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EDITORIAL

Announcing MMSC XI

Simon Paul Attard Montalto

The last Malta Medical School Conference, the Xth in this series, was held quite some time ago in 2018. Since then, there has been a lot of water under this particular bridge, not least because the COVID 19 pandemic effectively scuppered the projected schedule for the MMSC XI that was due sometime in 2021. The conference was eventually rescheduled for 2024 but these plans were seriously derailed by an inordinate increase in bureaucracy and regulations relating to events involving large sums of money. Despite having made significant progress toward 'landing' in 2024, the Organising Committee was instructed to re-issue tenders (twice!), resulting in lengthy delays. Unfortunately, the MMSC Organising Committee, as an entity within the Faculty of Medicine and Surgery, was obliged to work within the rules pertaining to the UOM, and with all the bureaucracy that that entails. Ultimately, the Committee settled for a venue acceptable to the establishment, but this incurred a further 12-month delay and an-almost-doubling of the initial projected costs!

Simon Paul Attard Montalto
Editor
Malta Medical Journal

COVER PICTURE

'Valletta'

Victor Grech is a consultant paediatrician with a special interest in paediatric cardiology. He finds photography and painting relaxing pastimes. He curated the world's first collective AI (artificial intelligence) exhibition in 2023 at Esplora Malta and this was his entry.

Following all these pre-conference tribulations, the Organising Committee is finally pleased to announce that the green light for the MMSC XI has now switched to 'On'! This prestigious event will be held at the Mediterranean Conference Centre in Valletta on the 4-6th December, 2025. The general format will be unchanged, with 5 main plenaries lectures followed by several breakout sessions over two and a half days. Given the long hiatus from the last conference, the Organising Committee anticipates an increased number of abstract submissions, and this can only enhance the quality of the science that will be accepted. Presentations will include oral and poster formats, and will be selected by peer review panels under the guidance of the MMSC Scientific Committee.

The conference is, by default, diverse in nature and will cover a plethora of disciplines and subspecialties. Some, like Medicine and Surgical specialities will require several break-out sessions whilst others such as O&G and Paediatrics always manage to submit enough suitable material to cover at least two breakouts. Nevertheless, the OC would welcome material from smaller disciplines and those that, traditionally, have been conspicuous by their absence. Certainly, the Scientific Committee will endeavour to populate the programme with as much quality material as possible. Furthermore, poster sessions will be run electronically on numerous designated poster stations, thereby increasing the number of presentations in this format considerably. The conference will be 'green' and, to this end, will do away with conference booklets, paper posters, etc.

The MMSConference series flies the flag of the Malta Medical School, and offers a platform whereby the work and research carried out by Maltese doctors and allied disciplines can be show-pieced. It is the largest, recurrent academic event of its kind organised within this University and has been a success in years gone by: we hope that the XIth in the series will continue where X left off and won't disappoint. Nevertheless, the Organising Committee will rely heavily on the enthusiastic support of colleagues to register, participate and contribute to the Conference to ensure its success, and looks forward to welcoming all in Valletta in December.

The Conference website has just been launched and can be accessed on: **www.mmscXI.com**

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ORIGINAL ARTICLE

Climate change, global warming and the upper respiratory airways-a review

Adrian Mark Agius

The progressive rise in air pollution has been linked to increased respiratory morbidity and mortality. Recent decades have seen increased demands for medical treatment accompanied by an increased risk of hospitalization and rise in premature deaths. Climate change contributes to air pollution by affecting the dispersal of primary pollutants, principally particulate matter $PM_{2.5}$ and by increasing the formation of secondary pollutants, mainly surface ozone close to ground level. Climate change is inherently associated with an increase in the prevalence of rhinitis, and its associated deterioration in quality of life.

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Climate change and air pollution involve a complex web of inter-relationships with various elements affecting human respiratory health. This paper reviews the relationship between the different principal elements associated with climate change and their effects on respiratory epithelium. The main contributing factors to nasal and pulmonary pathology are discussed and include carbon dioxide, ozone and particulates. The pathological mechanisms acting on nasal and bronchial mucosa are also described.

CLIMATE CHANGE

Global warming and the increase in emissions causing air pollution have caused a progressive deterioration in air quality. Since airborne allergens and air pollutants are frequently increased contemporaneously in the atmosphere, an enhanced IgE-mediated response to aeroallergens and enhanced airway inflammation could account for the increasing frequency of rhinitis and asthma in atopic subjects in the last 5 decades.[1]

Increasing carbon dioxide concentration in the earth's atmosphere is the main contributor to the greenhouse effect with increased mean temperatures. Higher surface temperatures lead to evaporation of water from soil so the land loses the ability to cool down with further trapping of heat. Extreme weather events such as lightning and heat waves have been predicted to become more common.[2]

Climate extremes are encouraged by increased water vapour concentrations in the air due to rising surface sea temperatures.[3]

Increased heat extends the pollination season of grasses and their geographical range resulting in more widespread and prolonged dispersal of pollens.[4] Pollens react with diesel particulates and ozone to increase their immunogenicity.[5,6]

Climate change is likely to influence the seasonal period and therefore grass growth, reproductive cycles and intensity of allergenic pollen load. In addition, weed species are expected to proliferate. These changes may vary from one region to another, due to the variation in amounts of UV radiation and rainfall.

The annual number of weeks in the year with high air pollen and mould spore concentrations has been progressively rising over time and has been shown to be positively correlated with temperature rise.[7]

Due to environmental pollutants which also act as irritants to skin and mucous membranes, pollen grains can be altered in the atmosphere leading to the release of lipid mediators (so-called pollen-associated lipid mediators) having pro-inflammatory effects.[8] Exposing ragweed plants to doubled CO_2 atmospheric concentration experimentally increased pollen production by 61%. In addition, ragweed pollen collected along roads with high traffic showed more allergenicity then the same pollen in rural areas.[9]

There is increasing evidence that climate change with events such as flooding may increase the dampness of buildings and therefore the growth of indoor moulds.[10] Increased fungal spore counts have been associated with an increase in asthma symptoms, increase in asthma medication and hospital admissions.[11,12]

Our forecasts of the future impacts of climate change depend on weather forecasts and may vary according to the weather models used which assume different scenarios of greenhouse gas concentrations.[13]

EXTREME WEATHER CONDITIONS

An increasing body of evidence correlates the occurrence of severe asthma epidemics with thunderstorms in the pollen season. Several epidemics of asthma have been reported following thunderstorms in various geographical zones, prevalently in Europe and Australia.[13]

In the first 20-30 minutes of a thunderstorm, there is evidence of increasing concentrations of air-borne allergens. This is due to dry updrafts that waft whole pollens into the cloud base where humidity is high. Here pollens may rupture and cold downdrafts carry the fragments to ground level where outflows distribute them. Whole pollen grains are too large to penetrate the deeper airways. However fragments may manage to do so thus enhancing bronchial hyperreactivity.

Due to strong electric fields that develop during thunderstorms, positive ions are released from the ground and could attach to pollen particles enhancing pollen rupture.

CARBON DIOXIDE

Carbon dioxide is the commonest greenhouse gas which is released by the burning of fossil fuels. Its concentration in the atmosphere is presently approximately 400 parts per million (ppm). Compared

to pre-industrial levels of 280 ppm, this is a rise of 43%. The trapping of heat by greenhouse gases has caused a rise in average global temperature of approximately 1°C. If atmospheric carbon dioxide continues to increase, projections calculate a further global average rise of between 2 and 6°C. [14]

Burning of fossil fuels contributed 75% of anthropogenic (man-created) CO_2 emissions to the earth's atmosphere.[15]

Tropical forests have acted as a carbon sink by taking up carbon dioxide from the atmosphere. Deforestation and clearing with burning of tropical forests contribute almost 25% of CO_2 emissions-the largest proportion of anthropogenic CO_2 emissions after fossil fuel combustion.[16]

OZONE

Ground-level ozone is a secondary pollutant formed by the interaction of the ultraviolet component of sunlight[17] with precursors which include nitrogen oxide emissions from traffic pollution, volatile organic compounds coming from plant metabolism and methane from bovine sources.[18,19]

Ground-level ozone is recognized as one of the worst urban pollutants. In experimental human and animal models, exposure to ozone impairs pulmonary function, increases airway responsiveness, and induces inflammation in the lower airways. At the cellular level, ozone can trigger epithelial cellular membranes to discharge cytokines and arachidonic acid metabolites such as cyclooxygenase and lipoxygenase derivatives. In addition, ozone can indirectly decrease mucociliary clearance and free radical production.[20]

The other main urban pollutant besides traffic related air pollutants (TRAP) is Particulate Matter (PM) of various dimensions.

PARTICULATE MATTER (PM)

Particulate matter is defined as coarse or fine. Coarse particles between 2.5 to 10 microns in diameter are deposited in upper airways while fine particles less than 2.5 microns in diameter are deposited into the lung. Particles can directly exacerbate existing respiratory disease such as asthma.[21] They can also further promote climate change by affecting ambient temperatures.[19] $PM_{2.5}$ levels are associated with anthropogenic sources like soot particles which absorb heat and increase local temperature.[22]

Particles may originate from anthropogenic sources such as construction activity, burning fossil fuels and forest fires, but also from natural sources such as volcanic eruptions and sand in dust storms.

Pollutant emission and dispersal or deposition are influenced by meteorological variables.[23] Reduced air quality affect humans directly but also affect humans indirectly by impacting ecosystems.

In the future, air quality is expected to worsen in cities.[24] Southern Europe is projected to be more affected than Northern regions.[25]

DIESEL EXHAUST PARTICLES (DEP)

DEP has a solid aggregate of elemental carbon and metals, in addition to a gaseous phase composed mainly of non-toxic inorganic gases such as oxygen and nitrogen. Organic components of DEP such as benzene, pyrenes, and others, are collectively termed poly-aromatic hydrocarbons, or PAH.

Based on epidemiological data, WHO and the International Agency for Research on Cancer have classified DEP as highly carcinogenic to humans.[26,27] through possible pulmonary genetic damaging effects and inflammatory toxicity.

Furthermore, climate chamber studies involving both ragweed and house dust mite (HDM) allergic patients also suggest a synergistic effect of DEP on atopic inflammatory mediators following respective allergen challenge and exposure[20] However consistent experimental simulation of real-life exposure conditions in animal studies is difficult to achieve due to the high complexity of DEP composition.

TRAFFIC RELATED AIR POLLUTANTS

Urban traffic related air pollutants (TRAP) have a complex structure composed of solid and gaseous phases, namely black carbon from diesel exhaust with gases like nitrous oxides and carbon monoxide, originating from general traffic and petrol exhaust. Other constituents include metals like zinc and copper originating from car brakes and tyres, respectively.[28]

Nitrogen dioxide contributes to ground level ozone formation which causes an inflammatory effect on the respiratory tract.

EFFECT ON THE RESPIRATORY SYSTEM

In a large epidemiological study from Brazil children living in polluted areas reported a 7% incidence of rhinitis compared to those living in non-polluted areas where the incidence was only 4%.[29]

Following the reunification of Germany, declines in air pollutant levels in Eastern Germany were correlated with a decrease in questionnaire-based respiratory tract symptoms.[30]

A 1°C rise in temperature is associated with increased mortality from respiratory causes, particularly in the elderly.[31]

Due to increased urbanization of populations and increased time spent working remotely means more exposure to indoor air pollutants such as House Dust mite and animal dander (eg cat) and possibly tobacco smoke. Tobacco smoking in the home has been identified as a factor increasing particulate matter (PM) and toxic chemical agents.[32] Remote working increased recently due to the SARS 2 pandemic.

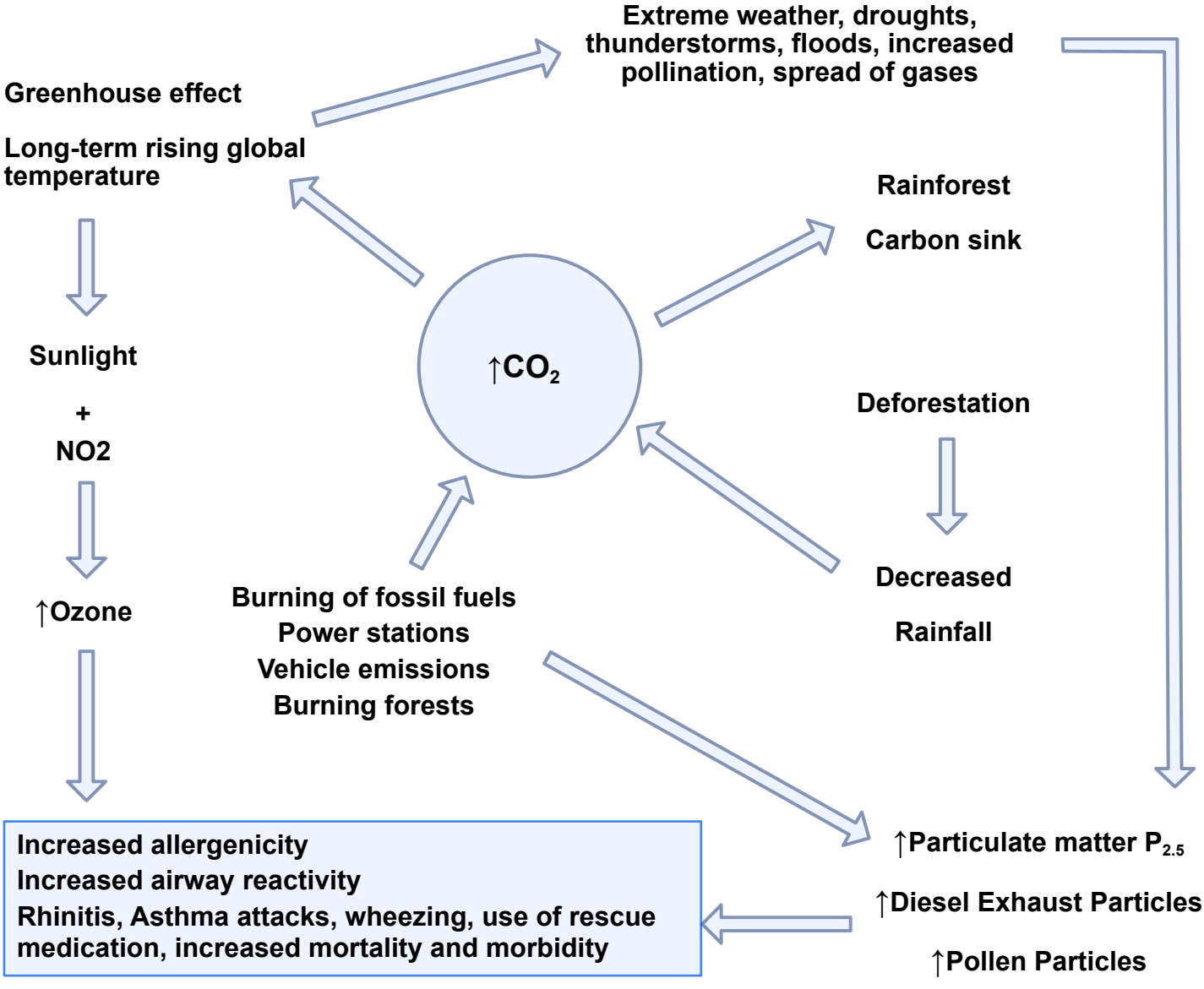
There is also an overlap between indoor and outdoor pollutants due to air exchange between outdoor and indoor environments. Cooking or heating using solid fuels in some cultures (coal, wood) can produce fine and coarse indoor particulate matter, nitrogen dioxide, carbon monoxide and sulphur dioxide.

The immuno-modulatory changes which air pollutants exert on respiratory diseases include recruitment of neutrophils and eosinophils in airway mucosa. Nonspecific airway reactivity with increased IL-33 expression and secretion of molecules from dying cells (damage associated molecular patterns, DAMP) activates and boosts the response of the innate immune system leading to increased IL-1b and decreased IL-10 production, and enhanced response to -inhaled allergens.[20,33,34,35]

DISCUSSION

Figure 1 summarises the principal connections between various elements involved in climate change, air pollution and rhinitis.

Table 5 *Interrelationships in Climate Change*



Emerging clinical data may be used to encourage governments into further action in order to mitigate the effects of climate change. Climate mitigation is any action taken to permanently eliminate or reduce the long-term risk and hazards of climate change to human life and property. Climate adaptation refers to the ability of a system to adjust to climate change (including climate variability and extremes) in order to reduce potential damage.

CONCLUSION

In conclusion clinicians are to expect an increase in incidence and morbidity due to rhinitis and asthma as a result of climate change. Allowances should be made in terms of health budgets and time dedicated to the burden of this condition in the coming decades.

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ORIGINAL ARTICLE

Practices of Sun Protection after Skin Cancer Surgery in Malta

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Background

Overexposure to Ultraviolet (UV) radiation is well known to be linked to the development of skin cancer. Our study aims to identify changes in patient practices after being diagnosed with skin cancer. Moreover, we identify areas of improvement which clinicians and healthcare staff can work on to improve patient awareness of harmful effects of UV radiation.

Methods

97 patients who had a skin cancer procedure performed at the Plastic Surgery and Burns Unit at Mater Dei Hospital, from January to March 2020, were included. Questionnaires were sent out, the data was anonymized and then inputted into an excel sheet.

Results

A response rate of 63.9% was obtained. 51% of the patients stated that they avoided midday sun exposure before and after their surgical procedure and 24% started avoiding the midday sun after their cancer diagnosis. 48% of the patients used sun protection accessories before and after their surgery, 16% started using them after their surgery and 32% do not use accessories to protect themselves from the sun. 33% of the patients used sunscreen before and after the procedure, 22% of them claimed that they started using sunscreen after the surgery but 45% of them said that they do not use sunscreen at all.

Conclusion

This study shows that a number of skin cancer patients are still not aware of the dangers of sun exposure. Therefore, more work needs to be done locally, not only in terms of primary prevention but also in secondary prevention following a skin cancer intervention.

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Mediterranean countries including Malta are well-known for their sunny weather. Being close to the equator however, makes Malta more susceptible to higher ultraviolet (UV) radiation levels compared to Northern European countries.[1]According to the World Health Organisation (WHO) data, Malta places thirty-fifth in terms of melanoma among both sexes of all ages (30+) attributable to UV radiation exposure.[2]

Whilst a small amount of UV radiation is beneficial for vitamin D production, overexposure to UV radiation is well-known to be linked to harmful effects including the development of skin cancer.[3]

Emphasis on primary prevention and protection from UV radiation, being the main avoidable risk factor in skin cancers, has been well-known and looked at for years, including in our local population.[4]

According to World Health Rankings, skin disease in Malta ranks as the 32nd cause of death, with a death rate of 1.86 per 100,000. It also places 73rd worldwide, with regards to deaths due to skin disease.

According to the Malta National Cancer Registry annual cancer report (1996-1997), non-melanoma skin cancer (NMSC) accounted for 15% (1001 cases) of all cancers registered between 1993 and 1997. 10 deaths were attributed to NMSC in this period. These cancers rarely cause death and are readily treatable, hence they are often excluded from cancer registries. In view of this, no more recent data from cancer registries was identified.

With regards to melanoma, the incidence between 2004 and 2014 was that of 544, of which 248 were males and 296 females.[5]

Our study aims to identify changes in patient practices after being diagnosed with skin cancer that required surgical intervention. Moreover we identify areas of improvement which clinicians and health care staff can work on to improve patient awareness of harmful effects of UV radiation and sun protection behaviours.

MATERIALS AND METHODS

Data Protection and Ethical approval were obtained. 97 consecutive patients who had a skin cancer procedure at the Plastic Surgery and Burns Unit at Mater Dei Hospital from January to March 2020, were identified. Questionnaires were sent out to these patients with questions regarding:

- Patient-related questions - age, gender, skin type, co-morbidities, presence of family history of skin cancer and site and number of lesions.
- Procedure-related questions - use of grafts or flaps and post-operative complications.
- Sun protection behaviours before and after the skin cancer procedure
- Patient perception on behaviours and healthcare professionals' advice

The data was anonymized and inputted into an excel sheet.

RESULTS

A response rate of 63.9% (n=62) was obtained. Out of the 62 patients who answered the questionnaire, 40% were females (n=25) and 60% were males (n=37). The age of the patients varied between 48 and 89 years. 24% (n=15) of the patients had multiple lesions excised on the same day.

18% (n=12) had a family history of skin cancer, 74% (n=45) did not have family history of skin cancer and 8% (n=5) did not know. The patients described their skin type as shown in Table 1. This was done according to the Fitzpatrick skin classification.

Table 1 *Patients' skin type according to patient perception*

Fitzpatrick Skin type	Number of patients
I	6
II	16
III	12
IV	20
V	5
No reply	3

Table 2 *Frequency of outdoor activities*

Frequency of outdoor activities	Number of patients
Daily	29
More than once a week	3
Weekly	8
Monthly	3
Less than once a month	3
Rarely	2
Never	7
No reply	4

84% (n=52) did not report any complication, 16% (n=9) said they had a complication namely an infection. Of note, four out of the seven patients who reported an infection had a history of diabetes (n=3) and breast cancer (n=1). 34% of the patients (n=21) reported that they had a graft or flap as part of their reconstruction after the skin cancer. Only 1 of these patients reported a complication, which was described as delayed healing.

Table 2 shows the frequency of outdoor activities in patients with skin cancer. One patient reported that they go out daily in summer only.

51% of the patients (n=32) reported avoiding midday sun exposure before and after the skin cancer excision. 8% (n=5) reported avoiding sun exposure but did not specify whether this was prior to or post skin cancer procedure. 24% of patients (n=15) changed their practice after the skin cancer diagnosis. 15% (n=9) claimed that they do not avoid sun exposure. One patient did not answer this question.

48% of the patients (n=30) used some kind of protective accessories before and after our intervention such as hats, sunglasses, umbrella or long sleeves. 16% of patients (n=10) started using protection after the intervention and 32% (n=20) do not use any protection when exposed to the sun. One patient who uses sun protection did not specify whether this was from before or after the procedure. One other patient did not reply to this question.

33% of patients (n=20) used sunscreen before and after the procedure. Two patients in this category specified that they only use it when swimming. 22% of the patients (n=13) started using sunscreen after the procedure and 45% (n=27) said that they do not use sunscreen at all. 1 patient claimed that he or she uses sunscreen only rarely; before and after the procedure and another one did not specify whether this was before or after the procedure. One patient did not reply to this question.

76% (n=26) of those using sunscreen said they use SPF 50+, 6% (n=2) use SPF 30+, 2% (n=1) use SPF 30+ or 50+, 2% (n=1) use 100+, 12% (n=4) did not know what sunscreen SPF they use. 71% of patients (n=24) said that they apply sunscreen a few minutes prior to sun exposure or just before they leave the house, 15% (n=5) apply it thirty minutes prior to sun exposure, 12% (n=4) apply it one hour before exposure. One patient was not sure about timing prior to exposure.

Figure 1 demonstrates patient awareness of being at an increased risk of having further skin cancers in the future.

60% (n=37) said that they know that UV rays are harmful, 6% (n=4) of which specified causation of skin cancer. 5% (n=3) said one should avoid UV when UV index is high. 6% (n=4) said UV rays are needed in moderation, while 3% (n=2) said they are beneficial. 13% (n=8) said that they do not know and 11% (n=7) did not reply.

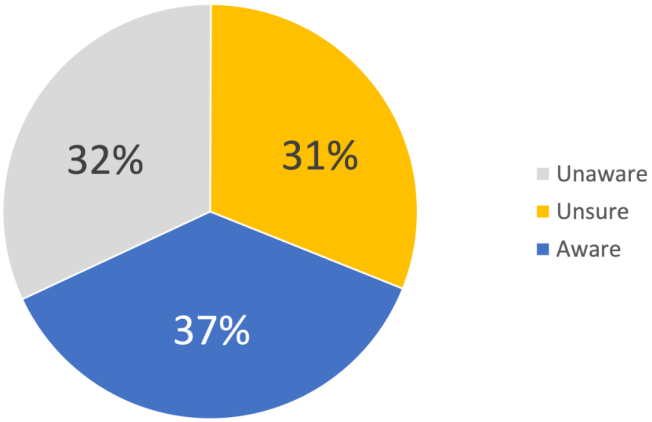

Figure 1 *Awareness of being at increased risk of having further lesions in the future.*

Several suggestions were made from the patients regarding education of the general public and increasing awareness via different means – social media, television, radio, sharing of experiences and real stories. Others included distribution of free sunscreen products especially to vulnerable people, cheaper sunscreen products and increasing shaded areas for people to avoid direct sunlight and/or sunburn.

With regards to healthcare professionals' advice on sun protection, 67% (n=42) reported that they had been advised to use sun protection measures, 30% (n=19) reported that they were not given advice and 3% (n=2) did not reply.

DISCUSSION

Excessive exposure to UV radiation from the sun can lead to skin cancer.[6] There are two main types of skin cancer: melanoma and non-melanoma skin cancer (NMSC).

Whilst NMSC rarely cause death unlike the rarer melanoma skin cancers, they can cause significant morbidity in patients in view of their frequent location in visible areas such as face, head, neck.[7] Increasing patient awareness may lead to patients seeking medical attention early on and potentially decreasing the morbidity and cosmetic problems that are associated with delayed presentation.[8] Additionally, a history of NMSC places patients at a higher risk of developing a second lesion.[9] Patients with basal cell carcinoma have ten times increased risk of developing a second similar lesion.[10] Patients having a cutaneous squamous cell carcinoma can

develop recurrent lesions with 95% of recurrent lesions occurring in the first 5 years.[9]

Incidence of skin cancers is known to correlate with ultraviolet light exposure.[1] Several measures have been implemented to promote and share information on skin cancer prevention, early diagnosis and treatment. One such project is the Euro-Melanoma campaign which is mostly co-ordinated by dermatologists.[11]

There seems to be less focus on secondary prevention in terms of patient knowledge and sun protection practices after skin cancer procedures.[12] To our knowledge, this is the first study of its kind in Malta that looks into patient perception on patient perceptions of sun protection measures and behaviours after skin cancer procedures. Improving our services by working on weak areas of knowledge and practices could be an opportunity to reduce the risk of patients presenting with further lesions. Therefore the focus of this study is to identify weak areas and false perceptions to improve patient education, reinforce good sun protection measures and to engage patients in developing and maintaining good practices.

Several studies performed have shown a correlation between skin type and risk of skin cancer as well as sun protection behaviours. In a study by Wheless et al it was found that high-risk skin cancer phenotypes are more receptive to skin cancer prevention education.[13]In this study, retrospective data was sought and therefore, patient self-reported skin type was looked at. Further studies could explore patients' knowledge with regards to awareness of skin type and risk of skin cancer according to skin type.

Overall, in all the areas assessed in this study, even though a minority, a number of patients:

- lacked knowledge with regards to presence of risk factors
- were not compliant with sun protection measures and
- were not provided with advice on skin cancer facts and risk reduction measures.

This suggests that further work needs to be done on educating patients with regards to sun protection behaviour. All the patients who reported application of sun protection measures said that they had been provided with advice on sun protection except for one patient.

Our patients seem to practice more sun avoidance behaviour rather than sunscreen application. Literature suggests that topical sunscreen should not be the first choice for skin cancer prevention.[14,15]

SUMMARY BOX

What is already known

- Overexposure to ultraviolet radiation is linked to the development of skin cancer.
- Sun exposure between 11am and 3pm should be avoided.
- Sun protection cream SPF50+ should be used daily and reapplied every 2 hours when exposed to the sun.
- Protective accessories such as umbrellas, clothing and hats should be used to protect the skin from the sun.

What are the new findings

- Patients improved their sun protection practices after their skin cancer diagnosis.
- 45% of the skin cancer patients do not use suncreen at all.
- 75% of the patients had no family history of skin cancer.
- 67% recall that they have been advised to use sun protection measures.

Whilst our study is one of the first to provide information on local perceptions after skin cancer surgery, it is not free of limitations. A limiting factor in our study is the small number of patients included. Another possible limiting factor is the fact that it was based on self-reported anonymous data rather than objective data.

CONCLUSION

This study shows that a number of skin cancer patients are still not aware of the dangers of sun exposure. A number of patients were given advice by healthcare professionals and do implement secondary prevention measures, however, there are still several patients who do not. Therefore as a number of international entities, including the world health organisation, emphasise the importance of sun protection, more work needs to be done locally, not only in terms of primary prevention but also in secondary prevention following a skin cancer intervention. This can be done by following local and worldwide tools and guidelines that include: explanation of the diagnosis, risk factors including risk of further lesions, advice on sun protection measures and self-examination.

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ORIGINAL ARTICLE

Burnout among mental health professionals working in an inpatient setting within the Maltese NHS

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Background

The aim of this study was to quantitatively explore the prevalence of job related burnout in mental health professionals working in an inpatient setting. The phenomenon of burnout is understood as a process involving three core features: emotional exhaustion, depersonalisation and low personal accomplishment.

Method

The study population consisted of all the psychiatry doctors, nurses, occupational therapists, psychologists, psychotherapists and social workers working in an inpatient psychiatric setting in the Maltese Islands. A cross-sectional anonymous self report survey was administered, this included demographic and job related questions and the Maslach Burnout Inventory (MBI-HSS-MP).

Results

The response rate was 71%. The burnout levels in this cohort of healthcare workers were similar to those found in other countries. 13.9% of the study population reported all the core features of burnout. 70.4% appeared to be moderately to highly emotionally exhausted.

Conclusion

This study identified the need for services to start assessing and working to improve the mental wellbeing of the mental health service providers in Malta.

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Job related burnout emerged as a concept in the 1970s and extensive research has been conducted to understand its nature.[1] In the research community, burnout is viewed as a process by which the psychological resources of an employee are gradually depleted as a consequence of prolonged stress at work.[2]

For the purpose of this study, burnout is considered as a three-dimensional process consisting of three constructs:

1. Emotional exhaustion - feeling emotionally drained and exhausted by one's work;
2. Depersonalization - negative or very detached feelings toward clients or patients;
3. Reduced personal accomplishment - evaluating oneself negatively and feeling unsatisfied with positive job performance and achievements.

This model was proposed by Maslach and Jackson and is the basis for the widely used Maslach Burnout Inventory adopted in this study.[3] In this theory, the concept of burnout is understood as a continuous variable and the authors emphasized that the Maslach Burnout Inventory does not produce a total score for burnout. This means that the prevalence of burnout cannot be interpreted as clinical burnout but a research measure.

