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Chief Editor
Borneo Journal of Medical Sciences
Faculty of Medicine and Health Sciences
Universiti Malaysia Sabah
Jalan UMS
88400 Kota Kinabalu
Sabah, Malaysia
Tel: +60 88 320000 Ext 5620
Fax: +60 88 320928
Email: bjms@ums.edu.my

PUBLISHER

Penerbit Universiti Malaysia Sabah (UMS)
Ground Floor, Library
Universiti Malaysia Sabah
Jalan UMS
88400 Kota Kinabalu
Sabah, Malaysia
Tel: +60 88 320 789
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EDITORIAL

Monkeypox: A Rising Threat

Sadia Choudhury Shimmi*

Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, 88400 Kota Kinabalu, Sabah, Malaysia

*Corresponding author's email: shimmi_cmc40@ums.edu.my

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Monkeypox (mpox) has recently emerged as a global health emergency. This zoonotic disease is caused by the monkeypox virus (MPXV), an enveloped double-stranded DNA virus belonging to the Orthopoxvirus genus in the Poxviridae family, which also includes viruses such as variola (smallpox), cowpox, and vaccinia. The monkeypox virus is part of the same family as the virus that causes smallpox. In 1958, two outbreaks of a pox-like disease occurred in colonies of monkeys kept for laboratory research in Denmark. It remains unclear what causes the disease, despite its name. African rodents and non-human primates might transmit the virus to humans, like monkeys. The first recorded human case of MPXV infection occurred in 1970 in the Democratic Republic of Congo (DRC), involving a nine-month-old child. After this initial case, the virus spread to several countries in Central and West Africa, where it became endemic. The spread of the virus has often been linked to travel or the importation of animals from these regions. A significant outbreak in the DRC in 1997 reportedly resulted in 88 infections and three deaths, all among children under the age of three.

In 2022, mpox spread globally, marking a significant shift in its epidemiology. Starting in May of that year, cases were reported in several non-endemic countries, including Sweden, Portugal, Austria, Italy, Germany, France, Germany, Belgium and Spain. Notably, most of these cases indicated a new pattern of transmission with no direct travel history to the endemic areas. As the outbreak progressed, numerous clusters and cases of mpox were

reported simultaneously across both endemic and non-endemic countries, covering vast geographical regions.

The global mpox outbreak a Public Health Emergency was declared by the World Health Organization (WHO) on 23 July 2022 which was International Concern. Between January and October 2022, WHO reported that mpox was in approximately 77,000 cases and 36 deaths from 109 countries. The majority of cases, over 65%, were reported in the Americas, with 32% occurring in Europe. Several mpox-related deaths were due to complications like encephalitis, particularly among immunocompromised patients.

In humans, the febrile rash illness as a first-ever case was reported in Indiana, Illinois and Wisconsin between the end of May and the beginning of June 2003. Prairie dogs (Cynomys) which were purchased recently and housed with recently shipping African rodents were the causes of mostly affected individuals. In April 2023, for the pet trade, these African rodents shipped to the United States were identified as the source of the infection.

From 2022, 1 January to 2024, 30 June, the total number of cases of mpox which were confirmed by the laboratory was 99,176, including deaths, 208 from 116 countries across all WHO regions, according to the United Nations Health Agency. WHO noted that, outside of Africa, "the outbreak continues at a low level of transmission" globally.

Globally, in June 2024 alone, a total of 934 new mpox cases were reported. The highest cases (567 cases) were in Africa. The second highest (175 cases) was in the Americas. Europe reported 100 cases, except for the Eastern Mediterranean region, the Western Pacific reported 81 cases, and Southeast Asia reported 11. During this period, 61% of the cases were reported by the African Region, 19% by the Americas, and European Region 11%.

According to the Africa Centres for Disease Control and Prevention (Africa CDC), in 2024, a total of 17,541 suspected and confirmed mpox cases (14,719 suspected and 2,822 confirmed) have been reported across the African continent. There were more cases of mpox in 2024 rather than in 2023 in African countries with 17,500 cases this year in contrast to approximately 15,000 in 2023. Most vulnerable groups are children, with around two-thirds of infections in the DRC occurring in individuals under the age of 15.

In Malaysia, from July 26, 2023, when the first case was detected to November 2023 when the last case was reported, the total number of cases was nine. The Health Ministry stated that in all cases, there was the involvement of high-risk activities among the affected individuals with fully recovered and no death was reported. "Based on our monitoring, no new imported mpox cases have been reported," the ministry said in a statement on August 15, 2024. The ministry also advised avoiding risky activities and maintaining a healthy lifestyle for those travelling to endemic and non-endemic countries.

Two distinct clades of the MPXV have been recognised: the Congo Basin clade (Clade I) and the West African clade (Clade II). In 2022–2023, the Clade IIb was the primary strain for the mpox global outbreak. In 2024, both Clade I and Clade II have been detected. The case fatality ratio for mpox in Africa is approximately 10% for the Congo Basin clade, with the highest mortality rates occurring in children and individuals without prior vaccination. Outside of Africa, the fatal Clade I was detected in a single patient in Sweden.

Mpox is transmitted to humans through infected animals, physical contact with an infectious person, or contaminated materials. In the current outbreak, most cases were reported among young men, with transmission primarily occurring through skin and mucosal contact during sexual

activities. The most commonly reported sexual orientation among affected individuals is men who have sex with men within connected social-sexual networks. Additionally, a higher prevalence of human immunodeficiency virus (HIV) infection has been reported among patients with mpox.

The incubation period of mpox normally ranges from 6 to 13 days. Although it may vary from 5 to 21 days. Mpox symptoms usually begin within a week after exposure, though they can appear anywhere from 1 to 21 days post-exposure. Mpox symptoms are generally milder than those of smallpox. Usual symptoms are a skin rash or mucosal lesions with 2 to 4 weeks duration, along with fever, low energy, muscle aches, headache, back pain, and obvious swollen lymph nodes.

However, classic mpox infection is divided into two stages: the prodromal stage and the rash stage. The prodromal stage lasts within 1 and 4 days and is characterized by symptoms such as fever (over 38.5°C), headache, sore throat, myalgia, fatigue, and lymphadenopathy. Lymphadenopathy is a key differentiating feature of mpox, distinguishing it from other diseases such as smallpox, chickenpox, hand-foot-and-mouth disease, or measles. Swelling of the lymph nodes may occur on either the bilateral or unilateral side of the submandibular, cervical, axillary, or inguinal regions.

In 1 to 3 days, the rash stage begins after the onset of fever. The rash typically first appears on the face and after that palms and soles to all parts of extremities. The lesions vary in size and shape from vesicles, macules, pustules, and papules to crusts, then scabs and eventually drop off as the skin heals. The rash generally concentrates more on the face (95%) and the palms and soles (75%) than on the trunk, displaying a centrifugal distribution. Skin lesions are often at the same stage of development (monomorphic). This disease affects the conjunctiva, cornea, oral mucosa, and genitalia.

However, in the recent global outbreak, the clinical features of mpox differ from those of previously reported classic cases. Patients are now exhibiting more mucosal lesions, which often localize in the genital, perineal/perianal regions, as well as on the eyes and in the mouth. The rashes may be confined to only a few lesions, may not always appear on the palms and soles, and may present at different stages of evolution. Notably, rashes may develop before the onset of typical prodromal symptoms, such as fever and fatigue. Anorectal pain and bleeding have also been frequently reported, making diagnosis challenging; therefore, a high index of suspicion for monkeypox is required in the current outbreak.

Mpox is generally a self-constraining disease, and its symptoms last from 2 to 4 weeks. Before the rash, from one day to 21 days, infected persons are contagious after the initial symptoms up to all skin scabs have fallen off. However, severe cases occur more commonly among immunocompromised individuals, children, and pregnant women. Complications of monkeypox can include secondary skin infections, keratitis, sepsis, bronchopneumonia, encephalitis, and which may lead to vision loss. Polymerase chain reaction (PCR) is the preferred laboratory test if symptoms are noticed. Specimens are collected from the rash including fluid, skin or crusts by robust swabbing for diagnosis. If no significant skin lesions are present, anal, rectal or oropharyngeal swabs testing is done.

The main principles of mpox management include providing supportive care, preventing complications, and controlling the outbreak. Many patients with mpox experience mild infections and recover without medical intervention. Infected patients should be isolated and adhere to infection control precautions until all skin lesions have dried and fallen off. During

isolation, supportive care-such as adequate hydration, nutritional support, antipyretics, pain control, and psychosocial support-should be provided.

Patients should be advised to stay away from picking or scratching skin lesions to prevent secondary infections. Topical antiseptics can be applied to excoriated skin lesions, and any skin infection or signs of sepsis should be monitored closely. Secondary skin infections should be treated with antibiotics, while warm sitz baths or topical lidocaine may be offered for symptomatic relief of anorectal or genital lesions.

Antivirals such as tecovirimat and brincidofovir, approved for the treatment of smallpox based on animal models and safety trials in healthy individuals, are also predicted to be effective against mpox.

Prevention remains crucial. Mpox is prevented by avoiding physical contact with infected individuals. Some countries approved vaccines and therapeutics that were developed for smallpox that can be used for mpox in certain circumstances. Immunization against mpox was previously achieved with smallpox vaccination. However, due to waning immunity and the cessation of vaccination efforts, mpox has emerged as the most prevalent orthopoxvirus following the eradication of smallpox. Currently, the World Health Organization (WHO) recommends the use of LC16 or MVA-BN vaccines, with the ACAM2000 vaccine as an alternative when the others are unavailable. For individuals at risk, such as close contacts of confirmed mpox cases or in high-risk groups, vaccination is helpful to prevent infection. However, mass vaccination is not yet recommended.

In Malaysia, the Ministry of Health (KKM) has integrated mpox monitoring into the MySejahtera application, amid the spread of this rare but potentially fatal disease in several countries. The health minister announced that the new feature on the government's mobile application includes alerts for travellers arriving in Malaysia from countries where mpox is endemic or where cases have been confirmed. The alert instructs travellers from these regions to monitor themselves for 21 days-the incubation period of mpox-and if they develop symptoms, try to find quick medical attention. The management of mpox follows established guidelines.

On August 14, mpox was again declared a public health emergency worldwide by WHO, just after 15 months the WHO previously declared mpox emergency on July 23, 2022. This declaration calls for global cooperation and resource allocation to enhance surveillance, treat infected individuals, and halt the outbreak. Diagnostics, surveillance, community engagement, and risk communication remain central to stopping the outbreak and eliminating human-to-human transmission of mpox in all contexts. Therefore, it is essential to be vigilant about the transmission, signs, and symptoms of mpox. We must protect ourselves, especially when in close contact with high-risk individuals or travelling to high-risk regions, to prevent this endemic disease from escalating into an epidemic or pandemic.

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ORIGINAL ARTICLE

Horizontal Inequality in Healthcare Utilisation in Rural Sabah, Malaysia

Adilius Manual[1]*, Mohd Yusof Ibrahim[2], Ho Chong Mun[3], Norazah Mohd Suki[4]

[1] Institute for Health Systems Research, National Institutes of Health, Ministry of Health Malaysia, Jalan Setia Murni U13/52, Seksyen U13 Setia Alam, 40170 Shah Alam, Selangor, Malaysia
[2] Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Jalan UMS, 88400 Kota Kinabalu, Sabah, Malaysia
[3] Faculty of Science and Natural Resources, Universiti Malaysia Sabah, Jalan UMS, 88400 Kota Kinabalu, Sabah, Malaysia
[4] Othman Yeop Abdullah Graduate School of Business, Universiti Utara Malaysia, 27b, Jalan Raja Muda Abdul Aziz, Chow Kit, 50300 Kuala Lumpur, Wilayah Persekutuan Kuala Lumpur, Malaysia

*Corresponding author's email: adilius.m@moh.gov.my

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ABSTRACT

Ensuring universal access to healthcare is essential for societal equity. However, significant inequalities exist within global healthcare systems, resulting in unequal access to services and divergent health outcomes. Socioeconomic inequity, poor living conditions, and inadequate healthcare infrastructure perpetuate poor health among poor communities. Despite greater healthcare needs, economically disadvantaged populations face substantial barriers to obtaining necessary services. This research evaluates the equitable aspect of healthcare utilisation in Sabah's rural areas to guide policy formulation. Nabawan, a rural area in Sabah with high poverty rates, was selected to assess income-related inequality and inequity in healthcare utilisation. Using the horizontal equity index and decomposition analysis, it was found that economic status significantly influences healthcare distribution, typically favouring the affluent. Central to this analysis is the concept of "equal treatment for equal need," ensuring individuals with similar healthcare needs receive similar care regardless of economic status. Results indicate that wealthier individuals are slightly more likely to utilise healthcare services, although the difference is minimal. To address disparities, enhancing targeted financial assistance programs like PeKa B40 could reduce out-of-pocket expenses for low-income households. Additionally, increasing healthcare funding for rural infrastructure and training local healthcare workers can ensure equitable access for all households.

INTRODUCTION

Ensuring universal access to healthcare is a cornerstone of societal fairness, echoing the principles outlined in the Universal Declaration of Human Rights by the United Nations (United Nations, 1948). Unfortunately, healthcare systems worldwide face significant inequalities, leading to divergent health outcomes and unequal access to services (Dickman et al., 2017; Guo et al., 2020; Mostafavi et al., 2020). The presence of socioeconomic inequity, substandard living circumstances, and insufficient healthcare infrastructure contribute to a continuous cycle of ill-health and increased rates of both mortality and morbidity among poor communities (Korda et al., 2007; Zhang et al., 2017). Ironically, economically poor populations have significant obstacles in obtaining necessary services, despite having larger healthcare need, whilst higher-income groups receive better treatment (Atun et al., 2016). This unequal access exacerbates poverty and ill-health, as impoverished households allocate a disproportionate share of their resources to healthcare expenses.

Furthermore, inequity or disparities persist not only between affluent and impoverished populations, but also within specific regions of countries (Atun et al., 2016; Ilinca et al., 2019). Rural, remote, and poor areas encounter unique challenges, exacerbating existing healthcare inequities. Addressing these disparities requires identifying and dismantling systemic barriers to equitable access. Horizontal equity, advocating impartial treatment based on "healthcare needs" rather than financial status, emerges as a crucial principle (Lu et al., 2007). It is imperative to focus on addressing underlying determinants such as economic status and health conditions.

While Malaysia has made significant strides towards universal healthcare coverage (Abu Bakar et al., 2019; Fadzil et al., 2020; Rannan-Eliya et al., 2016) adapting its system to mitigate financial barriers to essential services, the state of Sabah faces distinct challenges (Ali, 2010; Goroh et al., 2020; Oo Tha et al., 2020). With a disproportionately high poverty rate (Department of Statistics Malaysia, 2022c) and concerning health indicators, including elevated rates of infant and maternal mortality (Ministry of Health Malaysia, 2020) and an increased prevalence of communicable (Goroh et al., 2020; Naserrudin et al., 2023) and non-communicable diseases (Hanafiah et al., 2020), addressing healthcare disparities in the region is imperative.

Effective provision of healthcare, particularly in rural areas, is pivotal in mitigating health issues. All Malaysians have access to heavily subsidised public health facilities, but limited research has explored disparities in health service utilisation within economically underdeveloped regions. Therefore, there is a critical need for comprehensive studies to uncover barriers hindering equitable access to healthcare. This manuscript aims to assess the principle of "equal treatment for equal need" in the context of health service utilisation in economically underdeveloped rural regions of Sabah, identify primary barriers to achieving equitable healthcare utilisation, and provide supporting data for governmental policy formulation.

MATERIALS AND METHODS

This is a cross-sectional study that took place over a period of four months in Nabawan, a rural area in Sabah marked by high levels of poverty. This is a cross-sectional study conducted over four months in Nabawan, a rural area in Sabah characterised by high levels of poverty. Poverty is defined as the lack of sufficient financial resources to meet basic living standards. The poverty rate, indicating the percentage of the population living below the poverty line, has consistently ranged from 26% to 35.6% between 2016 and 2019 (Department of Statistics Malaysia, 2022a). Situated as one of Sabah's seven interior divisions, it boasts an

estimated population of approximately 32,309 as of 2020 (Department of Statistics Malaysia, 2022b). During data collection, face-to-face interviews were conducted with residents who had been in the locality for at least two weeks prior to the interview. All household members in the selected houses, including those without blood relations, were interviewed regardless of citizenship. Newborn babies less than two weeks old were also included as part of the household members. If an adult household member was deemed unfit for an interview due to frailty or mental incapacity, a proxy respondent was chosen to answer on their behalf. This proxy could be another household member or a non-household member familiar with the respondent's health-related matters. To maintain consistency within the study group, individuals residing in institutional settings such as school hostels were excluded.

The sample size was determined using a single percentage formula, with a precision of 5% and a confidence level of 95%. The population variance of 33.2% was accounted for, representing individuals seeking healthcare advice or treatment in Sabah within the last two weeks (Malaysia Ministry of Health, 2015b). Considering Nabawan's population of 32,309 individuals and a non-response rate of 20%, the desired sample size was calculated to be 414 respondents. Respondents were identified by dividing the research areas into Enumeration Blocks (EBs), recognized geographical entities by the National Statistics Department (Department of Statistics Malaysia, 2020a). A random sample of six EBs, totalling 96 random houses, was selected.

The study employed a questionnaire adapted from the Health Care Demand Module in the National Health and Morbidity Survey (NHMS) 2011 for its comprehensive content (Ministry of Health Malaysia, 2012). Prior to conducting interviews, all participants were required to provide consent in adherence to the guidelines set forth by the Medical Research Ethics Committee, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah (JKEtika 4/17(2)) and with a NMRR registration number 38145. Written informed consent was obtained from all research participants.

The interviews were conducted in Malay from February 23 to June 25, 2019. A locally hired translator was available to facilitate communication in other local languages if needed. Data entry was carried out using Epi Info version 7.2.2.6.

Dependent and Independent Variables

The dependent variable, healthcare service utilisation, was defined as having received any outpatient services within the previous two weeks or inpatient services within the past 12 months, irrespective of whether the visit was to a public or private health facility months (Ministry of Health Malaysia, 2012). Outpatient services include any medical consultations, treatments, or procedures that do not require an overnight stay, while inpatient services encompass any medical care that involves admission to a hospital at least one night (Aris et al., 2015). Meanwhile, independent variables were classified into two groups: need and non-need factors. Need factors encompassed gender, age, self-assessed health status, and daily functional limitations.

Gender and age are essential to horizontal equity analysis in healthcare because they directly influence healthcare needs and service use utilisation (Donnell et al., 2008). Gender affects needs due to biological differences, such as women's reproductive health and varying chronic condition prevalence. Age dictates healthcare at different life stages, from paediatric care for children to chronic disease management in middle age and intensive care for seniors (Kalseth & Halvorsen, 2020; Roth et al., 2022; Simons et al., 2023). Including these factors ensures healthcare access is evaluated based on true health needs rather than socioeconomic status.

Reported health status was assessed

using a Likert scale with response options ranging from "Very good" to "Very Bad," allowing respondents to classify their health as either positive (Very good, Good) or negative (Moderate, not good, Very Bad). Similarly, experienced activity limitations were measured by evaluating perceived restrictions in daily activities due to health conditions, also using a Likert scale. The response options included "Severe/unable to perform," "Moderate/mild," and "None," enabling respondents to categorize the severity of their limitations.

Non-need factors encompassed household income or socioeconomic status, education, and employment status. To determine socioeconomic status (SES), we followed World Bank guidelines by dividing household expenditure by household size, measured in adult equivalents according to the Organization for Economic Co-operation and Development (OECD) definition. The OECD definition is suitable because it accurately reflects household economic status by considering the differing resource needs of adults and children, ensuring comparability across studies (van Doorslaer et al., 2006). This method is widely recognised and utilised in socioeconomic analyses.

The calculation formula for adult equivalents (AE) in household h is represented as:

$$AE_h = (A_h + \alpha K_h)^{\theta}$$

(Organisation for Economic Co-operation and Development, 2008)

where,

AE_h is the adult equivalent in household h
A_h is the number of adults in household h
K_h is the number of children 0-14 years old
α (value is 0.5) is the "cost of children" and
θ (value is 0.75) reflects the degree of economies of scale.

After adjusting for adult equivalents, households were stratified into quintiles representing varying levels of economic status, ranging from the poorest to the most affluent. These quintiles were grouped into five categories, with quintile 1 representing the poorest 20% and quintile 5 representing the wealthiest 20% in Nabawan.

Statistical Analysis

The study investigated disparities in health services utilisation across various social demographics, employing both the Chi-square test and the Cochran–Armitage test. While the X^2 test was utilised to examine unordered categorical variables like employment status, the Cochran–Armitage test was applied to analyse ordinal variables such as age group, socioeconomic status, education level attainment, and self-assessed health status.

The concentration index (CI) was employed to gauge the extent of healthcare utilisation inequity linked to socioeconomic status. Further, it was decomposed to assess contributions from various components, encompassing both need and non-need factors. Additionally, the horizontal inequality (HI) index, factoring in health needs variations, was used to delineate healthcare utilisation inequity associated with socioeconomic status. The methodologies followed those outlined by Wagstaff et al. (1991). Wagstaff et al. (1991) examined various methodologies for measuring health inequalities, highlighting the significance of selecting appropriate metrics. They advocate for the slope index of inequality and the concentration index. These indices consider the entire population and accurately reflect socioeconomic disparities in health. The slope index measures the relationship between a health variable, such as the use of health services, and socioeconomic rank, while the concentration index evaluates how a health variable is distributed in relation to socioeconomic status, offering comprehensive insights into health inequalities.

Step 1: Health Services Utilisation Standardisation

The subsequent steps involved setting a benchmark for healthcare service utilisation. Initially, we calculated the distributions of actual service utilisation, expected service utilisation based on need, and standardised service utilisation based on need for each household income quintile. This allowed us to assess the distribution of service utilisation accurately, providing insight into the level of equity in healthcare distribution.

Predicted service usage, determined by "need variables," aimed to estimate the expected services required, distinguishing between situations of underuse and excess. Standardised service usage was employed to accurately evaluate the distribution of service utilisation, without factoring in variations in the distribution of health needs, in order to identify any inequities (Donnell et al., 2008). To compute the distribution of healthcare utilisation adjusted for need, considering its binary nature, we utilised a probit regression model in conjunction with an indirect standardization technique (Donnell et al., 2008; Zhang et al., 2022).

Step 2: Concentration Index and Decomposition

To assess socioeconomic disparities in service utilisation, we employed the concentration index (CI), a widely utilised metric in health economics research (Donnell et al., 2008). The CI ranges from -1 to +1, with zero denoting perfect equality and positive or negative values indicating disproportionate concentration of service utilisation among higher or lower socioeconomic strata, respectively (Xu et al., 2003). We calculated the CI using the formula:

$$C = \frac{2}{\mu} cov(h, r)$$

The *h* signifies the ranking of individuals regarding their utilisation of healthcare services, while *r* denotes the ranking of individuals based on their socioeconomic status, and μ represents the average level of healthcare utilisation across the population. Then, a decomposition analysis of the concentration index (CI) was undertaken to delineate the specific contributions of need variables and non-need factors to the socioeconomic inequity observed in service utilisation.

This analysis was facilitated through a probit regression model, expressed as (Wagstaff et al., 1991):

$$\gamma_i = \alpha + \sum_j \beta_j^m \chi_{ji} + \sum \gamma_k^n Z_{ki} + \varepsilon_i$$

In this equation, γ_i represents the likelihood of utilising health services, χ_{ji} stands for need factors, Z_{ki} stands for non-need factors, β^m_j and γ^n_k signify the effects of each variable, α serves as an intercept, and ε_i indicates the error term.

Subsequently, the decomposition of the CI is expressed as (Donnell et al., 2008):

$$C = \sum_j \frac{\beta_j^m \chi_j}{\mu} C_j + \sum_k \frac{\gamma_k^m Z_k}{\mu} C_k + \frac{GC_\varepsilon}{\mu}$$

In this equation, μ denotes the mean of *γ*, C_j and C_k represent the concentration index of χ_j and Z_k respectively, and GC_ε measure how much the error term *ε* contributes to the overall concentration index.

Step 3: Horizontal Inequity Index Calculation

Next, the horizontal inequity (HI) index was calculated and a positive HI indicates that individuals with high socioeconomic status are utilising more services than needed, while a negative HI implies that less affluent individuals accessing more services than needed (van Doorslaer et al., 2000).

$$HI = CM - CN$$

CM denotes the concentration index of actual

health service utilisation, and *CN* denotes the concentration index of the need-expected health service utilisation. *HI* lies in the range of (-2, 2), with a positive (negative) value indicating pro-rich (pro-poor) inequity (Lu et al., 2007).

All analyses were conducted using Stata version 18.0.

RESULTS

From the total of 438 respondents were interviewed, 21.2% (93) reported use of health care services. Based on Table 1, our analysis found notable associations between gender, age, and healthcare utilisation. Specifically, individuals aged 45–64, irrespective of gender, exhibited higher service utilisation compared to other age groups. Conversely, individuals aged 65 and older, regardless of gender, displayed lower service utilisation, ranging from 6.4% to 10.9%.

Self-assessed health emerged as a significant factor of healthcare utilisation. Individuals reporting very good health exhibited the highest service utilisation at 45.2%, followed by those reporting good health at 29.0%. Health limitations showed a significant association with healthcare utilisation. Individuals with severe or unable-to-perform health limitations had a service utilisation rate of 9.7%, those with moderate or mild limitations had a higher utilisation rate of 51.6%, while individuals reporting no health limitations had a utilisation rate of 38.7%.

Surprisingly, socioeconomic status did not demonstrate a significant association with healthcare utilisation. Utilisation across different socioeconomic quintiles ranged from 15.1% to 26.9%, with no discernible pattern based on socioeconomic status. Activity status showed as a significant association with healthcare utilisation. Employed individuals had an 8.6% utilisation, compared to 33.3% for self-employed individuals. In contrast, individuals not currently working exhibited the highest utilisation rate at 58.1%. This category also included children under the age of seven, who were automatically classified as not working. Only those aged seven to 17 were queried about their employment status, which encompassed any involvement in their parents' primary economic activities. Additionally, this group provided data on the number of household members dependent on others for financial support, either through employment or self-employment.

To explore the equitable aspect of healthcare utilisation, Table 2 illustrates the distributions of actual, need-expected, and need-standardised likelihoods of reporting healthcare utilisation, categorised by quintiles. These distributions are derived from predictive factors, including demographic variables, self-assessed health, and functional limitations of daily activities. Upon examining the actual distribution, there is a slight inclination towards favouring higher-income individuals and those in the poorest 20%. In contrast, the need-expected distribution shows a clear pro-rich bias. This means that the factors that determine healthcare needs-such as age, gender, and health conditions-are more common among wealthier people. Higher-income individuals often have better access to healthcare, allowing them to manage their health better, which affects their overall health conditions. Additionally, demographic factors like older age, which usually means higher healthcare needs, are more often found in wealthier groups because they tend to live longer and healthier lives. This connection between healthcare needs and higher income explains why wealthier individuals seem to need and use more healthcare, creating a pro-rich bias in the expected distribution of healthcare needs.

Consequently, the top two wealthiest segments of the population exhibit probabilities of reporting healthcare utilisation that are respectively 0.4% and 10.6% lower

Table 1: Social demographic characteristics, health status, and health services utilisation.

Variable	Number	Healthcare service utilisation		X2 or Z	p-value
		Number	Column %		
Need-factors Gender and age (years)					
Men				**17.19**	**0.004****
Less than 16	93	11	23.4		
16-34	50	11	23.4		
35-44	28	4	8.5		
45-64	40	15	31.9		
65-74	7	3	6.4		
Older than 74	5	3	6.4		
Women				**11.90**	**0.036***
Less than 16	78	13	28.3		
16-34	64	9	19.6		
35-44	18	3	6.5		
45-64	38	15	32.6		
65-74	15	5	10.9		
Older than 74	2	1	2.2		
Self-assessed health				**48.15**	**0.000*****
Very good	315	42	45.2		
Good	84	27	29.0		
Moderate/ Not good	33	20	21.5		
Very bad	6	4	4.3		
Health limitations				**51.97**	**0.000*****
Severe/unable to perform	14	9	9.7		
Moderate/mild	120	48	51.6		
None	304	36	38.7		
Activity Status				**7.12**	**0.028***
Employed	48	8	8.6		
Self-employed	101	31	33.3		
Not working#	289	54	58.1		
Education				**9.55**	**0.049***
Never attended schooling	36	14	15.1		
Completed primary	204	43	46.2		
Completed secondary	116	18	19.4		
Completed tertiary	22	3	3.2		
Children less than 7 y/o	60	15	16.1		

Notes:
1. # Children under the age of 7 were classified in this category. Those aged 7 to 17 were queried about their employment status, encompassing any involvement in their parent's primary economic activities.
2. Q = Quintile; y/o = years old
3. For non-ordinal categories like 'activity status,' the association was assessed using the chi-square test ($\chi 2$), whereas the remaining ordinal independent variables were examined using the Cochran–Armitage test (Z).
4. * $0.01 \leq p < 0.05$; ** $0.001 \leq p < 0.01$; *** $p < 0.001$

than expected given their need averages, compared to 15.8% lower in the poorest 20%. This highlights the disparity in healthcare utilisation based on socioeconomic status.

Following standardisation, the need-standardised distribution accentuates the pro-rich trend among the richest quintiles even further compared to the actual distribution. This disparity underscores the necessity for targeted interventions to address inequities in healthcare access and utilisation across socioeconomic strata. The p-value associated with the need-standardised utilisation of healthcare services evaluates the significance of the difference between the actual utilisation and the standardised utilisation, which adjusts for differences in healthcare needs across socioeconomic quintiles. A statistically significant difference p-value suggests potential inequity in healthcare utilisation even after accounting for differences in healthcare needs.

Table 2: Distribution of actual, need-expected, and need-standardised use of healthcare services.

Household Socioeconomic quintiles	Actual	Need-expected	Need-standardised
Poorest 20%	0.266	0.224	0.224
2nd poorest 20%	0.163	0.182	0.191
Middle	0.163	0.172	0.209
2nd richest 20%	0.230	0.229	0.206
Richest 20%	0.235	0.210	0.231
Standard error	0.053	0.052	0.024
t-ratio	0.268	0.544	0.304
p-value	0.053	0.052	0.024*

Notes:
1. The p-values for Actual, Need-Expected, and Need-Standardised columns represent the significance level for the respective variables.
2. * 0.01 ≤p < 0.05; ** 0.001 ≤p < 0.01; *** p < 0.001

Table 3 shows the decomposition analysis of the concentration index for healthcare utilisation in Nabawan, aimed at elucidating the underlying factors contributing to socioeconomic-related disparities in access to healthcare services. Among the need factors examined, age-sex groups exhibited a negative contribution of -0.007 (-42.7%), indicating a marginal alleviation of socioeconomic-related inequality associated with age and sex. Conversely, self-assessed health demonstrated a substantial negative contribution of -0.014 (-91.7%), underscoring its significant role in attenuating healthcare utilisation disparities across individuals with varying health perceptions.

Table 3: Decomposition of Concentration Index for health care utilisation.

	Absolute Contributions to concentration index	Percentage contributions
Need factors		
Age-sex groups	-0.007	-42.7
Self-assessed health	-0.014	-91.7
Functional limitations	0.009	57.7
Subtotal	-0.012	-76.7
Non-need factors		
Socioeconomic status	0.058	371.8
Activity status	-0.004	-24.0
Education	-0.014	-91.1
Subtotal	0.040	256.7
Residual	-0.014	-80.0
Total	0.014	
Horizontal Inequity Index	0.027	

Notes:
1. The p-values for Actual, Need-Expected, and Need-Standardised columns represent the significance level for the respective variables.
2. * 0.01 ≤p < 0.05; ** 0.001 ≤p < 0.01; *** p < 0.001

Interestingly, functional limitations displayed a positive contribution to the concentration index (0.009, 57.7%), suggesting a correlation between heightened limitations and increased healthcare utilisation, despite the overall negative impact of need factors on socioeconomic-related inequality.

Analysing non-need factors revealed varied influences on healthcare utilisation disparities. Socioeconomic status emerged as a notable contributor, demonstrating a positive impact (0.058, 371.8%) and emphasizing the pronounced effect of socioeconomic status on healthcare access. Conversely, both activity status and education exhibited negative

contributions, albeit to different extents (-0.004, -24.0% and -0.014, -91.1% respectively), suggesting a potential mitigating effect on healthcare utilisation disparities.

Furthermore, the positive horizontal inequity index (0.027) underscores residual inequality in healthcare utilisation, even after accounting for differences in healthcare needs. This finding highlights a persistent trend wherein individuals of higher socioeconomic status tend to exhibit greater healthcare utilisation compared to their counterparts of lower socioeconomic status.

DISCUSSION

Analysing income-related inequality and inequity in healthcare utilisation is essential for promoting social justice. It reveals disparities in access to essential services based on income levels (van Doorslaer et al., 2000). These disparities often lead to poorer health outcomes among marginalised populations and contribute to inefficiencies within healthcare systems. By identifying and addressing these disparities, policymakers and healthcare providers can develop targeted interventions to improve access to care for those with lower incomes, ultimately leading to better health outcomes, reduced economic costs, and a more equitable society founded on principles of fairness and ethical healthcare provision.

This paper presents a pioneering examination of income-related inequality and inequity in healthcare utilisation within a rural area of Sabah, Malaysia. Using the HI and decomposition analysis, it is evident that economic status significantly influences healthcare distribution in this region, typically favouring the affluent. For context, Van Doorslaer et al. (2000) analysed data from the early 1990s across ten OECD countries and found the HI for doctor visits ranged from 0.047 in the Netherlands to -0.010 in Germany, and for hospitalisations from -0.076 in Denmark to -0.047 in Switzerland. In comparison, Nabawan's HI for healthcare utilisation in 2019 was 0.027, similar to Sweden's 0.034 and more pro-poor than Denmark, Finland, the Netherlands, and the US from the 1990s. Additionally, Nabawan's HI is more favourable than Brazil's 0.037 (MacInko & Lima-Costa, 2012). Broader comparisons indicate that in rural Iran, the outpatient HI was 0.039 and the inpatient HI was -0.068 (Mostafavi et al., 2020), while in rural China, the outpatient HI was 0.029 and the inpatient HI was 0.16 (Guo et al., 2020). These disparities highlight the significant impact of economic inequalities on healthcare access across different healthcare systems and policies, underscoring the need for targeted interventions to improve equity in rural areas like Sabah.

The Universal Coverage Scheme (UCS) in Thailand was introduced in 2001 to make healthcare more accessible, particularly for the poor, by reducing financial barriers (Somkotra, 2011). The UCS includes a referral system ensuring access to necessary health services without prohibitive costs. After its implementation, the Health and Welfare Survey of 2005 reported that the HI for outpatient care was -0.067 and for inpatient care was -0.061, indicating a shift towards more equitable healthcare access (Somkotra, 2011). Before the UCS, healthcare utilisation favoured wealthier individuals due to high out-of-pocket costs. The UCS has reduced these financial barriers and aimed to standardise the quality of care across income groups by improving infrastructure, increasing the number of medical personnel in rural areas, and ensuring the availability of medications, thereby promoting horizontal equity in healthcare access.

Disparities in healthcare utilisation driven by non-need factors are predominant, with economic status, insurance coverage, and geographic location being primary contributors. In Nabawan, household socioeconomic status emerges as the most significant pro-rich contributor to inequality

in health service utilisation. The higher health service utilisation among affluent individuals can be attributed to their greater financial resources, better health literacy, geographic proximity to healthcare facilities, comprehensive employment benefits, cultural attitudes towards health, and potential response biases in data collection. Wealthier individuals generally have more disposable income, enabling them to afford healthcare services beyond the reach of lower-income groups, such as those not covered by public health systems, specialized care, and medications (Mackenbach, 2012). This financial capability significantly reduces barriers to healthcare access, resulting in higher utilisation rates among the affluent. Furthermore, higher education levels among wealthier people correlate with better health literacy, allowing them to understand the importance of healthcare, recognize symptoms early, seek preventative care, and navigate the healthcare system more effectively (Kickbusch, 2001; Nutbeam, 2000).

Affluent individuals often reside in urban or well-developed areas where healthcare facilities are more accessible and of higher quality, which minimises logistical challenges such as transportation issues or long travel times, barriers that are significant for those in rural or underdeveloped areas (Aday & Andersen, 1974; Feinstein et al., 2006). Additionally, many affluent people have jobs that provide comprehensive health insurance, significantly reducing out-of-pocket costs associated with healthcare services, and often covering preventative care, routine check-ups, and specialized treatments, thereby facilitating access to a wide range of healthcare services (Bodenheimer, 2005; Buchmueller et al., 2005).

Cultural differences also contribute, as wealthier individuals may place a higher value on regular check-ups and preventative care, which leads to higher healthcare utilisation among the affluent (Mechanic, 2002). The method of data collection via interviews could introduce response bias; wealthier individuals might be more likely to report their healthcare utilisation accurately, or there could be differences in how comfortable various socioeconomic groups feel about disclosing their health service usage (Sudman & Bradburn, 1974). This potential bias should be considered when interpreting the results. Collectively, these factors create a substantial disparity in healthcare access and utilisation between wealthier and lower-income groups, underscoring the need for targeted policies to address these inequities.

Income inequality remains significant in Sabah, and despite a noticeable decline in overall poverty rates over recent decades, rural areas continue to face higher poverty rates compared to urban areas (Ministry of Economy Malaysia, 2023), exacerbating healthcare access challenges. Sabah reports the highest poverty incidence in Malaysia at 19.5%, significantly surpassing the national rate of 5.6%, with rural areas bearing a disproportionate burden at 31.1% compared to 12.5% in urban areas (Department of Statistics Malaysia, 2020b). Additionally, Sabah has consistently high unemployment rates, ranging between approximately 5-8% over the past decade, about twice the national average. On top of that, the Institute for Public Health highlights Sabah as having one of the highest incidences of low health literacy among individuals aged 18 years and older (Institute for Public Health Malaysia, 2019). This combination of high poverty, high unemployment, and low health literacy, especially in rural areas, underscores the crucial link between socioeconomic factors and healthcare utilisation.

Geographic healthcare accessibility in Sabah presents a multifaceted challenge due to its diverse terrain, scattered population settlements, and infrastructure limitations. The state's expansive geography, encompassing remote rural areas and isolated islands, poses significant barriers to accessing healthcare services (Oo Tha Naing et al., 2020). Poor road

conditions and limited public transportation options further hinder healthcare access for remote communities (Ladin et al., 2020). The high prevalence of low-income households exacerbates these issues, as indirect costs like travel expenses can deter individuals from seeking necessary care. While urban centres like Kota Kinabalu may have relatively well-equipped healthcare facilities, rural and remote areas often face shortages of infrastructure, medical professionals, and essential supplies. Sabah's cultural and linguistic diversity adds complexity, as healthcare services may not always be culturally sensitive or accessible to indigenous populations (UN Permanent Forum on Indigenous Issues (UNPFII), 2015).

Accessing public hospitals can involve high fees, creating financial challenges, especially for low-income households. Specialist consultations range from RM 30 to RM 50, advanced diagnostic tests like MRI scans cost between RM 300 and RM 700, and surgical procedures vary widely, with minor surgeries around RM 100 and major ones potentially costing several thousand-ringgit (Governtment of Malaysia, 1951; Ministry of Health Malaysia, 2015). These costs, along with additional travel expenses, are particularly taxing for the low-income group. The combined financial burden of medical fees and travel can deter necessary care, explaining why Nabawan's HI tends to be more pro-rich, highlighting the need for targeted financial support and improved infrastructure to ensure more equitable healthcare access for all Malaysians.

The Malaysian government has taken proactive measures to improve healthcare accessibility, particularly in underserved regions like Sabah. Initiatives such as mobile clinics, flying doctor services (Koshy et al., 2013), 1Malaysia Clinics (Manual et al., 2014), the PeKa B40 Programme, and Skim Perubatan Madani (ProtectHealth, 2024) play a vital role. These efforts bring essential services to remote areas, making healthcare more affordable for vulnerable populations. By addressing both financial and logistical barriers, these programs aim to enhance healthcare equity and improve overall health outcomes in Sabah and other underserved regions.

Despite these initiatives, significant challenges persist in Sabah. Addressing these challenges effectively requires comprehensive strategies that encompass infrastructure development, capacity building for the healthcare workforce, health education programmes, and financial assistance initiatives. Only through such holistic approaches can equitably access to healthcare be improved for all residents of Sabah.

The "Residual" component in healthcare utilisation inequality analysis signifies the portion of the concentration index not accounted for by included variables, indicating unexplained disparities. Factors within the healthcare system itself, such as inefficient resource allocation and fragmented delivery systems, alongside cultural beliefs and social norms, contribute to disparities in healthcare access and utilisation (Zhang et al., 2022). Despite methodological limitations and variations in service coverage, this study illuminates disparities in healthcare utilisation within rural Sabah, emphasising the urgency of targeted policy interventions to rectify these inequities.

CONCLUSION

The expected utilisation of health services in Nabawan, based on standardised needs, is nearly equitable according to the horizontal equity index. This indicates that residents with similar levels of need for outpatient or inpatient care generally have equal access to healthcare services. Although wealthier individuals are slightly more likely to use these services, the difference is minimal.

Health service utilisation in Nabawan is generally better than in other rural areas

reviewed in the literature, indicating relatively good access to basic services. However, disparities may exist in the availability and quality of specialised care, such as cancer treatment, which often requires costly and time-consuming travel to urban centres. The variability in healthcare quality, with some clinics lacking resources for complex conditions, further exacerbates these issues. To address these disparities, comprehensive surveys and improved data collection methods are needed to accurately represent healthcare needs and service availability in Nabawan. This information will help policymakers and healthcare providers develop targeted interventions to enhance healthcare access and quality for all residents.

The horizontal equity index provides valuable insights for policymakers and healthcare stakeholders. It highlights areas where disparities in healthcare access exist and guides the development of targeted interventions to reduce these inequities, ensuring that everyone, regardless of socioeconomic status, has equitable access to healthcare services.

Effectively addressing these challenges requires a comprehensive approach. This includes developing infrastructure, training and deploying healthcare workers, initiating community outreach programmes, and fostering collaboration between government agencies, non-profit organisations, and local communities. By working together, we can ensure that all residents of Sabah have fair and equal access to the healthcare services they need.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethics approval was obtained from the Medical Research Ethics Committee, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah. The approval code is JKEtika 4/17(2). Written informed consent was obtained from all the participants.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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ORIGINAL ARTICLE

A Knowledge Assessment of the Surgical Safety Checklist among Operating Room Nurses in Malaysia

Khin Thandar Aung*, Nur Anis Sholehah Binti Mohd Asri

Critical Care Nursing Department, Kulliyyah of Nursing, International Islamic University Malaysia (IIUM), 53100 Kuala Lumpur, Selangor, Malaysia

*Corresponding author's email: khin_ta@iium.edu.my

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ABSTRACT

Surgical complications present a significant challenge worldwide. To address this issue, the World Health Organisation (WHO) introduced the Surgical Safety Checklist (SSC) as a means to decrease complications and fatalities during surgery. Nurses play a critical role in ensuring patient safety throughout the operation. A clear understanding of the checklist promotes effective communication within the surgical team, fosters a safety culture, and reduces complications. However, limited research has been conducted in accessing knowledge of operating room (OR) nurses regarding SSC, especially in the context of Malaysian healthcare. Therefore, this study was conducted to evaluate the level of knowledge of SSC among OR nurses in Malaysia. A quantitative approach with a descriptive design was used, involving ninety (90) OR nurses from Sultan Ahmad Shah Medical Centre (SASMEC@IIUM). The nurses completed a self-administered questionnaire and the results revealed good knowledge of the preoperative phase checklist (68.9%), intraoperative phase checklist (73.3%), and postoperative phase checklist (77.8%). However, a minority of nurses (around 20–30% across three different phases) needed improvement. This study suggests that the SSC has been effectively implemented at SASMEC@IIUM. However, it also emphasises the importance of ongoing education to ensure that all nurses have a thorough understanding of the checklist.

Keywords: *Surgical safety checklist, Operating room nurses, Awareness, Malaysia*

INTRODUCTION

Surgical procedures are essential to healthcare worldwide, but they come with risks. Each year, over 310 million surgical procedures are performed globally. There are varying estimates of morbidity and mortality, but recent data suggests that around 75 million patients experience postoperative complications, resulting in two million deaths annually. While surgeries are meant to save lives, complications can arise, with mortality rates ranging from 0.5% to 5% following major surgery, and up to 25% of patients experiencing complications after surgery (Abbott et al., 2018; Gong et al., 2021). These risks emphasize the need for patient safety measures in the operating room (OR).

One effective intervention to enhance surgical safety is the Surgical Safety Checklist (SSC). Checklists provide a simple and standardised approach to certain aspects of patient care. The World Health Organization (WHO) surgical safety checklist is the most commonly used checklist, consisting of 19 items across three domains: before anaesthesia induction, before surgical incision, and before the patient leaves the operating theatre. The "WHO Surgical Safety Checklist" is implemented globally to ensure patient safety during surgery and has shown potential in reducing surgical complications and mortality rates. The checklist improves patient safety, promotes interdisciplinary communication, and prevents avoidable complications by emphasizing existing safety procedures (Rego, 2019).

The SSC is a standardized tool that facilitates communication and verification of crucial steps throughout the surgical process, including the preoperative, intraoperative, and postoperative phases (Narayan, 2023). Studies have demonstrated that proper utilization of the SSC can significantly decrease surgical complications and shorten hospital stays (Barimani et al., 2020; Schwendimann et al., 2019).

The occurrence of surgical complications continues to pose a serious global concern, as preventable mistakes contribute significantly to illness and death (Dobson, 2020). The effectiveness of Surgical Safety Checklists (SSCs) in improving surgical outcomes and enhancing patient safety relies heavily on the understanding and proper execution by healthcare workers, including operating room (OR) nurses. The World Health Organisation (WHO) implemented the Surgical Safety Checklist to reduce the incidence of illness and death associated with surgical procedures. This is accomplished by establishing standardized safety checks that are performed before, during, and after surgery (Rego, 2019). However, obstacles to the implementation and regular use of SSCs may arise due to various factors, such as the level of knowledge and opinions held by operating room personnel (Wyss et al., 2023; Munthali et al., 2022).