The causal order of the three dimensions depends on the theoretical perspective adopted but it appears that high emotional exhaustion precedes high depersonalisation whilst high depersonalisation leads to high emotional exhaustion and low personal accomplishment.[4]

It is well known that burnout is very much present in healthcare professions[5] and that it is almost inevitable in such professions.[6] Lyndon continues by explaining that the healthcare environment is conducive at putting healthcare workers at risk. Issues that contribute for such environment include time pressures, emotional intensity, role conflict and difficult relationships between groups and with managerial strata of the organisation.

At the same time burnout affects service provision and ultimately service users.[7] Mental health workers represent one of the categories of health workers at highest risk of burnout.[8] According to Lasalvia et al, high levels of job distress affected nearly two-thirds of the psychiatric staff whilst one in five staff members suffered from burnout.[9] Psychiatrists and social workers were found to be affected the most. In Malta, Galea reported that in a sample of Maltese nurses (including mental health nurses), working in three state hospitals, symptoms of burnout were noted to be high.[10] He noted that 94% indicated low personal accomplishment, 88% scored high on depersonalisation and 33% scored high on emotional exhaustion.

The presence of burnout in the healthcare professional community is thus an established phenomenon in published literature leading to the next question that need to be elucidated, namely what factors contribute to burnout. Maslach and Leiter proposed that burnout develops as the result of mismatches between professionals and their job contexts in several areas of working life.[11] They proposed a mediation model whereby, a worker-job mismatch results in increased possibility of burnout. A subjectively experienced weak fit or incongruence in one or more aspects of working life can operate as a stressor and thereby threaten employees' well-being. In this line, a job-person mismatch maybe defined in terms of organizational-, job- or individual-weakness.[12]

The purpose of this study was twofold. The first aim was to investigate burnout affecting mental health professionals in Malta. The prevalence of burnout in mental health professionals who work closely with inpatient service users namely: Psychiatry Doctors, Psychologists/Psychotherapists, Nurses, Social workers and Occupational Therapists was studies. The other objective was to increase awareness with regards to the mental health wellbeing of service providers within the national mental health services.

MATERIALS AND METHODS

The method adopted for this study was a cross-sectional anonymous self-report survey. The Malta National Health System offers inpatient mental health services at Mount Carmel Psychiatric Hospital, Psychiatric Unit at Mater Dei Hospital and Short and Long stay wards at Gozo General Hospital. Managers in the respective units were contacted and informed of this study. Authorisation to contact the Human Resources department was obtained in order to identify the total population for this study and for the distribution of the survey.

The survey consisted of a questionnaire which entailed socio-demographics and job related questions together with the Maslach Burnout Inventory (MBI-HSS-MP). (Digital Supplementary File 1)

The survey was distributed to the different inpatient mental health locations as a pen and paper

questionnaire together with an information letter and a consent form. The choice to use a paper questionnaire was taken in an attempt to reach employees who do not use email or internet based surveys and hence to optimise response rate. The competition of the questionnaire was anonymous. Consent was understood as being present if the participant submitted the questionnaire. A collection checkpoint was established in a central area of the inpatient facility (Mount Carmel Psychiatric Hospital).

STATISTICAL ANALYSIS

Data collection was carried out over four weeks in the month of August 2018. The time period was chosen arbitrarily, taking into consideration the timeframe of the study. All data was stored in a password protected excel spread sheet.

Data collection was subjected to quantitative analysis and the results were compiled and evaluated in line with the literature review and objectives of the project. Statistical analysis was undertaken using IBM SPSS 20. Descriptive statistics together with Pearson co-relation and Analysis of variance (ANOVA) produced the results below.

These are structured according to the aims of the study. Statistically significant associations and correlations were considered at a p-value of 0.05.

The measure for burnout was attained by using the The Maslach Burnout Inventory Human services Survey for Medical Personnel (MBI-HSS-MP)

The Maslach Burnout Inventory (MBI), was initially published in 1981, and is considered to be a well-established tool for assessing burnout through a self-report survey. The MBI- HSS, adapted for Medical Personnel, also known as the MBI-HSS-MP, has slightly different wording. Instead of referring to "recipients", the MBI-HSS-MP, uses the term "patients".[13] It consists of 22 statements to be rated on a Likert scale assessing how often the statement occurs, ranging from 0 (Never) to 6 (Everyday). The 22 items are subdivided into three subscales measuring Emotional Exhaustion (9 items), Depersonalisation (5 items) and Personal Accomplishment (8 items). These represent the core components of burnout. The Cronbach Alpha co-efficient for the three subscales in this study were: emotional exhaustion α=0.91, depersonalisation α=0.64 and personal accomplishment α=0.82.

Previously defined cut-off scores by Maslach et al were used to determine low, moderate and high levels of each burnout feature:

- Emotional exhaustion: low ≤16, moderate 17 to 26, to high ≥27
- Depersonalization: low ≤6, moderate 7 to 12, high ≥13
- Personal accomplishment: low ≥39, moderate 32 to 38, to high ≤31

RESULTS

This survey included all the mental health professionals employed within the national health system whose work included inpatient care. The professionals included:

- Psychiatrists and trainees (N=42)
- Nurses (N=240)
- Occupational therapists (N=14)
- Psychologists/Psychotherapists (N=16)
- Social workers (N=10)

The total eligible number of employees was of 322 and 230 questionnaires were successfully completed and returned giving a response rate of 71%.

The response rates for the different professions were as follows:

- Psychiatry doctors (64.3%),
- Nurses (72.1%),
- Occupational therapists (85.7%),
- Psychologists/Psychotherapists (68.8%) and
- Social workers (70.0%).

57% were women and 43% males. The age distribution within the three categories (18-30, 31-50, 51 and over) was of 33%, 40% and 27% respectively. Thirty seven participants were of non-Maltese nationality representing 16.1% of the total population. 10.9% of the population were non-state employed, while only n=2.2 % worked on a part- time basis. 80.4% of the workforce constituted of frontlines, that is employees who deal directly with service users.

The mean scores for the three MBI sub scales are shown in **Table 1**. All the means fall within the moderate range for burnout as per Maslach et al.[14] **Table 2** shows the percentages in the study population falling within the different cut off categories. **Tables 3 - 5** illustrate the percentage scores within different professions for the three core burnout features.

Table 1 *Mean scores per MBI subscales and cut off scores as per Maslach et al.*[14]

MBI Subscales	Burnout Cut off scores			Results	
	Low	Moderate	High	Mean	SD
Emotional Exhaustion	≤16	17-26	≥27	23.79	12.31
Depersonalisation	≤6	7-12	≥13	8.04	5.49
Personal Accomplishment	239	32-38	≤31	33.93	8.62

Table 2 *Percentages Population per MBI Subscale*

MBI Subscale	Low (%)	Moderate (%)	High (%)
Emotional Exhaustion	29.6	30	40.4
Depersonalisation	42.6	39.1	18.3
Personal Accomplishment	30.4	41.3	28.3

Table 3 *Percentage Scores for Emotional Exhaustion by Profession*

Profession	Low (%)	Moderate (%)	High (%)
Social Workers	0	14.3	85.7
Psychology	15.7	57	27.3
Occupational Therapists	33.3	33.3	33.3
Nurses	27.1	33	39.9
Doctors	19.3	40	40.7

Table 4 *Percentage Scores for Depersonalisation by Profession*

Profession	Low (%)	Moderate (%)	High (%)
Social Workers	13	58.4	28.6
Psychology	63	97	0
Occupational Therapists	70	21.7	8.3
Nurses	38.9	40	21.4
Doctors	55	37.6	7.4

Table 5 *Percentage Scores for Personal accomplishment by profession*

Profession	Low (%)	Moderate (%)	High (%)
Social Workers	13	58.4	28.6
Psychology	63	97	0
Occupational Therapists	70	21.7	8.3
Nurses	38.9	40	21.4
Doctors	55	37.6	7.4

13.9% of the responders scored high on emotional exhaustion, high on depersonalisation and low on personal accomplishment and this can be considered as the prevalence of burnout in this cohort. On the other hand, 8.7% scored low on emotional exhaustion and depersonalisation and high on personal accomplishment. These could be considered as fully engaged employees. 15.2% scored high on both emotional exhaustion and depersonalisation while 14.3% scored high on emotional exhaustion and low in personal accomplishment.

DISCUSSION

Burnout levels found in this cohort of Maltese mental healthcare workers were comparable to results found in other published studies carried out in other European countries as summarised in Eurofound.[15] 13.9% of this study population scored up for all the three core features of burnout. These can be considered to be at the extreme end of the burnout continuum. At the other end of the spectrum 8.7% can be described as fully engaged at work with low emotional exhaustion, low depersonalisation and high personal accomplishment. Furthermore, although 71% responded to the questionnaire, 29% of the study population chose not to partake in the study. It could be hypothesised that people who are disengaged due to burnout contributed to a degree of nonresponse bias considering burnout as a subject matter.

When considering these results it is important to keep in mind that as Doulougeri et al[16] pointed out, calculating burnout using all the three core features (of burnout) is considered as a conservative approach. This can be understood depending on the perspective or paradigm used. If a one-dimensional concept of burnout is adopted, then this study would underestimate the prevalence of the phenomenon

under investigation. On the other hand, this study employs a multidimensional approach to remain truthful to Maslach and Leiter concept of burnout.[11] Nonetheless, it is valuable to investigate individual features of burnout to better understand the present wellbeing of service providers.

A key finding from this study was the high level of emotional exhaustion reported (40.4%). Emotional exhaustion is given particular attention in the literature and is considered by various authors as the core component of burnout and this is in line with the findings of this study.

Maslach and Leiter describe exhaustion as the first reaction to the stress of job demands or major change.[11] Some studies even measure emotional exhaustion to represent the existence of burnout and others measure emotional exhaustion in conjunction with either depersonalisation or low personal accomplishment as indicators of burnout.[16] Taking this into consideration and the fact that burnout is understood as a continuous variable and not a distinct phenomenon, people scoring high in one of the three components, particularly in emotional exhaustion, are at a higher risk of experiencing burnout.[17] This could mean that in this study there is a high proportion of the workforce who is at risk of becoming burnt out.

In contrast to depersonalisation and personal accomplishment, most demographic and work related factors in this study did not show statistical differences with regards to emotional exhaustion. This suggests that emotional exhaustion is experienced similarly across professions. The results of this study show that 70.4% of participants who responded appeared to be moderately to highly emotionally exhausted. Considering that emotional exhaustion is defined as 'wearing out, loss of energy, depletion, debilitation, and fatigue', further investigation is warranted to elucidate how widespread it is in the Maltese mental health inpatient services, whether this extends to community and out-patient services and ultimately how this affects the provision of healthcare services and patient care. Research shows that community mental health service workers exhibit higher scores of burnout when compared to those working in specialised community services and it would be informative to assess Malta's present situation.[18] High emotional exhaustion levels are related to heavy workloads, low supportive relations, and personal engagement, less quantity of staff members, professional development and understanding of burnout.[19] It would be valuable for the worker and the organisation alike to investigate these factors in relation to burnout within the mental healthcare services.

The depersonalisation and personal accomplishment components show a more complex relationship within the study population. As shown in the results, 18.3% and 30.4% of responders scored high for depersonalisation and low for personal accomplishment respectively. Depersonalisation and personal accomplishment show significant differences across a number of factors.

Of note were the higher levels of depersonalisation in males as compared to the female employees; and higher depersonalisation scores and lower personal accomplishment in non-Maltese employees and non-state employed. Depersonalisation is described in literature as starting off as a self-preserving mechanism from job stress, where a person utilises psychological withdrawal in the face of chronic stress. Ultimately this becomes a dysfunctional mechanism. As a result, depersonalization manifests itself as a negative, cynical attitude towards the service users or work in general.[20] It is interesting to note a gender difference in this aspect that was also documented in a meta- analysis by Purvanova and Muros.[21] It is valuable to research further this gender difference since if depersonalisation can be considered as a maladaptive coping mechanism to prolonged stress, males could benefit from coping skills training to improve their mental wellbeing. At the same time, it is difficult to ascertain whether gender differences are an attribution to the gender of the individual or the possible differing work environment or expected roles within a particular culture.

During the COVID pandemic and therefore, whilst this questionnaire was being filled out, ongoing changes were being carried out to the mental health system and its structure. This included closure of the psychiatric unit at Mater Dei Hospital and of long-stay wards at Mount Carmel Hospital. Furthermore, re-structuring of the acute wards was carried out and staff was functioning as ward-based rather than consultant-base. All of these changes were being implemented during the pandemic, hence adapting to a new working structure might have possibly added to the burnout being experienced.

Following this study, we formulated some recommendations to help tackle the issue of burnout amongst professionals.

Psycho education on burnout and its ramifications is essential at all organisational levels.[22] Employees

need to become more aware of their mental well being and the way the organisational environment affects them and their ability to offer reliable and safe service provision.[23] Workers who are already suffering from burnout or are at risk of burnout need to have the ability to recognise their situation and rectify their situation in an environment that fosters self-improvement and understanding.

Managerial awareness of employees' mental health and the possibility to provide organisational support is also crucial if burnout is to be reduced [24,25] Employee mental wellbeing needs to be integrated in organisational policy both for the employees' ability thrive in an organisation and for better service provision.[25]

Another recommendation is to invest more in further research into care provider wellbeing. Understanding the employees' needs and strengths will ultimately benefit the patient and service provision.

CONCLUSION

When analysing job related burnout, Eurofound report in 'Burnout in the workplace: A review of data and policy responses in the EU' that "The evidence pointed to increased risk of sickness absences, turnover intention, decreased work ability, lower performance in work and premature exit from the labour market".[15]

This study offers the possibility to initiate a discussion on the wellbeing of the service provider in an important health sector. It shows that the Maltese context follows closely international burnout levels and needs addressing to improve the workers' wellbeing and ultimately help in sustaining a safe environment for the service users.

Finally, it suggests areas where further research can be undertaken to better understand the health of the Maltese psychiatric services, and hopefully to initiate a brainstorming process of how to improve the present condition, both at an individual level and on the organisation plane.

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ORIGINAL ARTICLE

Impact of a weight loss programme on psychological wellbeing and quality of life

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Background

Prevalent conditions nowadays include mental disorders such as depression and anxiety as well as obesity which often co-exist together. Mental disorders may predispose individuals to gain weight through less exercise, increased stress hormones and binge-eating, whilst inversely obesity may lead to mental disorders through increased stress, low support and less independent functioning in everyday life. The aim of this study was to measure different parameters reflecting the psychological and mental wellbeing of individuals before and after completing a weight loss residential program at 'Dar Kenn Ghal Sahhtek'.

Method

A study was conducted on 36 individuals who enrolled into an 8-week program at 'Dar Kenn Ghal Sahhtek'. Parameters including age, gender, body mass index, levels of quality of life, depression and anxiety were collected upon admission and discharge. Statistical analysis was carried out on the data collected to compare the before and after data as well as check for any correlations between different parameters.

Results and Conclusion

From this study it was concluded that there is a statistical difference between the before and after data and that a significant decrease in all parameters was recorded upon completion of the program. Furthermore, a positive correlation was found between Beck's Depression scale and other parameters which confirms simultaneous causality between the different parameters.

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Mental disorders such as depression and anxiety have become a consistently prevailing issue in healthcare worldwide. These conditions may often coincide with Obesity which is another prevalent health concern.[1,2] The prevalence of obesity and overweight individuals in adults aged 18 years and older has trebled in the past 40 years and globally surpasses 37% of all adults.[3] In Malta adolescents and children have reportedly one of the highest prevalence of obesity and overweight individuals in the world.[4] According to statistics published by the National Statistics Office 25.5% of the Maltese population are obese which is significantly higher when compared to the 14.9% EU average. Statistics also show that the percentage of Maltese men who are obese is 27.5% whilst the percentage for women is 23.4%.[5] This is also supported by Malta having one of the highest prevalence of obesity in the European region as identified in studies by the World Health Organization.[4]

Mental disorders, predominantly depression and anxiety, are often diagnosed in obese and overweight individuals. This relationship between mental disorders and obesity has been noted to be especially common in adolescents and young adults.[3,6] An increased incidence of generalised anxiety disorder, panic disorder with and without agoraphobia and social phobia have been reported in obese and overweight individuals.[7]

The relationship between high Body Mass Index (BMI) and poor mental health may arise from several different origins and is often bidirectional in causality. People who have a BMI of more than 30 are usually observed to have a lower self-esteem, less support from people around them and usually suffer from multiple medical comorbidities such as hypertension, diabetes, joint problems and dyslipidaemia.[8] All these factors will contribute to increased emotional stress and decreased physical functioning, which may accumulate over time making them more vulnerable to mood disorders.[7]

In turn, mood disorders such as depression and stress have been associated with an increase in visceral fat accumulation and abdominal obesity.[9,10] Such patients tend to suffer from a binge-eating disorders and are less likely to be physically active due to their low mood. There may also be a physiological explanation as stress hormone cortisol levels have been found to be higher in patients who suffer from anxiety, Post Traumatic Stress Disorder (PTSD) and depression. This may in turn lead to increased levels of neuropeptide Y which cause an increase in food intake, aggravated further by low levels of Leptin (which usually acts as an appetite suppressant).[9] Furthermore patients who do suffer from mood disorders are often on antidepressants or atypical antipsychotics and weight gain is a common side effect of these medications.[11]

In Malta 'Dar Kenn Ghal Sahhtek' is a dedicated centre set up in 2014 for treating patients with eating disorders, including Obesity and Binge eating. It offers both residential and semi-residential facilities where patients suffering from obesity can enrol into a holistic weight reduction programme. During these programmes patients are guided by a multidisciplinary team consisting of psychiatrists, doctors, nurses, physiotherapists and psychologists in order to adopt a healthier lifestyle.[12] The goals of such a programme involve weight reduction to reach a healthy BMI, improved mental health and an overall better way of living.

METHOD

This retrospective study was conducted on a sample of anonymous records of 163 individuals who enrolled into the residential programme at 'Dar Kenn Ghal Sahhtek' between October 2014 and February 2017. The duration of the programme was 8 weeks, after which patients were followed up on an outpatient basis once weekly for a total period of 2 months. After this period, patients could join support group sessions which were held on a monthly basis. A study to analyse the impact and efficacy of this programme on the physical wellbeing of the participants has already been established in a separate study.[13] In this current study we analyse the impact this programme may have on the psychological aspects and quality of life of the participants.

On admission a set of parameters were recorded along with demographic data. These included;

- Demographic Data : Age , Gender
- Weight and Body Mass Index (BMI)
- Eating Disorder Quality of Life assessment (EDQOL)(15)
- Becks Depression Index scale (BDI)
- General Anxiety Disorder 7 item scale (GAD – 7)(16)

These parameters were repeated and documented upon discharge from the programme.

Statistical analysis on the data collected involved comparing the BMI, GAD, BDI and QOL taken on

admission and those noted down on discharge by using Wilcoxon signed-rank test. This type of paired difference test was used since the data collected from the sample was found not to be in normal distribution after using the Shapiro-Wilk test.

Such statistics compare and see if there is any significant difference between the means of the two groups; the before and after data for each different parameter.

Spearman's coefficient was also used to check for a positive or negative correlation between the different parameters measured.

RESULTS

A sample of 36 individuals was used for this study, which included 17 males and 19 females. These 36 individuals were chosen because they had complete data documented both at admission and follow up. Ages ranged from 19 to 67 years of age for male subjects and 15 to 69 years of age for female subjects. Values for weights of subjects taken before they entered the program ranged from 82 to 208 kgs for the male subjects and 90 to 188 kgs for the female subjects. BMI values taken before starting the program extended from 35.09 to 72.04 for the male participants and 32.47 to 82.02 for the female participants.

From the data analysis carried out, a significant statistical difference was found between the means of the Before and After data sets for each parameter, where the p value obtained by Wilcoxon signed rank test was less than 0.05 for each data set and therefore rejecting the null hypothesis (p=0.001, Z=-3.29) (Table 1). For Weight BMI, BDI score, GAD score and QOL score, a significant decrease was noted between the means of Before and After data sets (Table 1).

Using Spearman's coefficient, a moderative positive correlation was noted between BDI-Before and Weight-Before (ρ=0.53) and a moderate-weak positive correlation was obtained between BDI-Before and BMI-Before data sets (ρ=0.47). A stronger positive correlation was noted between BDI-Before and GAD-Before (ρ=0.66) and BDI-Before and QOL-Before data sets (ρ=0.72). Similarly a strong positive correlation was calculated between BDI-After and GAD-After (ρ=0.61) and BDI-After and QOL-After (ρ=0.78) (Table 2). When applying Spearman's rank correlation between GAD and QOL for both Before and After data sets, a weak-moderate positive correlation was noted (Before; ρ=0.43, After; ρ=0.47) (Table 3).

DISCUSSION

The results obtained after the participants completed the residential programme show a positive outcome. The Before and After data sets showed a significant reduction for all the different parameters. A considerable decrease can be noted in the Weight After the program when compared to the Weight taken Before the start of the program. Likewise the mean BMI, mean BDI score, mean GAD score and mean QOL scores significantly decrease

Table 1 *Descriptive statistics for the Before and After data sets collected for each different parameter and p values obtained for Wilcoxon signed rank test*

	N	Minimum	Maximum	Mean	Standard deviation	p
Age	36	15.0	69.0	42.7	14.7	
Weight Before	36	82.1	208.2	140.5	36.5	***<0.001***
Weight After	36	74.5	192.8	132.4	34.1	
BMI Before	36	32.5	82.0	52.3	12.1	***<0.001***
BMI After	36	31.4	79.1	49.3	11.4	
BDI-B	36	7.0	56.0	29.3	13.9	***<0.001***
BDI-A	36	1.0	48.0	14.5	13.7	
GAD-B	36	2.0	23.0	13.2	6.6	***<0.001***
GAD-A	36	0	41.0	8.1	9.6	
QOL-B	36	1.0	70.0	30.9	20.9	***<0.001***
QOL-A	36	0	37.0	10.6	10.5	

Table 2 *Correlations between Beck's Depression Index Before and After and different parameters using Spearman's rank correlation coefficient*

	Weight-B	BMI-B	GAD-B	QOL-B	GAD-A	QOL-A
BDI-B	0.53	0.47	0.66	0.72	0.19	0.32
BDI-A	0.08	0.04	0.1	0.12	0.61	0.76

Table 3 *Correlations between Generalised Anxiety Scale -7 (Before and After) and Quality of Life scale (Before and After) using Spearman's rank correlation coefficient*

	QOL-B	QOL-A
GAD-B	0.43	0.16
GAD-A	0.08	0.47

after completion of the residential program (Table 1). This shows that the residential program is a fruitful one resulting in loss of weight, a decrease in scores for Depression a decrease in scores for Anxiety and a decrease in the scores of Quality of Life (where a low score represents a good QOL).

A moderate positive correlation between Weight and BMI (taken before programme was commenced) and scores for BDI- Before was noted (Table 2). This portrays that an increase in weight and BMI will affect the score a patient will get on Beck's Depression scale. Since a positive correlation was obtained, then an increase in Weight or BMI will both have an effect and result in an increased score on Beck's Depression scale which increases the chances of that particular patient to suffer from depression and low mood. A stronger positive correlation was found between scores for BDI-Before and the scores for GAD-Before and QOL-Before respectively. This shows that a higher score in Beck's Depression Scale will affect both anxiety and quality of life of a patient, leading to an increased level of anxiety and poorer quality of life for the patient. Similarly scores between BDI-After and GAD-After and QOL-After respectively also show a strong positive correlation, further confirming the effect one's mood may have on the general mental wellbeing. A weak-moderate positive correlation was obtained between GAD-Before and QOL-Before and between GAD-After and QOL-After respectively (Table 3), thus showing that anxiety may also play a part in determining a patient's state of quality of life.

In order to fully assess the outcome of such a residential programme, follow-up of these patients in the community at Health centres or at Outpatient clinics for a few years after completing the programme would be ideal. After completion of the programme, it is important to check whether the participants have maintained the healthy lifestyle which they have been taught during the programme and thus check for a global improvement in mental and physical well-being.

Limitations of this study include the possibility of human error whilst conducting the BDI, GAD and QOL scales as well as human error during data collection and data entry which led to a sample size of 36 individuals out of 163 who had complete data inputted and available for analysis. The small sample size was also another limitation which possibly could have resulted in a Type II error, affecting the power of the study. Another limitation is the loss of follow-up

SUMMARY BOX

- Mental disorders and Obesity are common disorders found in the current society.
- Such conditions may precipitate one another and are often found present together.
- 'Dar Kenn Ghal Sahhtek' offers residential and semi-residential programs for individuals suffering from eating disorders.
- This study was carried out on 163 individuals who enrolled for a weight loss residential program in order to analyse different parameters before and after completion of program.
- A significant decrease was recorded for all parameters after completion of the program.
- A positive correlation was noted between different parameters thus confirming the simultaneous causality between obesity and mental disorders.

and further data collection after the programme was finished, in order to confirm whether this programme was truly efficient and whether the weight loss achieved was maintained in the long term. The lack of a control group whilst conducting the study may also influence the evaluation of the true outcome of this residential programme, but this would have led to individuals in the control group not having been offered the same treatment and interventions.

Prospective interventions at tackling the increasing incidence in high BMIs and co-existing mood disorders would include highlighting the importance of maintaining a healthy lifestyle to obese patients and how this may decrease their odds of developing lifetime mood disorders. Other possible strategies at tackling this issue include launching national public health campaigns to educate and inform the general public as well as educating children from a young age about nutrition and physical activity and encouraging a family-based approach to decrease and prevent obesity.[14] Such measures have already been implemented in the past few years here in Malta but more awareness and education are needed as Malta still has a higher percentage of obese people when compared to other countries.

ABBREVIATIONS

BMI	Body Mass Index
PTSD	Post Traumatic Stress Disorder
EDQOL	Eating Disorders Quality of Life scale
QOL	Quality of Life
GAD-7	Generalised Anxiety Disorder 7-item scale
BDI	Beck's Depression Inventory scale

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ORIGINAL ARTICLE

An Audit on Thyroid Scintigraphy Scan Requests in Benign Thyroid Disease

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Background

Thyroid scintigraphy has a useful role in the assessment of the thyrotoxic patient, particularly when thyrotoxicosis coexists with thyroid nodularity and when TSH- receptor antibody (TRAB) is negative. The aim of this audit was to assess the indication for thyroid scintigraphy in the assessment of patients locally, with reference to the European Thyroid Association (ETA) and National Institute for Health and Care Excellence (NICE) guidelines.

Methods

All scintigraphy scans carried out in adult patients with benign thyroid disease at Mater Dei Hospital in Malta, between January 2019 to December 2021, were analysed. The indications for the investigation and the imaging results were assessed using the hospital's electronic records, as were the thyroid function tests, TRAB levels, and thyroid ultrasound scans if available.

Results

In 55.95% of thyrotoxic subjects, there was no valid indication for thyroid scintigraphy, according to the ETA and NICE guidelines. 37.96% of these patients inappropriately referred for scintigraphy did not have a TRAB level checked prior to the scan date whilst 20.37% had a positive TRAB and no known thyroid nodules. 10.18% of scans were inappropriately ordered in euthyroid patients with thyroid nodules or euthyroid hyperthyroxinaemia.

Conclusion

TRAB levels should be checked in new-onset thyrotoxicosis. Thyroid scintigraphy is useful in the differential diagnosis of the thyrotoxic patient when there are co-existing thyroid nodules, especially if TRAB is negative. It is not recommended in the thyrotoxic patient with a positive TRAB and no known thyroid nodules or in the assessment of euthyroid patients with thyroid nodules.

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Thyroid scintigraphy scanning is a useful imaging modality, which is widely used in the investigation of thyrotoxicosis. Depending on the pattern of uptake, it can help to distinguish between Grave's disease (diffuse uptake), toxic adenoma (increased uptake at the site of the nodule with suppressed uptake in the surrounding thyroid tissue), toxic multinodular goitre (multiple foci of variably increased tracer uptake, with suppression of the remaining thyroid tissue) and thyroiditis (reduced or absent uptake).

Although it is a useful adjunctive test in the investigation of thyrotoxicosis, it is not necessarily a first-line or routine test and incurs additional costs to healthcare systems. According to the 2018 European Thyroid Association (ETA) guideline for the management of Graves' hyperthyroidism, the initial assessment should include measurement of the TSH-receptor antibody and an ultrasound scan of the thyroid. Thyroid scintigraphy scanning is suggested only when thyroid nodularity coexists with hyperthyroidism, and prior to radioactive iodine therapy.[1] NICE guidelines also recommend measuring TSH-receptor antibodies in all patients with thyrotoxicosis but suggest an ultrasound only when thyroid nodules are suspected clinically and suggest thyroid scintigraphy if the TSH-receptor antibody is negative.[2]

The aim of this audit was to assess the indications for thyroid scintigraphy scans being performed locally in adult patients with benign thyroid disease, in order to determine whether they comply with the European Thyroid Association guidelines and to assess whether they were necessary to establish the diagnosis and influence management.

MATERIALS AND METHODS

All thyroid scintigraphy scans carried out in adult patients (16 years of age and over) with benign thyroid disease at Mater Dei Hospital, Malta from January 2019 to December 2021 were included. These were analysed using the hospital's electronic records (including Centricity Clinical Viewer and iSOFT Clinical Manager) for imaging and blood investigations. Ethical approval was obtained from the local regulatory committee. The indication and actual result of each radio-isotope scan was reviewed for each patient. In addition, thyroid function tests, TSH-receptor antibodies, and thyroid ultrasound scans were reviewed for each of the patients, if performed prior to the scintigraphy scan.

RESULTS

A total of 216 thyroid scintigraphy scans were performed on adult patients over a three-year period between January 2019 and December 2021. The mean age of our study population was 60.5 years (range: 19-94 years) with a female predominance (66.6%). The female average age was 59.06 (range 19-90) and the male average age was 63.66 years old (range 26-94). 71.8% (n=155 patients) of the population had overt thyrotoxicosis, and 17.59% (n=38 patients) of the population had subclinical hyperthyroidism. 10.18% (n=22 patients) of the population were euthyroid, whilst 1 patient (0.46%) had no thyroid function test available on iSOFT. 31.48% of the study population had positive TSH-receptor antibodies whilst a TSH-receptor Ab was not available in 26.38% of the population.

The 2018 ETA Guideline recommends scintigraphy of the thyroid in thyrotoxic patients with co-existing thyroid nodularity on imaging.[1] 126 patients of the study population who were being evaluated for overt or subclinical thyrotoxicosis (65.28%) satisfied this criterion (**Table 1**).

The 2019 NICE Guideline recommends scintigraphy of the thyroid gland in TSH-receptor Ab-negative thyrotoxic patients.[2] Only 85 patients (44% of the thyrotoxic sub-population) fulfilled this criterion. Analysis of the data pertaining to the remaining 108 patients with thyrotoxicosis (55.95%) inappropriately referred for scintigraphy, revealed that 41 patients (37.96%) did not have a TSH-receptor antibody sampled prior to the scintigraphy scan, while 22 patients (20.37%) had a positive TSH-receptor antibody with no known thyroid nodules (**Table 1**).

In our cohort, thyroid scintigraphy scans added significant information to narrow the differential diagnosis of thyrotoxicosis in patients with negative TSH-receptor antibody status and in those with positive TSH-receptor antibody status associated with thyroid nodules.

In those patients with positive TSH-receptor antibody status and no known thyroid nodules, thyroid scintigraphy scans altered the diagnosis in 2 patients out of this sample (i.e. 2 out of 22 patients). One of these two patients had a thyroid scintigraphy scan suggestive of a toxic adenoma and an ultrasound performed later confirmed the presence of a thyroid nodule whilst the other patient had a scintigraphy scan indicative of thyroiditis.

Table 5 Thyrotoxic patient cohort and their respective TRAB, US and Scintigraphy findings. The scintigraphy cases highlighted in green are the ones that are recommended as per the 2018 ETA guideline. The scintigraphy cases highlighted in yellow are the ones that are recommended as per the 2019 NICE guideline. The scintigraphy cases highlighted in grey are the ones that are recommended as per both the 2018 ETA and the 2019 NICE guidelines.

TRAB	Nodules on US	Diffuse Uptake	Uptake suggestive of TMNG	Uptake suggestive of TA	Reduced / Absent uptake	Normal uptake	Ectopic thyroid tissue
Positive	No	4			1	3	
Positive	N/A	11		1		2	
Positive	Yes	26	6	5		9	
Negative	No	8	1		3	5	
Negative	N/A	3		1	4	5	
Negative	Yes	16	9	12	3	15	
Not available	No						
Not available	N/A	7		1	2	5	
Not available	Yes	10	2	8	1	4	

TRAB: TSH-receptor antibody; US: ultrasound; TMNG: Toxic multinodular goitre; TA: toxic adenoma

39.09% of thyrotoxic subjects with diffuse and normal thyroid uptake had a negative TSH-receptor Ab status.

Toxic adenomas were more common in females in this study. Using the chi-square test, a p-value of 0.048 was achieved (< 0.05).

In the euthyroid cohort (n=22 patients), the two most common reasons for ordering thyroid scintigraphy scans were:

1. to assess whether a nodule is hot, cold, or warm (54.5%) and
2. in patients with euthyroid hyperthyroxinaemia (31.8%).

In one euthyroid individual, a thyroid scintigraphy scan was requested to assess for ectopic thyroid tissue as a previous ultrasound of the neck had revealed a soft tissue nodule of uncertain origin.

DISCUSSION

Thyroid scintigraphy plays an important role in the assessment of the thyrotoxic patient in selected cases. It is based on the thyroid's ability to take up iodine via the sodium-iodide symporter. Technetium-99m (99mTc) is an analogue of iodine which is also transported to thyroid cells by means of the sodium-iodide symporter, allowing its use in thyroid scintigraphy in order to visualize the distribution of active thyroid tissue.[3]

According to the 2018 European Thyroid Association (ETA) guideline for the management of Graves' hyperthyroidism, thyroid scintigraphy scanning is suggested only when thyroid nodularity coexists with hyperthyroidism, and prior to radioactive iodine therapy.[1] The 2019 NICE Thyroid Disease: Assessment and Management guideline recommends measuring TSH-receptor antibodies in all patients with thyrotoxicosis but suggests an ultrasound only when thyroid nodules are suspected clinically and suggests thyroid scintigraphy if the TSH-receptor antibody is negative.[2]

Based on the results obtained in this audit, thyroid scintigraphy scans were particularly useful in establishing a diagnosis in those individuals with thyrotoxicosis and co-existent thyroid nodularity, especially when the TSH-receptor antibody was negative. In this audit, thyroid scintigraphy was not found to add any relevant information in thyrotoxic patients with a positive TSH-receptor antibody (TRAB) and no known thyroid nodules.

The presence of Graves' disease does not necessarily exclude the presence of thyroid nodules. In this audit, 46 patients (23.8% of the cohort with thyrotoxicosis) had positive TSH-receptor antibody status and co-existent thyroid nodules. 13% (n=6 patients) of this patient cohort had a thyroid scintigraphy pattern suggestive of toxic multinodular goitre whereas 10.8% (n=5 patients) had a thyroid scintigraphy pattern suggestive of a toxic adenoma. This is important, as by distinguishing Graves from other causes of thyrotoxicosis, scintigraphy will influence management in the long term. Patients with a toxic multinodular goitre or toxic adenoma usually should ideally be treated with a definitive option such as

surgery or radioactive iodine therapy if feasible, since long-term antithyroid drugs (ATDs) would otherwise be necessary as maintenance to control thyrotoxicosis. On the other hand, a 12 to 18-month course of ATDs is an established first-line approach in most cases of Graves' disease with tapering of ATDs then attempted based on TFTs and TRAB levels with subsequent monitoring for relapse.[1,4]

The use of TSH-receptor antibody in patients presenting with thyrotoxicosis is a useful and cost-effective measure which, if elevated, often leads to a rapid and accurate diagnosis of Graves' disease. The latter is reflected in the current guidelines. However, a study by Angell et al identified the presence of positive TSH-receptor antibody in thyrotoxic patients without Graves' disease.[5] Albeit rare, the above clinical possibility highlights that scintigraphy may have a role in patients presenting without pathognomonic evidence of Graves' disease and minimally elevated TSH receptor antibody levels.

One instance wherein thyroid scintigraphy may be useful in the initial assessment of a thyrotoxic patient is when an acute form of thyroiditis is suspected, especially silent thyroiditis or postpartum thyroiditis. In addition to the clinical presentation and thyroid function tests, scintigraphy scans play a complementary role in such instances as it may differentiate thyroiditis from other forms of thyrotoxicosis, with reduced uptake expected in cases of thyroiditis.[6]

In this audit, it was noted that 54.5% of euthyroid subjects, (i.e., 5.6% of the total study cohort), underwent thyroid scintigraphy in order to assess the functionality of a thyroid nodule. Although thyroid scintigraphy is an effective imaging method for assessing the functional aspect of a thyroid nodule, an ultrasound performed by an experienced ultrasonographer is the gold standard for the structural assessment of a thyroid nodule. In the assessment of thyroid nodules, thyroid scintigraphy should only be performed when the TSH level is suppressed in order to assess whether a nodule is 'hot', 'cold', or 'warm'. The presence of a cold nodule in Graves' disease carries a higher risk of malignancy than a cold nodule in the absence of autoimmune thyroid disease.[7] In these instances, information obtained from scintigraphy can be used in addition to careful assessment of the nodular sonographic features and fine-needle aspiration in order to better characterize and stratify the risk of thyroid nodules in patients with Graves' disease, with priority given to FNA sampling of cold nodules. However, in the euthyroid patient, thyroid scintigraphy is not indicated and assessment for risk of malignancy should be performed via ultrasound with FNA sampling being dictated based on the nodule's size and characteristics on ultrasound.[8]

In this audit, we also observed that a number of patients with diffuse homogenous uptake on their

SUMMARY BOX

What is already known about this subject?

- Checking serum TSH-receptor antibody (TRAB) is a cost-effective investigation in the diagnosis of Graves' disease and is recommended in the assessment of new-onset thyrotoxicosis.
- Thyroid scintigraphy is a useful adjunctive investigation in the assessment of the patient presenting with thyrotoxicosis when there is coexisting thyroid nodularity, as recommended by the European Thyroid Association (ETA) guidelines.
- Thyroid scintigraphy is recommended by the National Institute of Clinical Excellence (NICE) in the assessment of the patient presenting with thyrotoxicosis when TRAB is negative.

What are the new findings?

- In this audit, 55.95% of thyroid scintigraphy scans ordered during investigation of thyrotoxicosis at Mater Dei Hospital in Malta between the beginning of 2019 and the end of 2021 were not indicated according to the ETA and NICE guidelines, where 37.96% of this patient cohort inappropriately referred for scintigraphy did not have a TRAB level checked prior to the scan whilst 20.37% had a positive TRAB with no known thyroid nodules.
- 5% of euthyroid subjects (5.6% of the total study cohort) were inappropriately referred for thyroid scintigraphy to assess the functionality of a thyroid nodule, though in euthyroid patients the risk of malignancy of thyroid nodules should be evaluated based on ultrasound characteristics followed by fine needle aspiration (FNA) if necessary.
- Increased awareness on the indications for thyroid scintigraphy is likely to reduce unnecessary costs and waiting times by prioritising this investigation for those patients in whom it is likely to influence management namely in thyrotoxic individuals with co-existing thyroid nodularity, particularly if TRAB is negative.

thyroid scintigraphy scans had a negative TSH-receptor antibody status. It is possible that some of these patients had already been started on ATDs prior to the TRAB levels being checked. Since effective treatment with ATDs is associated with a lowering of TRAB titres[1], a proportion of this cohort might have exhibited TRAB positivity had this been checked earlier. Autoantibody-negative Graves' disease is a subject of debate as Graves' disease is proposed to be a systemic disease.[9] Studies have revealed that autoantibody-negative Graves' disease does exist, albeit rare.[10] This may occur for a number of reasons. Scatti Regàs A et al suggest that the tests for the detection of TSH receptor antibody may not be sensitive enough to detect low antibody concentrations.[11]

Another postulated explanation is that patients might exhibit TSH receptor mutations leading to chronic TSH receptor stimulation. The latter leads to a similar clinical and biochemical picture to that seen in Graves' disease, but without any detectable TSH receptor antibody.[12]

Yet another potential explanation for the occurrence of TSH-receptor antibody negative Graves' disease, is that the production of TSH-receptor antibody may be restricted solely to the thyroid. This hypothesis is based upon evidence that lymphocytes isolated from the thyroid of a patient with TSH receptor antibody seronegative autoimmune thyroiditis, could produce anti-thyroid antibodies,[11, 13-14] despite undetectable levels in serum.

CONCLUSION

Thyroid scintigraphy plays an important role in the assessment of the thyrotoxic patient and is particularly useful in patients who also have thyroid nodules. All patients presenting with new-onset thyrotoxicosis should have blood sampled for TSH-receptor antibody levels. Most patients presenting with thyrotoxicosis with positive TSH-receptor antibody levels will have Graves' disease. In the absence of thyroid nodules, a thyroid scintigraphy scan is unnecessary in thyrotoxic patients. However, if thyroid nodularity coexists, a thyroid scintigraphy scan is indicated to help distinguish between Graves' disease, toxic multinodular goitre and toxic adenoma. A case can be made for ordering a thyroid scintigraphy scan if acute thyroiditis is suspected based on the clinical presentation since the pattern of reduced uptake is diagnostic. Euthyroid or hypothyroid patients found to have thyroid nodules do not benefit from thyroid scintigraphy and should instead be investigated via an ultrasound scan of the thyroid. A decision to proceed with US-guided FNA should be guided by the patient's thyroid ultrasound characteristics. This audit revealed that a number of thyroid scintigraphy scans performed locally between 2019 and 2021 were not necessary for accurate diagnosis and management. Through this audit, we hope to raise awareness that thyroid scintigraphy scans should no longer be ordered to assess thyroid nodules in euthyroid or hypothyroid patients and is also unnecessary in patients with clinical and biochemical evidence of TSH-receptor antibody positive Graves' disease if thyroid nodularity does not coexist. Such a diagnostic approach will help reduce unnecessary costs and optimise the allocation of healthcare resources.

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ORIGINAL ARTICLE

Accident and Emergency Presentations in Patients in their Last Year of Life

Nicole Sciberras, Rebecca Galea, Daniela Marino, Amy Chircop, John Paul Tabone, Doreen Pace

Presentation of patients with incurable, terminal illness to the emergency department (ED) may prove distressing for patient and caregivers alike. The last year of life has been widely used as a proxy for patients with palliative needs. This retrospective study is the first local study to determine how many patients presenting to the ED are in their last year of life, and thus by association, what percentage of patients presenting to the emergency department would require palliative care. In Malta, 16.66% of patients presenting to the ED were in their last year of life, and despite this value being lower in comparison to overseas, it is still significant keeping in mind that locally palliative care caters only for oncology cases. There was no observed gender difference, and the mean age was of 77.6 years. Most patients presented more than one time to the ED more than once, and the largest cohort of patients presented 3 times to the ED in their last year of life. Community- based palliative care has been shown to reduce presentations to the emergency department and our focus must therefore shift towards strengthening this field.

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The World Health Organisation defines palliative care as 'an approach that improves the quality of life of patients (adults and children) and their families who are facing problems associated with life-threatening illness'.[2] Presentation of patients with unmet palliative need to the Emergency Department (ED) may prove distressing for patient and caregivers alike. There are multiple reasons for presentation, which may be secondary to the condition requiring palliative care, as well as for unrelated complaints. Several studies have attempted to gain insight into the nature of these complaints, as well as categorise the emergency presentations into avoidable and unavoidable. Locally, this is the first study of emergency presentations by patients in their last year of life.

The aim of this study was to ascertain the percentage of patients, that are considered palliative upon presentation at the ED over a period of two months.

The objectives are twofold:

- Elicit demographic data
- Identify any correlation between patient demographic and frequency of presentation at the ED

METHOD

Ethical approval was obtained from the local regulatory body and data anonymised to comply with data protection regulations. Data was collected retrospectively by identifying patients who presented to the ED in Mater Dei Hospital, the only local hospital with an ED, during the months of January and July 2017. Data collected involved checking for patient survival to at least one year from date of emergency presentation, and in those who did not, patient demographics were tabulated as follows: age, sex, number of presentations to the ED in the last year of life. The unpaired t-test was used to identify any statistically significant relation between the demographic variables. ANOVA was utilised to determine any link between age at death and the number of presentations to the ED in the last year of life. Exclusion criteria were as follows: mechanical trauma, paediatric age and patients who passed away at the Accident and Emergency Department.

RESULTS

2713 patients presented to the Accident and Emergency department in the months of January and June 2017. The number of deaths within one year from Accident and Emergency presentation was of 452(16.66% of sampled population). Of these, 226 deaths occurred within one year for patients who had presented to the Accident and Emergency Department in January and 226 in those who had attended in July 2017. With regards to deceased patients' demographics, the male: female ratio was of 1.14:1 (241 males and 211 females) and age range was 23 to 107 years, with a mean age of 77.6years. There was no statistically significant difference between both sexes in relation to the number of presentations to the Accident and Emergency Department (p=0.44, 95% confidence interval). However, we did observe a significantly larger number of re-presentations to the Accident and Emergency Department in patients who had presented in the month of January (p=0.029, 95% confidence interval).

The number of Accident and Emergency encounters within the last year of life is displayed in **Figure 1**. The largest cohort of patients had 3 presentations to the ED in their last year of life (78 patients), followed closely by 2 presentations (77 patients). 16 patients

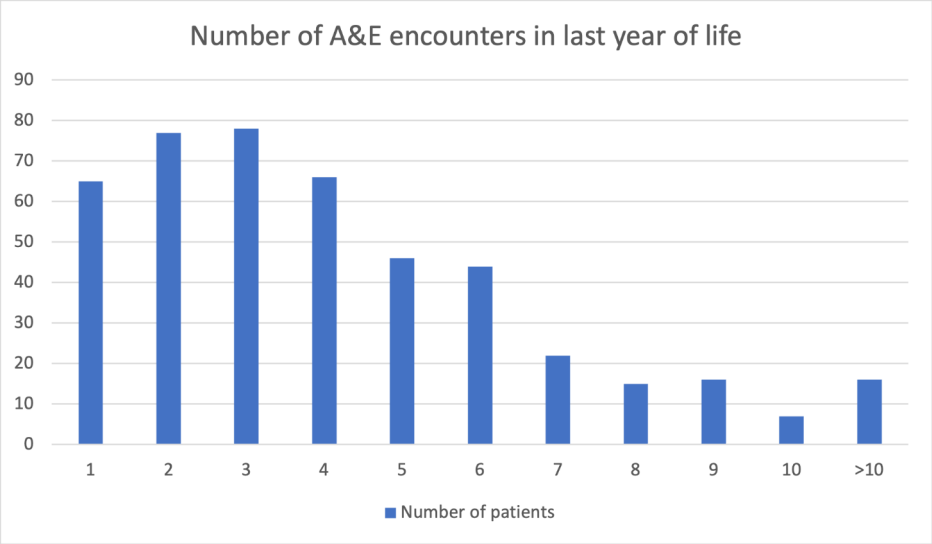

Figure 1 *Number of Accident and Emergency encounters in last year of life*

Table 1 *Average Number of Visits to Accident and Emergency Department per age group*

Age Range	No. of Patients	Average No. of Visits
20-40	8	6.125
41-60	33	5.487
61-80	196	4.448
81-100	215	3.651

had over ten presentations to the Accident and Emergency Department in the last year of life. We also observed that younger patients in their last year of life are more likely to visit the ED, as the average number of visits decreases with increasing age. This observation reached statistical significance (p=<0.0001) and is displayed in Table 1.

DISCUSSION

This study shows that 16.66% of patients presenting to the ED are in the last year of life, and that patients in their last year of life are likely to make use of emergency services more than once. The average number of visits decreases with increasing age. There was no difference in number of patients in their last year of life presenting to the ED between Winter (January) and Summer months (July).

Locally, this was the first study of its nature and highlights the need for better understanding of emergency presentations amongst patients with incurable, terminal illness. Malta has one ED to cater for the whole country so this can be considered a national study which covers the entire population. In 2017, there was a total of 141, 758 presentations to the Maltese ED (3). Extrapolating the above calculation to the whole year, this percentage translates to 23,532 patients presenting to the ED in 2017 who had palliative care requirements. Similar studies conducted on an international level reveal overall higher percentages of one year mortality following hospital admission.

The incident cohort study by Moore et alwas the most alike to ours in terms of study outcomes, with the additional outcome of identifying patient factors contributing to higher mortality risk. Based in Scotland, it included patients admitted to 22 hospitals within two weeks in March 2015, and 22.4% passed away within one year of hospital admission (not solely emergency admission as in our study). Malignancy (33.8%), cardiovascular disease (22.5%) and respiratory disease (17.9%) accounted for slightly less than 75% of all deaths.[1] One possible explanation for the discrepancy in mortality rates would be that due to the Maltese ED service being easily accessible and free of charge, Maltese patients might present earlier than in Scotland.

Further insight is provided by the 2012 NHS National End of Life Care Intelligence Network report, which reveals that around 78% of people will be admitted to hospital at least once in their last year of life. In contrast to our results, it also states that on average, people who have emergency admissions in the last year of life have two or less admissions.[4] With these statistics and chronic conditions in mind, one attempts to identify the root cause for repeated emergency presentations. In their study of elderly patients (over 70years) presenting to the ED, the authors comment that while unexpected return presentations to the ED within one month were often not preventable, healthcare professionals must still attempt to anticipate factors that may prompt return to Accident and Emergency, disease progression and potential unmet needs.[5]

The 'Better End of Life' 2022 report notes that emergency department attendance is relatively low and stable for most of the final year of life, but rises in the final three months of life, with out-of-hours visits increasing more than in-hours visits, especially in the last month of life.[6] Our study did not assess the timing of the Accident and Emergency visits, or whether the visits occurred out-of-hours.

Other studies on the same topic attempted to split emergency presentations of patients with advanced cancer under palliative care into avoidable and unavoidable, and the results highlight that most visits are unavoidable, despite being under the palliative care team. The unavoidable presentations were mostly due to pain as well as for referrals requiring admission following an outpatient review. On the other hand, avoidable admissions made up almost 25% of presentations and were related to complaints such as constipation. In conclusion, the authors argue that avoidable presentation rate would decrease with improved communication between palliative appointments.[7] As previously explained, our study does not go into the merits of individual cases but seeks to measure palliative need in the population, by using emergency admissions in the last year of life as a surrogate.

In a small study of 30 patients, further avoidable presentations are identified; these made up at least half of the emergency presentations by patients under the specialist palliative care register. In the

authors' words, a 'comprehensive, coordinated specialist palliative care approach across community and acute services' would prevent such avoidable presentations.[8] Having said this, several obstacles may be encountered when attempting to construct a streamlined approach as mentioned above. In a study based at an Accident and Emergency Department, emergency doctors named lack of access to medical records as well as lack of continuous availability of the palliative care team as the two main barriers to offering optimal palliative care services at the department. The Accident and Emergency physicians also voiced their concern that ward-based doctors and emergency-based doctors may use different criteria with respect to palliative care consultations.[9]

On a similar note, a critical review of patients with palliative care needs who present to the ED note that there is a lack of data in this respect and emphasised that palliative care is defined differently across healthcare systems.[10] These factors may therefore present another barrier to palliative care patients and physicians alike. Separate studies taking place in Australia agree that eliciting models of emergency and inpatient use for different disease courses is the first step in planning appropriate services for individuals with conditions where mortality is expected.[11]

Besides communication and coordination within the specialist palliative care system, Wright et alpoint out that timing of initiation of community-based care is also a vital factor in reducing emergency presentations, as when started before the last six months of life, it was associated with a lower mean rate of unplanned hospitalizations in the last 6 months of life.[12] Timely referral to community-based palliative care is also supported by McNamara et alwho identified a higher number of emergency presentations in patients who had been referred later to community-based palliative care.[13]

LIMITATIONS

The study period was over two separate months and it is thus not fully reflective of Emergency Department presentations over the rest of the year. Patient's past medical history and reason for presentation to Accident and Emergency were not recorded. The outcome of the Accident and Emergency visit (discharged or hospital admission) was not recorded.

CONCLUSION

In 2017, there was a total of 141, 758 presentations to the Maltese ED. In the span of two separate months, we calculated that 16.6% of patients are in their last year of life when presenting to the ED. Extrapolating this calculation to the whole year, this percentage translates to 23,532 patients presenting to the ED in 2017 who had palliative care requirements. Furthermore, when compared to international statistics, one may see that patients in their last year of life present more often to the Accident and Emergency Department locally. The latter raises the question whether there might be an unmet palliative care need in Malta. Moving forward, we must further attempt to identify patterns of ED presentations for various chronic diseases and develop the appropriate referral criteria, both of which will aid liaison between the ED and the palliative care team. A larger-scale study, possibly even using a time frame in the post-COVID period, would be ideal to identify changes in presentations since 2017, as well as attempt to pinpoint patterns of presentations as described earlier. In summary, keeping in mind the physical and psychological implications related to chronic disease burden, it is essential for doctors across different departments to anticipate patients' and relatives' needs from the palliative care team and thus to refer early to community based palliative care.

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ORIGINAL ARTICLE

Retrospective audit on the management of newly diagnosed non-muscle-invasive bladder cancer patients and their oncological outcomes

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Background

Non-muscle-invasive bladder cancer (NMIBC) is a heterogenous subclassification of urothelial carcinoma with variation in risk of recurrence and progression. The aim of this audit was to assess whether the clinical management of NMIBC was being carried out according to the recommendations provided by the European Association of Urology (EAU) guidelines.

Method

154 patients who were newly diagnosed with NMIBC were selected. Details about presentation, risk factors and clinical management were collected for analysis. The clinical standard of care used was the EAU Non-muscle-invasive Bladder Cancer Guidelines 2020. Oncological outcomes for this patient group was also documented. The European Organisation for Research and Treatment of Cancer (EORTIC) risk table was used to predict recurrence and progression in NMIBC. The risk group stratification table in the EAU guidelines (2020) was used to classify tumours according to their characteristics. SPSS and Kaplan Meier curves were used to analyse the results.

Results

TURBT was carried out in 52.9% of indicated patients; intravesical therapy in 14.1% of indicated patients; CT-IVU follow up according to guidelines in 64.3%; urine cytology follow up according to guidelines in 66.9% patients. Cystoscopy carried out after 3 months showed a recurrence rate of 12.3%

Conclusion

The clinical management of NMIBC has an important bearing on the progression of the cancer. Stricter adherence to the guidelines will enable the clinician to strike a balance between cost cutting and reduced tumour progression.

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Bladder cancer is the 7th most common cancer in males and the 17th in females worldwide.[1] In Malta bladder cancer is the 6th most common cancer, having accounted for 6.1% of all cancers diagnosed in 2020.[2]

Around 75% of cases present with non-muscle-invasive disease.[1] This group of patients represents a heterogeneous population with variable risk of recurrence and progression. This risk assessment is based on morphological and histopathological variables and stratifies non-muscle-invasive bladder cancer (NMIBC) into low risk, intermediate risk, high risk and very high risk groups.

Recurrence rates range from 31% to 78% and progression rates range from 0.8% to 45% at 5 years.[3] This implies that NMIBC will often require lifelong follow ups. Different grades of carcinoma exhibit differences in behaviour, aggressiveness and prognosis. Low-risk tumours are usually characterized by a relatively benign behaviour but often do recur although disease progression is rare, intermediate risk tumours have a higher recurrence rate but a low progression rate while high risk tumours have both a high recurrence and progression rate. These differences will require specific follow up strategies and treatment methods.

In this audit we looked into the clinical management of NMIBC including Trans-urethral removal of bladder tumour (TURBT), intravesical therapy, cystoscopy, CT intravenous urogram (CT-IVU) and urine cytology and assessed if it was carried out according to the recommendations provided by the European Association of Urology (EAU) guidelines.

MATERIALS AND METHODS

Patients who were newly diagnosed with NMIBC between January 2015 and December 2017 were selected from biopsy results obtained from the pathology department at Mater Dei Hospital (MDH). This excluded patients with muscle invasive bladder cancer, de novo metastatic disease, as well as patients with recurrent NMIBC diagnosed before 2015.

Distinction between new onset and recurrent NMIBC as well as details about presentation, risk factors and clinical management were obtained from the patient dashboard, MDH electronic database and the patients' medical notes. The primary outcome measured was the use of intravesical therapy in patients with NMIBC and their follow up. The clinical standard of care used as gold standard was the EAU Non-muscle invasive Bladder Cancer Guidelines 2020.[4] on intravesical therapy. Secondary outcomes measured included diagnostic and therapeutic interventions performed as well as oncological outcomes using Kaplan Meier curves.

The European Organization for Research and Treatment of Cancer (EORTC) risk table was then used to predict the recurrence and progression in stage Ta and T1 bladder cancer patients. The risk group stratification table in the EAU guidelines\(2020\) was used to classify the tumours into low, intermediate, high and very high risk according to their characteristics. Statistical Package for the Social Sciences (SPSS) was used to analyse the results and Kaplan Meier curves were used for survival analysis.

RESULTS

The cohort consisted of 154 patients who were newly diagnosed with NMIBC between 3rd January 2015 and 18th December 2017. Patient age ranged from 39 to 93 years. 129 patients (83.8%) were male while 25 patients (16.2%) were female.

84 patients (54.5%) presented with visible haematuria; 8 patients (5.2%) presented with microscopic haematuria; 6 patients (3.9%) presented with lower urinary tract symptoms (LUTS); 4 patients (2.6%) had pelvic pain while 1 patient (0.6%) presented with an upper tract obstruction. 22 patients (14.3%) were found incidentally while in 29 (18.8%) cases, the data was not available.

From our cohort of patients, 83 (53.9%) were classified as low risk; 21 (13.6%) were intermediate risk; 35 (22.7%) were high risk while 15 (9.7%) were classified as very high risk.

2nd look TURBT was indicated in 51 cases (33.1%) and performed in only 27 cases (52.9%).

Peri operative single dose mitomycin was administered in 36 patients (23.4%).

Intravesical therapy after primary diagnosis was indicated in 71 patients (46.1%) (intermediate, high and very high risk) but was only given in 10 patients (14.1%).

In the intermediate risk group 9.5% were given intravesical therapy. In the high risk group 5.7% of patients were given intravesical bacillus Calmette-Guerin (BCG) for 6 weeks; 5.7% were given intravesical BCG for 6 weeks with 2 years' maintenance while 8.6% were given intravesical BCG for 6 weeks with 3 years' maintenance. 80% of high risk cases were not given any form of intravesical

therapy. In the very high risk group 93.3% of patients were not given any form of intravesical therapy.

Cystoscopy was carried out after 3 months in 81 patients (52.6%). 10 of these patients (12.3%) had a recurrence. 3.6% of low risk cases had a recurrence; 14.3% of recurrences were in the intermediate risk group; 5.7% were in the high risk group while 13.3% were in the very high risk category.

CT-IVU follow up was carried out according to guideline in 99 cases (64.3%) while in 55 cases (35.7%) CT-IVU was not performed as recommended by EAU guideline. In the high risk group, 25.7% underwent CT-IVU as per EAU guidelines. In the very high risk group, 26.7% underwent CT-IVU.

In 103 cases (66.9%), urine cytology follow up was according to guideline while in 51 cases (33.1%) urine cytology was not performed according to the EAU guidelines. In the high risk category 11.4% underwent urine cytology according to the EAU guidelines. However none of the very high risk cases had urine cytology follow up carried out.

In 137 patients (89.0%), detrusor muscle was absent. Of these only 5 (3.6%) had a 2nd look TURBT performed.

Recurrence on follow up was noted in 31 out of 83 (37.3%) low risk cases, 15 of 21 (71.4%) intermediate risk cases, 21 of 35 (60%) high risk cases and 11 of 15 (73.3%) of very high risk cases. Average time to 1st recurrence was noted to be 491.2 days in low risk cases, 431.9 days in intermediate risk cases, 414.1 days in high risk cases and 266.1 days in very high risk cases.

In terms of prognosis, 61 of 83 patients (73.5%) with low risk NMIBC were found to be alive and disease free while 7 of 83 (8.4%) died of cancer. 10 of 21 patients (47.6%) with intermediate risk NMIBC were disease free while 2 of 21 (9.5%) died of cancer. 27 of 35 patients (77.1%) with high risk NMIBC were disease free while 5 of 27 (18.5%) died of cancer. 6 of 15 patients (40%) with very high risk NMIBC were found to be disease free while 9 of 15 (60%) died of cancer.