Understanding the level of awareness among operating room nurses is crucial for several reasons. Firstly, nurses play a vital role in ensuring patient safety throughout the entire surgical process. Their knowledge and understanding of the SSC enable them to actively participate in completing checklists and raise any concerns as necessary (Chellam & Arulappan, 2023). Additionally, a comprehensive understanding of the checklist promotes effective communication among the surgical team, fosters a safety-oriented environment, and reduces the likelihood of errors (Abbott et al., 2022).

Previous research has highlighted the importance of support and active involvement from the surgical team, with nurses playing a critical role in the effectiveness of Surgical Safety Checklists (Urban et al., 2021). Despite confirming the benefits of SSCs, there is a lack of studies specifically examining the level of awareness among OR nurses regarding these checklists, particularly within the healthcare

system of Malaysia.

This study aimed to assess the knowledge level of operating room nurses at Sultan Ahmad Shah Medical Centre (SASMEC) in Pahang, Malaysia, regarding Surgical Safety Checklists. The findings will provide valuable insights into the current implementation status of SSCs within the hospital and guide specific initiatives to enhance their effectiveness in maintaining patient safety. Furthermore, the results of this study have the potential to inform legislative modifications and educational initiatives aimed at improving surgical safety measures in Malaysia.

MATERIALS AND METHODS

Research Methodology and Location

This study employed a quantitative, descriptive cross-sectional design. Data were collected from operating room (OR) nurses at Sultan Ahmad Shah Medical Centre (SASMEC), Pahang, Malaysia, between April and July 2023.

Sampling and Participants

The sample size for this study was calculated using Raosoft software. The recommended sample size was determined to be 90 participants from a total population of 117 OR nursing staff at Sultan Ahmad Shah Medical Centre (SASMEC), located in Kuantan, Malaysia. The calculation was conducted with a margin of error of 5%, a confidence level of 95%, and a response distribution of 50%.

The study's inclusion criteria consisted of OR nurses employed at SASMEC with a minimum of six months of experience, possessing any level of nursing-related education (diploma, degree, diploma with post-basic, degree with post-basic, master, and PhD), and expressing a willingness to participate in the research. On the other hand, the exclusion criteria included nurses who worked outside of SASMEC, individuals with less than six months of experience, those without a nursing-related educational background, and those who were not willing to participate in the study.

Data Collection and its Tools

The objective of this study was to assess the knowledge of the surgical safety checklist (SSC) among operating room (OR) nurses at SASMEC. Printed questionnaires in English were used for data collection. These questionnaires were adapted from the World Health Organisation's (WHO) surgical safety checklist (SSC), SASMEC's perioperative checklist, and guidelines provided by the Malaysian Ministry of Health (KKM) (Patient Safety Unit, Ministry of Health Malaysia, 2018). The questionnaire was designed to align with these sources and cover the preoperative, intraoperative, and postoperative stages of the surgical safety checklist. To ensure accuracy and relevance, a panel of experts, including an OR nurse educator, a surgeon, and a methodologist, thoroughly reviewed the questionnaire. A pilot test was conducted on a separate sample of twenty-seven (27) operating room nurses at a different hospital to assess the questionnaire's reliability. The internal consistency of the data was evaluated using Cronbach's Alpha coefficient, resulting in a value of 0.973, indicating a high level of reliability.

The survey instrument was divided into four sections. Part A collected information on the sociodemographic characteristics of the participants. Part B aimed to assess the level of knowledge among nurses regarding the preoperative phase checklist. This assessment utilised a Likert scale consisting of 10 items, with a score of 5 indicating strong agreement and a score of 1 indicating significant disagreement. The maximum score achievable for part B was 50. Part C investigated nurses' knowledge of the intraoperative phase checklist using a Likert scale consisting of 4 items with a maximum score of 20. Part D assessed knowledge of the postoperative checklist using a Likert scale consisting of 4 items, with a maximum score of 20.

The data collection process involved approaching OR nurses at Sultan Ahmad Shah Medical Centre (SASMEC) who met the specific inclusion criteria and obtaining the required sample size. After obtaining informed consent, the researchers provided a detailed explanation of the study and gave participants the choice to withdraw their participation. Subsequently, participants individually completed the entire questionnaire. Throughout this process, researchers were available to address any inquiries. Once completed, the surveys were collected, and participants were thanked for their participation.

Data Analysis

The data analysis was conducted using IBM SPSS Statistics version 27.0 software. Descriptive statistics were used to summarise the collected data. Total scores were calculated for Parts B, C, and D of the questionnaire, which assessed knowledge of the preoperative, intraoperative, and postoperative phases, respectively. A score of 48 or higher out of 50 on Part B indicated a high level of knowledge of the preoperative checklist, while a score below 48 indicated a need for improvement. Similarly, a perfect score on the 20-point Parts C and D indicated a high level of knowledge of the respective intraoperative and postoperative checklists, while scores below the maximum suggested areas for improvement.

Ethical Considerations

Before the study began, ethical approval was obtained from the relevant authorities at SASMEC and the IIUM ethical committee with reference number IREC 2022-KON/72. Participation was voluntary, and informed consent was obtained from all participants. The data's anonymity and confidentiality were ensured throughout the research process.

RESULT

Part I: Socio-demographic Data of Participants

The participants' socio-demographic characteristics were analysed to gain insights into the sample composition. Table 1 summarises the distribution of participants based on their age, gender, years of experience, and educational level.

Table 1: Sociodemographic data of participants (n=90)

Variables		Frequency (n)	Percentage (%)
Age	21-25 years old	5	5.6
	26-30 years old	15	16.7
	>30 years old	70	77.8
Gender	Female	73	81.1
	Male	17	18.9
Race	Malay	88	97.8
	Chinese	2	2.2
Marital status	Single	12	13.3
	Married	76	84.4
	Divorcee	2	2.2
Educational background	Diploma	69	76.7
	Diploma with Post-basic	14	15.5
	Degree	6	6.7
	Degree with post-basic	1	1.1
Years of working	6 months – 1 year	1	1.1
	1 year – 3 years	10	11.1
	>3 years	79	87.8

Most respondents were older than 30 years old, with 70 out of 90 respondents (77.8%). Out of these respondents, 73 (81.1%) were female, while the remaining respondents were male. Most of the respondents were Malay, accounting for 88 respondents (97.8%), with only two respondents being Chinese (2.2%). Among the respondents, 76 (84.4%) were married, outnumbering the single respondents (12 or 13.3%) and the divorced respondents (2 or 2.2%). In terms of educational background, most of the respondents (69 or 76.7%) held a diploma, while 14 respondents (15.5%) had a diploma with post-basic qualifications. Only 6 respondents (6.7%) possessed a degree certification, and there was only one

respondent (1.1%) who held a degree with post-basic qualifications. Additionally, just one respondent (1.1%) had been working as an OR nurse for 6 months to 1 year. On the other hand, many of the respondents (79 or 87.8%) had been working as operation room (OR) nurses for more than 3 years, with the remaining respondents having worked between 1 year and 3 years in this role.

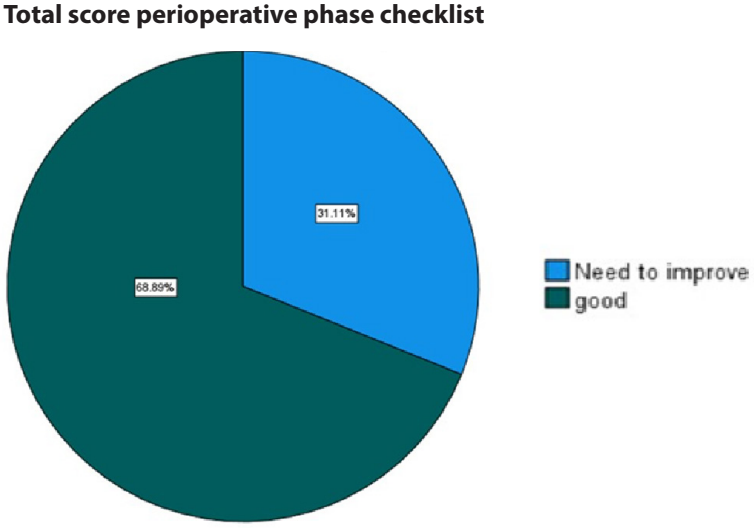

Figure 1: Level of knowledge on the perioperative checklist of SSC among OR nurses

Part II: Level of Knowledge on Preoperative Checklist of SSC

The participant's level of knowledge regarding the preoperative checklist of the Surgical Safety Checklist (SSC) was assessed. Table 2 presents the distribution of responses to the preoperative checklist items.

Table 2: The Level of Knowledge on the Perioperative Checklist of SSC

Variables	Total score	Frequency (n)	Percentage (%)
Knowledge of the OR nurse			
Good	48-50	62	68.9
Need to improve	10-47	28	31.1

The data showed that 62 (68%) of the respondents had a good understanding of the preoperative checklist for the Surgical Safety Checklist (SSC). However, 28 of them (31.1%) still needed to improve their knowledge regarding the preoperative checklist. It is shown in Figure 1. Overall, participants demonstrated a high level of knowledge when it came to the items on the preoperative checklist. The majority correctly identified important components such as patient identification, verification of the surgical site, and verification of consent. This indicates that they have a good grasp of the essential elements of the checklist.

Part III: Level of Knowledge on Intraoperative Checklist of SSC

The analysis also investigated participants' comprehension of the intraoperative checklist of the SSC. The responses to the items on the intraoperative checklist are presented in Table 3.

Table 3: The Level of Knowledge on the Intraoperative Checklist of SSC

Variables	Total score	Frequency (n)	Percentage (%)
Awareness of the OR nurse			
Good	20	66	73.3

Need to improve	4-19	24	26.7

According to the data, 66 respondents (73.3%) have a good understanding of the intraoperative checklist of the Surgical Safety Checklist (SSC), while 26.7% of the respondents need to improve their understanding. It is shown in Figure 2. Overall, the results show that participants have a strong understanding of the items on the intraoperative checklist, such as verifying essential equipment and communicating with the surgical team.

Table 2: The Level of Knowledge on the Perioperative Checklist of SSC

Variables	Total score	Frequency (n)	Percentage (%)
Knowledge of the OR nurse			
Good	20	70	77.8
Need to improve	4-19	20	22.2

Only 20 respondents (22.2%) needed improvement in their understanding of the

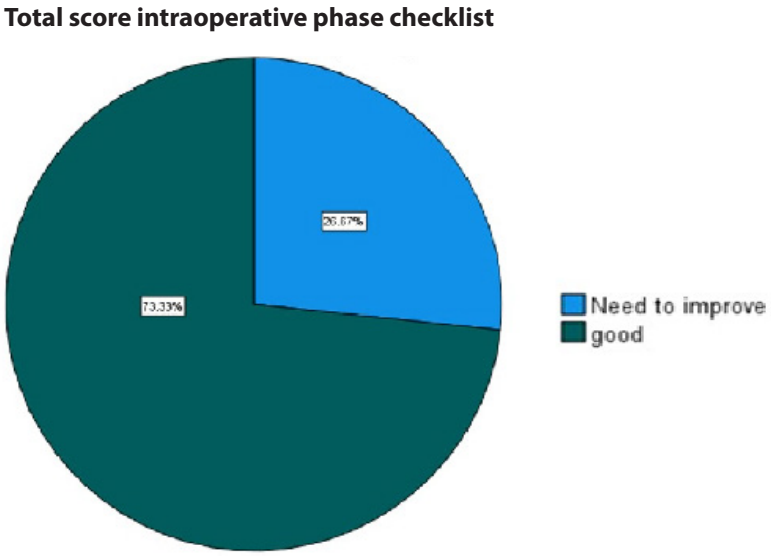

Figure 2: Level of knowledge on the intraoperative checklist of SSC among OR nurses

Part IV: Level of Knowledge on Postoperative Checklist of SSC

Lastly, the study assessed participants' understanding of the postoperative checklist for the Surgical Safety Checklist (SSC). Table 4 displays the distribution of responses to the individual items on the postoperative checklist.

Out of the 90 respondents, 70 (77.8%) of the OR nurses at Sultan Ahmad Shah Medical Center (SASMEC) demonstrated good knowledge of the postoperative checklist for the Surgical Safety Checklist (SSC).

postoperative checklist. Participants showed proficiency in items on the postoperative checklist, such as documenting procedures performed and communicating handover information. It is shown in Figure 3.

Overall, the findings suggest that operating room nurses at Sultan Ahmad Shah Medical Centre in Pahang, Malaysia, have a satisfactory level of knowledge about the components of the Surgical Safety Checklist. Specifically, 62% of OR nurses exhibited good knowledge of the preoperative checklist, 73.3% of the intraoperative checklist, and 70% of the postoperative checklist. However, a notable proportion of respondents need

improvement in their understanding across all phases, indicating the need for further education and training.

that adhere to the principles of simplicity, applicability, and measurement capacity to ensure comprehensive safety measures. The SSC should be utilised at critical points in the

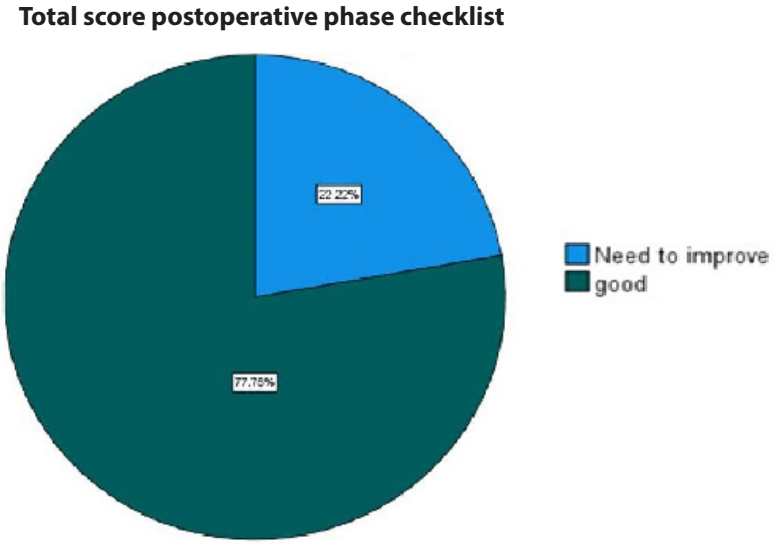

Figure 3: Level of knowledge on the postoperative checklist of SSC among OR nurses

DISCUSSION

Sociodemographic Characteristics of Participants

The sociodemographic characteristics of the participants revealed several notable trends. Firstly, the majority of respondents were over 30 years old, indicating an experienced workforce in the OR setting. This aligns with nursing, as age tends to correlate with experience. Additionally, the predominance of female respondents is consistent with the global nursing demographics, as women make up a significant majority of the nursing workforce. The sample was primarily Malay, reflecting the demographic makeup of Malaysia, where Malays are the largest ethnic group. Moreover, the high proportion of married participants suggests stability and commitment, which can positively influence their approach to patient care.

Level of Knowledge on Preoperative, Intraoperative, and Postoperative Checklists

The Surgical Safety Checklist (SSC) is a crucial tool for enhancing patient safety during surgery. It incorporates various components

surgical process, such as before the patient leaves the operating room before anaesthesia is administered, before the surgical incision, and at the end of the procedure (Bergs et al., 2014; Armstrong et al., 2022). By emphasising factors such as patient information, safety indicators, and early detection of adverse events, the SSC aims to ensure that the correct patient, surgery, and side are always considered. A systematic review by Treadwell et al. (2014) found that surgical checklists were associated with improved communication among operating staff, reduced surgical complications, and increased identification of potential safety hazards. To ensure the successful implementation of the checklist, strategies included involving institutional leaders as local champions, incorporating staff feedback for adaptation, and avoiding redundancy with existing information collection systems. Furthermore, Storesund et al. (2020) conducted a non-randomised clinical trial to evaluate the clinical effectiveness of the World Health Organisation's Checklists in Surgery and the Combined Surgical Patient Safety System. The results showed a decrease in the frequency of complications, reoperations,

and readmissions.

The evaluation process for OR nurses' knowledge level is meticulous and involves a specialised committee. This committee comprises experts in surgical nursing care, surgical nursing specialisation, patient safety, and surgery (Lim, et al., 2023). Working together, these professionals assess the proficiency and comprehension of OR nurses in various aspects of their discipline. The committee evaluates theoretical knowledge, adherence to safety protocols, and the ability to respond effectively in critical situations, as well as practical skills. By leveraging the diverse expertise of committee members, a comprehensive evaluation of OR nurses' knowledge base can be achieved, ensuring the delivery of high-quality care in surgical settings (Mamatkulov et al., 2022).

The study aimed to determine the level of knowledge that operating room (OR) nurses at Sultan Ahmad Shah Medical Centre (SASMEC) in Pahang, Malaysia, had regarding the Surgical Safety Checklist (SSC). The results indicate that the majority of OR nurses possessed sufficient knowledge about the SSC across all three stages: before surgery (68.9%), during surgery (73.3%), and after surgery (77.8%). This suggests that the implementation of the SSC at SASMEC has been successful and that OR nurses are well-informed about the essential measures required to ensure patient safety during surgical procedures. The nurses' strong understanding of safe surgical practices is particularly evident in their competence in key checklist items such as patient identification, surgical site verification, and communication with the surgical team.

In contrast, a study conducted by Sokhanvar et al. (2018) in Iran evaluated the attitude, awareness, and acceptability of the Surgical Safety Checklist (SSC) among operating room (OR) personnel. The study found that 92% of the participants were aware of the SSC, and 73.9% understood its objectives. Similarly, Delgado Hurtado et al. (2012) discovered that 93.8% of the 147 surgical personnel in Guatemala City were aware of the World Health Organisation (WHO) Surgical Safety Checklist, with 88.8% of them familiar with its objectives. Nevertheless, despite its widespread acceptance, there may be gaps in knowledge regarding the checklist's proper scheduling that could hinder its effective implementation.

The study's results indicate that a significant percentage of respondents (31.1% for preoperative, 26.7% for intraoperative, and 22.2% for postoperative) have a limited understanding of the Surgical Safety Checklist (SSC). To address these gaps, targeted educational interventions are necessary. It is recommended that individuals participate in refresher training programmes that are specifically tailored to each phase of the checklist. This approach will enhance comprehension and ensure consistent implementation throughout the surgical procedure. Swarjana et al. (2024) identified barriers to implementing the SSC, such as a lack of initiative, insufficient collaboration, and inadequate support from senior surgeons. They suggested that educational interventions effectively improve compliance with the SSC completion requirement. Additionally, Skarsgard (2016) emphasises the importance of consistently using the SSC in paediatric hospitals. According to the Paediatric Surgical Chiefs of Canada, this practice positively influences the safety culture in operating rooms. The study underscores the need for continuous monitoring and evaluation of OR nurses' knowledge regarding the SSC. Regular assessments can help identify emerging knowledge gaps and guide the development of tailored training programmes. Ultimately, this cyclical approach will foster a culture of patient safety in the OR by ensuring ongoing competence and adherence to the SSC.

This checklist is essential for ensuring that all necessary measures are taken to

protect the patient and prevent complications during surgery. Implementing surgical protocols has been proven to enhance communication among the surgical team, reduce complications, and identify potential safety hazards (Delisle et al., 2020). The focus is on improving clinical care and patient safety standards as protocols become more common in perioperative settings. The development and validation of a comprehensive surgical safety checklist aims to significantly decrease postoperative complications and streamline the verification process (Taplin et al., 2020). Additionally, operating room protocols like "time outs" provide an extra layer of assurance by allowing critical information to be re-verified before beginning surgical interventions (Birkmeyer, 2010; Poon et al., 2013). The implementation of these structured tools and protocols has enabled the OR nurses in SASMEC, Pahang, to deliver high-quality care and achieve optimal patient outcomes during the perioperative period.

Limitations

This study was limited by its cross-sectional design, which cannot establish causality. Additionally, the use of a convenience sample may not represent the entire population of OR nurses at SASMEC. Furthermore, the study's sample was limited to OR nurses at a single medical centre in Pahang, Malaysia, which may restrict the generalizability of findings to broader populations of OR nurses. Further research with a larger and more diverse sample population across various healthcare institutions is recommended to enhance the generalizability of the findings. Additionally, the study relied on self-reported data, which may be susceptible to response bias. Future research could incorporate objective measures of knowledge, such as direct observation of checklist use during surgical procedures, to provide a more comprehensive picture of OR nurses' adherence to the SSC.

Implications for practice and future research

The results of this study have important implications for both practice and future research in surgical settings. Firstly, the study highlights areas where nurses can enhance their knowledge and proficiency. This information can then be used to tailor targeted educational interventions aimed at improving nurses' understanding of the SSC components. Implementing continuing education programs, workshops, and simulation-based training sessions that specifically focus on checklist implementation and adherence could be highly beneficial in reinforcing best practices among nursing staff.

Additionally, the findings underscore the significance of organizational support and resource allocation to support ongoing training and professional development initiatives for nurses working in the operating room. Institutions should prioritize the provision of resources and infrastructure that foster high standards of patient safety and quality care delivery.

In terms of future research, it is important to explore the effectiveness of different educational interventions in enhancing nurses' adherence to SSC protocols, as well as their impact on patient outcomes. Conducting longitudinal studies that track changes in knowledge, attitudes, and practices following educational interventions would provide valuable insights into the sustainability and effectiveness of training programs.

CONCLUSION

Overall, this study offers valuable insights into the level of knowledge that OR nurses at SASMEC have regarding the SSC. While most nurses demonstrate a good understanding of the checklist, there is still room for improvement for a significant portion. To address this, we propose implementing targeted educational interventions and maintaining ongoing monitoring. This will ensure that all OR nurses possess the necessary

knowledge to successfully implement the SSC, ultimately enhancing patient safety during surgical procedures.

CONFLICT OF INTEREST

The authors have not declared any conflict of interest.

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REVIEW ARTICLE

Hesitancy to COVID-19 Vaccine Among Healthcare Workers: A Scoping Review

Azidah Abdul Kadir, Ng Ying Ying*

Department of Family Medicine, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, 15200 Kota Bharu, Kelantan, Malaysia

*Corresponding author's email: ngyingying@usm.my

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ABSTRACT

Vaccine hesitancy is a global concern and a significant barrier to vaccine uptake. Healthcare workers (HCWs) are more likely to contract COVID-19 and are the most trusted source of patient vaccine-related information. This scoping review summarized the rates of hesitancy against COVID-19 vaccine and booster dose among HCWs. We also explored the determinants of COVID-19 vaccine hesitancy and acceptance. The review method was described according to the PRISMA extension for scoping reviews. Literature search from PubMed, Google Scholar, Scopus, and EBSCOhost was conducted for studies published from January 2020 to August 2022. Themes were generated using inductive and deductive methods to identify the determinants for hesitancy and acceptance of COVID-19 vaccine. Overall, a total of 157 articles were included in this review. The hesitancy rate varied before the COVID-19 vaccination rollout ranging from 3.8% to 79.0%, while the hesitancy rate was 1.1%-73.3% in studies conducted after the vaccination rollout. Six themes were generated for hesitancy and seven themes for acceptance of COVID-19 vaccines. The themes identified for vaccine hesitancy and acceptance were trust issues in vaccines or authority; vulnerability to COVID-19 infection and its complications; information and misinformation; personal and past vaccine experience; religious and ethical; and socio-demographic and work factors. Professional integrity was the additional theme for vaccine acceptance. Safety and

effectiveness issues, trust, perceived risk of infection, and misinformation were among the common factors. It is recommended that the government develops strategies, guidelines, or more transparent information about the vaccines to improve the acceptance of COVID-19 vaccinations.

INTRODUCTION

The outbreak of the new coronavirus disease 2019 (COVID-19) has been declared a worldwide pandemic by World Health Organization (WHO) on 11 March 2020 (Cucinotta & Vanelli, 2020). The pandemic's catastrophic consequences underscore the urgent need for an effective vaccine. Vaccine hesitancy, defined as the delay in acceptance or refusal of vaccination despite availability, is a growing concern worldwide (Dubé et al., 2014). HCWs are at high risk of infection as their job requires close personal exposure to infected patients, which may contribute to the spread of the disease (Luo et al., 2021). When HCWs contract COVID-19, it reduces the workforce and further impacts the healthcare system significantly (Kwok et al., 2021). The WHO emphasizes that HCWs can be crucial to effective vaccination programs, as they can promote vaccinations and serve as role models for the general population (Avakian et al., 2022). Therefore, it is crucial to boost HCWs' confidence in vaccines and involve them in addressing vaccine hesitancy among patients.

The COVID-19 vaccines remain the best option for protection, although their efficacy varies by different strains of the virus (Haque & Pant, 2022). Recent literature has reported that the vaccination provides stronger, long-lasting protection against serious hospital outcomes and death than against symptomatic and asymptomatic illness (Hall et al., 2022). The emergence of new variants, new information, new policies, newly reported vaccine risks, and changes in policies have contributed to COVID-19 vaccine hesitancy (Larson et al., 2022). All these changes are amplified by the digital media platforms, leading to vulnerability of the hesitancy status over time (Larson et al., 2022). Therefore, continuous monitoring of HCWs' vaccine perceptions is pertinent to successful vaccination program and safeguards the healthcare system. Rapidly growing literature regarding COVID-19 vaccine hesitancy and acceptance in HCWs globally underscores the need to update the community and government on these issues.

To our knowledge, 13 reviews and meta-analyses (up until August 2022) had been conducted on COVID-19 vaccine hesitancy or acceptance among HCWs, with most searches completed by July 2021. Peterson et al. conducted a literature search in April 2022 but did not specify the number of studies. (Peterson et al., 2022). A review by Willems et al. reported on 22 cross-sectional studies and four qualitative studies, that did not specify the description of the continent or booster hesitancy rates (Willems et al., 2022). The highest number of studies reported about this issue was on 75 studies conducted through a literature search up to May 2021 (Crawshaw et al., 2022). A systematic review by Galanis et al. has highlighted that the acceptance rate of the COVID-19 vaccine among HCWs was 63.5%, which linked to factors like male gender, older age, white ethnicity, physician profession, higher education, comorbidities, previous flu vaccination, stronger vaccine confidence, positive attitude toward COVID-19 vaccine, fear about COVID-19, individual perceived risk about COVID-19, and contact with COVID-19 patients (Galanis et al., 2021).

We noted numerous studies have been done since 2021 that mandate an update on the topic. Furthermore, we pointed out that the attitude to the vaccine may fluctuate based on several factors that have not been discussed in previous reviews such as the period during vaccine rollout and towards the booster dose. As a result, we aim to conduct a scoping review to identify and summarize the COVID-19 vaccine and booster hesitancy

rates, as well as factors that could contribute to COVID-19 vaccine hesitancy or acceptance among HCWs worldwide. This review will help the health authorities and policymakers understand the hesitancy factors and strategy to improve acceptance of COVID-19 vaccination to enhance the vaccination uptake and future emerging vaccines.

We identify several objectives for this scoping review as follows:

- To map out the descriptions of the COVID-19 vaccine and booster hesitancy among HCWs in terms of types of studies, year of study, studies conducted during or before vaccine rollout, types of HCWs, and hesitancy rate.
- To explore the themes regarding determinants for hesitancy and acceptance of COVID-19 vaccines.

METHODS

The review method was described according to the PRISMA ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping reviews) (Tricco et al., 2018). This scoping review was performed following the methodological framework proposed by Peters et al. 2022 (Peters et al., 2021).

Eligibility criteria

Studies that met the following criteria were included. The inclusion criteria were:

1. Population: HCWs were defined as all individuals employed or studying in a healthcare setting, including physicians, nurses, and allied HCWs, as well as ancillary staff (e.g., healthcare administration and support staff).
2. Study design: cross-sectional, survey, cohort, qualitative.
3. Outcomes: studies examined attitudes/ hesitancy/acceptance of COVID-19 vaccination and analyzed related factors.
4. Language: English

The exclusion criteria were:

1. Population: the public or health-based students
2. Study design: an interventional study, review, systematic review and meta-analysis or scoping review
3. Outcomes: studies did not assess the COVID-19 vaccine attitude or related factors
4. Others: retraction, not peer-reviewed

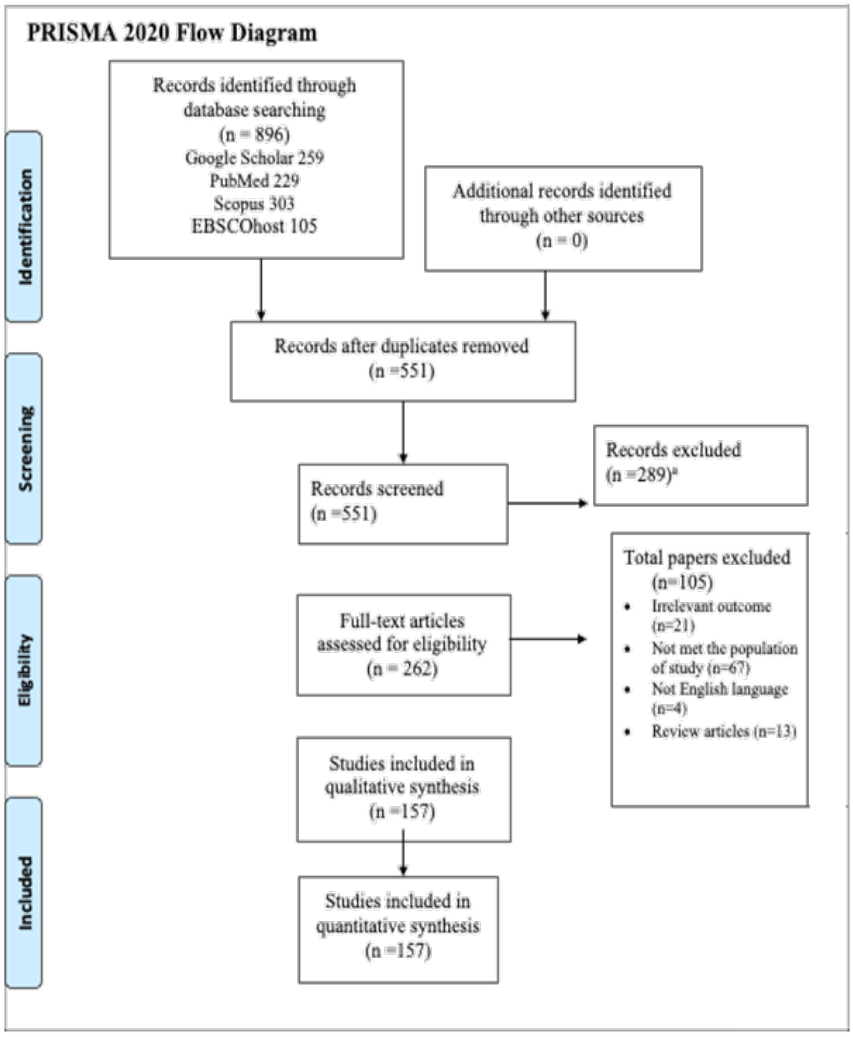
Search strategy

Four English databases (PubMed, Google Scholar, Scopus, and EBSCOhost) were comprehensively retrieved for relevant literature published from January 1, 2020 to August 25, 2022. Various combinations of topical terms were utilized as key phrases; COVID-19 or SARS-CoV-2 or 2019-nCoV AND healthcare workers or healthcare personnel or physicians or nurse AND vaccines or vaccination or immunization AND hesitancy or attitude or acceptance. The search strategy keyword was shown in Supplementary 1. Original articles written in English performed strictly among HCWs of both genders and containing sufficient data of interest were considered. Studies not reporting the rate of vaccine acceptance/hesitancy toward COVID-19 vaccination among HCWs were not included. Information on the author, publication year, country, data collection date, sample size, the population involved, vaccine availability, acceptance/hesitancy and prevalence rate towards COVID-19 vaccine, and associated factors were collected from studies of interest. "Hesitancy rate" was calculated considering both negative and uncertain answers showing refusal to be vaccinated (e.g., "probably no", "unlikely", or "somewhat disagree"). In that study which reported only vaccine acceptance rates, the vaccine hesitancy rates were calculated using the formula: (100%-vaccine acceptance rate%).

A two-step study selection was used in this review. The first exclusion by title and abstract was made by using the inclusion/exclusion criteria, by the author (NYY), then another researcher (AAK) retrieved the full text for further screening to determine whether studies to be included or excluded. Any divergences in screening results were resolved by discussion between reviewers and, if necessary, consulting a senior reviewer to reach a consensus. Endnote software was used to import search results from all databases and remove duplicates. After duplicate removal, the researchers screened titles, abstracts, and full text of the results independently. The differences were resolved through joint discussions or consultations with a third party.

Charting the data

A standardized set of data extraction items guided by our research question were developed and piloted at the protocol stage to extract key data from the included studies. Data extractions were performed by author AAK and checked by another author (NYY). Variables were extracted for the following key groupings: Title, article language, the author of article, publication date, publication year, country of studies, data collection period, sample size, study design, HCWs population, characteristics of participants, study tools, vaccine rollout, hesitancy or acceptance rate, booster hesitancy rate and determinants of hesitancy or acceptance.



[a] Did not evaluate COVID-19 vaccine-related hesitancy or acceptance among HCWs.

Figure 1: Flowchart of retrieval articles.

Data synthesis and analysis

Microsoft excel and word were used for the data extraction. Then these data were imported into NVIVO 12.0 and were coded according to the study objectives. Inductive and deductive methods were performed by AAK to get the themes and subthemes for the determinants of vaccine hesitancy or acceptance. Next, all the themes extracted from the papers were reviewed by the NYY. Both authors came to a consensus about the themes identified.

RESULTS

Our initial literature search yielded 896 articles from four databases (Figure 1). After removing duplications, 551 studies remained and were screened for titles and abstracts. Next, 289 articles were identified that fall in the category of unrelated and ineligible articles. The excluded publications consisted of 21 irrelevant outcomes, 67 studies that were not in the population of interest, 13 review articles, and four non-English full texts. As a result, the number of studies included was 157 publications.

Table 1 shows the descriptive characteristics of the studies. There were a total of 157 studies, with 147 cross-sectional studies (Supplementary 2) and ten qualitative or mixed-method studies (Supplementary 3). Most of the studies were conducted in 2021 (54.8%). Out of the 147 cross-sectional studies, 134 were studies on primary dose and 13 were studies including booster dose.

Survey characteristics

Forty-nine studies were conducted mostly before the COVID-19 vaccine's rollout, thus these studies analyzed people's attitudes and intentions about future COVID-19 immunizations based on the assumption that the vaccine would be accessible. Ninety-eight cross-sectional studies and 10 qualitative surveys were completed after the COVID-19 vaccine was available. Thirteen out of 98 cross-sectional studies conducted after vaccine rollout further studied the intention for booster doses among HCWs. Five cross-sectional studies involved collaborating with many countries, with the maximum number involving 91 countries (Askarian et al., 2022). The sample size for cross-sectional studies ranged from 108 to 85216 participants. There were various variances in the sample group, but most studies included physicians, nurses, or both. Clinical officers, lab technologists, allied health workers, administrative, and support employees were all included in the sample population of several studies.

COVID-19 hesitancy rates before and after vaccine rollout

Data on the COVID-19 vaccine hesitancy rate were retrieved from 147 cross-sectional studies. Based on our findings, 49 studies were conducted before the COVID-19 vaccination rollout and 98 studies were conducted during the vaccination campaign. The hesitancy rate varied before the COVID-19 vaccination rollout ranging from 3.8% to 79.0%, while the hesitancy rate was 1.1%-73.3% in studies conducted during the vaccination program rollout. Among highly hesitant countries included Egypt (74.0%-79.0%), Taiwan (76.4%), Congo (72.3%), and Cyprus (70.0%). In contrast, vaccine hesitancy was low in Italy (1.1%), followed by the United States (1.5%), Uganda (2.3%), and the Asia-Pacific region (3.8%).

Determinants and reasons associated with hesitancy to take the COVID-19 vaccine

We identified six themes and further sub-categorized them into 23 contextual determinants or reasons for COVID-19 vaccine hesitancy (Table 2). The themes were categorized into; trust issues in vaccines or authority, vulnerability to COVID-19 infection and its complications; information and misinformation; personal and past vaccine experience; religious and ethical; sociodemographic and work factors. Vaccine safety and efficacy seemed to be the most common factors found in many studies (Table 2). Concerns on the effect of the vaccine on

pregnancy, breastfeeding, and fertility were found in several studies (Fotiadis et al., 2021; Quiroga et al., 2021; Townsel et al., 2021; Xu et al., 2021). The socio-demographic factors for vaccine hesitancy revealed that females, younger age group, lower education level, and non-medical or clinical based paramedics were more likely to be hesitant. Most qualitative studies explored the attitudes and perceptions toward COVID-19 vaccines, with safety concerns and potential adverse effects being the most discussed aspects (supplementary data 3).

Table 1: Descriptive characteristics of the studies

Variables	Number of studies
Year of Study conducted	
2020	60
2021	86
2022	11
Continents of study	
America	34
Europe	36
Asia	58
Africa	23
Australia	1
>1 continent	5
Types of HCWs	
General	140
Physicians	4
Nurses	9
Pharmacists	3
Clinical Radiographers	1
Sample size	
<1000	88
1000-2000	31
2000-5000	25
5000-10000	7
>10000	6
Studies before vaccine rollout	49
Studies during vaccine roll-out (including booster dose)	108

Determinants and reasons associated with acceptance to take the COVID-19 vaccine

The themes for acceptance were almost the same for the hesitancy determinants but it had one different theme that was not found in the hesitancy factor (Table 3). This theme was professional integrity which included only one subtheme which was moral and work responsibility. A qualitative study and a few cross-sectional surveys identified this issue for HCWs' acceptance of the vaccine (Adejumo et al., 2021; Cuschieri & Grech, 2021; Kuter et al., 2021; Woodhead et al., 2021). Those HCWs who had a history of acceptance with the recommended vaccine, perceived higher susceptibility to infection, and having occupational risk are factors identified. Male, older age group, higher education level, having higher income, front liners and higher working experience are the socio-demographic characteristic of this group of HCWs.

Hesitancy to COVID-19 vaccine booster dose

A total of 13 studies were conducted to assess the hesitancy or acceptance of HCWs for the COVID-19 vaccine booster dose. The hesitancy rates for booster doses were ranged from 13.0% - 58.8%. The determinants for hesitancy to COVID-19 vaccine booster dose were almost similar to the determinants for hesitancy to the primary dose. Lower education level, younger age, concern about safety and side effects of the vaccine, and lack of information were all factors associated with hesitancy for COVID-19 vaccine booster dose. There were particularly some factors that were different from the factors associated with hesitancy to COVID-19 primary dose. These included post-vaccination adverse reactions that may cause work absenteeism, having received the Moderna vaccine (Chrissian et al., 2022), and increased fear of a second booster dose/new COVID-19 vaccine (Galanis, Vraka, et al., 2022). A study in Singapore found that if the HCWs were

Table 2: Themes for hesitancy factors to COVID-19 vaccines among HCWs.

Theme 1: Trust issues in vaccines or authority	
Concern about the safety and efficacy of the vaccines	(Adejumo et al., 2021; Amin & Palter, 2021; Aoun et al., 2021; Arslanca et al., 2021; Aurilio et al., 2021; Avakian et al., 2022; Baghdadi et al., 2021; Baynouna Al ketbi et al., 2021; Browne et al., 2021; Castañeda-Vasquez et al., 2021; Chrissian et al., 2022; Chudasama et al., 2022; Costantino et al., 2022; Cuschieri & Grech, 2021; Dara et al., 2021; Di Valerio et al., 2021; Dzieciolowska et al., 2021; Elharake et al., 2021; Fakonti et al., 2021; Haddaden et al., 2021; Hoffman et al., 2022; Hulen et al., 2022; Ilori et al., 2022; Kaufman et al., 2022; Kim et al., 2021; Manby et al., 2022; Mehta et al., 2022; Nasr et al., 2021; Ofei-Dodoo et al., 2021; Oliver et al., 2022; Otiti-Sengeri et al., 2022; Parente et al., 2021; Razzaghi et al., 2022; E. D. Robinson et al., 2021; Schrading et al., 2021; Shekhar et al., 2021; Unroe et al., 2021; Vignier et al., 2021; Yoon et al., 2022; Zaidi et al., 2021; Zaitoon et al., 2021; Zheng et al., 2021)
Concern about the effect of COVID-19 vaccines on fertility, pregnancy, or breastfeeding	(Aw et al., 2022; Dara et al., 2021; Fotiadis et al., 2021; Galanis, Moisoglou, et al., 2022; Ofei-Dodoo et al., 2021; Perez et al., 2022; Quiroga et al., 2021; Townsel et al., 2021; Xu et al., 2021; Yoon et al., 2022; Zheng et al., 2021)
Lack of trust in authorities such as health authorities, pharmaceuticals, or government	(Adejumo et al., 2021; Aemro et al., 2021; Al-Sanafi & Sallam, 2021; Alhassan et al., 2021; Alle & Oumer, 2021; Baynouna Al ketbi et al., 2021; Botwe et al., 2021; Dubov et al., 2021; Elharake et al., 2021; Famuyiro et al., 2021; Gadoth et al., 2021; Gogoi et al., 2022; Christopher Holzmann-Littig et al., 2021; Hulen et al., 2022; Qunaibi et al., 2021; Verger et al., 2021; Vignier et al., 2021; Woodhead et al., 2021; Yoon et al., 2022; Youssef et al., 2022; Zaidi et al., 2021; Zürcher et al., 2021)
Personal preference for a particular vaccine	(Al-Sanafi & Sallam, 2021; Dzieciolowska et al., 2021; Hulen et al., 2022; Quiroga et al., 2021; Sirikalyanpaiboon et al., 2021)
Theme 2: Vulnerability to infection and its complications	
Confidence in natural immunity or their immune system to protect them from COVID-19 infection	(Aemro et al., 2021; Amin & Palter, 2021; Bauernfeind et al., 2021; Castañeda-Vasquez et al., 2021; Chudasama et al., 2022; Costantino et al., 2022; Dubov et al., 2021; Galanis, Moisoglou, et al., 2022; Kara Esen et al., 2021; Kociolek et al., 2021; Mehta et al., 2022; Ofei-Dodoo et al., 2021; Pacella-LaBarbara et al., 2021; Qunaibi et al., 2021; Shehata et al., 2021; J. Wang et al., 2020; Yendewa et al., 2022; Zaitoon et al., 2021)
Perceived low risk of getting COVID-19 infection	(Aemro et al., 2021; Bauernfeind et al., 2021; Fotiadis et al., 2021; Pacella-LaBarbara et al., 2021; Sirikalyanpaiboon et al., 2021; Zürcher et al., 2021)
Confidence in complementary medi-cine	(Castañeda-Vasquez et al., 2021; Zaidi et al., 2021)
Fear of contracting COVID-19 infec-tion through the vaccine	(Barry et al., 2021; Chew et al., 2021; Kuter et al., 2021)
Theme 3: Information and misinformation	
Perceived inadequate knowledge about the vaccines	(Aemro et al., 2021; Alle & Oumer, 2021; Angelo et al., 2021; Aoun et al., 2021; Avakian et al., 2022; Baniak et al., 2021; Bauernfeind et al., 2021; Baynouna Al ketbi et al., 2021; Browne et al., 2021; Cuschieri & Grech, 2021; Di Gennaro et al., 2021; Dubov et al., 2021; Dzieciolowska et al., 2021; Gadoth et al., 2021; Christopher Holzmann-Littig et al., 2021; Kuter et al., 2021; Otiti-Sengeri et al., 2022)

Apprehension of social media negative stories	(Al-Sanafi & Sallam, 2021; Aw et al., 2022; Di Gennaro et al., 2021; Elkhayat et al., 2022; Christopher Holzmann-Littig et al., 2021)
Negative influence from surroundings such as family members, friends, or personal doctor	(Elkhayat et al., 2022; Christopher Holzmann-Littig et al., 2021)
Theme 4: Personal and past vaccine experience	
History of hesitancy with recommend-ed vaccines	(Adeniyi et al., 2021; Bauernfeind et al., 2021; Cuschieri & Grech, 2021; Famuyiro et al., 2021; Fotiadis et al., 2021; Christopher Holzmann-Littig et al., 2021; Kara Esen et al., 2021; Kim et al., 2021; Oliver et al., 2022; Qunaibi et al., 2021; Shallal et al., 2021)
Fear of injection	(Baghdadi et al., 2021; Ye et al., 2021)
Cost issue	(Adejumo et al., 2021; Parente et al., 2021)
Theme 5: Religious and ethical	
Spiritual and religious belief	(Alhassan et al., 2021; Elharake et al., 2021; Woodhead et al., 2021)
Disagree with mandatory vaccine	(Woodhead et al., 2021)
Theme 6: Sociodemographic and work factor	
Female	(Afzal et al., 2022; Al-Sanafi & Sallam, 2021; Askarian et al., 2022; Aw et al., 2022; Barry et al., 2021; Bauernfeind et al., 2021; Ciardi et al., 2021; Digregorio et al., 2022; El-Sokkary et al., 2021; Famuyiro et al., 2021; Grochowska et al., 2021; Janssen et al., 2021; Khamis et al., 2022; Kim et al., 2021; Kociolek et al., 2021; Li et al., 2021; Pacella-LaBarbara et al., 2021; Papini et al., 2022; Qunaibi et al., 2021; Shehata et al., 2021; Sun et al., 2021; M. W. Wang et al., 2021; Yilma et al., 2022; Zürcher et al., 2021)
Lower education	(Afzal et al., 2022; Al-Sanafi & Sallam, 2021; Askarian et al., 2022; Chrissian et al., 2022; Janssen et al., 2021; Li et al., 2021; Pal et al., 2021)
Younger age	(Aemro et al., 2021; Afzal et al., 2022; Aw et al., 2022; Bauern-feind et al., 2021; Browne et al., 2021; Chrissian et al., 2022; Ciardi et al., 2021; Digregorio et al., 2022; Gadoth et al., 2021; Hoffman et al., 2022; Janssen et al., 2021; Kara Esen et al., 2021; Kim et al., 2021; Mehta et al., 2022; Pal et al., 2021; Puertas et al., 2022; Qunaibi et al., 2021; Turbat et al., 2022)
Higher income	(Castañeda-Vasquez et al., 2021; Li et al., 2021; M. W. Wang et al., 2021; Zigron et al., 2021)
Presence of co-morbidity	(Chew et al., 2021; Dara et al., 2021; Suo et al., 2021)
Working in rural areas	(Shehata et al., 2021)
Non-medical or clinical based para-medics	(Abdulle et al., 2022; Afzal et al., 2022; Bauernfeind et al., 2021; Cuschieri & Grech, 2021; Gadoth et al., 2021; Gag-neux-Brunon et al., 2021; Kara Esen et al., 2021; Kim et al., 2021; Lataifeh et al., 2022; Li et al., 2021; Martin et al., 2021; Papini et al., 2022; Puertas et al., 2022; Razzaghi et al., 2022; Schrading et al., 2021; Shallal et al., 2021; Townsel et al., 2021; Turbat et al., 2022; Vignier et al., 2021)

Table 3: Themes for acceptance factors for COVID-19 vaccines among HCWs.