The Kaplan Meier curves in **Figure 1** and **Figure 2** highlight the cancer specific survival and the overall survival for the patient cohort respectively. Patients at very high risk had the worst prognosis in both overall and cancer specific survival (**Figures 3, 4**). Low risk patients had better cancer specific survival rates compared to high risk patients (**Figure 3**). However the overall survival rates in low risk patients was

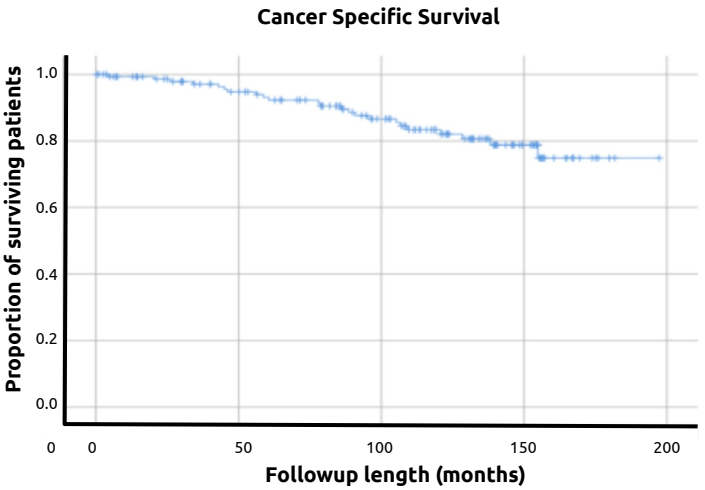

Figure 1 *Kaplan Meier Curve showing Cancer Specific Survival for whole cohort*

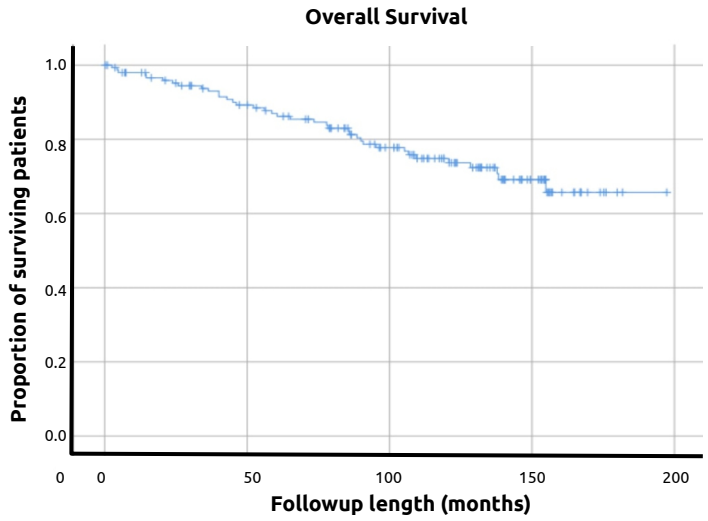

Figure 2 *Kaplan Meier Curve showing overall survival for the whole cohort*

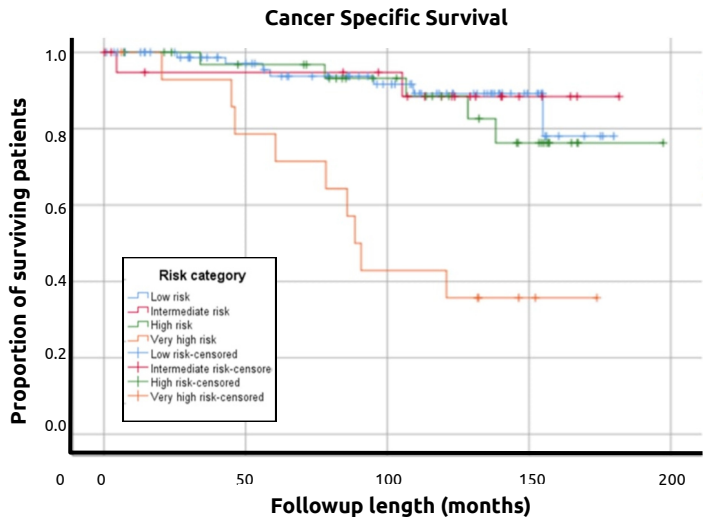

Figure 3 *Kaplan Meier curve showing cancer specific survival stratified by risk group*

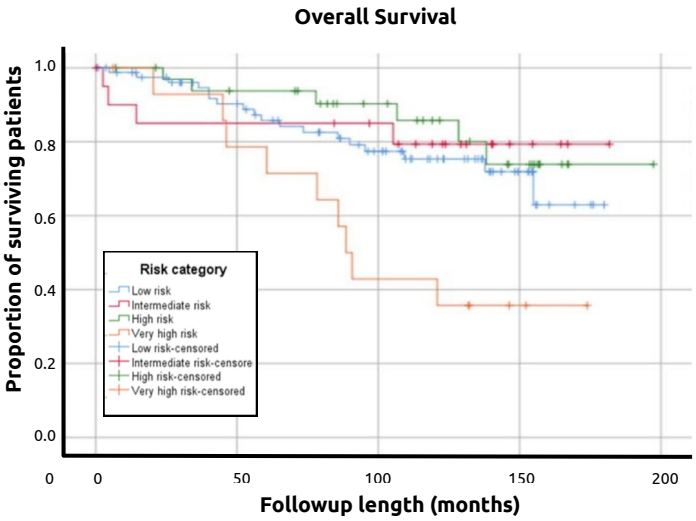

Figure 4 *Kaplan Meier curve showing overall survival stratified by risk group.*

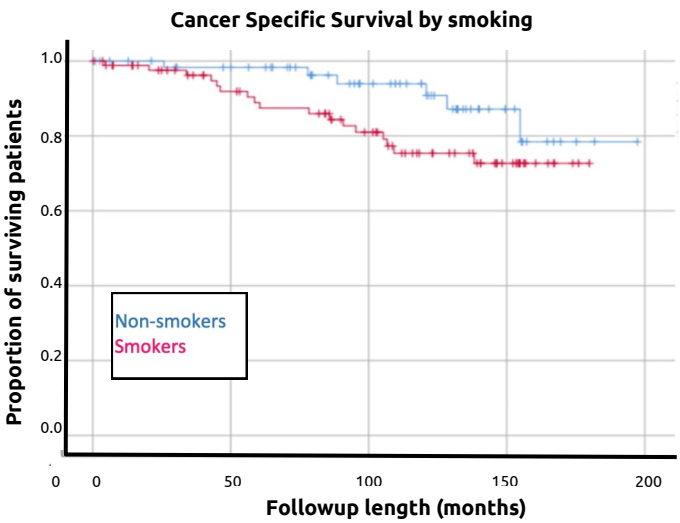

Figure 5 *Kaplan Meier curve showing cancer specific survival stratified by risk group*

lower than that of high risk patients (Figure 4). Non-smokers had better cancer specific survival than smokers (Figure 5).

DISCUSSION

The natural history of NMIBC is characterized by a high probability of recurrence, as well as by progression to muscle-invasive cancer in the presence of high-grade tumours. This mandates a follow-up strategy designed to identify recurrences and grade/stage progression in the bladder early in its evolution in order to facilitate timely intervention and ablation [5]

The EAU guidelines emphasize the importance of a focused patient history when diagnosing NMIBC In our study, we focused on age, gender, smoking status (smoker; ex-smoker; non smoker) as well as the patients' presentation.

Our cohort of patients consisted of a significantly higher number of males (83.8%) than females (16.23%). Studies show that the incidence and mortality for urothelial bladder cancer (UBC) are higher in men, whereas cancer specific mortality to incidence ratio is significantly lower for men than for women. This phenomenon could be partially explained by differences in exposure to bladder cancer carcinogens. Studies also show that female gender is associated with a higher stage at presentation.[6] In our study, 48% of females were diagnosed with NMIBC of a stage higher than pTaG1 no CIS compared to 43% of males.

Tobacco smoking is the most important risk factor for bladder cancer, accounting for approximately 50% of cases.[7,8].In our study, 57% of patients were smokers. Quitting smoking decreases the risk of developing bladder cancer by more than 30% after 1–4 years and by more than 60% after 25 years, but the risk never returns to the level enjoyed by non-smokers [9,10] However an association between tobacco consumption and progression or death resulting from bladder cancer has never been found.[9]

Haematuria is the most common finding in NMIBC[4] In our study, 54.5% of patients presented with visible haematuria. In addition, visible haematuria was found to be associated with higher stage disease compared to non-visible haematuria.[11]

Intravesical therapy after primary diagnosis was only given to 14.1% of eligible patients according to the EAU guidelines. The main reason can be attributed to a logistical restraint caused by the global shortage of intravesical therapy at present. The clinician has to therefore prioritize the allocation of the treatment to higher risk cases.

Patients who are on maintenance doses of intravesical therapy would have a survival advantage over those who only receive the 6-week induction doses.[12] In such cases where there is shortage of intravesical therapy, Frankhauser et al recommend splitting each dose of intravesical therapy into three separate doses.[13] while Mayor et al suggest that upfront cystectomy may be the most sensible option in high risk NMIBC [14]

The EAU guideline recommends that cystoscopy should be performed in all patients with symptoms suggestive of bladder cancer. It cannot be replaced by cytology or by any other non-invasive test. Patients with haematuria and/or urinary tract symptoms should undergo CT-IVU and/or renal and

bladder ultrasound.[4] From our cohort of patients, only 15% had a CT-IVU Urine cytology was performed in 5.8% of patients.

TURBT is a crucial procedure in the management of bladder cancer. It is used to make the correct diagnosis and completely remove all visible lesions. TURBT eradicates all visible tumours and provides tissue for pathological analysis and determination of histological type, grade and depth of invasion.[15] The quality of the initial TURBT specimen is extremely important.[16]

Detrusor muscle should be included in the specimen to rule out T2 disease and minimize the risk of under-staging. According to the EAU guidelines, 2nd look TURBT should be carried out when detrusor muscle is lacking in the specimen, if there is residual tumour at first resection, in pT1 as well as G3 tumours. In our case, 137 patients had absent detrusor muscle. Of these only 5 (3.6%) had a 2nd look TURBT performed. High grade tumours lacking detrusor muscle in the initial resection specimen are subsequently associated with residual tumour or muscle invasive disease in up to 50% of cases.[17,18]

Although TURBT alone can be effective method to treat TaT1 tumours, these tumours can recur or even progress to MIBC The high variability in the 3-month recurrence rate may be due to an incomplete TURBT, the implantation and growth of a circulating tumour cell at the time of TURBT or the presence of a very aggressive neoplasm.[19] Adjuvant therapy should be considered in all patients.

Following TURBT, immediate single instillation (SI) of chemotherapy significantly reduces the recurrence rate compared to TURBT alone.[20,21] Peri operative single dose mitomycin was administered in 36 patients (23.4%).

The prognosis of each tumour determines the need for additional adjuvant intravesical therapy. Patients with low risk tumours do not require further intravesical therapy.[20] In patients with intermediate, high and very high risk tumours, a single instillation is considered an incomplete treatment. 71 patients required further intravesical therapy. However this was only carried out in 14.1% of cases.

The EAU guidelines treatment recommendations in TaT1 tumours suggest that intermediate risk tumours should receive one-year full dose BCG treatment. Whereas high and very high risk tumours should receive full dose BCG instillations for 1 to 3 years. From our results, it is clear that guidelines were not followed especially in the high risk cases.

SUMMARY BOX

- The EAU guidelines emphasize the importance of a focused patient history when diagnosing NMIBC Age gender, smoking status and patients' presentation should all be considered.
- NMIBC is characterized by a high probability of recurrence and progression to muscle-invasive cancer in the presence of high-grade tumours.
- A follow-up strategy designed to identify recurrences and grade/stage progression in the bladder early in its evolution is needed in order to facilitate timely intervention.
- This audit showed that there must be stricter adherence to the EAU guidelines in the clinical management of newly diagnosed NMIBC

According to the EAU Guidelines it is recommended that the first control cystoscopy be performed 3 months after TURBT of the bladder tumour. This is a very important prognostic factor for recurrence and progression.[22,23] In our study, only 52.6% of patients underwent cystoscopy at 3 months. 12.3% of these patients had a recurrence. From our results we can note that the highest risk of recurrence was in the intermediate risk group (14.3% of recurrences), however this might not represent the true recurrence risk in view of low number of patients in the high and very high risk category.

Since the intermediate risk group is heterogenous (as seen in the Kaplan Meier curves), Kamat et al propose that this group be divided into three categories; one closely resembling low-risk tumours, another one resembling high-risk tumours in behaviour, and another category in between the two, based on a management algorithm for intermediate risk proposed by the International Bladder Cancer Group (IBCG).[24]

The Kaplan Meier curves in this study show that cancer specific survival is directly related to the cancer risk group. This compares well with international cancer specific survival rates where patients with high risk NMIBC and tumour progression have a poor prognosis.[25]

CONCLUSION

Leal et al looked at the economic costs of bladder cancer across the European Union (EU). These were €4.9 billion in 2012, of which health care costs were €2.9 billion (59%), productivity loss €1.1 billion (23%) and informal care costs €0.9 billion (18%).[26] From this audit we can conclude that the clinical management of NMIBC was carried out in accordance to the EAU guidelines in a minority of cases. Stricter adherence to the guidelines will enable the clinician to strike a balance between cost cutting (by reducing the number of unnecessary follow ups) and reduced tumour progression.

ABBREVIATIONS

NMIBC	Non-muscle-invasive bladder cancer
TURBT	Trans urethral removal of bladder tumour
CT-IVU	CT Intravenous Urogram
EAU	European Association of Urology
EORTC	European Organisation for Research and Treatment of Cancer
BCG	Bacillus Calmette-Guerin
SI	single instillation
IBCG	International Bladder Cancer Group
EU	European Union
SPSS	Statistical Package for the Social Sciences

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ORIGINAL ARTICLE

Psychiatric Admissions amongst the Substance Use Disorder Population to Malta's Mental Health Hospital

Admissions related to substance use disorder in Malta

Emma Camilleri, Caroline Vassallo, Kristian Sant

Background

The population of substance users is frequently stigmatised and under-represented. Their management often poses specific challenges secondary to complex presentations.

This study aims to establish a comprehensive picture of substance user presentations to the acute mental health hospital in Malta, focusing on the number of and reasons for admission. Any correlation existing between the length of stay and the presenting complaint was also analysed.

Methods

Data collection was carried out retrospectively over a 13-week period between 29th October 2021 and 31st January 2022 on all patients admitted to Malta's Mental Health Hospital. 113 total patients met the outlined inclusion criteria. Of these, 18 had incomplete information, and were excluded from the study, giving an overall number of 95 records analysed.

Results

58.8% of all psychiatric admissions were prompted by social reasons, 34.3% were admitted with comorbid mental health illness, and 6.9% were admitted for stabilisation, prior to entering a rehabilitation programme. Results showed that the length of stay was not significantly correlated with the reason for admission with a Spearman r value of 0.137.

Conclusions

Admission to Malta's mental health hospital is often utilised as a gateway to access social services. Instituting timely, easily accessible community services would allow individuals to receive community based care. Relevant training for staff, better education on service access as well as timely social service interventions could potentially decrease hospital admissions. We suggest the implementation of specifically catered community residences as well as communication with rehabilitation centres, to decrease waiting times prior to entry to rehabilitation programmes.

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The population of substance users is frequently stigmatised and under-represented. Their management plan often poses specific challenges secondary to complex presentations.[1] Individuals making use of substances suffer from multiple medical, psychological, psychiatric, financial, social, family and legal issues. This creates a significant burden both on these affected individuals as well as their families and society at large.[2] Additionally, the existing mental health services in Malta do not reflect the needs of this patient population. Locally, community psychiatry addiction services are limited. Thus, individuals suffering from substance use disorder (SUD) tend to desperately and excessively rely on hospital settings. This, unfortunately, burdens the currently existing mental health infrastructure.

Stigmatisation and social exclusion amongst individuals suffering from SUD is the norm rather than the exception.[3] These challenges provide additional barriers to accessing social services, including employment and housing.[4] Moreover, substance users often forgo existing community aid infrastructure and instead present in crisis via the accident and emergency department or an emergency general practitioner. This often prompts hospitalisation for social rather than acute medical or psychiatric complaints. However, acute medical facilities are often unable to provide immediate solutions for long-standing social issues.

This prompts patients to request early discharge and impulsive treatment dropout prior to having their underlying social problems adequately addressed. This generates an unfortunate perpetual cycle of late and complex presentations to inappropriate facilities and early discharge prior to patient needs being met.[5]

Thus, the aim of this study is to establish a comprehensive picture of substance user presentations to Malta's Mental Health Hospital, focusing particularly on the number of presentations requiring admission. The primary reason prompting admission and whether a correlation exists between the length of stay and the presenting complaint was also analysed.

MATERIALS AND METHODS

This study evaluated admissions to Mount Carmel Hospital, which caters for a population of circa 516,000.[6] Data collection was carried out retrospectively over a 13-week period between 29th October 2021 and 31st January 2022.

Upon admission to Mount Carmel Hospital, all patients undergo a urine toxicology screening for opiates, cocaine, tetrahydrocannabinol (THC), synthetic cannabinoid receptor agonists (SCRA) and amphetamines. Patients appropriate for study inclusion were identified via a positive urine test upon admission. A diagnosis of substance use disorder was made by the responsible specialist depending on DSM-5 criteria. This was documented in the patient's clinical notes and/or discharge summary. Patients who did not fit the criteria for a substance-use disorder diagnosis in accordance with the DSM-5 were excluded.

Once these records were identified, information was collated using iClinical Manager v 2.4 that provided patient demographics, including age, gender and length of stay. The patients' clinical notes and discharge letters were utilised to determine the reasons for admission, the primary mental health diagnosis which was most clinically significant, if any, and categorization of severity of substance-use disorder.

All identifiable patient data was anonymised prior to data analysis to ensure protection of all sensitive and personal details. We identified 113 total patient admissions meeting the outlined inclusion criteria, with 25 of those admissions being readmissions. Of the 113 episodes identified, 18 had incomplete information, and were excluded from the study, giving an overall number of 95 records analysed 20 of which were readmissions. Data analysis was carried out using the GraphPad Prism® 9.4 version. Descriptive statistics were presented graphically using Excel™.

RESULTS

DEMOGRAPHICS

The percentages of male and female individuals included in the study were 78.9% and 21.1%, respectively. The mean age was ~25 years (Table 1).

Table 1 *Demographic data of the patients recruited*

Variables	Participants
Total	113
Documented	95
Percentage Males (%)	78.9
Percentage Females (%)	21.1
Average Age (years)	24.8

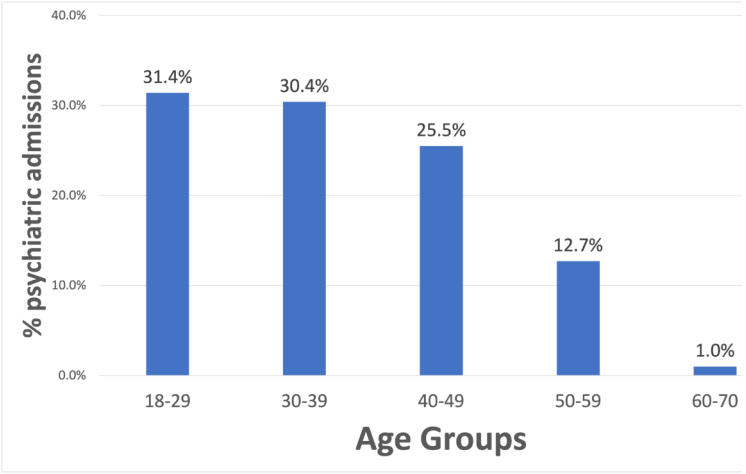

Figure 1 *Psychiatric admissions according to age*

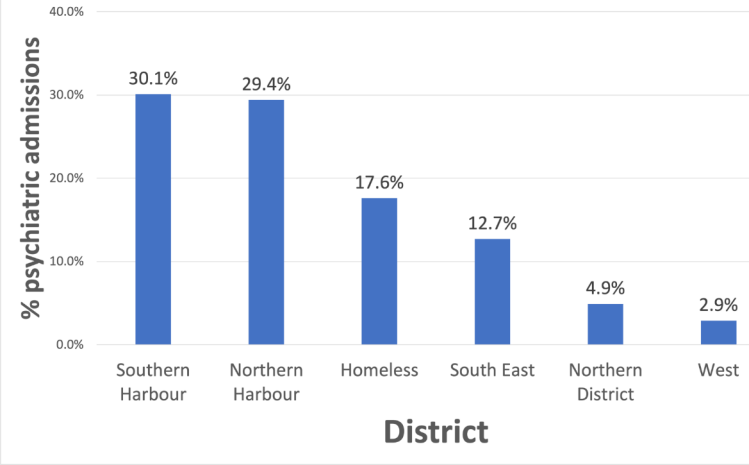

Figure 2 *Psychiatric admissions according to district*

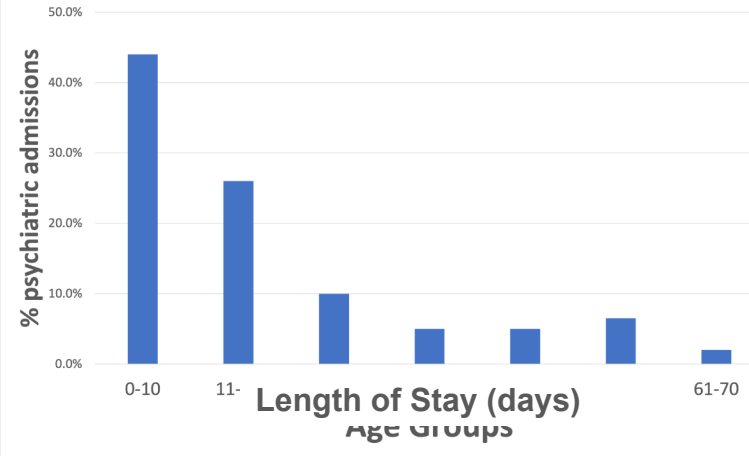

Figure 3 *Psychiatric admissions and length of stay*

Around a third (31.37%) of all admissions were in the 18-29yr age group, whilst only 0.98% of all admissions were in the 60-70yr age group. Another approximate third (30.39%) of admissions were between 30-39 years of age, whilst 26.47% were between 40-49 years, and 10.78% were between 50-59 years of age. The average age of all patients was 24.8, the median age was 67, and the mode was 45 (Figure 1).

The Nomenclature of Territorial Units for Statistics (NUTS) of the National Statistics Office (NSO) 2022 edition.[6] was used to assign the localities according to district. The most common district was the Southern Harbour with a percentage of 30.39%, whilst the Northern Harbour had a percentage of 29.4%. Interestingly, 17.65% of patients were homeless. 4.9% and 2.94% of patients originated from the Northern and Western district respectively. (Figure 2)

LENGTH OF STAY

Almost half (44.12%) of all psychiatric admissions spent between 0-10 days hospitalised, and around one-fourth (26.47%) of all patients spent between 11-20 days in hospital. The length of admission ranged from 1 to 64 days, with the median length of stay being 12.5 days. The average length of stay was 17.5 days (Figure 3, Table 2).

REASONS FOR ADMISSION

Significantly, more than half of all psychiatric admissions were due to social reasons, with a total of 58.8%. This contrasts with the initial reason for the majority of referrals which was often stated to be a decompensation of mental state or suicidal ideation. Around a third (34.3%) of patients were admitted with comorbid mental health illness, and 6.9% were admitted for stabilisation, prior to entering a rehabilitation programme.

This included detoxification from opioid substitution treatment or other medical stabilisation required. Social issues included lack of social support, financial instability, unemployment and homelessness.

Table 2 *Psychiatric admissions and length of stay*

Range length of stay (days)	**1 - 64**
Median length of stay (days) [IQR]	12.5 [5 – 21.75]
Average length of stay (days)	17.5

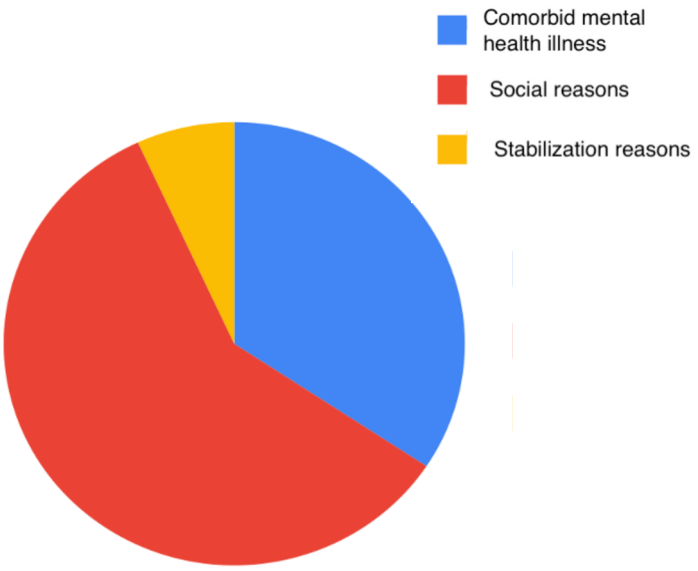

Figure 4 *Reason for Psychiatric admission*

Around half of all psychiatric admissions admitted with comorbid mental health illness experienced affective disorders, including: depressive disorders, anxiety disorders, and post-traumatic stress disorders. Another 25% of all comorbid mental health illness admissions were due to substance-induced psychosis (Figure 4, Table 3).

TYPE AND QUANTITY OF SUBSTANCE USED

During data collection, the type and number of substances used by the patients included in the study were also noted. More than half of all admissions (55.75%) were using more than one substance prior to admission. The term 'polysubstance' was therefore used to define the use of more than one substance within the same timeframe. Cocaine was the substance that was most prevalently used (67.3%), followed by opiates (34.5%), cannabis (33.6%) and synthetic (18.5%).

Table 3 *Percentage of psychiatric admissions according to dual diagnosis*

Comorbid mental health illness	Percentage (%)
Neurotic disorders	51.02%
Substance-induced psychosis	24.5%
Schizophrenia	2.04%
Personality Disorders	22.45%

CORRELATION ANALYSIS

A Spearman rank-order correlation coefficient was calculated between the length of stay and reason for admission. The Spearman r value was 0.137, with a confidence interval (CI) of -0.0724 to 0.3348. This implies that the length of stay was not significantly correlated with the reason for admission.

DISCUSSION

Data collected establishes three main cohorts of individuals suffering from SUD that are admitted to Mount Carmel Hospital. These include individuals with 1) comorbid psychiatric pathology 2) a relatively stable mental state who seek mental health services prior to engaging with rehabilitation programmes and 3) those admitted primarily in view of social issues. The vast majority (58.8%) of patients fell into the third cohort. Social issues prompting admission included financial instability, unemployment, housing issues and a lack of social support.

The results of this study clearly show the link between social issues and hospital admissions of substance users, in keeping with what has been previously published in literature [4] The pattern noted in international research reflects the current situation in Malta. Admission to Malta's mental health hospital is being utilised as a gateway to access social services, which are not readily accessible in the community. Our findings shed light on the lacunae in social services and access for substance users.

Access to social services in Malta is often a lengthy process which individuals may not be well versed in or may not be appropriately guided to do so. Such services are often not catered for individuals who make use of substances. Results show that hospitalisation is representing an immediate access to social services as the only viable alternative left to these individuals. This is often a last resort with patients preferring hospital admission, rather than continuing to tackle their social issues within the community.

The aforementioned social reasons affect society as a whole as they place a strain on the economy and have a significant impact on our countries' development.[7] According to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) and the National Audit Office (NAO) of Malta, 59% of substance-users were unemployed

and this accounted for 10% of the unemployment registry in 2012.[89] Updated figures from the Key Issues - Drug Situation in Malta document published in 2022 state that this percentage has fallen to 48% of substance users on average being in stable employment.[10] When each substance is viewed individually, 41% of heroin where in regular employment, whilst 56% and and 55% of cocaine and cannabis users respectively were in active employment [10]

In data published in 2012, 82% of substance-users held no tertiary academic qualifications.[8] In available data published 10 years later, it was noted that only 69% of substance users reached a secondary level of education.[10] 75% of heroin users completed secondary education but only 7% completed higher education.[10] 62% of cocaine users completed secondary education with 17% completing higher education and 64% and 17% of cannabis users completed secondary education and higher education respectively.[10] This significantly reveals the strong association between addiction and lack of educational attainment.

Vulnerable individuals are often socially excluded in view of poverty, which in turn may lead to criminality, risky drug related practices, unemployment and an inability to integrate within society.[11] Reassuringly 92% of Maltese regular substance users were noted to be in stable accommodation.[10]

The Malta Sustainable Development Vision for 2050s' aims are to improve education and training, which would allow for better employment opportunities and would in turn help eradicate poverty, social exclusion and socio-economic instability.

This being said, our results did not show a significant correlation between the length of stay and the reason for admission. Rather, results showed that individuals diagnosed with SUD frequently discharge themselves against medical advice, and present for re-admission soon after. This could be due to a variety of reasons. Individuals diagnosed with SUD in the pre-contemplative phase of change are often chaotic in their use, seeking admission for a couple of days prior to re-establishing their substance use within the community.

Individuals forming part of the second cohort, often are required to wait for weeks, if not months to enter rehabilitation, which causes significant frustration. This inevitably leads to request for discharge against medical advice, and often, is followed by a relapse into substance misuse. This further perpetuates any social issues, consequently leading to hospital readmission. Out of the 20 patients who were readmitted during the time of study, 13 were readmitted due to social reasons, whilst 7 were readmitted due to dual diagnosis. This cohort of 13 patients found difficulty coping in the community in view of social reasons, causing social instability and with little alternatives, early readmission to hospital. Substance users who seek admission to deal with social issues such as unemployment or financial issues are often faced with a lengthy process to deal with these problems, which also in turn leads to seeking early discharge.[12]

SUMMARY BOX

What is already known about the subject

- Stigmatisation and social exclusion amongst individuals suffering from substance use disorder is the norm rather than the exception.
- Literature shows that individuals making use of substances suffer from multiple medical, psychological, psychiatric, financial, social, family and legal issues.
- Social reasons affect society as a whole as they place a strain on the economy and have a significant impact on our Malta's development.

New Findings

- More than half of all substance use disorder related psychiatric admissions were due to social reasons, with a total of 58.8%.
- Results did not show a significant correlation between the length of stay and the reason for admission.
- Results showed that individuals diagnosed with SUD frequently discharge themselves against medical advice, and present for re-admission soon after.
- Improvement of community services, including relevant training for staff working with individuals diagnosed with SUD, better education on service access as well as timely social service interventions could potentially decrease hospital admissions.

LIMITATIONS

The following patients and data were not included in the study due to the following limitations:

1. Incomplete information from 18 patient records.
2. Substance use related admissions to Gozo General Hospital.
3. Patients with neuro-developmental disorders were not included as no formal testing for their diagnosis was available during their inpatient stay.
4. Patients with personality disorders were included depending on the DSM-5 criteria, but did not undergo formal personality psychometric testing.

CONCLUSION

Numerous improvements can be implemented to reduce the burden on the already overstretched Mental Health services Hospital - Mount Carmel. Despite a recently updated admission protocol, which specifies admission of individuals who post a significant risk to themselves/others, SUD individuals are often admitted due to difficulty in gatekeeping. Medical staff currently face significant challenges when such patients present to crisis services due to the lack of services available for referral within the community. For the admission protocol to achieve success robust community services must be in place to offer alternatives for substance use disorder patients.