Theme 1: Trust issues in vaccines or authority	
Confidence in the safety and efficacy of the vaccines	(Abdulle et al., 2022; Adeniyi et al., 2021; Aemro et al., 2021; Alhassan et al., 2021; Aoun et al., 2021; Arslanca et al., 2021; Baghdadi et al., 2021; Baniak et al., 2021; Bauernfeind et al., 2021; Botwe et al., 2021; Browne et al., 2021; Castañeda-Vasquez et al., 2021; Chew et al., 2021; Costantino et al., 2022; Cuschieri & Grech, 2021; Dara et al., 2021; Di Gennaro et al., 2021; Elharake et al., 2021; Fakonti et al., 2021; Famuyiro et al., 2021; Fares et al., 2021; Fotiadis et al., 2021; Gadoth et al., 2021; Gagneux-Brunon et al., 2021; Galanis, Moisoglou, et al., 2022; Grochowska et al., 2021; Kim et al., 2021; Kuter et al., 2021; Laiyemo et al., 2022; Ledda et al., 2021; Mehta et al., 2022; Oduwole et al., 2021; Otiti-Sengeri et al., 2022; Parente et al., 2021; Puertas et al., 2022; Robbins et al., 2021; E. D. Robinson et al., 2021; Shekhar et al., 2021; Sirikalyanpaiboon et al., 2021; Sun et al., 2021; Verger et al., 2021; Xu et al., 2021; Yassin et al., 2022; Youssef et al., 2022; Zaitoon et al., 2021; Zigron et al., 2021; Zürcher et al., 2021)
Trust in authorities such as health au-thorities, pharmaceuticals, and gov-ernment	(Khalis et al., 2021; Kim et al., 2021; Malik et al., 2021; Maraqa et al., 2021; Puertas et al., 2022; Shallal et al., 2021; M. W. Wang et al., 2021; Youssef et al., 2022)
Theme 2: Vulnerability to COVID-19 infection and its complications	
High perceived susceptibility to infec-tion and occupational risk	(Adejumo et al., 2021; Angelo et al., 2021; Dzieciolowska et al., 2021; Elkhayat et al., 2022; Gagneux-Brunon et al., 2021; Ilori et al., 2022; Khalis et al., 2021; Kukreti et al., 2021; Li et al., 2021; Nasr et al., 2021; Noushad et al., 2021; Noushad et al., 2022; Otiti-Sengeri et al., 2022; Pacella-LaBarbara et al., 2021; Parente et al., 2021; Patelarou et al., 2021; Paudel et al., 2021; Shehata et al., 2021; Sirikalyanpaiboon et al., 2021; Štěpánek et al., 2021; Vignier et al., 2021; Yassin et al., 2022; Ye et al., 2021)
Protecting self and families	(S. W. C. Koh et al., 2022; Kuter et al., 2021; Nasr et al., 2021; Oliver et al., 2022; Sun et al., 2021; Yassin et al., 2022)
Self and family history of COVID in-fection	(Afifi et al., 2022; Aurilio et al., 2021; Bauernfeind et al., 2021; Boche et al., 2022; Fotiadis et al., 2021)
Theme 3: Information and misinformation	
Perceived adequate knowledge about the vaccines	(Abdulle et al., 2022; Afifi et al., 2022; Avakian et al., 2022; Baniak et al., 2021; Ciardi et al., 2021; Dara et al., 2021; Elkhayat et al., 2022; Fotiadis et al., 2021; Galanis, Moisoglou, et al., 2022; Kaufman et al., 2022; Khalis et al., 2021; Lataifeh et al., 2022; Maraqa et al., 2021; Nasr et al., 2021; Noushad et al., 2021; Patelarou et al., 2021; Sirikalyanpaiboon et al., 2021; Sun et al., 2021; Youssef et al., 2022; Zigron et al., 2021)
Media positive information	(Kim et al., 2021)
Gather information about vaccines from health authorities	(Barry et al., 2021; Sirikalyanpaiboon et al., 2021; Ye et al., 2021)
Theme 4: Personal and past vaccine experience	
History of acceptance with recom-mended vaccines	(Aurilio et al., 2021; Avakian et al., 2022; Bauernfeind et al., 2021; Costantino et al., 2022; Elkhayat et al., 2022; Fotiadis et al., 2021; Maraqa et al., 2021; Patelarou et al., 2021; Saddik et al., 2021; Štěpánek et al., 2021; Ye et al., 2021; Youssef et al., 2022; Zaitoon et al., 2021)

Getting back to normality	(Chew et al., 2021; Kuter et al., 2021; Noushad et al., 2022; Ofei-Dodoo et al., 2021; Woodhead et al., 2021; Yoon et al., 2022)
Theme 5: Religious or political issues	
Compatible with religious belief	(Oduwole et al., 2021; Wiysonge et al., 2022)
Political or policy influence (incen-tives, policies)	(Baynouna Al ketbi et al., 2021; Dubov et al., 2021)
Theme 6: Professional integrity	
Moral or work responsibility	(Adejumo et al., 2021; Aoun et al., 2021; Cuschieri & Grech, 2021; Digregorio et al., 2022; Gadoth et al., 2021; Hulen et al., 2022; S. W. C. Koh et al., 2022; Kukreti et al., 2021; Kuter et al., 2021; Ofei-Dodoo et al., 2021; Pacella-LaBarbara et al., 2021; Razzaghi et al., 2022; Saddik et al., 2021; Štěpánek et al., 2021; Wiysonge et al., 2022; Woodhead et al., 2021)
Theme 7: Sociodemographic and work factors	
Male	(Afifi et al., 2022; Aoun et al., 2021; Baynouna Al ketbi et al., 2021; Briko et al., 2022; Dzieciolowska et al., 2021; Elharake et al., 2021; Elkhayat et al., 2022; Gagneux-Brunon et al., 2021; Kaufman et al., 2022; Kuter et al., 2021; Maraqa et al., 2021; Noushad et al., 2022; Nzaji et al., 2020; Parente et al., 2021; Patelarou et al., 2021; Paudel et al., 2021; Saddik et al., 2021; Štěpánek et al., 2021; Unroe et al., 2021; Youssef et al., 2022)
Higher education level	(Adejumo et al., 2021; Dubov et al., 2021; Fotiadis et al., 2021; Kuter et al., 2021; Nohl, Afflerbach, et al., 2021; Parente et al., 2021; Paudel et al., 2021; E. D. Robinson et al., 2021; Shallal et al., 2021; Shekhar et al., 2021; J. Wang et al., 2021; Xu et al., 2021)
Older age	(Alle & Oumer, 2021; Baynouna Al ketbi et al., 2021; Briko et al., 2022; Dzieciolowska et al., 2021; Fossen et al., 2021; Gagneux-Brunon et al., 2021; Kaufman et al., 2022; Kuter et al., 2021; Nohl, Afflerbach, et al., 2021; Noushad et al., 2021; Noushad et al., 2022; Shaw et al., 2021; Shekhar et al., 2021; Sirikalyanpaiboon et al., 2021; Štěpánek et al., 2021; Unroe et al., 2021; Wiysonge et al., 2022; Ye et al., 2021; Zaitoon et al., 2021; Zürcher et al., 2021)
Higher income	(Dubov et al., 2021; Paudel et al., 2021; Shekhar et al., 2021)
Presence of co-morbidity	(Angelo et al., 2021; Dara et al., 2021; Elkhayat et al., 2022; K. Wang et al., 2020)
Living in major cities or working in tertiary centers	(Elkhayat et al., 2022; Kaufman et al., 2022; Malik et al., 2021)
Working as front liners	(Adejumo et al., 2021; Aw et al., 2021; Briko et al., 2022; El-Sokkary et al., 2021; Fossen et al., 2021; Malik et al., 2021; Nohl, Ben Abdallah, et al., 2021; Ye et al., 2021; Youssef et al., 2022)
Longer duration of service in health	(Adejumo et al., 2021; Baghdadi et al., 2021; Baniak et al., 2021; Fakonti et al., 2021; Fotiadis et al., 2021)

reluctant for the first dose, they were likely to be hesitant for the booster dose. However, in the same study, they reiterated that the HCW were less booster hesitant compared to the first dose (Sky Wei Chee Koh et al., 2022).

DISCUSSION

This review utilized the most current and comprehensive reviews of the literature on COVID-19 vaccine hesitancy and acceptance among HCWs globally, including 157 articles up to August 2022. A scoping review comprised 147 cross-sectional and ten qualitative or mixed-method studies. The proportion of HCWs intending to be vaccinated against COVID-19 varies widely across countries or regions, influenced by different demographics, beliefs, and other contextual factors (Aw et al., 2021). We identified six themes for hesitancy and seven for acceptance. The most common theme for hesitancy and acceptance was trust issues in vaccines or authority. Under this theme, concern about the safety and efficacy of the vaccines including concerns about the effect of the vaccines on pregnancy, lactation, or fertility was noted in many studies.

Overall, the COVID-19 vaccine hesitancy rate of HCWs before the vaccine's rollout was higher compared to during or after the vaccine campaign, which was 35.6% compared to 27.3% in mean. In this review, Egypt and Taiwan showed higher hesitancy rates up to 79.0% and 74.0% respectively before the COVID-19 vaccine was made available in the country (Fares et al., 2021; Kukreti et al., 2021). HCWs expressed mainly concerns about the fast-tracked development of a vaccine, a lack of enough clinical trials, and fear of side effects of vaccine (Fares et al., 2021). The acceptance of the vaccine was low also due to the safe status of COVID-19 infection as there were no community outbreaks during the study in Taiwan and therefore, the perception of infection with COVID-19 was low (Kukreti et al., 2021). The effect of time should be considered to rationalize the high hesitancy rate among HCWs in the early period.

COVID-19 vaccine willingness can vary substantially with time, experience with actual vaccine administration, and the ongoing pandemic's time-varying morbidity and mortality values (Sallam, 2021). A longitudinal study among HCWs in Los Angeles found that attitudes toward COVID-19 vaccines had improved and vaccine uptake intent had nearly doubled in the second survey after the vaccination campaign had been running for some time. It was believed as a result of increased communication about vaccine candidates, an increase in public confidence in leadership that oversees vaccine messaging, regulation, and supply, an increase in the number of cases and fatalities, evidence of the high efficacy and safety of COVID-19 vaccines and reports from others in their communities who had successfully vaccinated (Halbrook et al., 2022).

When the COVID-19 vaccine was made available, some countries still reported a high hesitancy rate. The two highest hesitancy rates recorded were 73.3% and 66.7%, respectively, from studies among Arabian HCWs and these studies shared almost similar factors which were fear of the side effects, not adequate time to verify the vaccine's safety, doubtful of the credibility of the producing company, and distrust of the healthcare policy applied by the government (Qunaibi et al., 2021). Another earlier study of Arab countries among the public showed that the low levels of COVID-19 vaccination uptake willingness despite the burden of COVID-19 was severe, due to the low trust in the government, low levels of education, and worse conspiracy beliefs (Sallam et al., 2021). The effects on public health could be imminent if these conspiracy theories are not refuted with fact-checking and evidence-based scientific knowledge.

Our analyses identified that confidence or concern in safety and efficacy of the COVID-19 vaccines, and trust in authorities

were the main top determinants for the attitude of HCWs toward the vaccines. These include factors on concerns about the short-term or long-term side effects, vaccine development velocity, and lack of trust in the information provided by the authorities. Among the fears were an allergic reaction, effect on the unborn child or breastfeeding baby, and long-term carcinogenic effects (Haddaden et al., 2021; Mehta et al., 2022; Ofei-Dodoo et al., 2021). Some of the HCWs delayed their vaccination, preferred to observe the effect on other people, and wait to review more data and gather more information before deciding on themselves (Peterson et al., 2022). On the other hand, the effectiveness and safety of the vaccines had an impact on the choice to adopt COVID-19 vaccination (Norhayati et al., 2021). An early study of the acceptance of a potential COVID-19 vaccine increased as the hypothetical effects of the vaccine increased (Alqudeimat et al., 2021).

The issue pertaining to trust in authorities are the vaccine development, approval process, pharmaceutical industry, conspiracy theories, and health politics (C. Holzmann-Littig et al., 2021). The same findings are noted globally either in the USA, the middle east, Africa, and European countries (Alhassan et al., 2021; Elharake et al., 2021; Verger et al., 2021). Lack of trust in the pharmaceutical companies or concerns about government-controlled of pharmaceutical companies in the epidemic raising vaccine hesitancy (Adejumo et al., 2021). Due to worries and memories of incidents involving inadequate unethical research practices, scepticism and eventually, they did not trust that vaccine development is salient (Woodhead et al., 2021). They believe that a short development period will affect vaccine efficacy and are concerned about the long-term side effects of the vaccine injection, leading then to doubt about the vaccine's ability to counter SARS-CoV-2 attack.

COVID-19 vaccine hesitancy was found to be higher in females than the male which is in line with other reviews (Caiazzo & Stimpfel, 2022; E. Robinson et al., 2021). Females expressed more concerns about vaccine safety and negative feelings toward vaccination were significantly higher among those attempting pregnancy, pregnant and lactating (Perez et al., 2022). In another study, pregnant ladies were six times more likely to delay their COVID-19 vaccination and twice as likely to refuse the vaccine (Townsel et al., 2021). Female has been also found to have lower vaccination rates in other vaccinations such as influenza and pandemic influenza vaccinations (Chor et al., 2009; Paudel et al., 2021). Males had better health-seeking behaviours and appreciation of advice about COVID-19 vaccines (Elkhayat et al., 2022). The association between younger HCWs and COVID-19 hesitancy may be due to increased public attention on prioritized vaccination among the elderly while on the other hand, older individuals perceived higher risk of serious illness and a greater likelihood of the presence of medical co-morbidities (Aw et al., 2021).

Perceived lack of information about the vaccines, apprehension over social media negative stories, and negative influence from others were factors derived from the theme of information and misinformation. The spread of misinformation regarding vaccines on social media had become a major driving factor in declining the recommendation by the government for vaccination (Nohl, Ben Abdallah, et al., 2021) According to a study, two-thirds of HCWs depend on television, internet, and friends who choose to refuse the vaccine (Elkhayat et al., 2022). These summarises the importance of social media as a primary source of information nowadays. Anti-vaccination groups employed all propaganda techniques on social media such as pressing issues on vaccine safety and inefficacy and blaming pharmaceutical companies for working illegally to produce vaccines in bulk (Sobkowicz & Sobkowicz, 2021).

We also identified that perceived

vulnerability to COVID-19 infection was a major factor. Perceived low risk for infection or confidence in natural immunity or their immune system were among the contextual factors. HCWs were hesitant to take the shot due to the belief that they were already naturally immune because they had contracted the disease at least once before (Shehata et al., 2021). Some of hesitant HCWs were confidence and preferred complementary and alternative medicines (CAM) use to protect them from COVID-19 infection (Castañeda-Vasquez et al., 2021). Examples of CAM used for COVID-19 prophylaxis include vitamins, minerals, herbal medicine, yoga and other dietary supplements. (Bulatova et al., 2022). On the other hand, those HCWs who perceived that they were at higher risk of contracting the infection would be more likely to be vaccinated (Pacella-LaBarbara et al., 2021; Yoon et al., 2022). Many studies have also shown that the high perceived susceptibility to infection increased the HCWs' intention for vaccination to protect themselves, their families, and patients (Kuter et al., 2021). Thus, it is not surprising that those working as front liners were more likely to accept the vaccines (S. W. C. Koh et al., 2022).

The emergence of SARS-CoV-2 mutants, waning immunity, and breakthrough infections prompted the use of booster doses of the COVID-19 vaccine to fight against the pandemic. In this review, the hesitance of the primary dose of the COVID-19 vaccine may predict the delay of booster doses of the vaccine. In a few observational studies, HCWs who were hesitant toward the first dose were three to five times more likely to be hesitant toward the booster doses (Sky Wei Chee Koh et al., 2022; Paul & Fancourt, 2022). The hesitancy to receive booster doses may also reflect a general hesitancy to receive other forms of vaccination (Pal et al., 2021).

Authentic information and tools to manage adverse events motivate vaccination. Misinformation causes vaccination hesitancy, which requires education of eligible vaccine recipients, according to previous studies (Muric et al., 2021; J. Wang et al., 2021). The significance of education aimed at HCWs has been underlined in studies of other vaccines (Song et al., 2006). Since the HCW vaccination coverage rate was suboptimal in other vaccines, some countries have implemented mandatory vaccination policies among HCWs for vaccine-preventable diseases (Maltezou et al., 2019). The USA had widely adopted a mandatory influenza vaccination campaign for HCWs in healthcare facilities with excellent results (uptake rate of >90%) (Black et al., 2018). This results in some counties implementing mandate COVID-19 vaccination for HCWs as well as public servants.

This review has limitations. First, our review excluded non-English published papers and may miss some relevant articles. Second, most included studies were cross-sectional studies with variable sampling methods, possibly explaining differing hesitancy rates even within a single country. Third, these studies mainly focus on vaccination intentions, which do not predict future vaccine uptake. Further studies should investigate the actual vaccine uptake, as intentions do not necessarily translate into action. Finally, some potential determinants of vaccine hesitancy were not mentioned due to data constraints.

CONCLUSION

We conclude that there were six themes for hesitancy and seven themes for acceptance of COVID-19 vaccines. Safety and effectiveness issues, trust, perceived risk of infection, and misinformation were among the common factors. The hesitancy rates varied across countries, gender, job position, education level, and economic status. Vaccine testing must adhere to worldwide best practices and remain unbiased by politics, religion, or race. Accurate information should be disseminated to build HCWs' confidence, as their encouragement is vital for patient vaccination. Knowing the reasons for vaccine hesitancy and acceptance

can guide and aid in the implementation of education and policy-level initiatives to improve future immunization programs.

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CONFLICT INTEREST

The authors do not have any conflict of interest to declare.

SUPPLEMENTARY DATA

Supplementary 1
Supplementary 2
Supplementary 3

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CASE REPORT

A Young Girl with Recurrent Fallopian Tube Carcinoma (FTC): An Interesting Case Report

May Zaw Soe[1]*, Elaine Chung[2], Suguna Subramaniam[3], Yeap Boon Tat[4], Abdel Mohsen Mohamed Ahmed Abdel Hafez[1], Tin Tin Thein[5], Ehab Helmy[1]

[1] Department of Obstetrics and Gynaecology, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Jalan UMS, 88400 Kota Kinabalu, Sabah, Malaysia
[2] Tawau Hospital, P. O. Box 67, 91007 Tawau, Sabah, Malaysia
[3] Department of Obstetrics and Gynaecology, Sabah Women and Children's Hospital, Locked Bag No. 187, 88996 Kota Kinabalu, Sabah, Malaysia
[4] Department of Medical Education, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Jalan UMS, 88400 Kota Kinabalu, Sabah, Malaysia
[5] Department of Pathology and Microbiology, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Jalan UMS, 88400 Kota Kinabalu, Sabah, Malaysia

*Corresponding author's email: maysoe@ums.edu.my

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ABSTRACT

Primary fallopian tube carcinoma (FTC) is a rare disease which frequently occurs among post-menopausal women. It is often grouped under the epithelial ovarian cancer umbrella. The treatment of choice is surgery and chemotherapy. Our patient was a young teenage girl with recurrent FTC who responded well to surgery and chemotherapy. We discuss on the epidemiology, risk factors, principles of management and prognosis of FTC.

INTRODUCTION

Primary fallopian tube cancer (FTC) is one of the rare gynaecological malignancies. It accounts for 0.14% to 1.8% of female genital malignancies (Kalampokas et al., 2013). From literature, FTC was identified in the year 1847 but the first case report was published in 1888 by Orthmann. Its global incidence is 0.36-0.41 per 100,000 women per year (Marina et al., 2019). Around 40% to 60% of the tumours that are classified as high-grade serous carcinomas of the ovary or peritoneum might have originated from the fimbriae of the fallopian tube (Kindelberger et al., 2007). It is often associated with chronic tubal inflammation, infertility, tuberculous salpingitis and tubal endometriosis (Mladenovic, 2009). Similar to ovarian cancer, breast cancer 1 (BRCA 1) and tumour protein 53 (TP53) mutations are associated with fallopian tube malignancies (Senturk et al., 2010).

We report a case of a young girl who presented to us with gross ascites. An elective right salpingo-oophorectomy was performed. The histopathological examination (HPE) confirmed the diagnosis of right FTC. Despite on adjuvant chemotherapy and regular follow up, recurrence occurred after three years of remission. An extrafascial hysterectomy, left salpingo-oophorectomy, omentectomy, appendectomy and lymphadenectomy were done and she responded well to another cycle of carboplatin based chemotherapy.

CASE PRESENTATION

A healthy teenage virgin girl (weight = 60 kg, height = 1.7 metres), presented to us with a history of progressive abdominal distension for four weeks. It was associated with loss of appetite and weight for two weeks. She attained menarche at 11 years old and her menstrual cycle was normal and dysmenorrhea was not associated. She denied any history of trauma or fever. Her family history was unremarkable of any malignancies.

On examination, she was alert, conscious but cachexic. Her blood pressure (BP), heart rate (HR), respiratory rate (RR) and oxygen saturation (SaO2) were 112/75 mmHg, 92 beats per minute, 22 breaths per minute and 97%, respectively. Clinical examinations were unremarkable except for massive ascites.

INVESTIGATIONS

Her full blood count (FBC) revealed haemoglobin (Hb) of 10.2 g/dl (normal values: 11-13 g/dl), total white blood cells (TWBC) of 9.8 x 109/L (normal values: 7-12 x 109/L) and platelets of 273 x 109/L (normal values of 150-450 x 109/L). Other biochemical parameters, including the arterial blood gases (ABG), liver and renal function tests were within normal ranges. Tumour marker values such as carbohydrate antigen (CA) 19-9, carcinoembryonic antigen (CEA), alpha fetoprotein (AFP), lactate dehydrogenase (LDH), beta hCG and oestradiol were within normal values.

However, the cancer antigen 125 (CA-125) was grossly elevated at 457.1 U/ml (normal values: 0-35 U/ml). Ultrasound abdomen and pelvis revealed severe exudative ascites with mesenterial pseudocyst and omental thickening suggestive of tuberculous peritonitis with less probable differential diagnosis of peritoneal carcinomatosis. Peritoneal tapping was done and straw-coloured ascites fluid was sent for cytology, acid fast bacilli (AFB) and bacterial culture. The results were no malignant cell seen, no AFB seen, no bacterial growth respectively. Her computed tomography (CT) of thorax, abdomen and pelvis (TAP) showed extensive amount of ascites fluid and a cystic and vascularised lesion superior to the right side of uterus measuring 4.2 cm x 4.4 cm x 4.2 cm with thick and enhancing wall. There was a small cystic lesion at the left para adnexa region measuring 2.9 cm x 2.5 cm x 2.2 cm suggestive of ovarian cystic mucinous adeno-carcinoma (Figure 1).