Improvement of community services, with specialised Addiction Mental Health Service Development including relevant training for staff working with individuals diagnosed with SUD is needed. This together with better education on service access and timely social service interventions could potentially decrease hospital admissions.

Instituting timely, easily accessible community services would allow these individuals to receive community based care. In turn this would greatly lessen the frustration, difficulties and stigma faced by people forming part of the third cohort in this study. Inpatient services would benefit from a decreased burden on hospital staff, increased bed space availability, decreased hospital costs and commodity in limited resource allocation. When it comes to patients forming part of the second cohort - we postulate that they too could be better served within the community.

Increasing links and communication with rehabilitation centres on the Maltese Islands, as well as decreasing waiting times prior to entry to rehabilitation programmes would lessen the quantity of admissions to hospital as well as their length. We suggest the implementation of community residences specifically catered for individuals diagnosed with SUD who are often turned away from other community residences based on the fact that they make use of substances. Should these changes be implemented we hypothesise that both the second and third cohort of patients mentioned in this study would receive timelier, appropriate care within the community allowing inpatient services more time, funds and staff to offer optimal care to patients forming part of the first cohort.

Finally, and most importantly, a collective effort by all organisations experienced in the management of patients suffering from SUD is required to effectively address the social issues of these patients. Thus, we would be able to provide better care, which is vital for the healing process of substance users.

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ORIGINAL ARTICLE

Comparative study of iris-claw intraocular lens implantation and implantable collamer lens

patient-reported outcomes

Matthew Azzopardi, Franco Mercieca

Background

Iris-claw phakic intra-ocular lenses (pIOLs) and implantable collamer lenses (ICLs) are the main pIOLs in use. We aim to compare for the first time patient experience and satisfaction of these two techniques.

Methods

A cross-sectional study design, with no randomization or control groups was utilised. Patients who underwent either surgery between 2010 and 2020 were identified from hospital records. Phone interviews, performed in June 2021 used a semi-structured questionnaire divided into pre-operative build-up, patient experience and post-operative issues. A five-point Likert scale was used for standardisation. Perioperative data was collected from their medical files.

Results

After exclusions, 20 ICL patients (40 eyes) and 17 iris-claw patients (34 eyes) were included. A higher proportion of the ICL cohort completely agreed that the surgery has improved their vision significantly (ICL n=18, 90%; iris-claw n=8, 47%; P=.03) and that they would recommend it (ICL n=19, 95%; iris-claw n=8, 47%; P=.01). Postoperative issues were comparable, but iris-claw patients experienced more long-term glare (iris-claw n=8, 47%; ICL n=1, 5%; P<.01). Both techniques eliminated contact lens use. Astigmatic ICL patients were more satisfied, with 89%(n=17) completely agreeing that they would recommend the surgery, in comparison to 50%(n=6) of astigmatic iris-claw patients (P=.015).

Conclusion

ICL is superior to iris-claw in terms of patient satisfaction, efficacy and long-term issues, and also in astigmatic patients. Short-term issues were comparable. Both types of surgery succeeded in decreasing contact lens use, further contributing to an improved quality of life. Clinically this could help guide phakic intraocular lens technique selection for better patient satisfaction.

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Uncorrected refractive error is the second commonest cause worldwide of visual impairment after cataracts, with 43% of global visual impairment attributed it.[1] In a study published in 2015, over half of Europeans aged between 25 and 90 were estimated to have a refractive error, with the greatest burden being myopia.[2] Similar results were reported in the United States with half of individuals aged 20 or older having a clinically significant refractive error.[3] Uncorrected refractive error was also found to exert a significant economic impact, with the total productivity loss in international dollars estimated to be around a thousand times greater than the global number of cases.[4]

In phakic intraocular lens (pIOL) implantation a specially designed lens is inserted in front of the patient's own anatomical lens with the aim of correcting the ametropic error. pIOLs are mainly subdivided into three groups, based on their final position in the eye and fixation mechanism. Angle-supported anterior chamber pIOLs (ACIOLs) and iris-fixated ACIOLs lie anterior to the iris, whilst posterior chamber pIOLs (PCIOLs), such as implantable collamer lenses (ICLs), lie between the iris and the anatomical lens.[5] In practice, they are generally preferred as options for high-grade refractive error, with other refractive surgery techniques being used for lower degrees of ametropia. In fact, various studies have shown that pIOL implantation seems to be safer and a more effective in the treatment of moderate to high myopia in comparison to corneal-based refractive surgery, such as laser in situ keratomileusis (LASIK) and excimer laser refractive surgery.[6-8] It also seems to avoid the risks of retinal detachment and corneal ectasia, which are linked to refractive lens exchange and excimer laser surgery, respectively.[6] However caution and appropriate consideration is advised in patients with active anterior segment disease, cataracts, previous ocular surgery, glaucoma or raised intraocular pressure, pre-existing macular pathology, retinal disease, anomalous irises or pupils and systemic diseases associated with poor postoperative healing, such as diabetes mellitus.[5]

The main pIOL implantation techniques in use are the Verisyse (Artisan in Europe) iris-claw ACIOL and the Visian ICL, both of which are approved by the United States Food and Drug Administration (FDA) for correction of myopia with or without astigmatism of up to 2.5 Diopters (D).[5] A meta-analysis published in 2014 concluded that the refractive outcome of these two pIOLs was comparable, as was the safety. However while ICL implantation was found to have a better predictability, more complications were associated with it such as anterior subcapsular cataract.[9] On the other hand, Boxer Wachler et al reported that ICL had better refractive outcomes and binocular uncorrected visual acuity (UCVA) in comparison to iris-claw.[10] At our center, these are the main pIOL implantation techniques used. Patient selection for either pIOL surgery is based on published inclusion and exclusion criteria.[5] The only addition at our center is that patients who have a corneal thickness of less than 490µm are also considered for pIOL implantation in preference to corneal-based refractive surgery.

However to date there are no studies that compare the two widely-available pIOLs in terms of patient-reported outcomes. Through this study we aim to compare for the first time the experience of patients who underwent iris-claw pIOL implantation to that of patients who underwent ICL implantation, at our center. We aim to compare the effect the surgeries had on their lives, including post-operative short-term and long-term issues, and their degree of satisfaction.

MATERIALS AND METHODS

The study design chosen was a non-randomized cross-sectional study without a control group. Ethical approval was obtained from the University of Malta Faculty Research Ethics Committee on 4 June 2021. Patients who underwent iris-claw pIOL or ICL implantation at our center between May 2010 and May 2020 were identified from hospital records. To eliminate bias due to differing technique, only those operated on by Surgeon A, the only surgeon who used both surgical techniques, were included in the study. Due to the SARS-COV2 pandemic, data was collected via phone interviews in June 2021, ensuring at least one year of post-operative follow-up. Verbal informed consent was obtained prior to the interview. A semi-structured questionnaire subdivided into pre-operative build-up, patient experience, and post-operative issues was used. Patient experience was categorized and standardized through the use of a five-point Likert scale. Following the interviews, perioperative data was collected from their medical files, after obtaining consent. This included details about pre-operative refractive correction used, implanted lens power and position, corneal data, intra-operative details and any post-operative follow-ups. All of the data gathered was compiled in a secure database and analyzed using SPSS software.

RESULTS

PRE-OPERATIVE DATA

26 patients who underwent ICL implantation and 28 patients who underwent iris-claw pIOL implantation were eligible for the study. Due to patient preference or non-response to the participation invitation, some patients were excluded leaving a final number of 20 ICL implantation patients (40 eyes; 77%) and 17 iris-claw pIOL implantation patients (34 eyes; 61%). The age range of iris-claw patients was 22 to 52 years with an average age of 31.94 years, while the age range of ICL patients was 19 to 44 years with an average age of 33.55 years. No statistically significant difference was found in between the age of the two cohorts (Mann–Whitney U=133.5, n1=17, n2=20, P=.271 two-tailed).

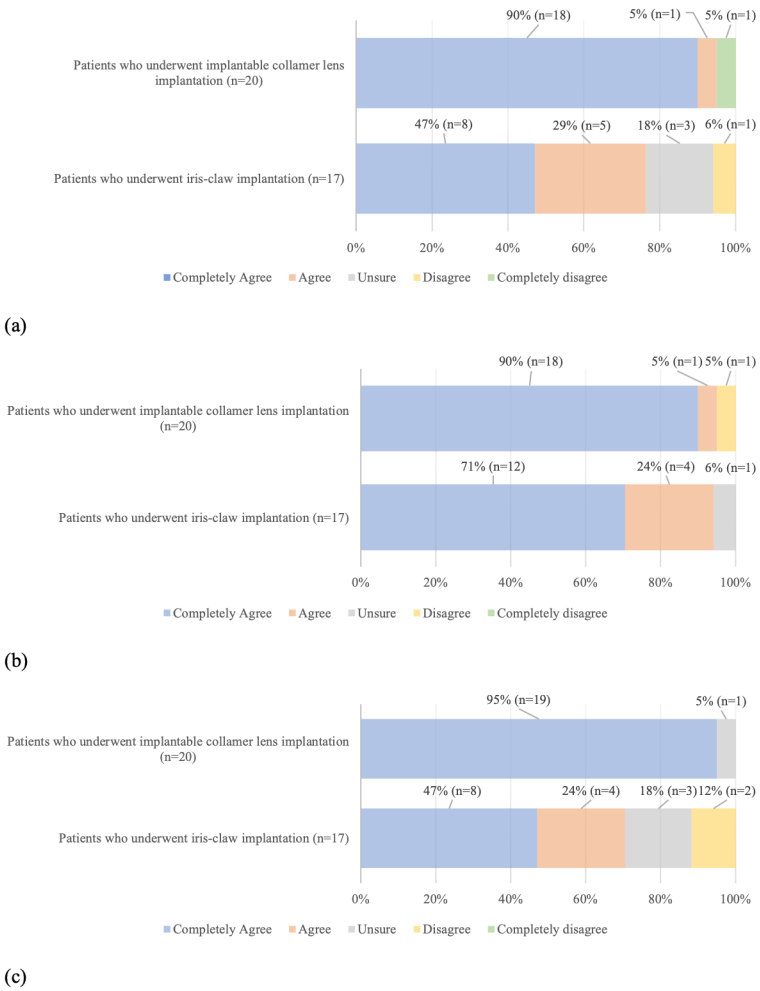

Figure 1 *Patient response to the following statements (a) 'The surgery has improved my vision significantly' (Mann–Whitney U=99.5, n1=17, n2=20, P=.03 two-tailed) (b) 'The surgery was a life-changing procedure' (Mann–Whitney U=139, n1=17, n2=20, P=.35 two-tailed) (c) 'I will definitely recommend this surgery to friends and family, if they require it' (Mann–Whitney U=89.5, n1=17, n2=20, P=.01 two-tailed)*

In negative cylinder notation, the refraction of the patients who underwent iris-claw implantation ranged from -4D to -18.5D of myopia and -0.5D to -4.5D of myopic astigmatism, per eye. On the other hand, those who underwent ICL implantation ranged from -3.5D to -16.25 of myopia and -0.5 to -4.5D of myopic astigmatism, per eye. Also the average subjective visual acuity in LogMAR was 0.11 (SD=0.15) for ICL patients and 0.26 (SD=0.12) for iris-claw patients. The average thinnest corneal thickness of iris-claw patients was 514.27µm (SD=36.45) compared to 533.63µm (SD=39.96) in ICL patients.

Pre-operatively iris-claw patients used predominantly a combination of glasses and soft contact lenses (CLs) (n=10, 59%), whilst the rest used glasses only (n=5, 29%) or a combination of glasses and hard CLs (n=2,12%). Similarly ICL patients used mainly a combination of glasses and soft CLs (n=17, 85%), followed by only soft CLs (n=2, 10%) or glasses only (n=1, 5%).

PATIENT SATISFACTION

To gauge patient satisfaction post-operatively, all patients were asked to rate their level of agreement with 3 statements in the form of a Likert scale. The statements were 'The surgery has improved my vision significantly', 'The surgery was a life-changing procedure', and 'I will definitely recommend this surgery to friends and family, if they require it'. The results are depicted in **Figure 1**.

POST-OPERATIVE RECOVERY AND ISSUES

Post-operatively 59% (n=10) of iris-claw patients did not require any further refractive correction, whilst 35% (n=6) required glasses and 6% (n=1) required further surgery and glasses, amounting to a total of 41% (n=7) who required further correction. On the other hand, 85% (n=17) of ICL patients did not require any further refractive correction, with the remaining 15% (n=3) requiring glasses (n=2, 10%) or further surgery (n=1, 5%) (P=.14, Fisher's exact test[FET]).

71% (n=12) of iris-claw patients reported an immediate satisfactory improvement of vision postoperatively, whilst 18% (n=3) said it took more than 1 day but less than 1 week, 6% (n=1) more than 1 week but less than 1 month, and a further 6% (n=1) more than one month. On the other hand, 95% (n=19) of ICL patients reported an immediate satisfactory improvement in vision post-operatively, with the remaining 5% (n=1) reporting that it took more than 1 day, but less than 1 week (Mann–Whitney U=127.5, n_1=17, n_2=20, P=.20 two-tailed).

The reported post-operative adverse events were subdivided into post-operative complications and post-operative issues to differentiate potentially preventable adverse events, termed 'complications', from non-preventable 'issues' that arise due to surgery. The post-operative issues were further subdivided into short-term issues lasting less than 6 months and long-term issues (unresolved issues or issues which lasted more than 6 months).

With regards to short-term post-operative issues, 76% (n=13) of iris-claw patients and 80% (n=16) of ICL patients reported that they had at least one (P>.99, FET). Between 1 and 4 issues were reported in 65% (n=11) of iris-claw patients and 75% (n=15) of ICL patients, with 12% (n=2) of iris-claw patients and 5% (n=1) of ICL patients reporting 5 or more issues. No short-term post-operative issues were reported in 24% (n=4) of iris-claw patients and 20% (n=4) of ICL patients. A further breakdown of the short-term issues along with their duration is provided in **Figure 2**. Fisher's exact test (FET) was used to calculate significance.

On the other hand, with regards to long-term post-operative issues, 65% (n=11) of iris-claw patients reported that they had between 1 and 4 issues. The remaining 35% (n=6) had no long-term issues. Meanwhile 40% (n=12) of ICL patients reported that they experienced between 1 to 4 issues, with the remaining 60% (n=8) claiming to have had no long-term issues (P>.99, FET). A further breakdown of the long-term issues is provided in **Figure 3**.

None of the iris-claw patients had any post-operative complications. However 2 ICL patients (10%) had a complication (P=.49, FET). One had post-operative torsion of the ICLs whilst the other had an absent vault between the left ICL and the anterior capsule, requiring explanation of both ICLs.

ASTIGMATISM AND PIOL IMPLANTATION

82% (n=14) of the iris-claw cohort and 90% (n=18) of the ICL cohort were astigmatic. 21% (n=3) of astigmatic iris-claw patients and 94% (n=17) of the astigmatic ICL cohort were corrected with a toric pIOL (P<.001, FET). An analysis of the astigmatic patients' responses is provided in **Figure 4**.

DISCUSSION

All of our study participants had some sort of refractive correction pre-operatively showing that they all deemed their uncorrected vision to be insufficient for daily life. The main aim of refractive surgery and hence pIOL surgery is to change the

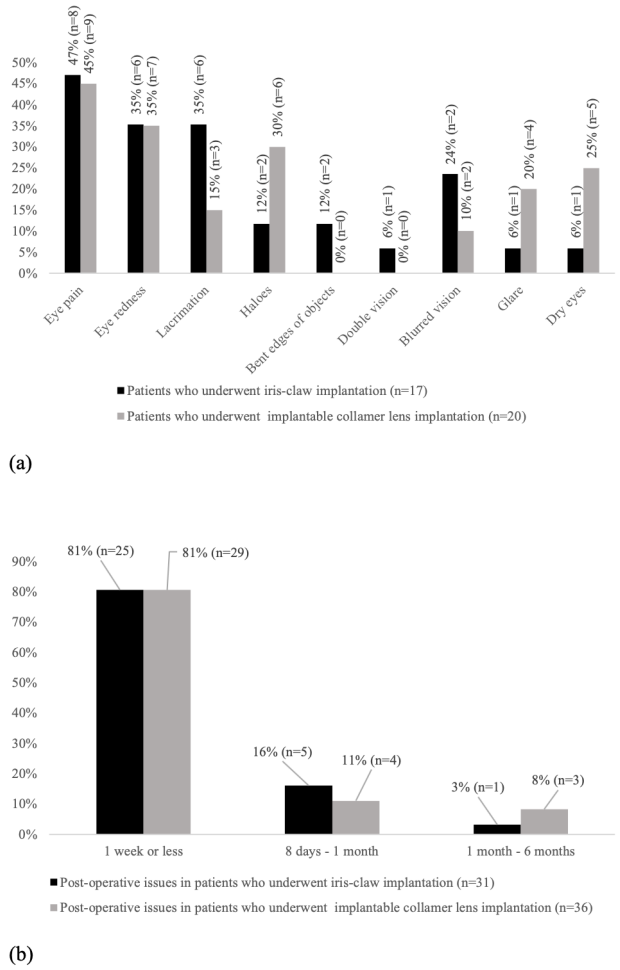

Figure 2 *a) Commonest short-term post-operative issues (occurred in first 6 months and are now resolved) reported by the 2 patient cohorts [eye pain: P>.99; eye redness: P>.99; lacrimation: P=.25; haloes: P>.99; bent edges: P=.20; double vision: P=.46; blurred vision: P=.38; glare: P=.35; dry eye: P=.19] (b) Duration of the short-term post-operative issues (Mann–Whitney U=552, n1=31, n2=36, P=.94 two-tailed)*

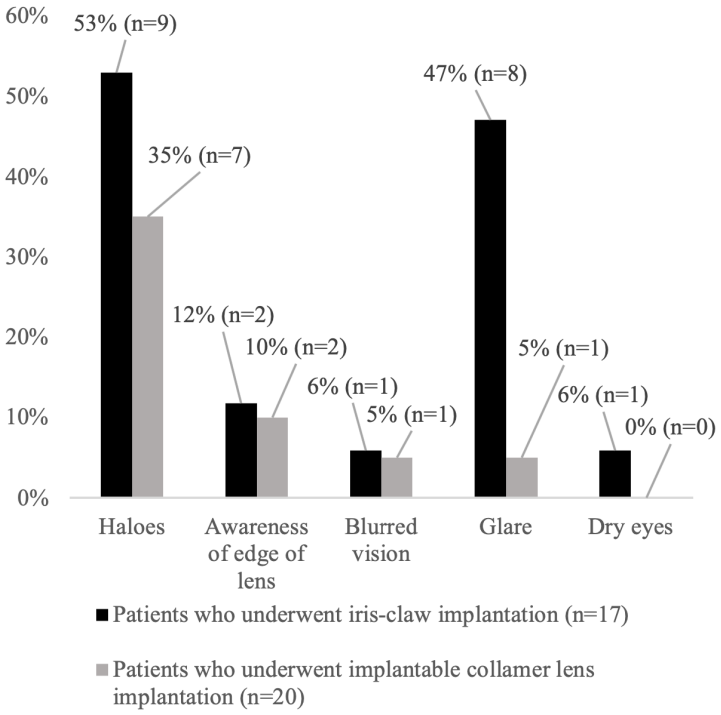

Figure 3 *a)Commonest long-term post-operative issues (still unresolved) reported by the 2 patient cohorts [haloes: P=.33; awareness of lens edge: P>.99; blurred vision: P>.99; glare: P=.006; dry eye: P=.46]*

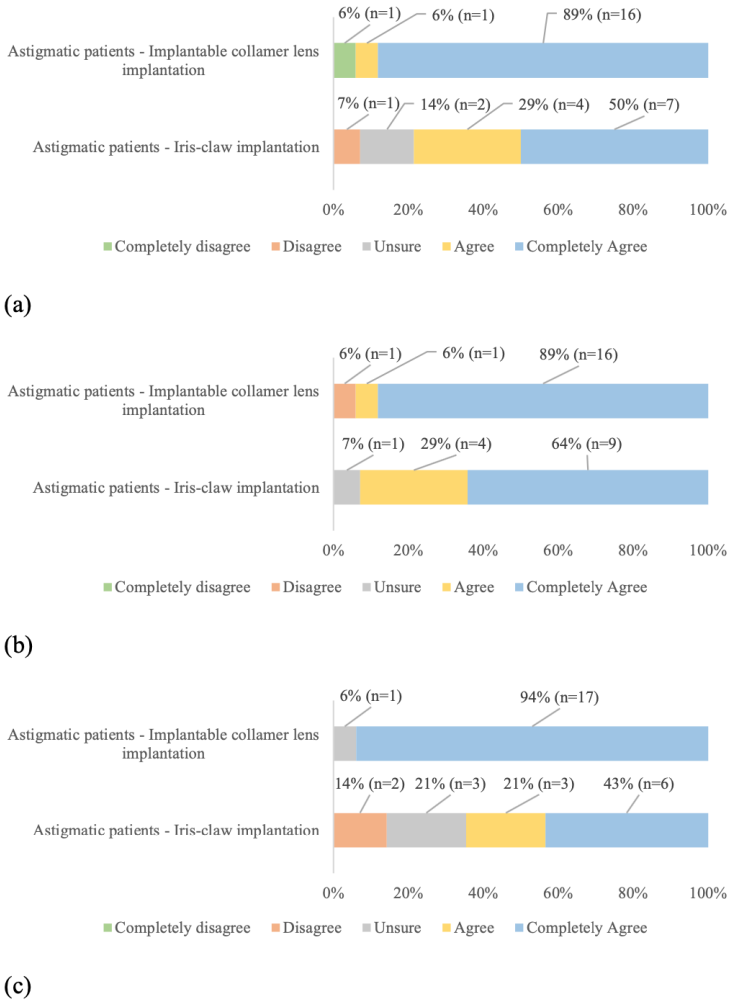

Figure 4 *Comparison of astigmatic patient response to the following statements (a) 'The surgery has improved my vision significantly' (Mann–Whitney U=82, n1=14, n2=18, P=.099 two-tailed) (b) 'The surgery was a life-changing procedure' (Mann–Whitney U=99.5, n1=14, n2=18, P=.32 two-tailed) (c) 'I will definitely recommend this surgery to friends and family, if they require it' (Mann–Whitney U=61.5 n1=14, n2=18, P=.015 two-tailed)*

A lot of published studies compare these two surgical techniques objectively, but our study is the first to compare them in terms of patient-reported outcomes. When asked whether the surgery has improved their vision significantly, 85% of ICL patients compared to 47% of the iris-claw cohort completely agreed. This shows that a significant improvement in vision post-operatively was noted in a statistically significant (P=.03) higher proportion of the ICL cohort. Furthermore with respect to whether they would recommend the surgery to friends and family, a higher proportion of ICL patients (90%) completely agreed in comparison to iris-claw patients (59%), with this difference being statistically significant (P=.01). Similar to these results, the surgery was also deemed to be life-changing by a higher proportion of ICL patients (90% ICL versus 71% iris-claw). However this was not statistically significant (P=.35).

From the responses obtained to these statements, ICL implantation resulted in higher patient satisfaction in comparison to iris-claw implantation, with the results for two out of the three statements found to be statistically significant.

In our study, post-operative adverse events were subdivided into post-operative complications and post-operative issues, to differentiate potentially preventable adverse events, termed complications, from non-preventable issues that arise due to surgery. In the iris-claw cohort, no significant complications were reported. On the other hand, in the ICL cohort 2 patients (10%) had a significant documented complication, one of which required explantation of the ICLs. Patient A, who had bilateral toric ICLs implanted, presented 2 months post-operatively with a rotated right toric ICL, which was followed by torsion of the left toric ICL 4 months later. The patient was subsequently offered femto-LASIK, but opted to use glasses instead. On the other hand, patient B had to have the ICLs explanted 1 week post-operatively due to the absence of a vault in between the left ICL and the anterior capsule. Patient B's myopia was subsequently treated with the small excision lenticule extraction (SMILE) procedure.

Unsurprisingly Patient B completely disagreed with the first statement, disagreed with the second statement, and was unsure whether they would recommend the surgery to friends and family. Interestingly however, Patient A completely agreed with all 3 statements, even though both ICLs rotated post-operatively. This could further show that whilst the objective result was different to the planned end-point, the patient still perceived a significant change in visual acuity and was satisfied to use low-powered glasses as an adjunct to the ICLs.

Post-operative issues were further subdivided into short-term and long-term issues. No statistically significant difference was found between the short-term and long-term issue rates in both cohorts (P>.99), however the iris-claw cohort reported a higher prevalence of long-term glare when compared to the ICL cohort (P=.006), raising the possibility that differences in lens design could have contributed to this.

The commonest long-term issues in iris-claw patients were haloes (53%), glare (47%) and awareness of the edge of the lens (12%). In the ICL cohort, haloes were also the commonest long-term issue (35%), followed by awareness of the edge of the lens (11%), blurred vision (5%) and glare (5%). This follows that while both cohorts had similar long-term effects, these occurred at a lower frequency in the ICL cohort. With regards to short-term issues, the commonest

reported in either cohort were similar. Eye pain (47%), eye redness (35%), increased lacrimation (35%) and blurred vision (24%) were the commonest in the iris-claw cohort, whilst eye pain (45%), eye redness (35%), haloes (30%) and dry eyes (25%) were the commonest reported in the ICL cohort. With regards to duration, the majority of short-term issues lasted 1 week or less in both cohorts (81% in both cohorts), whilst all issues which lasted more than 6 months were still unresolved.

Another lower-order aberration that needs to be taken into consideration is astigmatism. In our study, a comparable proportion of iris-claw patients (82%), and ICL patients (90%) were astigmatic. However much less astigmatic iris-claw patients (21%) were implanted with a toric pIOL in comparison to ICL astigmatic patients (94%), due to the technical difficulties in alignment and lack of surgeon experience with toric iris-claw implantation. This difference was found to be statistically significant (p<.001) and therefore limits the amount of comparisons that can be made between the two astigmatic cohorts.

With regards to the astigmatic patients' satisfaction postoperatively, 83% of astigmatic ICL patients completely agreed, in comparison to 50% of astigmatic iris-claw patients, that the surgery had improved their vision significantly (P=.099). With respect to whether the surgery was a life changing procedure, 89% of the astigmatic ICL cohort and 64% of the astigmatic iris-claw cohort completely agreed (P=.32). Finally 89% of the ICL astigmatic cohort completely agreed that they would recommend the surgery to friends and family, whilst only 50% of astigmatic iris-claw patients completely agreed with this (P=.015). This shows that a generally higher satisfaction was reported by the astigmatic ICL cohort. However a statistically significant difference between the responses was only found in the last statement.

Finally both of the significant complications mentioned above occurred with toric ICLs. Published studies indicate that toric ICLs have good rotational post-operative stability.[15,16] In one study, 90% of toric lenses were found to have rotated less than 5 degrees between all visit intervals.[16] In our study, of the 40 eyes implanted with toric ICLs only 2 (5%) suffered from clinically-significant rotation, whilst 94% did not. Although our results seem to concur with the published results, the degree of rotation was not measured, limiting further inferences.

Our study has a number of limitations. The SARS-COV2 pandemic national restrictions and patient preference made in-person patient interviews and examination difficult to organize. This would have allowed an objective comparison to be carried out alongside the subjective comparison of the two pIOL surgeries. Secondly even though all patients who underwent pIOL surgery at our center were included, the small sample size limits further conclusions. Finally only a small number of astigmatic patients

SUMMARY BOX

What is already known about this subject

- Uncorrected refractive error is the second commonest cause worldwide of visual impairment after cataracts, with 43% of global visual impairment attributed it.
- In phakic intraocular lens implantation a specially designed lens is inserted in front of the patient's own anatomical lens with the aim of correcting the refractive error.
- Various studies have shown that pIOL implantation seems to be safer and a more effective in the treatment of moderate to high myopia in comparison to corneal-based refractive surgery, such as laser in situ keratomileusis and excimer laser refractive surgery.
- The main phakic intraocular lens implantation techniques in use are the Verisyse (Artisan in Europe) iris-claw ACIOL and the Visian implantable collamer lens. A meta-analysis published in 2014 concluded that the refractive outcome of these two pIOLs was comparable, as was the safety. However to date there are no studies that compare the two widely-available pIOLs in terms of patient-reported outcomes.

What are the new findings

- Implantable collamer lens implantation is superior to iris-claw implantation in terms of patient satisfaction and post-operative need for refractive correction. It is also superior in astigmatic patients, but a larger cohort is required for statistical significance.
- Short-term issues were comparable between the two cohorts, but Implantable collamer lens patients reported a statistically significant lower incidence of long-term glare.
- Both types of phakic intraocular lens implantation surgery succeeded in decreasing contact lens use, potentially further contributing to an improved quality of life.

were implanted with a toric iris-claw which constricts direct comparison with toric ICLs and major inferences about the astigmatic cohorts.

In conclusion, ICL implantation was found to be superior to iris-claw implantation in terms of patient satisfaction, efficacy and long-term issues. It resulted in higher patient satisfaction, with a larger proportion of ICL patients reporting an immediate satisfactory improvement in vision and a lower need for further refractive correction post-operatively. Short-term issues were comparable between the two cohorts, but ICL patients reported a lower incidence of long-term glare. Both types of pIOL surgery succeeded in decreasing contact lens use, potentially further contributing to an improved quality of life. Finally a higher rate of patient satisfaction was reported with ICL implantation the astigmatic cohort, but larger studies are needed to confirm this. A comparison of the two pIOL implantation techniques with larger patient cohorts, potentially in a collaboration between different centers, could further consolidate this study's findings and help improve patient satisfaction post-pIOL surgery.

ACKNOWLEDGEMENTS

We would like to acknowledge Mr. Andrei Camenzuli who helped with data collection.

ABBREVIATIONS

ACIOL	Anterior chamber intraocular lens
D	Diopters
FDA	Food and Drug Administration
ICL	Implantable collamer lens
PCIOL	Posterior chamber intraocular lens
pIOL	Phakic intraocular lens
SARS-COV2	Severe acute respiratory syndrome coronavirus 2
SD	Standard deviation

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ORIGINAL ARTICLE

Pregnancy Outcomes among Patients with Inappropriate Sinus Tachycardia

Saba Ryadh Younis al-Obaidi, Abdulameer Jasim Jawad al-Gburi

Background

About one percent of the population is affected by inappropriate sinus tachycardia. Little is known about this condition during pregnancy. Our objectives were to get a deeper understanding of the natural course of inappropriate sinus tachycardia in pregnancy and to investigate maternal and foetal outcomes.