Figure 1: Coronal view of the pre-operative CT-TAP showing cystic and vascularised mass at the right adnexa.

DIFFERENTIAL DIAGNOSIS

Based on the clinical findings and scan, a diagnosis of a huge right ovarian tumour was made. Epithelial ovarian tumour was our provisional diagnosis since CA-125 was elevated (in cases of serous epithelial ovarian tumour) and cystic appearance of the tumour in CT scan. As she was not sexually active with no history of fever, thus, tubo-ovarian mass or abscess (pelvic inflammatory disease) was excluded. She also did not have any history of dysmenorrhea, thus excluding the diagnosis of endometrioma. Dermoid cyst was another possible differential diagnosis, but cystic appearance of the tumour was not the common feature of dermoid cyst in CT scan.

TREATMENT

Family conference was organised to discuss about prognosis of fallopian tube cancer and procedure before informed consent was taken. Our patient was posted for an elective laparotomy and excision of right ovarian tumour under general anaesthesia (GA). An epidural catheter was sited at the lumbar 3-4 (L3-4) vertebra level for perioperative analgesia. After that, she was intubated with a size 7 mm endotracheal tube and maintained with balanced anaesthesia which consisted of sevoflurane, morphine, rocuronium, and fractional of inspired oxygen (FiO2) of 40%. Ventilation was achieved with a peak airway pressure (PAP) of 29-32 cmH20 generating a tidal volume of 300-350 ml. Intraoperatively, uterus, the left fallopian tube and left ovary were noted to be healthy. However, there was a mass measuring 4.2 cm x 4 cm at the right fallopian tube with breached capsule, solid and irregular material seen. Tumour implant was seen at right anterior round ligament. Small intestine and large intestine were free from nodules. Urinary bladder was normal. A right salpingo-oophorectomy, omentectomy and peritoneal fluid sampling were performed and the samples were sent for histopathology examination (HPE).

She was extubated at the end of the surgery and sent to the intensive care unit (ICU) for monitoring and postoperative stabilization. She was discharged home four days later. Two weeks later, the HPE was reported as low-grade serous carcinoma of the right fallopian tube with invasive implant of low-grade serous carcinoma at the right round ligament. Theca luteal cyst was seen in right ovary. There was no malignancy on omentum. Our patient was staged with tumour, nodes, and metastasis (TNM) staging of TIIa N0 M0 which is equivalent to International Federation of Gynaecology and Obstetrics (FIGO) IIA. She was referred to the oncologist for chemotherapy.

Prior to chemotherapy, which commenced five weeks after the surgery, the CA-125 level decreased to 26.9 U/ml. She underwent a total of six cycles of paclitaxel-carboplatin chemotherapy regimen and the disease went into remission with the CA-125 level further dropped to 12.9 U/ml after six months. She was followed up closely in our gynaecological clinic with yearly CT TAP surveillance to monitor her disease progress.

However, three years later, she complained of intermittent lower abdominal pain for two months which was associated with loss of appetite and weight for one month. She also complained of abdominal distension with a left lower abdominal mass. On examination, the mass was palpable with a size of 8 cm x 6 cm at the left iliac fossa region. It was firm in consistency, mobile and there was no tenderness. Other clinical examinations were unremarkable. The CA-125 level was raised at 35.2 U/ml. Her repeated CT TAP showed an enlarged left adnexal complex cystic mass measuring 5.2 cm x 8.2 cm x 5.9 cm. However, there were no other localized or distant metastases seen (Figures 2 and 3).

Prior to elective operation, family conference was organised to discuss about fertility issue and advantages and disadvantages of hysterectomy. Family and

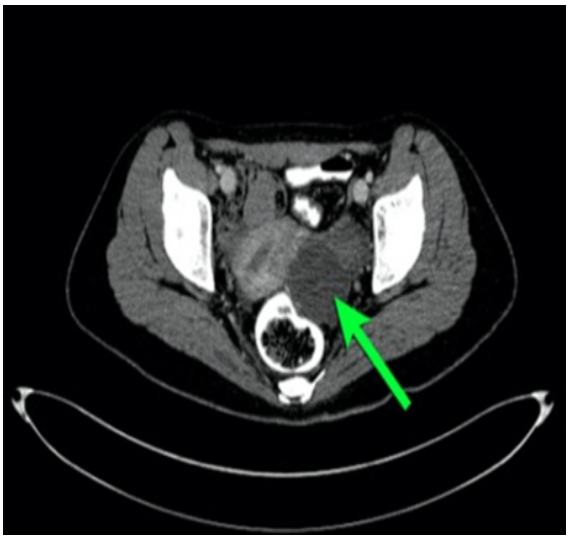

Figure 2: An axial view of CT-TAP which showed a huge left adnexal complex mass prior to the second surgery.

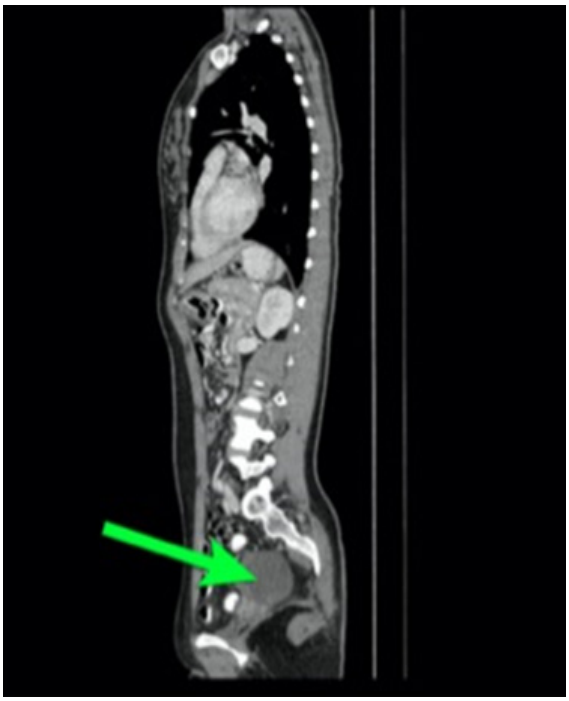

Figure 3: Sagittal view of CT-TAP prior to the second surgery.

patient were well aware of consequences and informed consent was taken. Oocyte harvesting was not done in view of the high cost. Genetic testing and molecular testing were not done pre-operatively. The option of hormonal suppression was not documented in case record She successfully underwent an elective laparotomy and left ovarian cystectomy three days later. The HPE of the left ovarian cyst revealed a serous borderline tumour with invasive implants on the uterus. A cycle of chemotherapy was urgently initiated after discussion with the oncologist. Recurrence of FTC was noted and the patient subsequently underwent an extra fascial hysterectomy, left salpingo-oophorectomy, omentectomy, appendectomy and lymphadenectomy.

OUTCOME AND FOLLOW-UP

Primary FTC is a rare gynaecological malignancy, accounting to 0.14-1.8 % of all gynaecological malignancy (Pectasides et al., 2006). It usually occurs in the postmenopausal elderly women with a mean age of 55 years old (age range of 17 to 88 years old) (Jeung et al., 2009). We believe that our unfortunate teenage girl was the youngest to be diagnosed to have stage II low grade serous FTC. Given the rarity of the disease, literatures on FTC and its recurrences are extremely limited.

The aetiology of this malignancy is unknown. High parity has been reported to be protective, and the use of oral contraceptives pills (OCP) decreases the risk of having FTC [Riska & Leminen, 2009). Theoretically, it is associated with tubal inflammation and endometriosis. Our patient was a nulliparous girl with no history of sexual relationship and nor consuming OCP.

Primary serous adenocarcinoma of the fallopian tube with papillary features is the commonest histological type. In comparison to ovarian carcinoma, FTC often presents at early stages, but with a worse prognosis. It is usually managed in the same manner as ovarian cancer (Kosary & Trimble, 2002).

In a retrospective study of 151 patients, it was shown that patients with FTC often present with abnormal vaginal bleeding (47.5%), lower abdominal pain (39%), abnormal watery vaginal discharge (20%) and a palpable pelvic/abdominal mass (61%) (Baekelandt et al.,

2000). Hundal et al. (2021) published a case of FTC in a pre-menopausal woman presenting with abnormal vaginal bleeding. Our patient initially presented with gross ascites, loss of appetite and weight. She did not present with abnormal vaginal bleeding and the other three symptoms. Therefore, it did not fit into the common clinical features of fallopian tube malignancy.

FTC can often be mistaken as tuberculous abdomen or salpingitis as tuberculosis is very common in Southeast Asian countries. Initial extensive radio-imaging results could not clearly reveal the diagnosis of primary FTC. The finding can mimic ovarian tumour, tubo-ovarian abscess in sonographic investigations (Haratz & Russell, 2004). Ovarian tumour diagnosis was even highlighted to be considered in the imaging report in our patient case. However, intraoperatively FTC diagnosis was confirmed. Therefore, operative findings predict the histological diagnosis, staging and prognosis (Berek et al., 2020).

Making the preoperative diagnosis could be assisted by measurement of the serum CA-125 levels, which is elevated in 80% of patients with FTC (Rezvani & Shaaban, 2011). It can also be raised in benign pelvic organ tumours such as endometriosis and pelvic inflammatory disease. Hefler et al. (2000) stated that median CA-125 level in patients with primary FTC preoperatively is 183 U/ml. Given that she was a young girl, FTC was not a likely diagnosis preoperatively despite a grossly elevated CA-125 (457.1 U/ml).

FTC spreads by local invasion, transluminal migration, lymphatics and haematological. It has a higher rate of retroperitoneal and distant metastases than that of epithelial ovarian cancer (Ajithkumar et al., 2005). The stage of disease at the time of diagnosis is the most important factor affecting the prognosis. Most of primary FTC cases are detected in early stage, in Taiwan >50% of patients are diagnosed to have stage I and II disease (Horng et al., 2014). Wethington et al. (2008) reported that the 5-year survival rate for Stage I tumour was 81%, and cancer-specific survival was 65% (95% CI 57–75) and 54% (95% CI 48–60) for Stages II and III, respectively. Survival rate for Stage I and II diseases has ranged from 37% to 95%, and for Stages III and IV tumour, from 0% to 69% (Wethington et al., 2008). The initial staging of our patient at the time of diagnosis was stage II, thus having a good survival rate.

The other clinicopathologic prognostic factors include residual disease after cytoreduction, the presence of ascites and the histological grading. Surgery is the treatment of choice, and the principles are the same as those used for ovarian cancer. Total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, selective pelvic and para-aortic lymphadenectomy for any stage for FTC is commonly performed. Lymph node metastasis is common in patients with FTC, therefore lymphadenectomy is highly recommended (Koo et al., 2011). However, due to the age of our patient and fertility sparing factor, a laparotomy right salpingo-oophorectomy and omentectomy were conducted.

Postoperative adjuvant chemotherapy with taxol and carboplatin every three weeks, which is similar to that used for ovarian carcinoma, is normally initiated (Katsumata & Noriyuki, 2013). Our patient was given a total of six cycles of carboplatin and taxol. She was under surveillance for three years while the disease was under remission.

The majority of patients who present with advanced epithelial cancers of the fallopian tube will relapse with a median time to recurrence of sixteen months (Berek et al., 2021). The treatment for relapse fallopian tube cancer is the same as relapse ovarian cancer. Parmar et al., (2003) proved that patients with a treatment-free interval of more than six months are considered to be platinum sensitive

and commonly treated with platinum-based chemotherapy. Genetic testing and hormonal suppression should be considered in serous fallopian tube cancer cases since this treatment option has been applied in ovarian cancer cases (Simpkins et al., 2013). The rationale of hormonal suppression is to stop production of oestrogen from the ovaries or to reduce circulating oestrogen levels. This option has been well used as treatment for breast cancer and ovarian cancer. Hormonal suppression can be either hormone or hormone blocking drugs, for example a) GnRH agonists (example goserelin, leuprolide) b) oestrogen receptor blockade (example tamoxifen) c) oestrogen synthesis suppression, aromatase inhibitors (example letrozole, anastrozole, exemestane) d) oestrogen receptor downregulation, oestrogen receptor antagonist (example fulvestrant) e) androgen receptor blockade, antiandrogen (example flutamide) f) progesterone receptor blockade, progesterone receptor antagonist (example mifepristone, medroxyprogesterone, megestrol acetate) (Li et al., 2021). Aromatase inhibitors can be used to treat low grade serous ovarian cancer. Genetic testing and hormonal suppression might be the treatment option for our patient however, both were not given as an option. In view of significant change in practice over the last 20 years, patients have been routinely followed up with regular CA-125 testing after completion of chemotherapy. Our patient had a relapse after three years. She was again given platinum-based chemotherapy for the recurrence and has been under regular monitoring of CA-125 level and CT TAP yearly. Currently, she is on remission and coping well.

CONCLUSION

- Fallopian tube malignancy is a rare gynaecological tumour which occurs commonly in post-menopausal elderly women.
- It is not uncommon for fallopian tube malignancy to occur in young patients.
- Common symptoms are lower abdominal pain, abnormal watery vaginal discharge and a palpable pelvic mass.
- The management of fallopian tube malignancy are surgery and chemotherapy.
- Hormonal suppression should be considered in fallopian tube malignancy which occur in young patients.

CONFLICT INTEREST

The authors do not have any conflict of interest.

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CASE REPORT

A Tenacious Trio of Retropharyngeal Emphysema, Pneumomediastinum and Subcutaneous Emphysema Secondary to Pulmonary Tuberculosis: A Case Report

Arjunkumar Asokan[1]*, Amalina Abu Othman[1], Stephanie Chen Kar Mun[1], Larry Ellee Nyanti[2], Nai Chien Huan[3], Hema Yamini Ramarmuty[3], Kunji Kannan Sivaraman Kannan[3]

[1] Department of Internal Medicine, Hospital Queen Elizabeth, 88400 Kota Kinabalu, Sabah, Malaysia
[2] Department of Medicine, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, 88400 Kota Kinabalu, Sabah, Malaysia
[3] Department of Respiratory Medicine, Hospital Queen Elizabeth, 88400 Kota Kinabalu, Sabah, Malaysia

*Corresponding author's email: rjunk28@gmail.com

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ABSTRACT

Retropharyngeal emphysema (RPE) is the presence of air in the retropharyngeal area. It may occur due to various etiologies or sometimes spontaneously due to an underlying lung pathology. This report describes a case of a 26-year-old gentleman with pulmonary tuberculosis on treatment who presented with acute breathlessness and dysphagia. His neck and chest radiograph showed retropharyngeal emphysema with pneumomediastinum and subcutaneous emphysema. This was further confirmed by a CT neck and thorax. The patient was managed conservatively with analgesia, antibiotics, IV corticosteroids and oxygen supplementation. Repeat chest radiograph after 17 days showed resolution of retropharyngeal emphysema. Clinicians should have a high index of suspicion for RPE in patients who present with unexplained acute breathlessness and dysphagia of a diseased lung.

INTRODUCTION

Retropharyngeal emphysema has classically been reported as a complication of pneumothorax (Suda et al., 2020), asthma exacerbation (Farouji et al., 2023), trauma to orofacial structures (AlEnazi et al., 2022), central venous catheters (Licina, 2019) or may occur spontaneously (Long, 2021). The trio of retropharyngeal emphysema, subcutaneous emphysema, and pneumomediastinum has

only been described once in literature as a complication of asthma (Khan et al., 2020). To our knowledge, this is the first report of this rare trio in a patient with smear positive pulmonary tuberculosis (TB).

CASE REPORT

A 26-year-old man with recently diagnosed smear positive pulmonary TB, presented to the emergency department with sudden onset breathlessness associated with dysphagia. He denied any stridor, chest pain, post-prandial regurgitation or recent trauma. He was compliant to his anti-tuberculosis medications which had been commenced two weeks prior. Vital signs revealed hypotension with a blood pressure of 92/60 mmHg, pulse rate of 100/min and oxygen saturation of 93% on room air. Physical examination revealed palpable crepitations extending from bilateral surfaces of the neck to the supraclavicular regions bilaterally. The trachea was centrally located, while lung examination was remarkable for coarse crepitations in the right upper lobe. There was no facial puffiness.

Chest radiograph showed subcutaneous emphysema with pneumomediastinum and diffuse patchy consolidations predominantly in bilateral upper lobes (Figure 1A). There was no evidence of pneumothorax. Patient was initially on 8L/40% venturi mask which was weaned to 3L nasal prong. Upper airway endoscopy by the otolaryngology team was unremarkable. Subsequently, lateral neck radiograph demonstrated a column of hypodensity anterior to the vertebral column, suggesting retropharyngeal emphysema (Figure 1B).

Computed tomography (CT) of the neck and

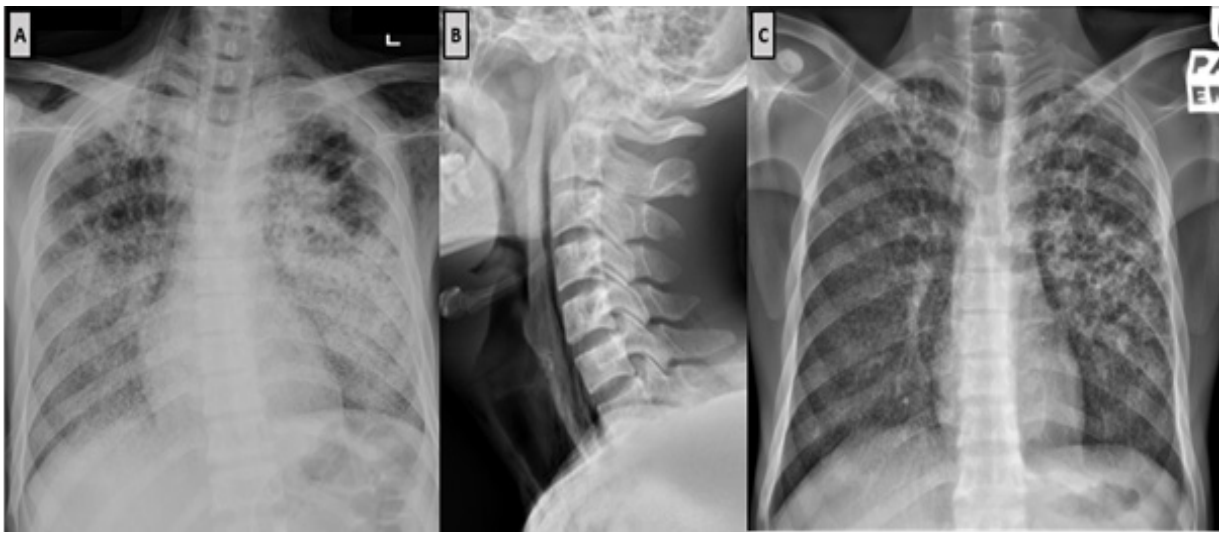

Figure 1: Anteroposterior chest radiograph on admission demonstrated consolidative and diffuse reticulonodular changes over bilateral middle to lower zones, with presence of linear lucency at the superior mediastinum extending to the mediastinal borders which is in keeping with pneumomediastinum. Subcutaneous emphysema can be elicited at the supraclavicular and upper chest region (A). Lateral cervical radiograph shows air at the retropharyngeal space extending to the skull base in keeping with retropharyngeal emphysema. There is also presence of prevertebral soft tissue swelling (B). Day 17 anteroposterior chest radiograph shows resolution of subcutaneous emphysema as well bilateral middle to lower zone consolidation and pneumomediastinum (C).

thorax showed retropharyngeal emphysema with extensive subcutaneous emphysema involving the neck spaces, left anterior chest, bilateral axilla and bilateral posterior chest; with extensive pneumomediastinum and pneumopericardium. There was no demonstrable tracheal wall, oesophageal wall, alveolar-pleural, or bronchial-pleural defects (Figure 2). He was referred to the Respiratory team, and a decision was made for conservative management as patient did not exhibit signs and symptoms of mediastinitis or worsening airway obstruction. On day four of admission, his subcutaneous emphysema reduced and dysphagia resolved with no intervention and he was able to be weaned off oxygen supplementation. His anti-tuberculous medications were continued. Repeat neck and chest radiograph on day 18, showed complete resolution (Figure 1C).

DISCUSSION

TActive pulmonary tuberculosis (TB) may be complicated by secondary pneumothorax with pneumomediastinum leading to subcutaneous emphysema (Vats et al., 2007), respiratory failure (Pratap et al., 2022), and even venous thromboembolism (Kumarihamy et al., 2015). In the absence of pneumothorax on chest radiograph, symptoms like acute dyspnoea and pleuritic chest pain warrant further urgent investigation.

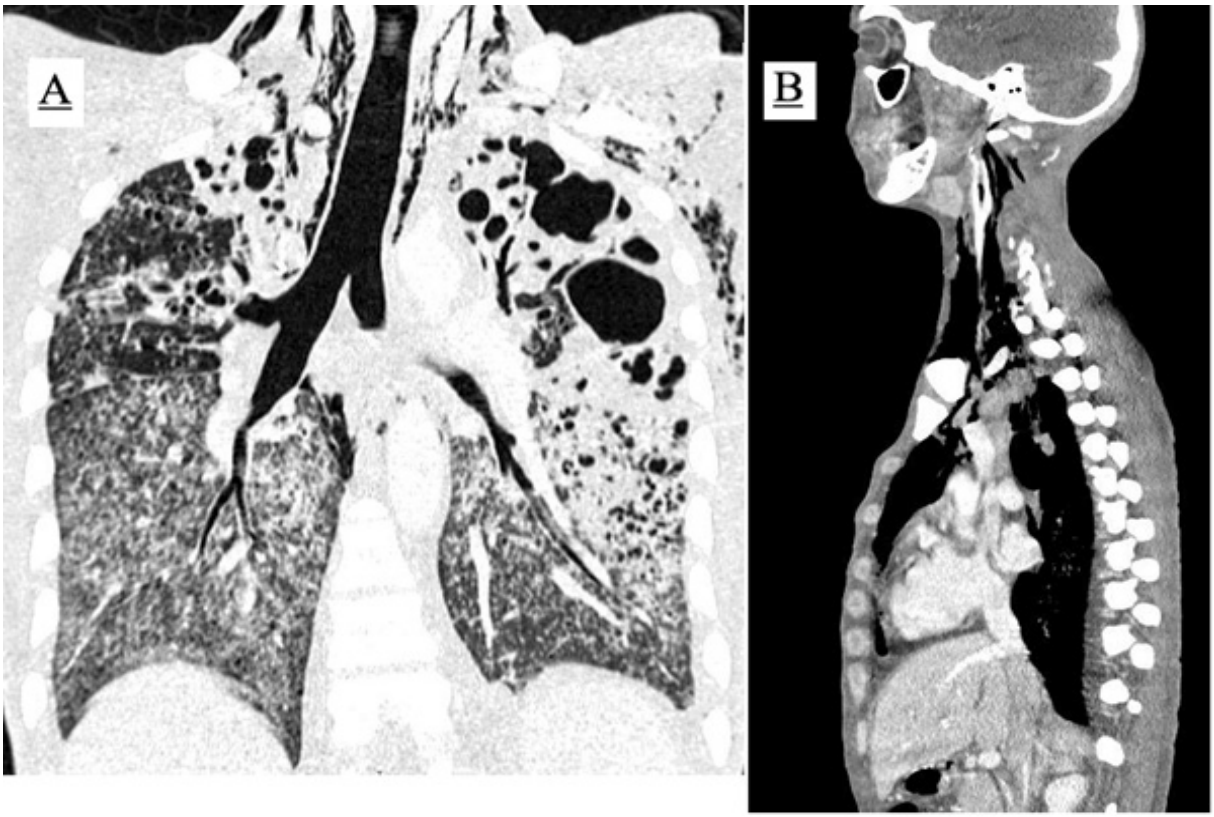

Figure 2: Coronal CT neck and thorax (multiplanar reformation) demonstrates pneumomediastinum with concurrent subcutaneous emphysema. Also seen are cicatrization collapsed with diffuse bronchiectatic changes and surrounding consolidation, predominantly at the bilateral upper lobes. Diffusedly scattered centrilobular nodules with tree-in-bud patterns in both lung fields (A). Saggital CT neck and thorax shows retropharyngeal emphysema and pneumomediastinum (B).