Methods

Forty-two pregnant women with symptoms consistent with inappropriate sinus tachycardia were included in this observational cohort study and compared to 42 control pregnant women.

Results

No significant difference was found in age, twin pregnancy, diabetes, blood pressure, and hemoglobin level while the gravida of the inappropriate sinus tachycardia group was significantly lower than control (p-Value=0.002). The symptoms resolved in the majority (83%) of cases within 2 weeks of delivery. Pregnant patients with inappropriate sinus tachycardia have higher unscheduled hospital visits (38.1 vs 9.5%; p-Value=0.002) and induction of labor (45.2% vs 23.8%; p-Value=0.039)

Conclusion

Hospital visits and induction of labor were higher in pregnant patients with inappropriate sinus tachycardia which may not be necessary with more emphasis should be on empathic care and patient education.

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Approximately one percent of the population is affected by the well-known but partially understood syndrome of inappropriate sinus tachycardia.[1] Task force guidelines describe it as (1) heart rate that is more than 100 beats per minute at rest in sinus rhythm;(2) 24-hour mean heart rate of more than 90 beats per minute;(3) no secondary causes; and (4) the presence of symptoms including palpitations.[2] Exercise intolerance, shortness of breath, and palpitations may be very incapacitating despite the "benign" nature of inappropriate sinus tachycardia.[1] In the literature, however, little is known about inappropriate sinus tachycardia during pregnancy including its development and management. Similarly knowledge is scarce about how inappropriate sinus tachycardia can affect fetal and maternal health in pregnant patients.

Previous studies on inappropriate sinus tachycardia during pregnancy indicate that it is a rather common but underrecognized condition.[3,4] To present, the literature has just two further case reports.[5,6] In light of this, we attempted to investigate the fetal and maternal outcomes of patients with this syndrome through an observational cohort study.

MATERIALS AND METHODS

This prospective study was done between September 2020 and May 2022 during which 42 women with symptoms consistent with inappropriate sinus tachycardia were referred to Ibn al-Bitar Specialized Center for Cardiac Surgery (Baghdad Iraq). A comprehensive diagnostic workup was performed before delivery to firmly establish the diagnosis according to the task force expert consensus.[2] A control group of 42 pregnant patients was included. We exclude patients with a history of known inappropriate sinus tachycardia, hypertension, current use of beta-blockers or non-dihydropyridine calcium channel blockers (for the control), patient with heart failure, and renal failure or pulmonary hypertension, and any significant cardiopulmonary disease (for both groups). The research was authorized by the Local Medical Ethics Council and participants provided written informed consent.

A full medical history review and physical examination were undertaken, with an emphasis on the potential reasons for sinus tachycardia, including thyroid illness, medicines, and substances. All patients were examined for any evidence of hypovolemia (skin turgor, jugular venous pressure, and postural hypotension). A 12-lead ECG was used to detect tachycardia and establish its sinus origin to distinguish inappropriate sinus tachycardia from other supraventricular arrhythmias. Postural tachycardia syndrome (POTS) was ruled out since its symptoms are often exclusively triggered by orthostatic changes. Other potential causes like physiologic and psychological factors, panic attacks, and occult substance abuse were ruled out. Intensive investigation including thyroid function test, complete blood picture, C-reactive protein, Glomerular Filtration Rate (GFR), troponin level, plasma metanephrines, NT pro-BNP level, and echocardiography was done to exclude secondary causes.

Blood pressures were determined in both arms using a calibrated and automated blood pressure instrument (Contec ABPM50, Contec medical systems co., ltd) with the participant seated. Twenty-four hours Holter monitoring was done using Contec TLC5000 12-Channel Monitor (Contec medical systems co., Ltd).

Maternal outcomes were documented which include unscheduled hospital visits, induction of labor, cesarian section, antepartum/intrapartum bleeding, and post-partum bleeding. Fetal outcomes were documented which include preterm labor, postterm labor, fetal distress, meconium aspiration syndrome, APGAR[7] at 1 minute, and APGAR at 5 minutes.

STATISTICAL ANALYSIS

A normally distributed continuous variables were represented as mean with standard deviation as a measure of dispersion and compared across groups using the unpaired Student's t-test. The Mann–Whitney test was used to compare continuous, non-normally distributed data and represented as median and interquartile range. Categorical variables were represented as a number (with percentages) and the Chi-Square test was used to compare groups. A p-Value less than 0.05 was used as a threshold for statistical significance. Microsoft Office Excel 2019 and Statistical Package for the Social Sciences (SPSS) Version 26.0 for Windows (SPSS Inc., Chicago IL, USA) were used for conducting the analysis.

RESULTS

CLINICAL PRESENTATION

A definitive diagnosis of inappropriate sinus tachycardia during pregnancy was established in forty-two ladies and all of them have palpitations at rest or on exertion with reduced exercise capacity.

Table 1 *Baseline characteristics of the two study groups*

	IST, n=42	Control, n=42	p-value
Age, years	23.35±7.63	24.18±9.09	0.653
Gravida	2.94 [1.92-4.60]	4.52 [2.72-6.81]	*0.002*
Twin, n (%)	3 (7.1)	2 (4.8)	0.645
Diabetes, n (%)	2 (4.8)	3 (7.1)	0.645
Systolic BP, mmHg	108.38±8.71	109.82±6.71	0.397
Diastolic BP, mmHg	69.47±9.99	69.73±7.73	0.895
Hemoglobin, mg/dL	10.39±1.52	10.73±1.53	0.312
Maximum HR, bpm	119.56±11.11	85.98±15.54	*<0.001*
Holter Mean HR, bpm	101.65±5.78	78.34±8.96	*<0.001*

Abbreviations: n stands for Number; IST stands for inappropriate sinus tachycardia; BP stands for Blood Pressure; bpm stands for beats per minute; HR stands for Heart Rate

The mean age at the time of presentation was 23.35±7.63 years with gravida 2.94 [IQR 1.92-4.60] (39 singletons, 3 twins). A detailed history indicated the development of symptoms during the index pregnancy at 20.86±5.68 weeks of gestation. Comparing the inappropriate sinus tachycardia and control groups, no significant difference was found in age, twin pregnancy, diabetes, blood pressure, and hemoglobin level while the gravida of the inappropriate sinus tachycardia group was significantly lower than control as shown in Table 1.

All participants have sinus rhythm with no pathological arrhythmias detected by resting electrocardiogram and Holter monitoring. The maximal documented rest heart rate was 119.56±11.11 bpm in the inappropriate sinus tachycardia group vs 85.98±15.54 bpm in the control group with mean 24-h heart rates of 101.65±5.78 bpm in the inappropriate sinus tachycardia group vs 78.34±8.96 bpm in the control group as shown in Table 1. On Holter monitoring, diurnal heart rate fluctuation was retained, with a typical night drop with many daytime tachycardias (of variable duration).

Among the inappropriate sinus tachycardia group, 10 patients (23.8%) described prominent cardiac symptoms outside of pregnancy with inappropriate sinus tachycardia already diagnosed out of pregnancy in 4 patients (9.5%). In patients with a history of inappropriate sinus tachycardia, the presenting symptoms during the index pregnancy were unique and new; they were not a continuation or worsening of earlier symptoms. Nineteen out of 31 multigravida women (>1) had a history of symptoms in previous pregnancies (61.3%). Beta-blockers were used in 12 pregnant patients with inappropriate sinus tachycardia (28.6%). The symptoms resolved in the majority (83%) of cases within 2 weeks of delivery. Figure 1 shows these findings.

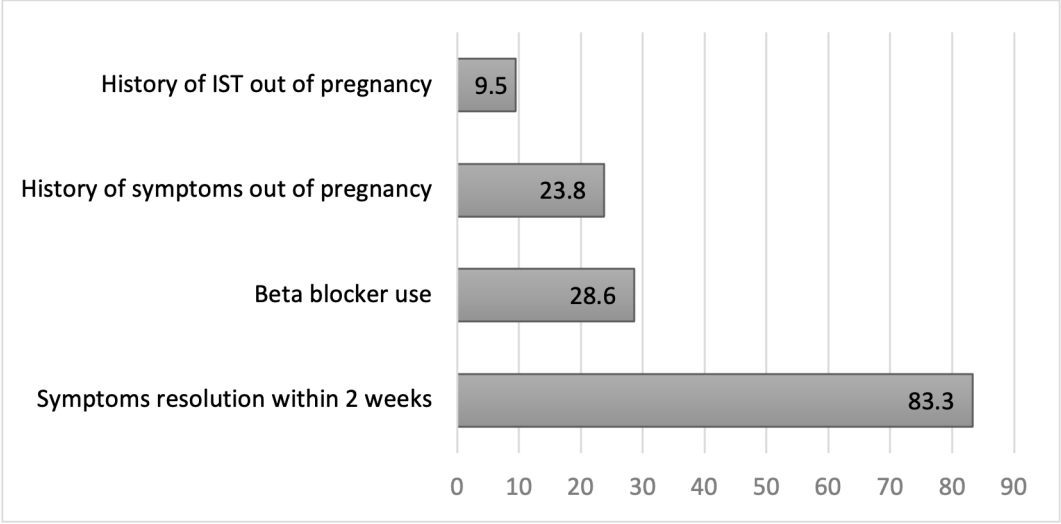

Figure 1 *Characteristics of patients with inappropriate sinus tachycardia, %*

MATERNAL AND FETAL OUTCOMES

Sixteen women (38.1%) with inappropriate sinus tachycardia had an unscheduled visit to the hospital on at least one occasion in comparison to 4 patients (9.5%) in the control group (p-Value=0.002).

No significant difference was found between the two groups regarding the rate of antepartum/ intrapartum and post-partum bleeding. During pregnancy, there were no maternal fatalities, cases of acute coronary syndrome or heart failure or thromboembolic, or hemorrhagic events.

There is a trend toward more Cesarian sections in the inappropriate sinus tachycardia group as compared to the control group which does not reach statistical significance (14 (33.3%) vs 7 (16.7%); p-Value=0.078). All cesarean sections were done for conventional obstetric reasons independent of the cardiac symptoms. The induction of labor was statistically higher (19 women; 45.2%); in comparison to the control group (10 patients; 23.8%) with a p-Value of 0.039. No significant difference was found between inappropriate sinus tachycardia and control groups regarding the rate of preterm or post-term labor, fetal distress, meconium aspiration syndrome, and APGAR at 1 and 5 minutes as shown in **Table 2**.

DISCUSSION

Our study demonstrates that pregnant women with inappropriate sinus tachycardia have lower gravida (which may be explained by a different personality traits and exaggerated response to emotional stress), more hospital admissions, and labor induction due to the poorly tolerable symptoms. An earlier study shares some of these findings but had a smaller sample size (19 patients) and lacks a control group, instead, it compares the findings to the background local and national rate.[4]

The inappropriate sinus tachycardia and control groups in this cohort generally have comparable characteristics. Given the small number of participating women, we acknowledge that care is required when assessing the relevance of the results.

The diagnosis of inappropriate sinus tachycardia based on task force guidelines [2] does not discriminate based on sex or the presence of pregnancy; thus, it may be used on pregnant women as in our cohort. Some may dispute this, arguing that the heart rate physiologic variations during pregnancy are more likely to cause sinus tachycardia at rest or exercise. Nevertheless we do not agree with that.

Hormones produced after conception cause vascular dilation and a decrease in peripheral arterial resistance. This is compensated by increasing the cardiac output to preserve an appropriate blood pressure (Cardiac output equal to stroke volume multiplied by heart rate). Stroke volume is enhanced by raising cardiac preload through fluid retention by the kidneys. Throughout pregnancy, the heart rate gradually rises by 10–20 beats per minute, from autonomic changes by baroreceptors, reaching a maximal heart rate in the last trimester.[8–10] Less than 10 percent of healthy pregnancies had heart rates greater than 100 beats per minute after 18 weeks of

Table 2 *Maternal and fetal outcomes in the study groups*

	IST, n=42	Control, n=42	p-value
Unscheduled Hospital Visit, n (%)	16 (38.1)	4 (9.5)	0.002
Induction of labor, n (%)	19 (45.2)	10 (23.8)	0.039
Cesarian Section, n (%)	14 (33.3)	7 (16.7)	0.078
Antepartum/Intrapartum Bleeding, n (%)	2 (4.8)	1 (2.4)	0.557
Post-Partum Bleeding, n (%)	3 (7.1)	4 (9.5)	0.693
Preterm Labor, n (%)	3 (7.1)	2 (4.8)	0.645
Post term Labor, n (%)	1 (2.4)	2 (4.8)	0.557
Fetal Distress, n (%)	1 (2.4)	0 (0)	0.314
Meconium aspiration syndrome, n (%)	0 (0)	1 (2.4)	0.314
APGAR at 1 minute	9.19±0.890	9.26±0.734	0.689
APGAR at 5 minutes	9.31±0.643	9.33±0.650	0.866

Abbreviations: n stands for Number; IST stands for inappropriate sinus tachycardia; APGAR stands for Appearance, Pulse, Grimace, Activity, and Respiration.

gestation and over 105 beats per minute after 28 weeks of gestation.[11–14] In the absence of an identified reason, we feel that a rest heart rate of more than 100 beats per minute during pregnancy should be regarded as abnormal. The usage of a mean heart rate higher than 90 beats per minute by 24-Hr Holter monitoring to diagnose inappropriate sinus tachycardia during pregnancy is not supported by evidence from studies that reported normal values specifically during pregnancy.

Most pregnant women in our study had symptoms only during pregnancy, with symptoms disappearance nearly immediately after delivery. In addition, around two-thirds of women had inappropriate sinus tachycardia-related symptoms during prior pregnancies with no symptoms out of pregnancy. This indicates that inappropriate sinus tachycardia during pregnancy may be a discrete condition.

Inappropriate sinus tachycardia during pregnancy may indicate an enhanced cardiac and autonomic physiological response in pregnancy, which is biologically acceptable. It is known that sympathetic tone increases and baroreceptor reflex sensitivity changes during pregnancy.[15,16] Women who developed inappropriate sinus tachycardia during pregnancy may have hormonal variations similar to those reported during the menstrual cycle, which may exacerbate these changes.[17] An increase in the HCN2 channel protein expression as reported in pregnant mice[18] may explain the raised sensitivity of the sinus node to the enhanced sympathetic tone.

The foundation of management is good communication and empathetic care. Regarding particular approaches, there is less data related to inappropriate sinus tachycardia in pregnancy; however, many of the treatments used to manage it in non-pregnant adults may be used.

Among the recommendations for a healthy lifestyle are adequate water intake and exercise.[19] These are useful in patients with postural orthostatic tachycardia and, given the number of similar physiological and clinical characteristics, may be used in women with inappropriate sinus tachycardia.[20,21]

It is possible to lower the sinus rate using pharmacological methods; however, it should be emphasized that this does not always result in symptom relief. Generally beta-blockers and non-dihydropyridine calcium channel blockers (diltiazem and verapamil) were utilized as first-choice treatments. But the use of these medications is limited by adverse effects.[22–24] Consequently ivabradine administered alone or with beta-blockers may alleviate symptoms, reduce heart rate, and improve patient tolerance.[25–30]

When prescribing during pregnancy, physicians are justifiably cautious. Labetalol has historically been the preferred beta-blocker during pregnancy, and its usage outside of the first trimester is not known to be detrimental. Bisoprolol, labetalol, metoprolol, and propranolol are classified as category C by the Food and Drug Administration (FDA). While atenolol should not be administered (category D). Breastfeeding is allowed if the mother is taking labetalol, metoprolol, or propranolol as stated by the American Academy of Pediatrics Committee on Drugs[31], while atenolol is present in breast milk at a higher level and is not included in their list.

Calcium channel blockers (diltiazem and verapamil) are considered category C by FDA The American Academy of Pediatrics Committee on Drugs states that breastfeeding is possible if the mother is taking verapamil or diltiazem.[31]

Although not specifically categorized, the FDA indicates that ivabradine may induce fetal injury during pregnancy as shown in animal research and

SUMMARY BOX

Facts known about inappropriate sinus tachycardia during pregnancy

- About one percent of the population is affected by inappropriate sinus tachycardia.
- Little is known about this condition during pregnancy
- Knowledge is scarce about how inappropriate sinus tachycardia can affect fetal and maternal health in pregnant patients

New findings from this study

- The gravida of the inappropriate sinus tachycardia group was significantly lower than control (p-Value=0.002).
- The symptoms resolved in the majority (83%) of cases within 2 weeks of delivery
- Pregnant patients with inappropriate sinus tachycardia have higher unscheduled hospital visits (38.1 vs 9.5%; p-Value=0.002) and induction of labor (45.2% vs 23.8%; p-Value=0.039)
- More emphasis should be on empathic care and patient education.

that its usage is not suggested during breastfeeding. Despite these warnings, ivabradine use during pregnancy has been reported to manage patients with inappropriate sinus tachycardia-induced cardiomyopathy.[5,6]

Sinus node ablation may be the most aggressive treatment option available. It is not always successful when applied to manage inappropriate sinus tachycardia in non-pregnant patients[32–36] and has the added harm of fetal irradiation in pregnant patients. Ablation has been reported as a therapy for severe tachyarrhythmias in pregnant women that are not caused by inappropriate sinus tachycardia.[37]

Specifically for inappropriate sinus tachycardia in pregnancy, labor often resulted in symptom alleviation. Numerous studies in different populations have shown that labor induction at term is safe for both mother and child[38–40], despite the fact that it is an intervention that not all women would prefer. All labor inductions were performed at term in our study. Given the "benign" prognosis of inappropriate sinus tachycardia, we emphasize the need for a conservative approach wherever feasible.

CONCLUSIONS

The pregnancies of women in this study were disrupted by many intolerable symptoms of exercise intolerance and palpitations with a higher incidence of labor induction and more unscheduled hospital visits. Inappropriate sinus tachycardia during pregnancy may constitute a unique arrhythmia, perhaps induced by an increased cardioautonomic reaction to pregnancy-related physiological changes. The emphasis of treatment should be on compassionate care, lifestyle modifications such as exercise and enough water intake, and patient education. Consider pharmacological treatments only for symptoms that are frequent and bothersome. We feel that this issue needs additional research with a higher sample number and longer follow-up; and investigation of therapeutic modalities. We anticipate that this publication will raise awareness of inappropriate sinus tachycardia during pregnancy.

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ORIGINAL ARTICLE

No birth sex ratio changes in the United States in 1977 following Elvis Presley's death

Victor Grech

Introduction

In humans, males are born slightly in excess of females such that male divided by total births (M/T) approximates 0.515. Many factors influence M/T, including acutely stressful events. This study was carried out to ascertain whether the death of Elvis Presley (1977) caused any perturbations in M/T in the following months in the United States.

Methods

Anonymous data (male and female births) was obtained from publicly available online datasets as white and non-white births.

Results

There were 3,235,291 (1658996 male and 1,576,295 female) births in 1977 with M/T=0.5128 (95% CI: 0.5122-0.5133). A seasonal pattern is evident in M/T for the United States for 1977. There were no obvious perturbations of this baseline after Presley's death including by race.

Discussion

Monthly cycles in M/T have been observed including in the United States. Acute stress has been shown to reduce M/T after the death of important and loved personages but this did not occur following the demise of Presley, possibly due to his slow career decline prior to his death.

In humans, males are born slightly in excess of females such that male live births divided by total live births (M/T) approximates 0.515.[1] Many factors influence M/T, including acutely stressful events.[2] This was observed for example after the September 11 attacks on the United States, where a sharp drop in male births was noted in the United States four months after this event,[3] and this correlated with a corresponding excess of male foetal loss in the same country in already pregnant women during that event.[4]

The demise of important personages has also been linked to similar dips in M/T, as evidenced after the demise of Lady Diana with a UK (only) dip in M/T 4-5 months later,[5] and the assassination of President John Kennedy with an M/T dip in the United States 4 months later.[6]

Elvis Presley was a popular musician, a loved figure and a loved icon whose death caused grief to many.[7,8] This study was carried out in order to ascertain whether the death of Elvis Presley (Born: January 8, 1935, Tupelo, Mississippi, United States - died: August 16, 1977, Graceland, Memphis, Tennessee, United States) caused any perturbations in M/T in the following months up to January of the following year (1978), five months later.

METHODS

Anonymous data (male and female live births) was obtained from the United States Office of Health Research via the publications vital statistics of the United States under Natality, and these are publicly available online.[9,10] Ethics approval and data protection were not applied for as these are inapplicable for the processing of datasets from such repositories. Data was available by state and by race (white and non-white). The degree of completeness was not specified. The equations of Fleiss were used to obtain confidence intervals for M/T (binomial).[11]

RESULTS

There were 3,497,642 (1,792,786 male and 1,704,856 female) births with M/T=0.5126 (0.5120-0.5131). A seasonal pattern is evident in M/T for the United States for 1977 (Figure 1). Visual inspection shows no obvious perturbations of this baseline. Breakdown by white and non-white populations also showed no baseline perturbations (Digital Supplementary File 1). Formal individual chi tests for November 1977, December 1977 and January 1978 versus the other months in the study confirmed the absence of significant fluctuations.

DISCUSSION

Monthly cycles in M/T are recognized and have been described for the United States in the same pattern as shown in this study.[12]

Acutely stressful events may precipitate spontaneous abortion in women who are pregnant with frail foetuses. Males are terminated in this way more than females in accordance with the Trivers-Willard hypothesis, which avers that nature has favoured parents who are able to influence offspring sex according to periconceptual and pregnancy conditions. This is because in polygynous species like humans wherein males have multiple mating

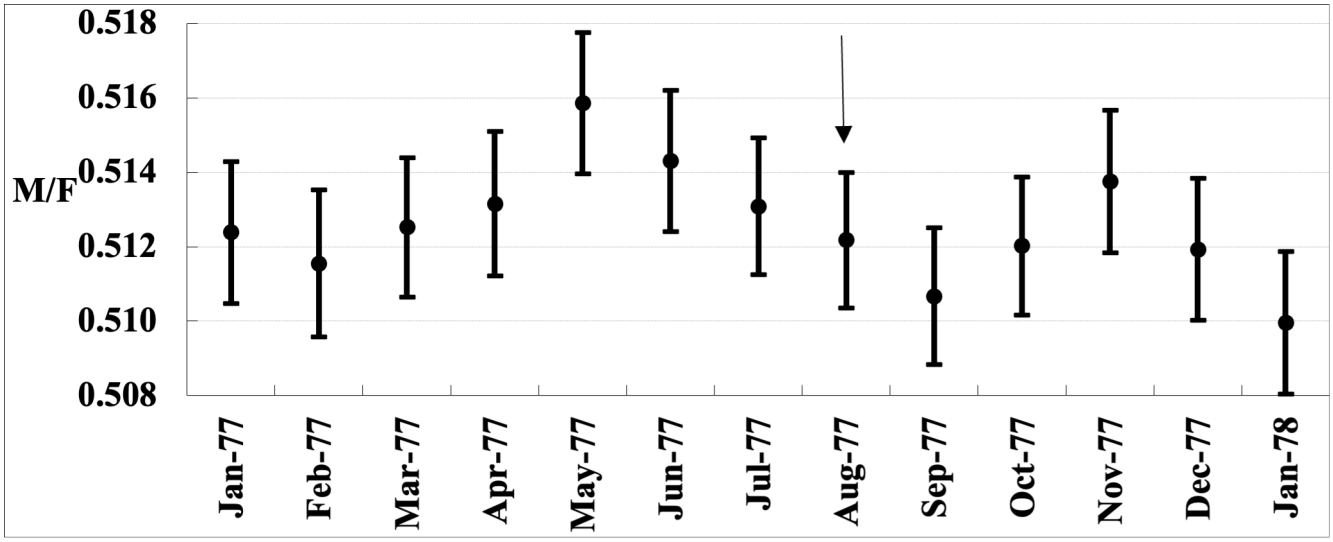

Figure 1 *Monthly M/T with 95% confidence intervals for the United States, January 1977 to January 1978 (White plus non-White). Arrow indicates month of Elvis Presley's death.*

opportunities, a strong male born in favourable conditions is likelier to pass on parental genes.[13] However, a frail male requires more resources to be gestated and in poor conditions, may not survive to term. Moreover, a frail male may not survive to adult life and in any case, would not be able to compete for mating privileges with stronger males. For this reason, in poor conditions, males are likelier to be culled in utero giving a potential mother an opportunity to retry pregnancy. If conditions remain poor and a female ensues, such a foetus requires less resources to be carried to term and in adult life will invariably be impregnated. On the other hand, if conditions improve and a male ensues, this further favours the parental passage of genes.[13]

Stress in its many forms has been shown to transiently reduce M/T and this was shown in a meta-analysis of terrorist events looking at population level M/T outcomes.[14] As already noted, the sudden death of a known and loved personage, whether accidental or by murder, resulted in a dip in M/T circa four months after the event, implying that already pregnant mothers miscarried disproportionately more male than female foetuses.[5,6] This was not witnessed after the death of Elvis Presley, as shown in this paper. Moreover, the assassination of President Kennedy had different effects on non-white vs. white populations,[15] and in this study, no such differences were noted.

It is possible that Presley's slow career decline may have attenuated the grief felt by his fans, who may also have become older and less likely to be of childbearing age and therefore also less likely to influence M/T despite outpourings of grief.[16]

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HISTORICAL PERSPECTIVE

A nation-wide support system for lepers in 14th century France

Charles Savona Ventura

Fear of contagion of leprosy had throughout the centuries led to the forced segregation of infected victims into communities supported by municipal or ecclesiastical authorities. These establishments or Lazar-houses often functioned in isolation of one another managed according to defined regulations based on a monastic life. The Crusader movement of the twelfth century led to the establishment of a widespread organization referred to the *fratres Sancti Lazari* extra muros Jerusalem leprosis that managed establishments according to a common rule. The expulsion of the Christian forces from the Outremer led to changes in how municipal and ecclesiastical authorities in France looked at the *fratres Sancti Lazari*, and events during 1320-21 led to an attempt to dismantle the organization in an effort to appropriate the supporting benefices of the establishment.

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It is generally accepted that the earliest possible account describing a skin condition resembling leprosy, the tumour of the God Xensu, is found in the Ebers Papyrus dated to about 1550 BCE.[1] However, the earliest absolute archaeological evidence of leprosy in Egypt is described in an Egyptian skeleton from the second century BCE. In contrast, archaeological evidence of leprosy from India dates to about 2000 BCE.[2] There is also a possible reference to the disease prior to the first millennium BCE in the Atharva Veda Sanskrit hymns.[3] On the basis of nucleotide polymorphisms of rare contemporary samples, it has been suggested that leprosy evolved first in Asia and subsequently transmitted to Europe, West Africa and later the Americas.[4] In Europe, the first accurate description of the disease, referred to as *elephas*, was written by Arataeus of Cappadocia around 150 ACE.[5]

Despite the empire expansion designs of Alexander the Great and later the Roman Empire, it appears that leprosy remained a relatively rare disease in Europe during the Classical Age. Its prevalence appears however to have increased in Medieval Europe with the east-west migration and trade exchanges that occurred during the first millennium ACE.[6] The increasing prevalence of the disease led to the enactment of legislation by secular authorities to arrest its diffusion emphasizing segregation of the infected from the health community in accordance to Biblical direction (*Leviticus* 13:45). This gave rise to the establishment of lazar-houses or leprosaria throughout Europe and the Middle East. The absolute segregation imposed by secular authorities caused ecclesiastical authorities to attempt establish means of addressing the rights of the segregated infected to religious practice. These rights, defined by the Council of Lateran in 1179, established that 'where a number of leprous people are gathered together in community they shall be permitted to enjoy to themselves a church, churchyard, and priest of their own. But they must take care that this be no ways injurious or pre-judicial to the rights of parish-churches'.[7] A lazar-house established in Jerusalem in the fourth century ACE was to gain European prominence after the First Crusade of 1099. This establishment known as *hospitali infirmorum sancti Lazari de Jerusalem* was to expand its sphere of influence throughout Europe and establish daughter houses in France (established 1154), England(1157), Hungary(1162), the Holy Roman Empire(1184), Kingdom of Two Sicilies(1226), and Kingdom of Castile.(1248) [8]

LAZAR-HOUSE MANAGEMENT

Shunned from the healthy community, leprous individuals formed permanent communities based on a monastic pattern supported by benefices and donations given by a wide range of benefactors. According to the Canon-Penitentiary of Saint-Victor at Paris Robert de Flamborough writing in 1208-1215, lepers living in leprosaria were to be considered religious communities since they lived according to a set of *regula* based on Christian principles similar to the monks and canons, the Templars and Hospitaller Orders, and the religious brothers or sisters who cared for the sick in general hospitals or hospices.[9] The first known *regula* regulating life in French leprosaria were those promulgated by Raymond Bishop of Montpellier in 1149-1158 (p.181-183).[10] In 1226, King Louis VIII of France further promulgated a code of laws to regulate the lazar-houses in his dominium.[11] Guy de Foulques, Bishop of Le Puy eventually elected Pope Clement IV, in 1256-1259 also drafted a very detailed set of leprosarium regulations written with the aim of guaranteeing the rights of the lepers in residence ensuring their self-government but ensuring segregation from the healthy members of the community to avoid spread of infection. These were very much in line with the edicts laid down by the Council of Lateran in 1179 (p.206-214).[10] Other surviving regulations pertaining to French leprosaria date to the late twelfth to fourteenth centuries (p.181-252).[10] These regulations suggest that these regional establishments functioned in isolation of one another being frequently managed by preceptors chosen by and from within the leper community. They were financially supported by the municipal secular or ecclesiastical authorities. While generally following similar precepts, the *regula* determining management within these regional establishments were distinct and separate from each other.