Spontaneous pneumomediastinum (SPM) is an uncommon entity describes as free air or gas present within the mediastinum that has occurred with no obvious cause. It has been associated with many conditions like bronchial asthma (Newcomb & Clarke, 2005), strenuous exercise (Partridge et al., 1997) and even

activities linked with the Valsalva manoeuvre (Panacek et al., 1992). Some mechanisms that could lead to SPM are: 1) rupture of alveoli; 2) bridge of mucosal or cutaneous barrier at the level of tracheobronchial tree or the oesophagus leading to gas/air leak into the mediastinum; 3) gas produced by organisms in the mediastinum (Murayama & Gibo, 2014).

According to Farouji et al. (2023), retropharyngeal emphysema (RPE) is a known complication of pneumomediastinum, along with subcutaneous emphysema. As described by Elnazi et al. (2022) and Long (2021), RPE is a condition that occurs when air is trapped in the retropharyngeal space and is postulated to be a sequela of abruptly increased intra-alveolar pressure leading to ruptured alveoli, thus allowing extraluminal gas to enter the retropharyngeal, space along the fascial planes.

The management of RPE is predominantly conservative unless the circulation or airway is compromised due to upper airway obstruction. In this situation an urgent tracheostomy is indicated or in more serious cases, a cardiothoracic consult is warranted (Suda et al., 2020). Otherwise, as described in several case reports such as Suda et al. (2020), Farouji et al. (2023), Elnazi et al. (2022) and Khan et al. (2020), conservative management involves supplemental oxygen, with some centres practicing administration of systemic corticosteroids. We opted for a conservative approach in our patient as there were no signs of respiratory distress. The absence of pneumothorax precluded the need for a chest drain. He was treated with supplemental oxygen, intravenous hydrocortisone 100mg thrice daily and intravenous amoxicillin clavulanic acid 1200 mg thrice daily for 2 weeks.

Literature has shown that dysphagia, more often than not, points towards oesophageal involvement or gastrointestinal tuberculosis (Paudel et al., 2021), (Rana et al., 2013). However, the acuteness of the presentation is a tell-tale sign that something more sinister and life threatening should be sought after. From this case it is evident that an acute history of sudden breathlessness coupled with dysphagia should raise a suspicion of RPE or subcutaneous emphysema (SE).

Subcutaneous emphysema is often observed in association with spontaneous pneumomediastinum, and both entities have been uncommonly reported in pulmonary tuberculosis (Saxena et al., 2013), (Phadte et al., 2018). In the absence of obvious traumatic causes, CT thorax is required to exclude concurrent spontaneous pneumomediastinum and the presence of caverno-pleuro-subcutaneous fistula; the latter was absent in our patient.

While non-traumatic subcutaneous emphysema is usually self-limiting due to reabsorption of air into capillaries by diffusion (Ahmed & Awouda, 2010), prompt intervention is required in non-resolving cases, to prevent hypoxia, cardiac tamponade and sudden death. The mainstay of treatment involves treating the underlying lung pathology. Additional high flow oxygen helps to correct hypoxia and denitrification of the blood which hastens reabsorption of subcutaneous air (Dixit & George, 2012). Other more invasive management methods include bilateral infraclavicular incisions down to the pectoralis fascia or placement of fenestrated catheters has been described in Saxena et al. (2013) and negative pressure wound therapy (Janssen et al., 2022).

CONCLUSION

In conclusion, a high index of clinical suspicion for TB must be kept in mind in patients from TB prevalent areas, presenting with dyspnoea and cough especially as it can be complicated with potential air leaks such as spontaneous secondary pneumothorax, subcutaneous

emphysema or pneumomediastinum. In cases of confirmed pulmonary TB presenting with sudden dyspnoea, the aforementioned potential air leaks must also be excluded. As displayed in this particular case, conservative management, when administered emergently can be effective in resolving air leaks at the same time avoiding unnecessary complications that may be posed with surgical intervention.

CONFLICT INTEREST

The authors do not have any conflict of interest.

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CASE REPORT

Cola Saves My Life: The Successful Treatment of Oesophageal Food Bolus Impaction with Cola Ingestion

May Honey Ohn[1]*, Khin Maung Ohn[2]

[1] St George's University Hospitals NHS Foundation Trust – Cardiology, Blackshaw Road London SW17 0QT, United Kingdom of Great Britain and Northern Ireland
[2] Department of Orthopaedic, Faculty of Medicine and Health Science, Universiti Malaysia Sabah, 88400 Kota Kinabalu, Sabah, Malaysia

*Corresponding author's email: mayhoney.ohn@gmail.com

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ABSTRACT

Oesophageal food bolus impaction, a serious emergency, requires immediate intervention to prevent complications, such as perforation or aspiration leading to respiratory distress. Severity varies based on factors such as the size of the ingested object, obstruction site, individual health, and the promptness of medical attention. In this report, we present the case of a middle-aged gentleman who presented to the emergency department with oesophageal food obstruction caused by a piece of lamb meat. Despite the initial unsuccessful attempts with first aid treatment, the patient experienced immediate relief of obstruction upon ingesting cola. This case highlights the potential use of cola in managing selected cases of oesophageal food impaction, offering a non-invasive alternative to oesophago-duodenoscopy. While cola emerged as a promising intervention in this case, its broader applicability and safety warrant further investigation through controlled trials. Establishing judicious cola use guidelines alongside traditional interventions can enhance patient care and safety.

INTRODUCTION

Oesophageal food bolus impaction is a frequently encountered scenario in the emergency department. In adults, it is predominantly unintentional, constituting approximately 95% of cases (Mosca et al., 2001). The presentation of this condition can vary significantly, ranging from individuals who recover without intervention to those

experiencing severe aspiration and imminent airway compromise leading to a peri-arrest state or oesophageal perforation. The management of this condition is diverse, and most of the oesophageal food bolus impaction relieves spontaneously (Chen & Beierle, 2001). Less than 20% necessitate endoscopy, and less than 1% undergo surgical intervention (Eisen et al., 2002). Traditional management strategies for oesophageal food bolus impaction involve the Heimlich manoeuvre, manual removal of foreign body, or endoscopic procedures such as oesophagoduodenoscopy. Here, we present an intriguing case in which cola consumption resulted in the immediate resolution of oesophageal food bolus impaction caused by a chunk of lamb meat.

CASE PRESENTATION

A 40-year-old gentleman with no prior medical history presented to the emergency department with food obstruction attributed to a 1x1 cm sized piece of lamb meat in his mid-oesophagus level. The patient had attempted various methods, including drinking water, juice, and consuming a banana, all of which induced vomiting but failed to dislodge the obstruction. First aid measures, including the Heimlich manoeuvre, proved ineffective in relieving the obstruction. Physical examination revealed no signs of airway distress. A plain radiograph showed no evidence of a bony foreign body obstruction in the digestive tract.

Following initial unsuccessful attempts to alleviate the obstruction, the medical team considered the administration of Glucagon and hyoscine butylbromide. Upon contacting the on-call gastroenterologist team, it was suggested to arrange an urgent oesophagogastroscopy procedure. However, before proceeding with these interventions, a trial of regular cola consumption was attempted. Remarkably, the patient reported immediate relief, with the oesophageal food obstruction being dislodged. Subsequent reassessment confirmed the complete resolution of the food obstruction in the oesophagus, resulting in a significant improvement in the patient's condition. Consequently, the patient was discharged home.

DISCUSSION

The successful resolution of acute oesophageal food impaction with cola consumption in our patient raises several interesting considerations and prompts further discussion. Acute oesophageal food bolus impaction can potentially be as serious emergency that requires immediate intervention, especially if it is associated with complications such as perforation or severe respiratory distress if aspirated. The traditional approach to managing acute oesophageal food impaction involves techniques such as the Heimlich manoeuvre, manual foreign body removal, or endoscopic procedures like oesophago-duodenoscopy. The preferred method for addressing this situation is endoscopic removal, which boasts a success rate exceeding 90% and a minimal complication rate < 5% (Aiolfi et al., 2018; Huang et al., 2018). However, in this case, the use of cola as an alternative intervention proved effective in relieving the food obstruction in the oesophagus.

Cola, a carbonated beverage containing carbon dioxide and other ingredients, has been suggested as a potential remedy for the dissolution of certain types of gastrointestinal obstructions. Several case reports and studies have explored the use of cola in managing chronic gastrointestinal obstructions (Karanjia & Rees, 1993). The selection of cola in this case report is based on its well-known effervescent properties and anecdotal evidence suggesting its efficacy in dislodging esophageal food impactions (David et al., 2019; Lee & Anderson, 2005). Baerends et al.'s (2019) retrospective study found that all patients with oesophageal food impactions were successfully treated with cola without significant adverse events. Carbonation creates gas bubbles, which can create pressure and aid in pushing or dislodging

the obstructing material. Furthermore, the acidic nature of cola may also help soften the bolus of food material, making it easier to pass through the oesophagus. Additionally, cola may stimulate peristaltic activity, promoting movement and clearance of the obstruction, although an in vitro study showed that Coca-Cola® did not induce significant movement of pieces of cooked chicken tightly squeezed in graduated syringes.

Shukla et al. (2012) conducted a study to investigate the effect of carbonated beverage (Pepsi[Pepsico India Ltd]) on transient lower esophageal sphincter relaxation (tLESR) and lower esophageal sphincter (LES) pressure in healthy subjects, revealing a significant increase in tLESR and decrease in LES pressure following ingestion. While other carbonated beverages may possess similar properties, the widespread availability and familiarity of cola among healthcare providers may have influenced its specific use in this context. Further research comparing the effectiveness of different carbonated beverages in managing esophageal food impactions could provide valuable insights.

However, upon conducting a comprehensive review of the management of oesophageal soft food obstruction (OSFBO), it becomes apparent that cola therapy does not yet represent the standard of care in the guideline due to a lack of strong evidence. Additionally, the use of hyoscine butylbromide for OSFBO appears to be based on a misinterpretation of a textbook reference. In contrast, when dealing with oesophageal food bolus impaction, it is worth noting that glucagon stands out as a cost-effective initial strategy (Haas et al., 2016). While surgical removal of OSFBO can be effective, it does carry potential risks. Nevertheless, emerging evidence suggests that surgical intervention within 24 hours of onset may be justified to proactively mitigate potential complications stemming from the initial obstruction.

Based on our observations from this case, we conclude that cola offers potential as a cost-saving, life-saving effective, and widely available over-the-counter treatment for dislodging acute oesophageal food obstructions. Its use should be tailored to individual patient factors, including obstruction location and risks. While suitable for conscious patients with intact gag reflexes, cola therapy is not universally applicable and should be supplemented with traditional interventions as needed. Further research, particularly randomized controlled trials, is essential to assess cola's safety, efficacy, and broader utility in managing oesophageal food obstruction. Such studies would enhance our understanding of its effectiveness, obstruction resolution rates, complication rates, and patient satisfaction.

CONCLUSION

In conclusion, the successful resolution of oesophageal food impaction in our patient with cola consumption underscores the potential role of cola as a non-invasive management option. Cola's unique effervescent properties, acidity, increase in tLESR and decrease in LES pressure capabilities may contribute to the dislodging of obstructing materials. However, further research is needed to establish its safety, efficacy, and applicability of cola in a wider range of food obstruction cases in the oesophagus. Clinicians should exercise discretion, considering individual patient characteristics, when contemplating cola as an alternative intervention. It is important to recognize that cola should not replace immediate life-saving measures when necessary, such as in unresponsive patients or when cola intervention is unsuitable.

CONFLICT INTEREST

The authors don't have any conflict of interest to declare.

CONSENT

The patient has given the written consent for publication.

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CASE REPORT

Role of Low Dose Intravenous Methylprednisolone in Pulmonary Hemorrhage Associated with Severe Leptospirosis

Irene Oh Huai En[1]*, Jerome Gan Jheng Rhong[1], Ew Ju Vern[1], Wong Peng Shyan[2]

[1] Department of Medical, Hospital Pulau Pinang, 10450 George Town, Pulau Pinang, Malaysia
[2] Unit of Infectious Disease, Department of Medical, Hospital Pulau Pinang, 10450 George Town, Pulau Pinang, Malaysia

*Corresponding author's email: huaien94@gmail.com

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ABSTRACT

Leptospirosis, an emerging zoonosis endemic in Malaysia, presents with diverse clinical manifestations, ranging from mild to potentially fatal illness. Pulmonary involvement in leptospirosis, particularly pulmonary hemorrhage, poses a significant risk of mortality, prompting exploration of various treatment strategies. While high-dose corticosteroid therapy has demonstrated efficacy in some studies, data on the use of low-dose corticosteroids in pulmonary leptospirosis remain scarce. Here, we report a case of successful treatment with low-dose methylprednisolone in a patient diagnosed with Weil's disease and pulmonary hemorrhage. The patient, initially presenting with fever, vomiting and hemoptysis, rapidly deteriorated, necessitating intubation due to respiratory distress. Prompt initiation of low-dose methylprednisolone alongside antibiotic therapy resulted in clinical improvement, resolution of pulmonary hemorrhage, and normalization of laboratory parameters. This case highlights the potential efficacy of low-dose corticosteroid therapy in managing severe pulmonary involvement in leptospirosis, offering insights into alternative treatment modalities for this challenging condition. Further studies are warranted to elucidate the optimal dosing and timing of corticosteroid therapy in leptospirosis-associated pulmonary complications.

INTRODUCTION

The fluctuating incidence rates of leptospirosis

in Malaysia from 2010 to 2020, ranging between 8.63 and 17.2 cases per 100,000 individuals, emphasize the critical importance of studying this disease. (Philip & Ahmed, 2023). Most cases of leptospirosis are self-limited while some progressed to severe disease with multi-organ involvement. Two clinical syndromes have been described, icteric or anicteric. Anicteric leptospirosis is typically a biphasic illness, with acute (septicemic) phase and immune phase. Icteric leptospirosis, also known as Weil's disease, occurring in 5-10% of cases, are often rapidly progressive and have a fulminant course. Pulmonary hemorrhage can often happen in icteric leptospirosis and carries a high mortality rate.

Literature reviews have demonstrated that high dose steroid (IV Methylprednisolone 1g OD) used in the early phase of illness reduce mortality and morbidity (Shenoy et al., 2006; Trivedi et al., 2001). Nevertheless, it is crucial to acknowledge that high-dose steroid therapy is associated with potential adverse effects, particularly an elevated susceptibility to infection among critically ill patients. In our case report, we present the application of low-dose steroid therapy in a young male diagnosed with leptospirosis and pulmonary hemorrhage.

CASE PRESENTATION

A 30-year-old gentleman with no known medical illness, presented to the emergency department ten days after jungle trekking and swimming in a river. His main complaints were fever, arthralgia, myalgia, vomiting and redness of both eyes for five days. The alarming symptom that brought him to medical attention was one episode of hemoptysis.

On examination, the patient was restless with acidotic breathing. He was noted to be jaundiced with conjunctival suffusion, blood pressure 88/60 mm Hg, heart rate 140 beats per minute, temperature 38.6°C, oxygen saturation 98% under room air and respiratory rate 28 breaths/min. Other systemic examinations were unremarkable.

Fluid resuscitation was commenced and intravenous (IV) Ceftriaxone 2g was served, however the patient soon deteriorated and desaturated to oxygen saturation of 80% under room air, requiring high flow mask oxygen 15 L/min.

Blood investigation revealed thrombocytopenia (Platelet $59X10^3$ µmol/L), acute kidney injury (Serum creatinine 395 µmol/L) and direct hyperbilirubinemia (40 µmol/L). Arterial blood gas showed severe metabolic acidosis with pH 7.01, bicarbonate 8.6 mmol/L and lactate 14 mmol/L. Liver enzymes and coagulation parameters were within normal range. Chest X-ray was unremarkable. Leptospirosis IgM ELISA test was negative. Nonetheless, severe leptospirosis was still suspected, taking into consideration of recent water activities.

Within 12 hours of admission, he was intubated due to worsening respiratory distress. Post intubation, fresh blood was noted upon endotracheal suction. Repeated chest x-ray showed bilateral diffuse alveolar space shadowing, consistent with pulmonary hemorrhage. IV Methylprednisolone 500 mg daily was administered.

The patient developed another episode of hemoptysis the next day. Blood parameters revealed worsening thrombocytopenia (Platelet 16 µmol/L) and direct hyperbilirubinemia (217 µmol/L), deteriorating kidney function (Serum creatinine 463 µmol/L) as well as rhabdomyolysis (Creatine kinase enzyme 2188 u/L). Repeated leptospirosis ELISA test IgM turned out to be positive.

After three days of steroids and antibiotic, he was able to wean off ventilator with chest X-ray showing resolution of pulmonary hemorrhage. Daily IV Methylprednisolone 500 mg was served for a course of three days and

maintenance dose was deemed not indicated due to significant improvement in clinical condition. IV Ceftriaxone was continued for a total of seven days. Notably within the next few days, platelet count, bilirubin and creatine kinase had normalized, and acute kidney injury recovered without requiring dialysis. The patient was discharged well on day 10 of admission.

DISCUSSION

Our case report highlights the successful management of a 30-year-old male presenting with severe leptospirosis complicated by pulmonary hemorrhage. This case underscores the importance of early recognition and treatment initiation in combating this potentially fatal disease.

Leptospirosis, endemic in Malaysia, often presents with nonspecific symptoms, posing a diagnostic challenge. In our patient, the initial presentation of fever, arthralgia, myalgia, and vomiting rapidly progressed to pulmonary hemorrhage, necessitating prompt intervention. This progression is consistent with the literature, which underscores the

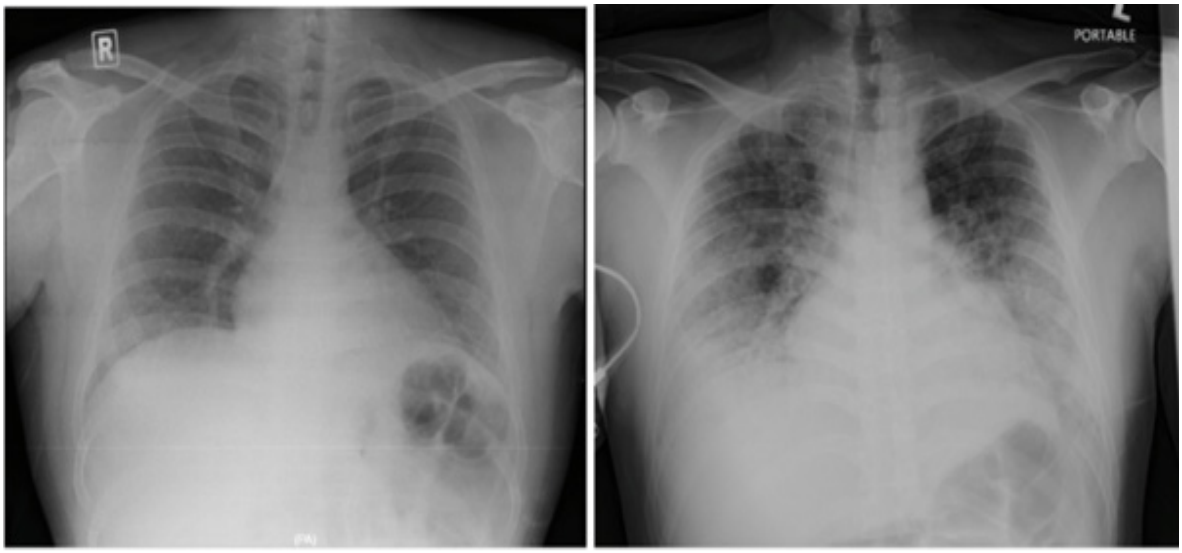

Figure 1: Chest X-ray (Left: Upon presentation, clear; Right: 12 hours post admission, bilateral diffuse alveolar shadowing).

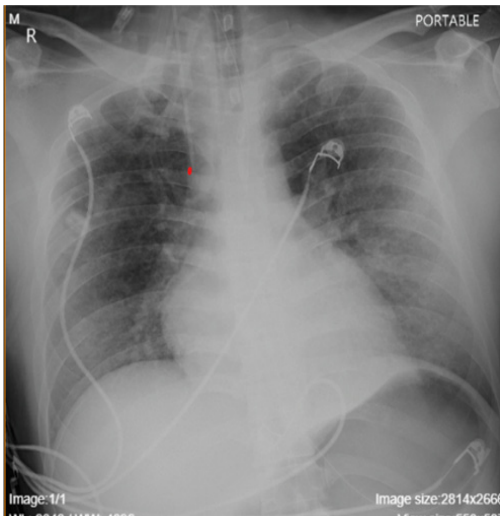

Figure 2: Resolution of chest X-ray changes after three days of IV Methylprednisolone 500mg OD.

need for heightened clinical suspicion and early initiation of appropriate therapy (Centers for Disease Control and Prevention, 2019).

While antibiotics like doxycycline and penicillin are recommended for leptospirosis treatment (Centers for Disease Control and Prevention, 2019), conflicting evidence regarding their efficacy necessitates exploring alternative therapeutic options (Brett-Major & Coldren, 2012; Charan et al., 2013; Watt et al., 1988). Despite initial negative serological tests, our patient received empirical antibiotic therapy, which likely contributed to his favorable outcome.

Pulmonary hemorrhage in leptospirosis, particularly in icteric forms (Weil's disease), is a severe complication with high mortality (Taylor et al., 2015). High-dose corticosteroids have been traditionally used to manage this, reducing mortality and morbidity when administered early. Intravenous methylprednisolone at 1g daily for three days, followed by oral prednisolone at 1mg/kg/day for seven days, has been shown to effectively treat pulmonary leptospirosis, reducing the need for ventilator support and improving outcomes if given within the first 12 hours of symptoms (Shenoy et al., 2006; Trivedi et al., 2001).

However, caution is necessary when using high-dose corticosteroids due to the risk of nosocomial infections. Hingorani et al. (2016) reported two cases of severe invasive fungal infections following steroid treatment for pulmonary leptospirosis. One patient received IV methylprednisolone 125 mg every 8 hours for six days, and the other received two bolus doses of 250 mg. Notably, only these two patients among others in the same ICU developed severe fungal infections. Further research is needed to determine the causal relationship between steroid use in leptospirosis and invasive fungal infections. Therefore, steroid use in pulmonary leptospirosis should be judicious, employing the lowest effective dose for the shortest duration possible.

Recent studies and case reports have suggested that lower doses of corticosteroids might be equally effective while potentially reducing the risk of adverse effects. For instance, Lim et al. (2018) reported successful treatment of pulmonary hemorrhage with a lower dose of 500 mg methylprednisolone once daily for three days without a maintenance dose, achieving complete recovery. Similarly, Kularatne et al. (2010) demonstrated the efficacy of 500 mg IV methylprednisolone daily for three days followed by 8 mg orally for five days in a cohort of severely ill patients, showing reduced mortality and improved outcomes.