In contrast, the European-based establishments managed by the *extra muros Jerusalem leprosis* were interlinked and regulated by a common *regula* primarily based on the Rule of Saint Augustin. The earliest extant compilation of these *regula* available was written during 1314-1321 by the preceptor of the house at Seedorf in Switzerland.[12] According to this *regula*, the leprous sick on admission to the establishment took the three monastic vows of chastity, poverty and obedience. They thus became full brothers who slept in a dedicated dormitory separate from the healthy brothers who formally joined the establishment to

assist the sick. The healthy and sick members were expected to participate in all the liturgical activities of the monastery keeping the canonical hours of matins to compline. The organization of the *fratres Sancti Lazari* was thus comparable to that of a traditional monastic community following the Rule of St. Augustine with all the establishments following the same rule and subservient to the mother house sited respectively in Jerusalem, Acre and Boigny, France.[13] Management in the mother house was originally left to a leprous master, but after 1253 pontifical permission was obtained from Innocent IV to appoint a non-leprous master.[14]

In 1265 with the Bull *Venerabilibus fratribus*, Clement IV confirmed the privileges of the *fratres Sancti Lazari* and placed all leper-houses in the West under their protection and government.[15] In the Kingdom of Sicily and Naples, Charles I of Anjou in 1268-1271 ordered that all the leprosaria in his domains were to be placed under the protection and government of the fratres Sancti Lazari. This arrangement was maintained after the War of the Sicilian Vespers resulted in the division of the Kingdom of Two Sicilies by letters patent from Robert of Anjou, King of Naples dated the 29 April 1315 who gave similar instructions within his realm.[16] However, it is not clear how many, if any, of the French establishments were managerially taken over by the *fratres Sancti Lazari*. France had a significant number of lazar houses said in 1226 to number not less than 2000 in total. The number of establishments continued to increase so that there was scarcely a town or burgh in the country that was not provided with a leprosarium.[17] While supported by religious and philanthropic benefices which provided care and shelter to the victims of leprosy, the leprous marginalized community was generally looked upon with suspicion and disdain by the healthy population supported by the belief that the disease symbolized sin or punishment for sin. This suspicion, coupled with the fear of a Muslim advance to France from the Iberian Peninsula, led to a paranoid fear that led to the Lepers' Plot hysteria of 1321 when it was alleged that lepers had, in cohesion with the Muslim Emir of Granada and the Jewish community, organized themselves to poison the wells throughout Europe in an attempt to either kill the healthy community or to transmit leprosy. The hysteria may well have been further fuelled by a desire of the monarchy and municipal authorities to appropriate the benefices of the various leprosaria and belongings of the Jewish community.

THE 1321 LEPERS' PLOT

The Lepers' Plot flourished in the wake of the 1320 Shepherds' Crusade, which saw rural mobs attack Jews in France and the neighbouring Kingdom of Aragon, despite being ordered to stop by Pope John XXII, King Philip V of France and King James II of Aragon. In France, the Bishop of Bazas Raymond-Bernard de La Mote reported that some of the apprehended mobsters of the Shepherds' Crusade had claimed to have found barrels filled with rotten bread while pillaging the leprosarium (possibly near Le Mas-d'Agenais) and further alleging that the lepers had intended to use the bread to prepare poisons for contaminating well water. Following these allegations, the mob's attention turned towards the lepers. Leprosaria were attacked and torched. The municipal authorities, on their part, undertook measures to attempt to appropriate the benefices accruing to the leprosaria in their region and thus attempted to "protect" the properties. In July 1320, the lieutenant of the porévot of Sauveterre-de-Guyenne forbade the torching of the leprosarium in the town.

News of the so-called Lepers' Plot spread rapidly to Aragon. King James of Aragon initially reacted by ordering the arrest and expulsion of all leprous foreigners. On 27 June, James ordered the arrest of lepers, destruction of their powders, and questioning under torture. He further ordered the arrest and expulsion of non-leprous foreigners, 'since it is difficult, truly even impossible, to recognize such and identify them'. Local inquisitions were set up. Those who confessed were burnt.[18]

In December 1320, the Bishop of Dax had all lepers in his diocese arrested, an act that may have helped precipitate the subsequent violence and contribute to the charges brought against the lepers in the spring of 1321. By February 1321, the communities of Toulouse, Albi and Carcassonne had petitioned the French monarchy to segregate the lepers and expel the Jews from France. The consuls further attempted to gain jurisdiction over the autonomous properties belonging to the leprosaria offering their services to administer the revenues and pious donation accruing to the lepers and provide for the leper's maintenance. These petitions were not favourably received by the king and the petitioners took matters into their hands. The Mayor of Pérginueux ordered lepers to be arrested and tortured by judicial officers.

Many who confessed under torture were burned at the stake. These arrests by the municipal authorities were considered a clear usurpation of royal prerogatives.[18]

While the actions against lepers and leprosaria were being taken by the various municipal authorities, King Philippe V was in Poitiers presiding over an assembly of the towns in the south of France. On the 21 June 1321, he issued an order declaring that this plot of poisoning the water supplies by the lepers constituted an attack on the king's majesty and therefore subject to the authority of the king's courts. In this way, all the seized leper belongings reverted to the Crown. Lepers who confessed their involvement in the plot were to be burned at the stake; those found innocent or who were aged under fourteen years were to be imprisoned in the leprosaria. On the 16 August, the king relinquished the seizure of the French leprosaria and a few days later pardoned all lepers who had been arrested and found guilty during the turmoil – in essence accepting these to be innocent and the Lepers' Plot to have been a hoax.[19,20] Many municipal secular and ecclesiastical authorities, including Albi, Narbonne, Carcassonne and Toulouse, contested the royal claims to ownership of the seized lepers' property forcing the king to release these to rival claimants.[21] Individuals accused of perpetuating the Lepers' Plot were brought before the Inquisitional Tribunal presided by Bishop Fournier (later elected Pope Benedict XII) at Palmiers in southern France.

INQUISITIONAL TESTIMONIES

There is no definite mention of the *fratres Sancti Lazari* in any of the surviving testimonies. However, the testimony given by Guillaume Agasse to the inquisitional court presided by Bishop Fournier suggests the involvement of a nationwide coherent group of interrelated leprosaria falling under one central organization that adhered to a specific chain of command structure involving superiors, commanders and preceptors – a structure very similar to that extant within the *fratres Sancti Lazari* in the 14th century.[22] In contrast, the twelfth to thirteenth century regulations drawn up for French leprosaria associated with municipal or ecclesiastical authorities suggest that these establishments were generally localised affairs that functioned independently from each other. They were managed by an internal management structure responsible only to the relevant municipal or ecclesiastical authority.

The case in question involved the leper Guillaume Agasse who served as a '*clerc lépreux commandeur de la léproserie de Lestang*'. Agasse was brought before the inquisitional court on the 4th June 1321 in Palmiers. He was charged with allegedly having been involved in the plot to poison the wells throughout France with a mixture that would either kill the healthy communities or infect them with leprosy.[23] A similar charge was brought earlier in May 1321 against the leper Johan de Bosco from Alterque who was arrested in Regale Ville. De Bosco had testified on oath, that he had been approached by brother Geraldus, the leper preceptor of the leprosarium of Alterque, and given two bags of pessimam powder to use for poisoning the water supplies of various villages. He was paid twenty sous for his involvement and given a further ten sous to cover expenses. He believed that the mixture he was given would cause anyone who drank it to become leprous or die within two months.[18]

The proceedings against Agasse lasted about a month with the sentence being delivered on the 5 July 1322. Torture was resorted to by the prosecutor during the first testimony but the subsequent two depositions were made without resorting to torture. Agasse testified that, in the previous year, he had been delivered a missive from the '*précepteur de la léproserie de la porte Arnaud-Bernard de Toulouse*' summoning him to immediately proceed to Toulouse '*pour traiter et decider de choses qui tourneraient á mon avantage et honneur*'. On his way to Toulouse, Agasse learned that Raimond, '*minister de la maison de Saverdun*', had also received a similar missive from the preceptor of the Toulouse leprosarium. They made their way to Toulouse together and on the 11 May 1320, attended a meeting of about forty to fifty lepers, many of whom were '*ministers et précepteurs*' from various regions of southern France, including '*Raimond minister de la léproserie de Saverdun, Pierre de Mazéres minister de la léproserie dudit lieu, et le minister des leproseries d'Unzent et des Pujols*'. Agasse could not confirm the attendance of '*les ministers des leproseries de Foix, de Varilhes et autres lieux du comet de Foix*'.

This meeting was addressed by the preceptor of the Toulouse leprosarium with the following statement: '*Vous autres voyez et entendez comme les chrétiens en bonne santé nous tiennent, nous autres maladies, en opprobre et en abjection, qu'ils nous rejettent de leir compagnie et frequentation, et qu'ols nous tiennent en derision, blaspheme, et mépris. C'est pour cela qu'il a*

été discuté, délibéré et ordonné par nos supérieurs que par tout le monde oú régnent les chrétiens, soient donnés et administers par les maladies aux chrétiens en bonne santé des poisons, des charmes et des philtres, par le moyen desquels ils meurent tous ou deviennent lépreux ou maldes. Et alors, les maladies et les ministers actuals auront l'administration et le pouvoir qu'ils détiennent, recevront leurs terres et les gouverneront, et même se les approprieront. Et pour obtenir et atteindre ce but, il a été délibéré et décidé entre les supérieurs de prendre le roi de Grenade comme allié et défenseur. Ce roi a déjà annoncé à quelques-uns de nos supérieurs qu'il était dispose à nous fournir sur ce point conseil, aide et assistance. Pour realiser et mener à bonne fin la chose, il a été décidé qu'en tout lieu de toute la chrétienté les maladies mettraient, dans les sources, les puits et les eaux courantes, des poudres, des charmes ou des philtres, don't ces eaux seraient infectées et corrompues, de telle sorte que ceux qui en boiraient deviendraient lépreux ou mourraient à bref délai. Et pour ce faire, ont été faites sur le conseil de médecins beaucoup de poudres, don't chaque personne ici présente recevra dans des sacs de cuir ou d'étoffe, et emportera avec elle pour les metre dans les eaux, chacune dans le lieu où elle habite'. The testimony further revealed that '*Les commandeurs supérieurs ont envoyé, pour traiter cela avec le roi [de Granda] et le Soudan [de Babylone], le commandeur de la léproserie de Bordeaux, et c'est li qui nous a rapporté cela de leur part*'. The Muslim potentiates had required the lepers to renounce Christ and to spit on the cross as a sign of their commitment.[23] Towards the end of his deposition, Agasse retracted the evidence he had given against the lepers Guillaume Normand and Fertand Espanol, and against Raimond de Saverdun (who has already been executed) and Pierre de Mazéres. He assumed full responsibility and stated that he had for three months believed that the Christian faith was of no value. The involvement of Muslim support for the leper conspiracy was false – there was no Sultan of Baghdad at the time. He was found guilty only on the charge of heresy and blasphemy and condemned to perpetual imprisonment. He was not found guilty of poisoning the water supply.[24,25]

The testimony by Agasse therefore confirms the existence of a nationwide French organization involving leprosaria. The management of this organization involved a chain of command linking a number of subsidiary village-based leprosaria managed by *commandeurs* and ministers to a larger regional one in Toulouse managed by a *précepteur* who in turn was responsible to a central government of *supérieurs*. These occasionally were summoned to meet and discuss important national issues.

The events leading to the 1320 Lepers' Plot and the apparent attack on the benefices and leprosaria managed by the *fratres Sancti Lazari* who had in previous decades enjoyed Royal patronage in France need to be placed into the historical perspective. The end of the thirteenth century saw the *fratres Sancti Lazari* who had assumed a military role in the Outremer, loose their raison d'être with the expulsion of the Christian forces from the Kingdom of Jerusalem following the fall of Acre in April 1291. The loss of the Outremer was partly blamed on the escalating rivalry that existed between the Militant Orders particularly the Hospitallers and the Templars. The events of the subsequent two decades were to determine the fate of the various Orders expelled from the Kingdom of Jerusalem. The Hospitaller Order of St. John remained centred in the Outremer initially in Cyprus but eventually in 1310 occupied Rhodes thus acquiring their own sovereign temporal domain ensuring their survival as an organization.[26] On the other hand, the Knights Templar Order maintained its status as a "state within a state" with a standing European-based army that had no allegiance to any monarchy. In 1305, criminal charges were brought against the Order by an ousted Templar accusing its members of heresy. In October 1307, Philip IV of France ordered the simultaneous arrest of the Templar grandmaster Jacques de Molay and the French Templar knights. Under torture, the accused confessed to the charges brought against them. This led to Pope Clement V to issue the bull *Pastoralis Praeeminentiae* dated 22 November 1307, which instructed all Christian monarchs in Europe to arrest all Templars and seize all the assets of the Order. In 1308, Clement V absolved the Templars of all heresies and in a letter addressed to Philip IV wrote that all Templars that had confessed to heresy were "restored to the Sacraments and to the unity of the Church". At the Council of Vienne in 1312, Clement issued the bull including *Vox in excelso* which officially dissolved the Order citing the reason for the disbandment as being the public scandal that had been generated by the confessions. An additional bull *Ad providam* handed over all Templar assets to the Hospitallers. Freed from torture, the grandmaster de Molay and the Preceptor of Normandy Geoffroi de Charney retracted their confession and insisted on their innocence. Declared relapsed heretics, they were sentenced to burn alive at the stake in Paris on the 18 March 1314.[27]

These events throughout Europe, but particularly in France, were to have a significant effect on the

general outlook towards the *fratres Sancti Lazari* with their central house stationed at Boigny in France. Royal letters patents confirming the protection and support of Philippe le Bel had been given to the *fratres* in July 1308 (p.xvii-xviii).[28]In spite of the Royal protection, attempts had been made by local and ecclesiastical bodies in France to appropriate the land holdings of the *fratres* or introduce taxation on previously exempted holdings. For example, the provost of Caen demanded taxes on the property belonging to the *fratres* within his region ignoring the tax exemptions previously given by Philippe Augustus II in 1200 and confirmed by Philippe le Bel in 1304. Legal proceedings were initiated with a decision that favoured the *fratres* in 1313. A similar attempt was made by the officers of the crown to appropriate the *fratres*' property at Boigny. This too was contested in court with a favourable decision being given to the *fratres* in 1317 (p.154-156).[28] This action led to a reconfirmation in 1317 by Philippe V of the *fratres*' ownership of Château de Boigny (p.xix-xx); [28] while John XXII promulgated a pontifical decree in 1318 granting the *fratres* exemption from local ecclesiastical authority and making the *fratres Sancti Lazari* dependent only to the Holy See (p.159-160 ftnote b).[28] The environment was therefore ripe for a suspicious mob to be directed by the municipal authorities to attack the leprosaria managed by the *fratres Sancti Lazari* and thus appropriate the management of the associated benefices. In 1358, Regent Charles dauphin de France through Royal Letters Patent again ordered the judicial officers in the realm to protect the Order from violence and oppression, and to allow them peaceful enjoyment of their possessions and privileges (p.172-173).[28]

The support of the various rulers to the individual regional houses was insufficient in creating a common targeted *raison d'être* for the *fratres Sancti Lazari* especially with the fall in the prevalence of leprosy in Europe following the Black Death epidemics and the effect these had on the socio-economic conditions in late fourteenth century Europe.[6] This in effect changed the *fratres Sancti Lazari* into a land-owning establishment using the resources to maintain itself and give solstice to those in need. This change in ethos failed to provide the driving force necessary to maintain the cohesion of the international organization and regional houses often functioned in isolation from the central mother house in Boigny, France. The breakdown in administrative cohesion appears to have occurred in the mid-fourteenth century. In 1370, in a petition addressed to the Holy See, the master general in the central house at Boigny Jacobi de Besnes was lamenting that over the previous twenty years, no oblations had been received from some of the houses in England, Apulia, Hungary, and France. The same brothers had failed to attend the Chapter General meetings of the Order; while some had actually reverted to a secular life. In response, Pope Urbane V sent a missive to the Bishop of Paris requiring him to ensure that the absent brothers regulated their obligations under the threat of ecclesiastical censure.[29] While administrative cohesion was eventually achieved in France, Hungary and the Holy Roman Empire; the *fratres Sancti Lazari* in England, the Kingdom of Two Sicilies, and Kingdom of Castile continued to follow separate management directions.

In the Maltese Islands, no documentary evidence exists for the presence of a leprosarium in the fourteenth century. However, it has been suggested that the Medieval *hospitalis Sancti Franciscj*, situated outside the Medieval walls of Mdina [modern-day National Archives] may have been originally established as a leprosarium.[30] The establishment was definitely extant in 1372 but probably had been established in earlier decades possibly after 1299 following the appointment by Pope Boniface VIII of Cardinal Bishop Gerardus of Sabina as Apostolic Delegate to the Kingdom of Sicily with powers to grant indulgences to the faithful who assist in the running of hospitals.[31] The first documented case of leprosy termed *erga corpore morbo lepre* is said to have affected a Gozitan woman Garita Xejbais who bequeathed land to the Church in 1492.[32] By the end of the 15th century, the available documentation relating to *hospitalis Sancti Franciscj* makes no mention of lepers but refers only to "*poveri abitanti*".[33]This is not surprising since the documented decrease in the European prevalence of leprosy caused by the 14th century Black Plague epidemic had resulted in 'closure' of many of the previously extant leprosaria. The Maltese Islands had also been ravaged by the plague pandemic in 1363.[34]

In Rhodes, the Order of Saint John had regulated stringent public health laws to limit the spread of the disease in the *Domini Sanatatis* promulgated during the reign of Grandmaster Emery D'Amboise (1530-1512). The "sick of Saint Lazarus" were beneficiaries of special charities from the Order and cared for in their homes. These regulations debarred infected individuals from having any social intercourse with healthy ones who in turn were prohibited under penalty of a hefty fine from receiving any goods from lepers. Furthermore, lepers were precluded from practicing certain occupations unless licensed by the sanitary authorities who ensured that material goods

belonging to lepers were not physically passed on to healthy people. It was however not deemed necessary to segregate the victims of this infection in dedicated leprosaria. The *Domini Sanatatis* regulations were introduced in Malta after 1532.[35]

In the Maltese Islands, therefore, there is no definite documented evidence of the existence of organized leprosaria during the Medieval Period. Victims of Hansen's disease were allowed to live in the community with only a minimal degree of restrictions to their movements. They were not enforceably segregated. Segregation of these individuals was only introduced in 1893 when the Council of Government issued the Lepers Ordinance No. VII entitled 'An Ordinance for checking the spread of the disease commonly known as Leprosy' setting up the St Bartholomew Leprosarium to house the infected cases. The last leprosarium, at Hal Ferha estate, closed down its services in 2001.[36]

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CASE REPORT

Osgood-Schlatter Disease in Adulthood: A Case Report

Marie Adrienne Zerafa Simler, Kirill Micallef Stafrace

Osgood-Schlatter disease is a common cause of anterior knee pain in the athletic adolescent population. It commonly presents with tenderness at the patellar tendon insertion site at the tibial tuberosity, usually caused by microavulsions or existing anatomical variations at this site. Its severity is dictated by the degree of repetitive strain activities such as jumping and sprinting. Although well described in the adolescent and the young athletic population, this disease is considerably rare in adults and consequently an unusual problem faced by physicians and surgeons alike. This case report explores an unusual case of Osgood-Schlatter disease in a 29-year-old male, in which the symptomatology, pathophysiology and images are used to investigate the case. Finally, different management options are explored with the aim of aiding medical practitioners treating such patients.

Several months following attempts at failed conservative management, this gentleman was referred to the Sports Clinic at the Orthopaedic Outpatients. On examination, his left knee was swollen with a minimal effusion and an area of erythema and deformity marking the proximal anterior aspect of the tibia over the tibial tuberosity. The knee was otherwise stable for its anatomical components. The patient had decreased range of motion secondary to severe pain on flexion of the knee to more than ninety degrees. The pain was specific to the area of erythema and deformity over the left tibial tuberosity.

Laboratory investigations revealed that relevant blood analysis were within normal parameters for pathologies such as infection, gout and inflammatory musculoskeletal and rheumatological disease. Plain radiographs of both knees revealed extensive calcification and soft tissue swelling over the insertion of the patellar tendon into the tibial tuberosity (**Figure 1**). An MRI was more sensitive and specific to these radiological findings and demonstrated further soft-tissue swelling and bone marrow oedema. Infrapatellar bursitis and severe thickening and calcification of the distal patellar tendon at its insertion into the tibial tuberosity was also noted (**Figure 2**).

Finally, an ultrasound once again indicated ossified cartilage with surrounding oedema of the surrounding soft tissues and thickening of the patellar tendon. Doppler investigation of the ossified component of the patellar tendon showed neovascularization around the significant ossification at the insertion of the patellar tendon into the tibial tuberosity.

DISCUSSION

Osgood-Schlatter disease was first described in the early 1900s when the two physicians Osgood and Schlatter reported an increased incidence of adolescents complaining of pain over the tibial tuberosity in their lower limbs on increased physical exercise. This pathological process, also known as tibial osteochondrosis, has in fact become one of the most common traction apophysitis and overuse injury in the knee of adolescent athletes.[1]

Although well described, the origin of this condition and its pathological process remains very controversial. Its pathophysiology involves loss of continuity of the patellar tendon-cartilage-bone junction of the developing tibial tuberosity through an inflammatory process secondary to chronic tendinitis and calcification. The most accepted theory for this process is repetitive knee extension mechanism contraction causing microavulsions at the insertion of the patellar tendon into the tibial tuberosity.[2,3] Anatomical variants also play a role as they may predispose to increased tension over the patellar tendon. The most significant variant noted was the position of the tibial tuberosity as this dictated the tension and extension forces over the patellar tendon during quadriceps contraction.[4]

Osgood-Schlatter disease has been explored in great detail in developing adolescents and children between eight and fifteen years of age. It is known to resolve once closure of the epiphyseal growth plates has occurred. Nonetheless, although rare, it is known to occasionally persist into adulthood in active individuals as in the case demonstrated in this report.[5] In fact, 10% of children and adolescents who develop Osgood-Schlatter disease continue to experience symptoms into adulthood. This is a rare but recognised condition in young adults which is an ongoing orthopaedics issue faced by physicians and surgeons alike.[5]

The treatment offered to both adults and adolescents is initially conservative. It involves restriction or adjustment of aerobic activities causing excess force over the patellar tendon to exercises such as stretching, swimming and cycling. These activities increase hamstring and quadriceps strength and flexibility and are known to accelerate recovery.[6,7] Protective pads, ice and elevation are also

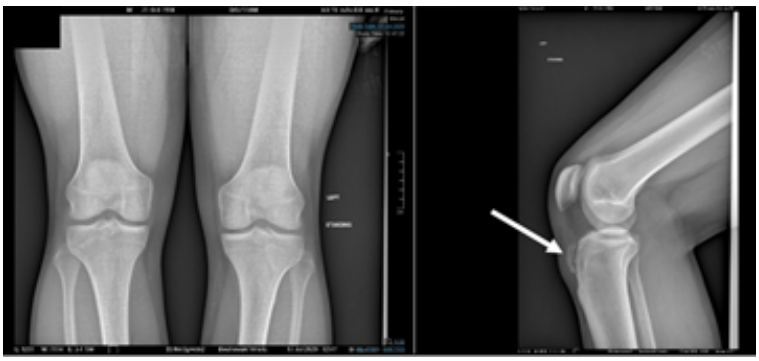

Figure 1 *X-Ray of knee*

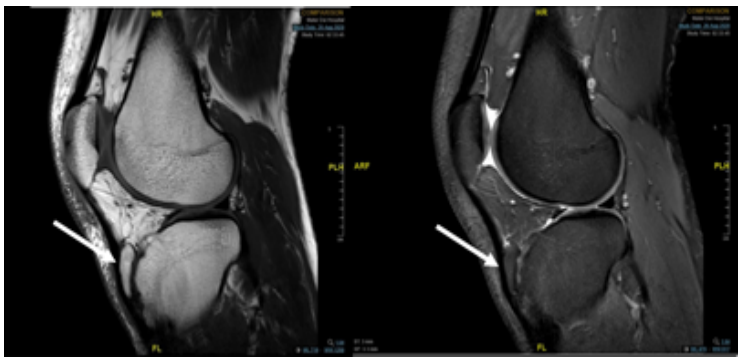

Figure 2 *MRI knee*

part of the usually prescribed conservative management. Such a regime is frequently accompanied by a short prescription of nonsteroidal anti-inflammatory drugs for bouts of increased pain.[6,7] Such management has reported good response with only refractory cases requiring further intervention.[7] Further intervention such as external shockwave therapy for the duration of over a month have proved to be successful when conservative management alone fails. External shockwave therapy is effective in reducing pain, enhancing patient-reported functional recovery, and improving performance-based functional outcomes in adults with Osgood-Schlatter disease.[8]

Corticosteroid injection into the patellar tendon is not recommended as a treatment for Osgood-Schlatter disease. This is mostly secondary to its high incidence of subcutaneous atrophy and rupture of the patellar tendon. Other injections such as hyperosmolar dextrose and autologous conditioned plasma are also available, however their efficacy alone is limited and are used as adjuncts to the conservative management options mentioned above.[9,10] Therefore, when all conservative management options fail, operative treatment is considered. Multiple procedures have been documented for the treatment of this disease, especially in adults. These include drilling of the tubercle, removal of loose fragments, autogenous bone peg insertion through the tubercle, tibial tuberosity excision and sequestration.[11]

Less invasive modalities such as arthroscopic surgery and bursoscopic excision have also shown promising results. Arthroscopic surgery was noted to be less invasive and spared the patellar tendon from incision and surgical trauma. This allegedly saves the patient from pain on kneeling unlike more invasive interventions.[12] Bursoscopic excision is even less invasive as such a procedure does not violate the infrapatellar fat pad and avoids meniscal and ligamentous iatrogenic injury. However, this approach does have a limited working space which inhibits adequate reduction of the described ossifications and abnormalities.[13,14]

CONCLUSION

In conclusion, this report notes that Osgood-Schlatter disease is a common pathology in children and adolescents. It resolves as the adolescent develops into adulthood, but may persist and cause ongoing unwanted symptoms as Osgood-Schlatter disease of the adult. As a result, adults who do not respond to conservative management may need to opt for surgical intervention for cure of this disease.

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CASE REPORT

Idiopathic plantar hidradenitis in a 5-year-old girl after exposure to wet footwear

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Idiopathic plantar hidradenitis (IPH) is characterised by tender erythematous papules and nodules which involve the soles of the feet. The pathogenesis of this condition remains obscure, with a temporal association between exposure to cold and moisture and the presentation of skin lesions which may allude to a possible pathogenic mechanism.

We report a five-year-old girl who developed plantar hidradenitis. The patient participated in a school outing wherein her feet were exposed to prolonged cold and damp. She complained of pain in the soles of her feet and was unable to walk the next morning. She was admitted to hospital with a suspicion of infection and discharged the next morning on oral antibiotics. Review by dermatology raised the possibility of plantar hidradenitis and a course of low dose oral steroids was given. The patient recovered fully in five days.

Familiarity with the inciting tiggers and symptoms of IPH in children allows a clinical diagnosis to be made without the need for hospitalization and further investigations. The authors believe that the instigating factors in our patient were prolonged exposure to wet footwear combined with strenuous activity. Further studies are needed to determine the aetiology of IPH.

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Idiopathic plantar hidradenitis (IPH) is characterised by tender, erythematous papules and nodules which involve the soles of the feet. This condition tends to affect younger children.[1] It is also known as 'traumatic plantar urticaria', 'palmoplantar eccrine hidradenitis' and 'plantar erythema nodosum'.[2–4] IPH is histologically similar to neutrophilic eccrine hidradenitis (NEH), with notable exceptions which include the presence of neutrophilic abscesses localized to the eccrine coils within the deep reticular dermis and the lack of syringosquamous metaplasia.[5,6] The pathogenesis of this condition remains obscure but there is a temporal relationship between exposure to cold and moisture and the presentation of skin lesions which may allude to a possible pathogenetic mechanism.[1] This case report aims to increase the awareness of this condition as a potential differential diagnosis in order to avoid unnecessary hospital admissions, histological investigations and treatments such as antibiotics.

CASE REPORT

We report the case of a healthy five-year-old girl who presented with bilateral erythematous, tender nodules after she participated in a school outing wherein children visited a valley and jumped in muddy puddles in the morning causing her shoes to become wet. On returning to school, her schoolteachers changed her into dry socks, but the child remained in her wet shoes until returning home around 6 hours later. Her behaviour was normal, and she did not complain of any pain. Her parents bathed and dried her thoroughly.

The child spent the rest of the day playing on a scooter and running around outside. She complained of some pain in her feet in the evening which her parents attributed to her eventful and physically demanding day. The patient slept through the night but, on waking up she, complained of bilateral sole pain and could not weight bear. She was therefore taken to the local emergency department.

On examination she was afebrile and systemically well, having only very tender bilateral erythematous nodules (Figure 1A) which precluded her from weight bearing. She was admitted for intravenous cefixime to cover for possible infection, given the history of exposure to potentially contaminated water. Bloods investigations included a full blood count which only showed marginally raised white cells (13.26 x10^9/L) with relative neutrophilia (8.39 x10^9/L) and a slightly raised CRP (6.2mg/L). A COVID swab and blood culture were unremarkable. She was therefore discharged with a 7-day course of cefpodoxime to cover for possible infection.

Outpatient dermatology review raised the possibility of plantar hidradenitis as the working diagnosis and introduced a course of low-dose oral steroids, 10mg prednisolone daily for 3 days. The following day, the erythematous nodules had reduced in size (Figure 1B) and the patient was on her feet with some pain and could manage walking on tip toes. She had almost completely recovered by that same evening, returned to school the next day, and even managed more strenuous activities such as tennis.

Significant improvement was seen once the course of steroids was completed (Figure 1C).

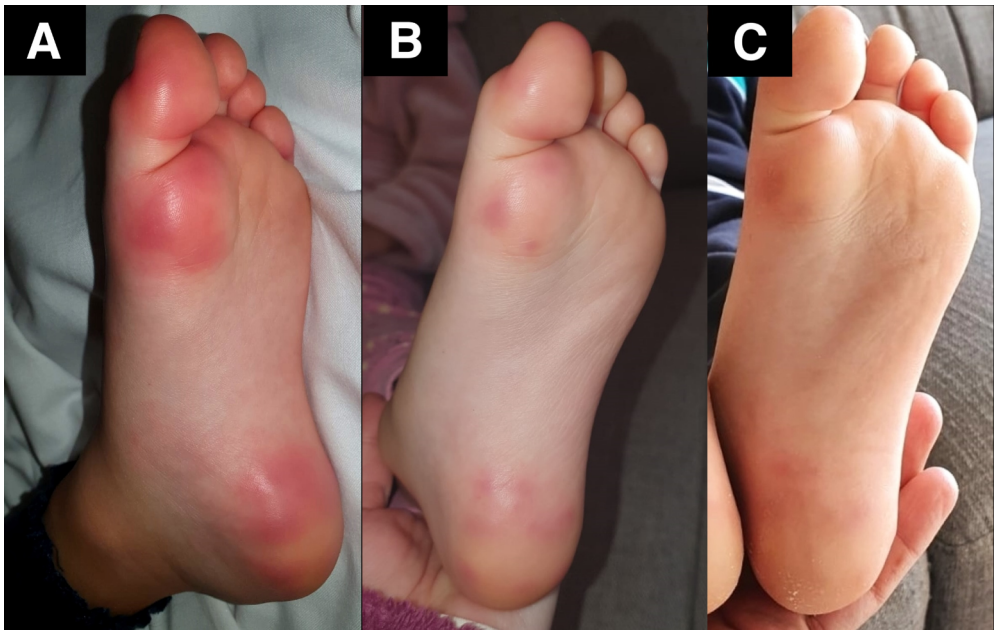

Figure 1 **A)** *On presentation before prednisolone was given. Erythematous nodules mostly present on the left heel, toes, and forefoot. B) One day post-prednisolone. Erythematous nodules on the left heel, toes, and forefoot smaller than the previous day. C) Significant improvement seen upon completion of the course of prednisolone.*

DISCUSSION

IPH is a condition characterised by the onset of erythematous and tender nodules on the plantar aspect of the foot. A variant of this condition may also affect the palms, when it is referred to as idiopathic palmoplantar hidradenitis (IPPH).[1,3] IPH was first reported in 1988 where its initial pathophysiology was thought to be related to strenuous physical activity.[2] It is now recognised that a number of inciting factors may trigger this condition.[1] These may include strenuous activity, trauma, heat, excessive moisture, perspiration and pseudomonas infection. The aetiology of this disease is uncertain although an association with intense physical activity and pseudomonas infection is under investigation.[7]

Reports of recurrent palmoplantar hidradenitis have also been made. This is a benign condition which may also be associated with low-grade fever. Resolution occurs in the absence of therapy making the disease self-limiting. It has been suggested that this entity may be more common than is reported in literature but is not routinely evaluated histologically given its transient nature.[8]

Our case fits within the typical clinical presentation of idiopathic plantar hidradenitis. The history of prolonged exposure to wet footwear combined with strenuous activity is concordant with other case reports of the same condition.[1,3]

The differential diagnosis of this condition may include erythema nodosum, Sweet syndrome, Behçet's disease, chilblains, Neutrophilic eccrine hidradenitis (NEH), Acute acral eruptions (AAE) secondary to SARS-CoV-2 infection and Pseudomonas hot-foot sysndrome.[6,9–11] The latter has also been described as one of the possible contributing factors of the condition. This case report discusses each of the listed differentials in the context of our case and how these were ruled out given the clinical picture.

Erythema nodosum is a cutaneous reaction consisting of inflammatory, tender, nodular lesions. The pathology may be associated with a plethora of diseases including infections, autoimmune disorders, inflammatory bowel diseases, sarcoidosis, rheumatologic diseases, medications and malignancy.[12] Our case involved a healthy child with none of the mentioned co-morbidities; erythema nodosum was therefore not likely. IPH should be distinguished from palmoplantar erythema nodosum as both are clinically characterized by tender erythematous nodules which appear after physical activity and that may involve the palms and/or soles of children.[12]

Sweet syndrome (SS), also known as acute febrile neutrophilic dermatosis and Behçet's disease (BD) form part of a heterogeneous group of inflammatory skin disorders known as neutrophilic dermatoses. BD typically presents in patients in their third to fourth decades while SS typically presents in patients between 47 and 57 years of age. Although both may present with the abrupt onset of painful erythematous nodules or plaques with predominantly neutrophilic infiltrates in the dermis, neither condition fits within the clinical picture of our case.[13]

Chilblains often appear in the differential diagnosis of IPH.[14] Chilblains usually resolve spontaneously and involve localized inflammation of the skin which occurs upon exposure to cold, wet weather. The inflammation is a result of a maladaptive vascular response to non-freezing cold.[15] The child in our case was exposed to cold, wet conditions however, dermatological input did not feel that the lesions were typical of chilblains and a course of steroids resulted in complete resolution. A clinical diagnosis of IPH was therefore made.

The clinical picture of IPH contrasts with that of with neutrophilic eccrine hidradenitis (NEH) which typically occurs in patients receiving chemotherapy for haematological malignancy. The clinical features of NEH are polymorphic and can affect other areas besides the palms and soles. While both clinical and histological investigations are needed to make a diagnosis of NEC, histological investigation is not required to make a diagnosis of PH.[8,16] Moreover, NEH typically resolves after cessation of chemotherapeutic treatment and the application of topical steroids.[10]

COVID-19 remains pandemic at the time of writing. Acute acral eruptions (AAE) secondary to SARS-CoV-2 infection have been observed in children and the clinical picture is similar that of IPH. AAE presents with heterogeneous features which include erythematous and violaceous papules and macules.[11] The patient in our case was asymptomatic and tested negative for COVID-19 on the day of admission. AAE was therefore not likely.

Pseudomonas aeruginosa is a recognized cause of folliculitis which arises after the use of swimming pools, hot tubs and contact with other bodies of water. Presenting features may include bilateral vesicular, pustular, or maculopapular lesions and pruritic folliculitis. Conversely, pseudomonas hot-

foot syndrome is a benign, self-limiting condition, the aetiology of which seems to involve *P. aeruginosa* infection. This condition, however, does not require antibiotic therapy.[9] The patient in our case was exposed to potentially contaminated water and thus, potentially, to P. aeruginosa. The authors do not exclude that the microbe may have contributed to the pathophysiology in this case as there have been documented reports of IPH triggered by *P. aeruginosa* infection.[7,9]

Familiarity with the inciting triggers and symptoms of IPH in children allows a clinical diagnosis to be made without the need for hospitalization and further investigations such as biopsy. Analgesic treatment, rest and topical or systemic steroid therapy seem to be the only effective treatment options. Biopsy to demonstrate eccrine gland neutrophil infiltration should only be carried out in abnormally prolonged cases or cases where there is an atypical presentation.[16,17] Increasing awareness of this condition may help avoid unnecessary investigations and treatments such as courses of antibiotics, especially given that the differential diagnosis often includes infective conditions such as pseudomonas hot-foot syndrome.[9]

The authors believe that the instigating factors in our patient were prolonged exposure to wet footwear combined with strenuous activity which induced trauma to the soles of the feet. We do not, however, exclude that *P. aeruginosa* exposure or infection may have contributed to the pathophysiology in this case.

LEARNING POINTS

1. Familiarity with the inciting triggers and symptoms of IPH allows a clinical diagnosis to be made without the need for hospitalization and further investigations.
2. Analgesic treatment, rest and topical or systemic steroid therapy seem to be the only effective treatment options.
3. Biopsy to demonstrate eccrine gland neutrophil infiltration should only be carried out in abnormally prolonged cases or in cases with atypical presentation.

CONCLUSION

Familiarity with the inciting triggers and symptoms of IPH in children may help avoid hospital admission, unnecessary investigations, and treatments, such as antibiotics. The importance of the multidisciplinary approach is highlighted in this case as the final diagnosis was only postulated once the patient had been seen by a general practitioner, paediatricians, and a dermatologist. Input from all members of the caring team and involving a specialist dermatologist allowed a clinical diagnosis to be made, appropriate treatment to be instituted and inappropriate treatment to be terminated. Further studies are needed to determine the aetiology of IPH and perhaps to allow more targeted treatment.

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CASE REPORT

Secretory Carcinoma of Parotid and Diagnostic Challenge of Salivary Gland Malignancy

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Secretory carcinoma (SC) or also known as mammary analogue secretory carcinoma (MASC) is a new distinct entity of salivary gland carcinoma that histopathologically resemble secretory carcinoma of breast. It was first documented in salivary gland in 2010 and included in World Health Organization classification in 2017. Formerly it was misdiagnosed as acinic cell carcinoma or adenocarcinoma in majority of cases, but comparably it is more aggressive. Present of translocation mutation t (12;15) (p13; q25) with fusion of ETV6-NTRK3 genes is typical feature for SC that absent in other salivary gland neoplasm. Diagnostic challenges are always seen in salivary gland tumor due to the morphological diversity, rapid change in nomenclature, some subtypes are extremely rare and lack of specific laboratory test in some center. Surgery is the mainstay of treatment same as other salivary gland carcinoma but increasing evidence of alternative medical treatment with tropomyosin receptor kinase antagonist that make SC more special.

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A 39-year-old male, with no underlying medical illness, presented to the Otorhinolaryngology clinic with a history of right infra-auricular swelling for 2 years duration. It was gradually increasing in size. Initially was painless but became painful on mouth opening over the past 2 months. It was associated with trismus and reduced oral intake for 6 months duration. There was no facial weakness, constitutional symptoms, or obstructive symptoms.

On examination, there was 4cm x 4cm swelling at the right angle of the mandible, hard in consistency, irregular surface, non-tender and appeared fixed to the overlying skin and underlying structures. The facial nerve was intact and no cervical lymph node was palpable. There was presence of trismus, but no medialization of the lateral oropharyngeal wall. Flexible nasopharyngolaryngoscopy revealed normal findings. Fine need aspiration cytology (FNAC) was performed which showed features suggestive of low-grade salivary gland tumour with differential diagnosis of low-grade mucoepidermoid carcinoma.

Computerized tomography (CT) scan of the neck, thorax, abdomen, and pelvis was performed for staging the tumour before surgery. The CT neck revealed homogenously enhancing multilobulated mass in the superficial lobe of the right parotid gland, measuring 4.2cm x 2.7 cm x 4.6cm, with foci of calcification seen within (Figure 1). The mass appears abutting masseter muscle anteriorly, trapezius muscle posteriorly and extending to the skin laterally without parapharyngeal extension medially. In addition, there was presence of enlarged cervical lymph nodes at levels II, III and V bilaterally. CT thorax, abdomen and pelvis showed no distant metastasis.

Subsequently the patient underwent right total parotidectomy and right modified neck dissection type 3. Intra-operatively the tumour involved superficial and deep lobes of the right parotid gland, measuring 10cm x 6cm, hard in consistency and attached to overlying skin laterally (Figure 2 and 3). The involved skin was removed together with the tumour. Furthermore the tumour was attached to the lower branch of the facial nerve and there was presence of multiple lymph nodes from level I to V Post-operatively the patient developed right facial nerve palsy, House Brackman grade III, otherwise no other complication. The facial nerve palsy fully recovered after six months.

Histopathology examination (HPE) of the tumour showed features suggestive of SC, circumscribed to the infiltrative and lobulated pattern of growth. It

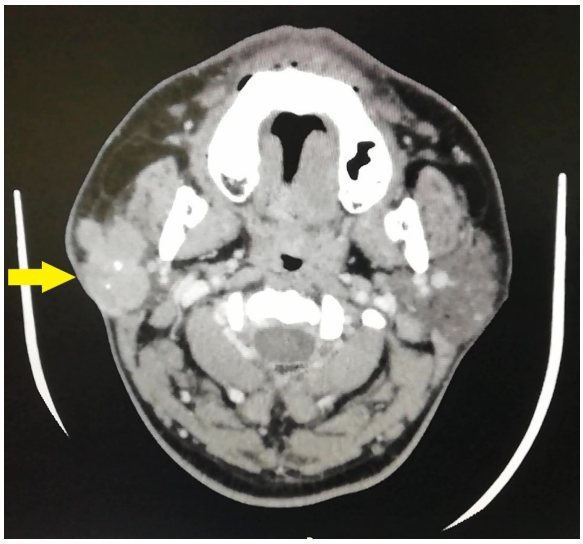

Figure 1 *CT neck shows homogenously enhancing multilobulated mass in superficial lobe of right parotid gland, measuring 4.2cm x 2.7 cm x 4.6cm, with foci of calcification. The mass appears abutting masseter muscle anteriorly, trapezius muscle posteriorly and extending to skin laterally without parapharyngeal extension medially.*

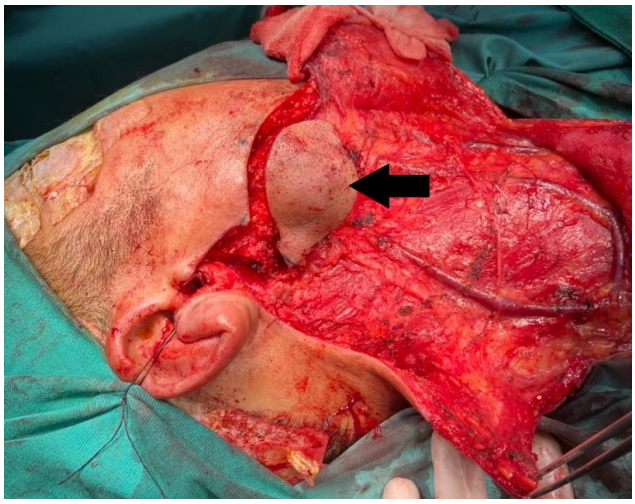

Figure 2 *Intra-operative picture show subplatysmal flap is raised and the tumour with involved overlying skin (arrow) plan to remove together. Lower part of neck is exposed for right modified radical neck dissection type 3.*

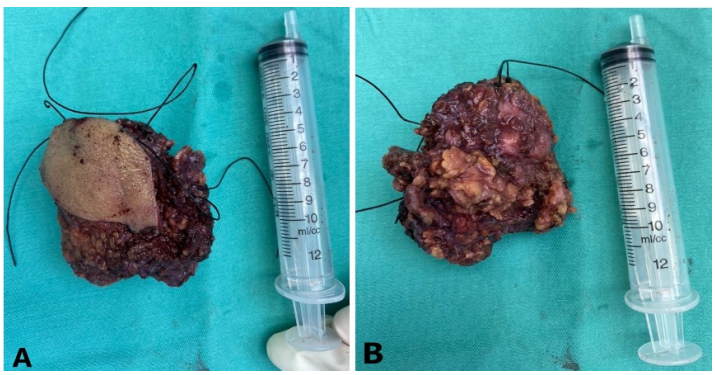

Figure 3 *Tumour in superficial lobe of parotid with involved skin, measuring 10x6cm (A) and tumour in deep lobe of parotid gland, measuring 12 x 6cm (B) were removed, tag with string and sent for histopathology examination.*

was displayed in microcystic, follicular and papillary-cystic structures with luminal secretion (Figure 4A). The immunohistochemical stains against S100 (Figure 4B), mammaglobin (Figure 4C) and CK7 were all positive. There was presence of perineural invasion (Figure 4D) and deep margin, as well as subcutis, were involved. Other margins were close to the tumour. Surprisingly no malignant cells were detected in the deep lobe of the parotid and all levels of the right cervical lymph nodes (levels I to V). The patient was subsequently referred to the oncology team for adjuvant radiotherapy.

DISCUSSION

The diagnosis of salivary gland tumours is always challenging due to the nature of salivary tumours that have marked morphological diversity with some of them showing overlapping features, some subtypes are extremely rare and rapid changes in nomenclature and classification in recent years.[7] In addition, limited samples for microscopic examination and lack of certain laboratory tests also contribute to the difficulty.

SC is currently recognized as a new distinct entity of salivary gland carcinoma and accounts for less than 0.3% of all salivary gland tumours and 5% of all malignant salivary gland tumours.[5,6] Majority of cases were misdiagnosed as acinic cell carcinoma or adenocarcinoma previously.[6,8,9] With the advance in molecular biology test, SC showed the typical characteristic of translocation mutation t (12;15) (p13; q25) which results in the fusion gene ETV6-NTRK3, which is absent in other salivary glands neoplasms.[8,9]

It showed male predominance in most series and commonly occur at 40 to 50 decades of life[3,6,9], which is consistent with our case. SC is generally classified as a low-grade carcinoma that usually presented with a painless slow-growing mass.[3] However it may show some features to suggest a more aggressive lesion as compared to acinic cell carcinoma, like a higher rate of cervical lymph node involvement and distant metastasis as well as local recurrence.[8] There was skin infiltration in our patient and the mass was abutting on the masticator muscle resulting in pain and trismus. In addition, there was microscopically perineural invasion and close surgical margin. Although the CT scan showed the presence of multiple cervical lymph nodes, HPE has proven no regional metastasis.

Due to the differences, thus it is important to differentiate the type of diseases to properly plan the management. FNAC is usually the first investigation of choice due to its generally good safety profile, low tumour seeding and high diagnostic accuracy.[10] However the clinical usefulness of FNAC in parotid gland lesions should be assessed

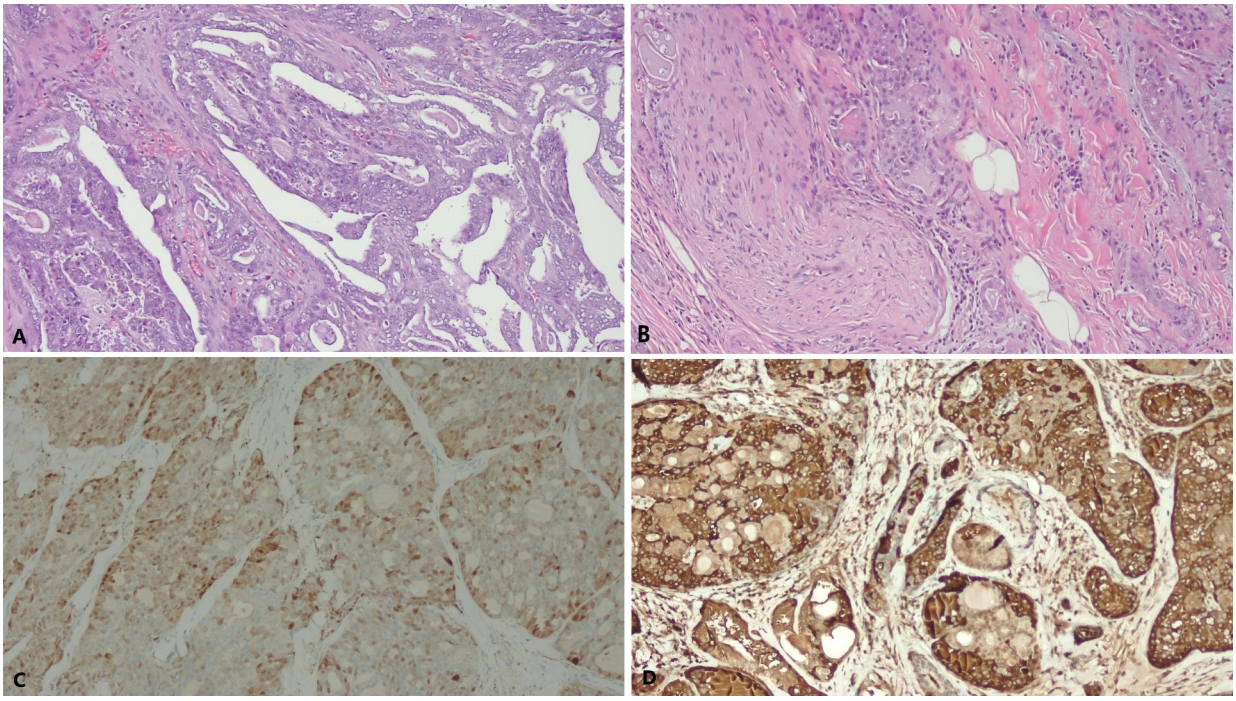

Figure 4 *HPE of the tumour shows circumscribed to infiltrative to lobulated pattern of growth, composed of microcystic, follicular and papillary-cystic structures with luminal secretion, and intracytoplasmic granules without zymogen granules, H&E, x200 (A). Immunohistochemical stains show positivity for S100, x100 (B) and mammaglobin, x100 (C). Tumour tissue invading into the perineural space surrounding a nerve, H&E, x100 (D).*

based on case-by-case and depend on local diagnostic performance, due to its wide variability of accuracy (sensitivity 52-100%, specificity 67-100%).[11] The accuracy varies depending on the experience of the FNAC operator, use of rapid onsite evaluation, cytologic preparation, the diagnostic experience of the cytopathologist, reporting terminology and characteristics of the salivary gland tumours.[12] Recently Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) has been developed to help standardize reporting system for salivary gland cytology, provide evidence-based risk stratification, guide in management and improve the communication between clinicians and pathologists.[13,14] Although the FNAC failed to provide an exact diagnosis consistent with the final HPE result in our case, it still gave important information that the lesion was malignant.

The gold standard investigation to diagnose SC is fluorescence in situ hybridization which can identify typical characteristic molecular alteration of t(12;15) (p13;q25) translocation.[9] This translocation that results in the fusion of genes ETV6 and NTRK3 will activate a signalling pathway leading to cell proliferation and neoplastic transformation is not seen in other salivary gland carcinomas. However unfortunately, some of the centres like ours are not well-equipped with this molecular test. A combination of histopathology study and immunohistochemical profile is believed to be sufficient for diagnosis in some typical cases.[9,15] Histopathologically SC has apocrine secretory epithelium morphology, papillary-cystic or microcystic pattern, abundant PAS-positive eosinophilic secretion, and absence of basophilic zymogen granules. Mammaglobin and S100 protein are among basic immunohistochemical profiles that suggest SC if positive.

The mainstay of treatment for parotid SC is parotidectomy, with or without neck dissection and adjuvant radiotherapy or chemotherapy depending on local disease extension and distant metastasis.[5,6,8] The principle of treatment is almost similar to other types of parotid carcinoma. The major difference is the presence of a promising alternative medical treatment with tropomyosin receptors kinase antagonists like crizotinib, entrectinib and larotrectinib, although still at the clinical trial level.[6]

CONCLUSION

SC is a newly recognized distinct entity of salivary gland malignancy in which most of cases were formerly misdiagnosed as acinic cell carcinoma or adenocarcinoma. Due to the different clinical characteristics and microscopic and molecular features, clinicians and pathologists should be alert to the existence of this entity. Surgery is still the mainstay of treatment, however there is promising alternative medical treatment with tropomyosin receptor kinase antagonists. Our case highlights a more aggressive form of SC which need post-operative adjuvant radiotherapy and challenges in diagnosis in a centre with limited laboratory resource.

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CASE REPORT

Successful treatment outcome of nasopharyngeal papillary adenocarcinoma following surgery:

a case report

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Nasopharyngeal carcinoma (NPC) is a common head and neck malignancy, endemic in East Asia and South East Asia. The rate of incidence varied in different countries based on the relative exposure of the population to different risk factors. The majority of NPC cases are squamous cell carcinoma subtypes. Primary nasopharyngeal papillary adenocarcinoma (NPAC) is an extremely rare subtype of NPC with characteristic adenocarcinoma cell structure. We present a case of NPAC treated by an endoscopic transnasal nasopharyngectomy with a successful outcome.

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Nasopharyngeal carcinoma (NPC) is the most common malignancy in the nasopharynx.[1] The majority of NPC cases are non-keratinizing and keratinizing squamous cell carcinoma subtypes. Primary nasopharyngeal papillary adenocarcinoma (NPAC) is extremely rare, constituting only 0.38–0.48% of all malignant nasopharyngeal neoplasms, albeit a few cases have been reported.[2–4] We report the successful outcome of a case of NPAC treated by endoscopic nasopharyngectomy.

CASE REPORT

A 40-year-old man presented with a complaint of epistaxis for several months. Endoscopic examination revealed a smooth surface, midline, pedunculated mass from the superior aspect of nasopharynx. A histopathologic examination of the nasopharyngeal mass demonstrated a NPAC Unfortunately patient defaulted follow up due to financial constraints. After 3 years, he came back with left nasal blockage and blood-stained mucus exacerbated by sneezing. There was no tinnitus, otitis media or aural fullness. A repeat endoscopic examination showed a pedunculated mass from the roof of nasopharynx in continuity with the posterior septal margin and adenoid tissue. The mass was confined to the midline with bilateral fossa of Rosenmuller intact. There were no cervical lymph nodes or anterior neck mass palpable and other physical examination were unremarkable. Computed tomography (CT) of base of skull and neck reported a small lobulated soft tissue lesion confined to the nasopharynx, with no surrounding bony erosion nor lateral pharyngeal recess and parapharyngeal space involvement (**Figure 1**).

An endoscopic transnasal nasopharyngectomy with posterior septectomy was done. Intraoperatively a lobulated mass measuring 0.5cm x 0.3cm was resected with wide margin using monopolar diathermy. The mass was successfully dissected off from the nasopharyngeal vault with clear margin and no evidence of bony invasion. No further adjuvant therapy was necessary. At one-year follow-up following surgery, the patient remained well with no evidence of tumor recurrence.

DISCUSSION

Primary nasopharyngeal malignant tumours can be divided into a few subtypes such as nasopharyngeal carcinoma (NPC), salivary gland tumours, soft tissue tumours, haematolymphoid tumours, notochord tumours, and a separate entity of nasopharyngeal papillary adenocarcinomas (NPAC).[5] The NPAC entity must not be confused with the closely-named entities of sinonasal adenocarcinomas, be it the intestinal type or non-intestinal type.

NPACs of the mucosal surface origin are low grade malignancies with a papillary configuration.[2] They are a rare type of epithelial tumor but may uncommonly present at the nasopharynx. Unlike its other malignant sinonasal tumour, NPAC is not associated with wood exposure or other known factors such as EBV infection. Histologically this type of papillary configuration is also seen in metastatic papillary thyroid carcinoma, hence the literature term of 'thyroid-like nasopharyngeal papillary adenocarcinoma' is not uncommonly-encountered. Thyroid primary was excluded in this case in the light of negative stains of thyroglobulin and normal thyroid gland on CT scan. Despite the three years lapse, owning to the slow growing low-grade tumor, we were able to remove the tumor with clear margins.

NPAC has no known etiological factors and has been reported to affect patients ranging from age 9 – 64 years with no sex predominance.[5] The most common

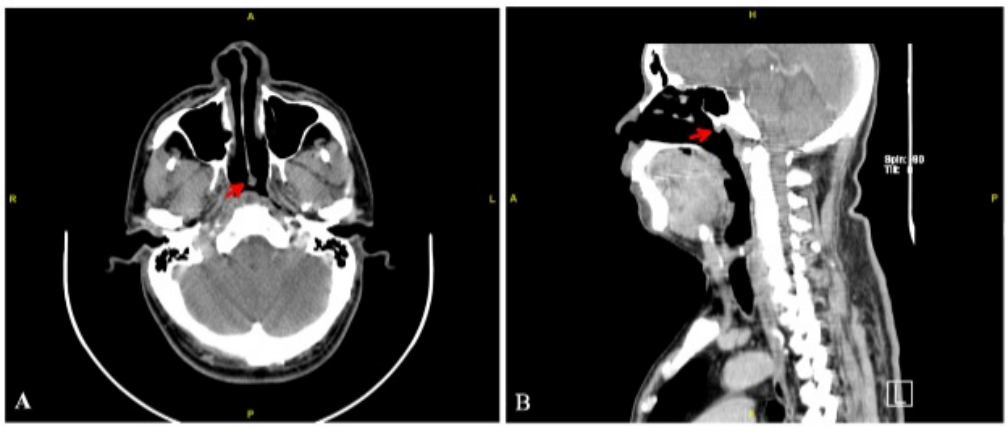
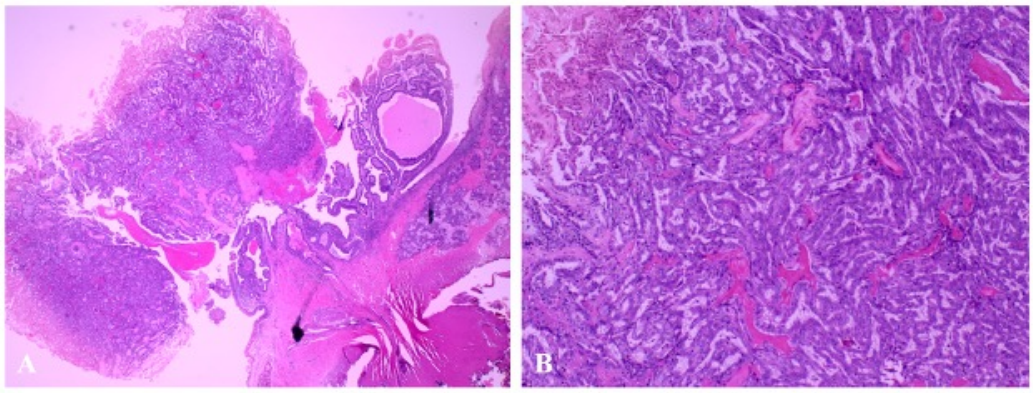


Figure 2 *(A) Polypoidal tumor tissue formed by the compact and complex papillary configurations with hyalinized fibrovascular core. (B) These papillae are lined by columnar and cuboidal cells, that display round to oval nuclei, fine chromatin pattern and small nucleoli. The intervening stroma shows pinkish collagenous appearance*



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presentations are nasal blockage and epistaxis. Other reported presenting symptoms include rhinorrhea, aural fullness, otitis media, blood stained sputum and reduced hearing.[2,5] NPAC is a remarkably well-behaved tumor with low percentage of local recurrence and no cervical lymphatic spread been described.[6] This is evidenced in our patient where there was no lymphatic involvement despite the three years delay in treatment. Endoscopically there was a smooth surface, midline, pedunculated mass arising from the roof of nasopharynx in continuity with the posterior septal margin. The differential diagnosis of a tumor in this location is the oft encountered NPC, keratinizing or non-keratinizing squamous cell carcinoma, which usually arises in the lateral nasopharynx as opposed to the midline and virtually never pedunculated.

In the case of NPAC, it can be challenging for pathologist to arrive at a diagnosis due to the similarity of the histological features with other tumors arising from mucosal surface, salivary gland or thyroid gland. Histological assessment of our specimen showed the tumor consists of compact and complex papillary configurations with hyalinized fibrovascular cores. The papillae are lined by cuboidal to columnar cells that have round to oval nuclei with generally fine chromatin pattern and small nucleoli (Figure 2). Some interpapillary areas form gland like structures that have bubbly appearance and contain periodic acid-schiff-diastase positive material. Varying amount of spindle cells were seen within the stroma, which partly merge imperceptibly with the epithelial component. Immunohistochemistry disclosed positivity for pan-cytokeratin, vimentin and thyroid transcription factor-1 (TTF-1), and negativity for thyroglobulin, glial fibrillary acidic protein (GFAP) and S-100 protein. In the event of ambiguous clinical presentations, given the similarities between NPAC and papillary thyroid carcinoma (PTC), a molecular genetic study can be performed to determine the mutational status of the BRAF-gene.[7]

Due to the rarity NPAC cases, the assessment and treatment options must be highlighted. A review by Xu et al[8] suggested that cranial nerve invasion, skull base erosion and the presence of positive cervical nodes should be considered on tumor staging. It is advocated that surgery with clear resection margins is adequate especially in early-stage tumor. An adjuvant radiotherapy (RT) is reserved for patients who are at high risk of developing recurrence.[8] The use of a more precise radiation techniques can help improve local control and spare radiation-induced damage to the surrounding structures. The low grade nature of NPAC has a good prognosis and allows less aggressive treatment measures to avoid unnecessary morbidities.

CONCLUSION

NPAC is a rare subtype nasopharyngeal malignancy with adenocarcinoma cell structure in papillary configuration that differs from NPC of squamous cell type in its propensity for a slow growth, low incidence of neck nodes metastasis and good prognosis if identified early. Therefore the use of a proper staging system and further deliberation of treatment options between surgical and oncological intervention will give better insight to help establish an optimal treatment strategy in the future.

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