Further supporting our approach, Thunga et al. (2012) and Pedro (2020) reported successful outcomes using tapering doses of methylprednisolone and equivalent hydrocortisone dosing, respectively, underscoring the flexibility and potential efficacy of various low-dose corticosteroid regimens.

Our patient's management aligns with these findings. The administration of 500 mg IV methylprednisolone daily for three days resulted in significant clinical improvement, resolution of pulmonary hemorrhage, and normalization of laboratory parameters without the need for a prolonged maintenance dose. This result suggests that lower doses of corticosteroids can be effective in managing severe pulmonary leptospirosis, potentially offering a safer alternative to high-dose regimens.

The successful outcomes observed across various steroid regimens underscore the adaptability of treatment approaches in managing pulmonary hemorrhage associated with leptospirosis. Despite differences in dosing and administration, these regimens share a common goal of modulating the immune response to mitigate pulmonary

damage.

CONCLUSION

Our case report demonstrates the successful use of low-dose methylprednisolone in managing severe leptospirosis with pulmonary hemorrhage. The findings underscore the potential of low-dose methylprednisolone as a viable treatment option for pulmonary complications in leptospirosis, offering a balance between efficacy and safety. However, it is crucial to note that our patient, like those in similar case reports, was young and without comorbidities. Further research is needed to validate these results across diverse patient populations and to establish standardized protocols for dosing and duration

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CONFLICT INTEREST

We have no conflict of interest to disclose.

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CASE REPORT

Subclinical Hypothyroidism and Placenta Abruption: A Dangerous Relationship During Pregnancy

Nadirah binti Zainoren*, Abdul Hadi bin Said

Department of Family Medicine, International Islamic University Malaysia (IIUM), Bandar Indera Mahkota, 25200 Kuantan, Pahang, Malaysia

*Corresponding author's email: nadirahzainoren@gmail.com

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ABSTRACT

This case report explores the intricate link between subclinical hypothyroidism and placenta abruption during pregnancy, emphasising the potential risks and clinical implications, through a detailed case study of a 28-year-old woman with a history of hyperthyroidism, non-compliance, and subsequent subclinical hypothyroidism, causing placenta abruption leading to intrauterine death. The report highlights the challenges in managing thyroid disorders during pregnancy. Limited Malaysian data on this association prompts a broader discussion of international findings, suggesting a correlation between subclinical hypothyroidism and adverse pregnancy outcomes. The study delves into potential mechanisms, including thyroid hormone impact on placental vascular function and the complexity added by autoimmune thyroiditis. Personalised treatments, thyroid function monitoring, and comprehensive antenatal care are emphasised for optimal pregnancy outcomes. This case underscores the need for increased awareness, proactive management, and preconception counselling to safeguard maternal and foetal well-being.

Keywords: *Hypothyroidism, Pregnancy, Placenta abruption, Pregnancy outcomes*

INTRODUCTION

The occurrence of thyroid dysfunction during pregnancy is a matter of great concern due to its potential to cause harmful effects on both the mother and the developing foetus. Subclinical hypothyroidism, a medical condition marked by normal amounts of thyroxine hormone (T4)

in the blood but increased levels of thyroid-stimulating hormone (TSH), has been linked to adverse outcomes during pregnancy, such as placenta abruption (CPG Management of Thyroid Disorders, 2019). Thyroid hormones are crucial for developing and maintaining a healthy pregnancy and foetus, as they regulate various metabolic processes and hormones during pregnancy. Thyroid hormones play an essential role in the growth and development of the placenta, ensuring optimal communication and nutrient exchange between the mother and foetus (Adu-Gyamfi et al., 2019; Alemu et al., 2016). The placenta is a vital conduit for nutrition and oxygen from the mother to the foetus and waste removal. As demonstrated by placental abruption, any interference with its regular operation might have severe consequences for the mother and the foetus (Schmidt, 2022). Placenta abruption is defined as early separation of the placenta from the lining of the uterus, occurring any time after 20 weeks of gestation and before the delivery of the foetus. It usually presents with sudden onset of vaginal bleeding, abdominal pain, uterine contractions and tenderness, and nonreassuring fetal well-being. (Schmidt, 2022).

This case report aims to provide a comprehensive analysis of the intricate association between subclinical hypothyroidism and placental abruption. It seeks to elucidate the underlying mechanisms and explore the potential consequences of clinical therapy.

CASE PRESENTATION

A 28-year-old Gravida 3 Para 2 came for booking at ten weeks of gestation. She is a non-smoker and denies recreational drug use. Her previous pregnancy was uneventful, and she delivered her baby via spontaneous vaginal delivery (SVD). She has no history of hypertensive disorder, and her blood pressure (BP) throughout pregnancy was normotensive. Further history revealed that she was diagnosed with hyperthyroidism in 2019 due to Grave's disease with positive thyroid stimulating hormone receptor antibody (TRAb) but defaulted to treatment and follow-up due to the COVID-19 pandemic. During booking, her body mass index (BMI) was 21kg/m^2, with initial investigation showing normal results, including a haemoglobin (Hb) level of 13g/dL. Clinically, she was euthyroid with no neck swelling. However, a thyroid function test (TFT) revealed an elevated thyroid-stimulating hormone (TSH) level of 6.1mIU/L alongside a normal thyroxine (T4) level of 12.6pmol/L. She was diagnosed with subclinical hypothyroidism attributed to Hashimoto's thyroiditis, as evidenced by elevated thyroid peroxidase (TPO) antibody levels (527 IU/ml). Other autoimmune screening was not performed. Treatment commenced with L-thyroxine 50mcg daily, and she was compliant with the medication. The dosage of L-thyroxine remained unchanged throughout her pregnancy. Her thyroid function was monitored monthly, and as her pregnancy advanced, her TFT was not normalized with a TSH level of 5.06mIU/L despite being on medication (Table 1).

Throughout her pregnancy, she remained healthy and clinically euthyroid. Her modified oral glucose tolerance tests (MGTT) were normal. Her transabdominal ultrasound scan (TAS) at booking shows a singleton foetus with crown-rump length (CRL) corresponding to her gestational age. Subsequent assessments of foetal growth parameters during the second and third trimesters correspond to her gestational age with adequate liquor. The placenta was located at the posterior upper segment with normal morphology. However, at 34 weeks of gestation, she presented with contraction pain and sought medical intervention at the hospital. There were no indications of leaking liquor, vaginal discharge, or bleeding, nor was there a history of trauma or vigorous massage. The absence of reduced foetal movements was also noted. Her vital signs remained

stable, her blood pressure was within the normal range, and palpation showed a tense abdomen. A transabdominal ultrasound revealed the absence of foetal cardiac activity, with a retroplacental clot measuring approximately 6cm x 6cm, although no free fluid was observed. Subsequently, a baby boy was delivered via spontaneous vaginal delivery with clear amniotic fluid, exhibiting no signs of life. Upon external examination, he weighed 2.63kg at birth with a grossly normal structure. No further post-mortem investigation was undertaken. During placenta inspection, it was noted that there was 1 Liter of retroplacental clots. It was complicated with massive postpartum haemorrhage secondary to abruption of the placenta and uterine atony with a total of 2.5L estimated blood loss. She was transfused with two pint-packed cells and was stabilised and admitted to a high dependency unit (HDU) for close monitoring and was discharged well after four days of admission.

Table 1: Thyroid function test results of the patient in different antenatal check-ups with the pregnancy-specific normal ranges.

GESTATION (WEEKS)	12W5D	22W6D	26W4D	32W4D
TSH (mIU/L)	6.1 (0 – 5.5)	1.433 (0.5 – 3.5)	3.767 (0.5 – 3.5)	5.065 (0.5 - 4)
FT4 (pmol/L)	12.6 (10 – 16)	10.3 (9 – 15.5)	8.6 (9 – 15.5)	10 (8 – 14.5)

DISCUSSION

TIn Malaysia, there is limited data available on the prevalence of placenta abruption and its association with subclinical hypothyroidism (CPG Management of Thyroid Disorders, 2019). Nonetheless, prior research from other countries has suggested a possible link between subclinical hypothyroidism and unfavourable pregnancy outcomes, including placenta abruption. A study in India discovered a positive correlation between subclinical hypothyroidism and significant negative consequences for both the mother and the foetus, including pregnancy-induced hypertension, intrauterine growth restriction, and intrauterine death (Sahu et al., 2009). Another study done in Pakistan highlighted the problems that might arise from subclinical hypothyroidism in pregnant women, such as preterm labour, gestational hypertension, placenta previa, and intrauterine growth restriction (Khan et al., 2020). Like our case study, pregnant women with subclinical hypothyroidism were found to have a high risk of placenta abruption, which may lead to intrauterine death (Alemu et al., 2016; Bankapur et al., 2023; Singh et al., 2024; Urgatz & Poppe, 2024; Vaishnav et al., 2023).

The consistent findings and case studies prompt significant inquiries regarding this connection's mechanisms. Although the precise underlying mechanisms are not yet fully understood, various factors may contribute to the heightened risk of placental abruption in patients with subclinical hypothyroidism. A possible explanation involves the influence of a lack of thyroid hormone on the placenta's vascular function. Thyroid hormones are essential for controlling the blood vessels. Insufficient thyroid hormone levels, even if just slightly below the normal range, might cause changes in the blood flow to the placenta.

This may cause placenta vascular insufficiency, thus increasing the risk of placenta abruption (Adu-Gyamfi et al., 2019; Spinillo et al., 2021; Vanes et al., 2013).

Moreover, the existence of autoimmune thyroiditis in this patient adds a degree of intricacy. Immunological dysregulation and persistent inflammation caused by autoimmune thyroiditis may affect the placental tissues. The presence of inflammation in the placenta may lead to compromised placental structure and increase the likelihood of clot formation and bleeding, as seen in this case (Alemu et al., 2016; Amin et al., 2010; Urgatz & Poppe, 2024).

The complex relationship between placental abruption and subclinical hypothyroidism, in this case, the report makes it imperative to think about the clinical ramifications and treatment options for expectant patients with comparable profiles. It is essential to monitor thyroid function closely, particularly in cases of autoimmune thyroiditis, to identify those who are more vulnerable to poor pregnancy outcomes. Any deviations from the normal range should be promptly identified and managed. The risk of placenta abruption may also be reduced by personalised treatments to optimise thyroid hormone levels and reduce the inflammatory response caused by autoimmune thyroiditis (Alemu et al., 2016; Amin et al., 2010; Urgatz & Poppe, 2024; Vaishnav et al., 2023).

Aside from monitoring thyroid function, the healthcare team must offer extensive antenatal care to tackle the heightened risk of adverse consequences linked to subclinical hypothyroidism. This may entail meticulous monitoring of foetal development, frequent assessments of blood pressure to detect preeclampsia, and patient education on the disease and complications. Open and informed discussions between the healthcare staff and the patient regarding screening and therapy's potential benefits and risks are crucial. This will empower the patient to make informed decisions regarding her antenatal care (Alexander et al., 2017; Maraka et al., 2018; Negro & Mestman, 2011).

In addition, the healthcare staff should provide the patient with information regarding the signs and symptoms of placenta abruption, such as vaginal bleeding, abdominal pain, and changes in foetal movement. Timely identification and immediate intervention in placenta abruption cases can improve neonatal outcomes. If there is suspicion or diagnosis of placenta abruption, prompt intervention should be given, which may involve expediting delivery for better outcomes for both the foetus and the mother. Support and counselling regarding the possible emotional effects of subclinical hypothyroidism and the potential for adverse outcomes, such as placenta abruption leading to intrauterine death, should also be given to the patient and her family (Alexander et al., 2017; Maraka et al., 2018; Negro & Mestman, 2011; Schmidt, 2022). As the pregnancy progresses, multidisciplinary care comprising family physicians, obstetricians, endocrinologists, and maternal-foetal medicine specialists is essential to address the possible impact of subclinical hypothyroidism on pregnancy outcomes. Working together to identify the best treatment plans for thyroid dysfunction during pregnancy may eventually lead to better outcomes for both the mother and the foetus (Alexander et al., 2017; Maraka et al., 2018; Negro & Mestman, 2011).

In this case report, it is observed that there is a transition from hyperthyroidism to hypothyroidism in pregnancy due to the significant physiological demands on the thyroid gland. An influential aspect in this transition is the impact of human chorionic gonadotropin (hCG), a hormone released by the placenta. In early pregnancy, hCG prompts the thyroid gland to produce more thyroid hormones, which might potentially worsen hyperthyroidism. As pregnancy advances, hCG's effects fade, and the thyroid gland

adapts to meet metabolic needs. The thyroid gland may struggle to maintain hormone levels, especially in autoimmune thyroiditis, causing hypothyroidism (Alemu et al., 2016; Amin et al., 2010; Urgatz & Poppe, 2024).

Optimising thyroid dysfunction treatment in pregnant women requires understanding this transition. Clinicians must be aware of the potential for hyper- and hypothyroid conditions during pregnancy. This emphasises the necessity of thyroid function monitoring and personalised therapies for gestational hormonal changes. This case report presents an intriguing illustration of the intricacies of managing thyroid disorders in pregnancy. This highlights the importance of increased awareness and proactive management measures to deal with the changing thyroid function in pregnant individuals, eventually ensuring the health and well-being of both the mother and the foetus (Alexander et al., 2017; Maraka et al., 2018; Negro & Mestman, 2011).

Lastly, in this case, the patient's pre-pregnancy hyperthyroidism was not managed before conception due to non-compliance with follow-up and medication. This likely contributed to the development of subclinical hypothyroidism during pregnancy, which in turn led to placental abruption and the subsequent intrauterine death of the foetus. The adverse outcomes observed in this case highlight the importance of preconception counselling and optimisation of thyroid function before attempting to conceive (Alexander et al., 2017; Maraka et al., 2018; Negro & Mestman, 2011).

CONCLUSION

The complexities of thyroid dysfunction during pregnancy impose a holistic and careful approach to protect maternal and foetal well-being. It is crucial for healthcare providers to keep updated on the latest evidence-based guidelines and to have open discussions with pregnant women about the risks and benefits of screening as well as treating subclinical hypothyroidism. Healthcare providers can collaborate to implement a collaborative approach that includes routine thyroid function monitoring, thorough antenatal care, and prompt intervention in case of any emerging issues to enhance pregnancy outcomes.

CONFLICT OF INTEREST

The authors declared no conflicts of interest related to this article.

CONSENTS

Informed consent was obtained from the patient before preparing this case report

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CASE REPORT

Systemic Mastocytosis presents as a solitary skull lesion in a child

Jennie Tan Geok Lim[1]*, Ng Chee Guan[2], Teh Kok Hoi[3], Teoh Pei Yeing[4], Normawati binti Mat Said[2]

[1] Department of Radiology, Sarawak General Hospital, Jalan Hospital, 93586 Kuching, Sarawak, Malaysia
[2] Department of Radiology, Tunku Azizah Hospital (Kuala Lumpur Women's and Children's Hospital), 50300 Kuala Lumpur, Malaysia
[3] Department of Pediatrics, Tunku Azizah Hospital (Kuala Lumpur Women's and Children's Hospital), 50300 Kuala Lumpur, Malaysia
[4] Department of Pathology, Kuala Lumpur Hospital, 50586 Jalan Pahang, Kuala Lumpur, Malaysia

*Corresponding author's email: jentan86@gmail.com

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ABSTRACT

Mastocytosis arises from the abnormal growth and accumulation of mast cells within the body's organ systems. Within the pediatric age group, systemic mastocytosis is exceptionally rare, with only a few reported cases in the medical literature. Here, we report a case detailing a solitary skull lesion in a 10-year-old child as the sole identified manifestation of systemic mastocytosis. She presented with neurologic symptoms without any allergic or systemic manifestation. The child was initially diagnosed with hemangiopericytoma, with the differential diagnosis of atypical meningioma. The patient underwent surgery and histopathological examination confirmed the diagnosis of systemic mastocytosis. Unfortunately, the patient presented with recurrence, necessitating another surgery that again confirmed the diagnosis. Multidisciplinary team collaboration integrating clinical, radiographic, and immunophenotypic correlations is vital in the diagnosis and management of this sporadic condition.

INTRODUCTION

Systemic mastocytosis is a rare condition, with an estimated global prevalence of 1 in 10000 individuals. It is due to the abnormal growth of mast cells which can affect the bone marrow, skin, or extracutaneous organs such as the liver, spleen, lymph nodes and gastrointestinal tract (George et al., 2011; Theoharides et al., 2015). While it can manifest at any age, it is more commonly observed in adults and can affect both sexes with a slight predominance in

males. KIT mutations have been demonstrated in over 95% of adults with mastocytosis (Valent, 2015), but less so in children, with recent literature indicating mutations in 25 to 64.3% of pediatric-onset mastocytosis (Verzijl et al., 2007; Yanagihori et al., 2005).

Due to its rarity in the pediatric population, there have been very few reported cases in the literature (Castells, 2006; Guenther et al., 2001). These cases are classified as mast cell neoplasms with lytic bone lesions and do not meet the diagnostic criteria for SM. Conversely, our case report presents a tumor that fulfils the criteria for SM, despite lacking systemic involvement. Thus, we describe a unique case of a child with a solitary skull lesion as the sole identified manifestation of systemic mastocytosis.

CASE PRESENTATION

A previously well 10-year-old Asian girl presented with headache, vomiting and left-sided visual loss. There was no history of urticaria or allergic manifestation. On examination, she had left temporal inferior quadrant hemianopia. The rest of the neurological examination was unremarkable. No cutaneous or other organ involvement was identified.

The initial non-contrast-enhanced CT scan of the brain (Figure 1) showed a solitary lytic bone lesion in the right occipital skull with an extra-axial mass causing adjacent cerebral vasogenic oedema. Contrast-enhanced MRI scan of the brain (Figure 2) confirmed the presence of an extra-axial mass which was isointense on T1- and T2-weighted sequences, with post-contrast enhancement and associated dural enhancement. No other intracranial abnormality was detected. The initial provisional diagnosis was meningeal hemangiopericytoma because of the locally aggressive enhancing extra-axial tumour with bone erosion.

Differential diagnosis included atypical meningioma or bone malignancy such as skull osteosarcoma with intracranial extension. Meningiomas are dural-based extra-axial tumours which show avid post-contrast enhancement with dural tail; these are commonly associated with calcification and adjacent bony hyperostosis, instead of erosion. Osteosarcoma typically exhibits permeative or moth-eaten appearance with aggressive periosteal reactions such as the sunburst-type, onion-skin or Codman triangle, which is not seen in this case.

The patient underwent right posterior craniotomy and excision of the tumour with titanium mesh cranioplasty. Intraoperatively, the tumour was noted to arise from the dura with involvement of both the outer and inner tables of the skull.

Histopathological examination (Figure 3) of tumour, skull and dura showed densely packed sheets of neoplastic cells with cytoplasm ranging from abundant eosinophilic to vacuolated in appearance. These neoplastic cells had round to oval nuclei, exhibiting clumped chromatin and some with small nucleoli. Mitoses were occasionally seen. Intermingled were scattered cells with irregular lobulated to reniform nuclear contours as well as multinucleated cells. A small number of neutrophils and eosinophils were present. There was no marked nuclear pleomorphism.

Immunohistochemical studies demonstrated diffuse positivity for CD117, CD43, CD25, CD68 and CD2. Additionally, there was focal positivity for tryptase, CD45 and CD30. Immunostains for CD163, myeloperoxidase (MPO), lysozyme, CD15, CD34, CD56, Langerin, S100, CD1a, epithelial membrane antigen (EMA), pan-cytokeratin (PanCK), glial fibrillary acidic protein (GFAP), D2-40, and E-cadherin all yielded negative results. The Ki67 proliferative index was approximately 10 percent. Toluidine blue staining revealed metachromatic granules in numerous neoplastic cells. Based

on the histological features and ancillary testing, the features were indicative of a mast cell neoplasm consistent with systemic mastocytosis.

The patient underwent re-craniotomy and tumour excision, during which a thin film of tissue was observed growing over the titanium mesh, which was also removed to

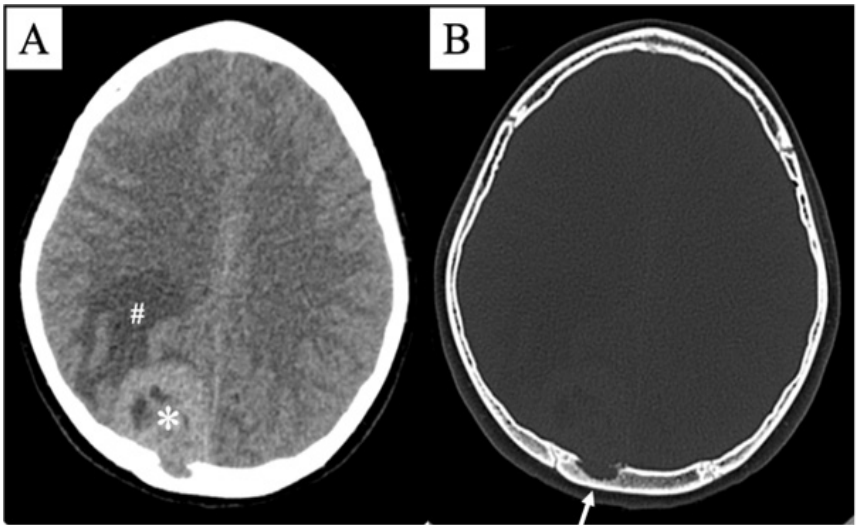

Figure 1: Non-contrast enhanced axial CT images of the brain at presentation. (A) Soft tissue window and (B) bone window showed a solitary right occipital extra-axial mass (asterisk) associated with cerebral vasogenic (hashtag) and adjacent bone erosion (arrow).

Bone marrow aspiration and trephine biopsy, along with immunophenotyping did not reveal any evidence of marrow infiltration. Genetic study for cKIT D816V mutation analysis was negative. Serum Tryptase were within the normal range. Full blood count was unremarkable with no signs of eosinophilia.

The patient's symptoms resolved after the surgery. Immediate post-operative CT brain study did not show residual tumour. Post-operative whole-body PET/CT scan did not show FDG-avid uptake to suggest another site of disease involvement. Following a multidisciplinary team discussion, the patient was followed up clinically without adjuvant chemotherapy or radiotherapy as she was asymptomatic.

However, two months after the surgery, the patient complained of headache. Subsequent contrast-enhanced MRI scan (Figure 4) revealed tumour recurrence.

prevent future recurrence necessitating re-surgery. Histopathological examination again confirmed tumour recurrence.

DISCUSSION

The 2022 World Health Organization (WHO) categorised mastocytosis into three major types: cutaneous mastocytosis (CM), SM, and mast cell sarcoma (MCS). The SM is further divided into bone marrow mastocytosis (BMM), indolent (ISM), smoldering (SSM), aggressive (ASM), SM with an associated hematologic neoplasm (SM-AHN), and mast cell leukaemia (MCL).

Cutaneous mastocytosis is predominantly observed in the pediatric age group, constituting 90% of cases with a bimodal distribution pattern. It typically peaks in the first three years of life, with a second smaller peak occurring after 15 years of age (Klaiber et al., 2017). Systemic mastocytosis makes up less than 10 per cent of the

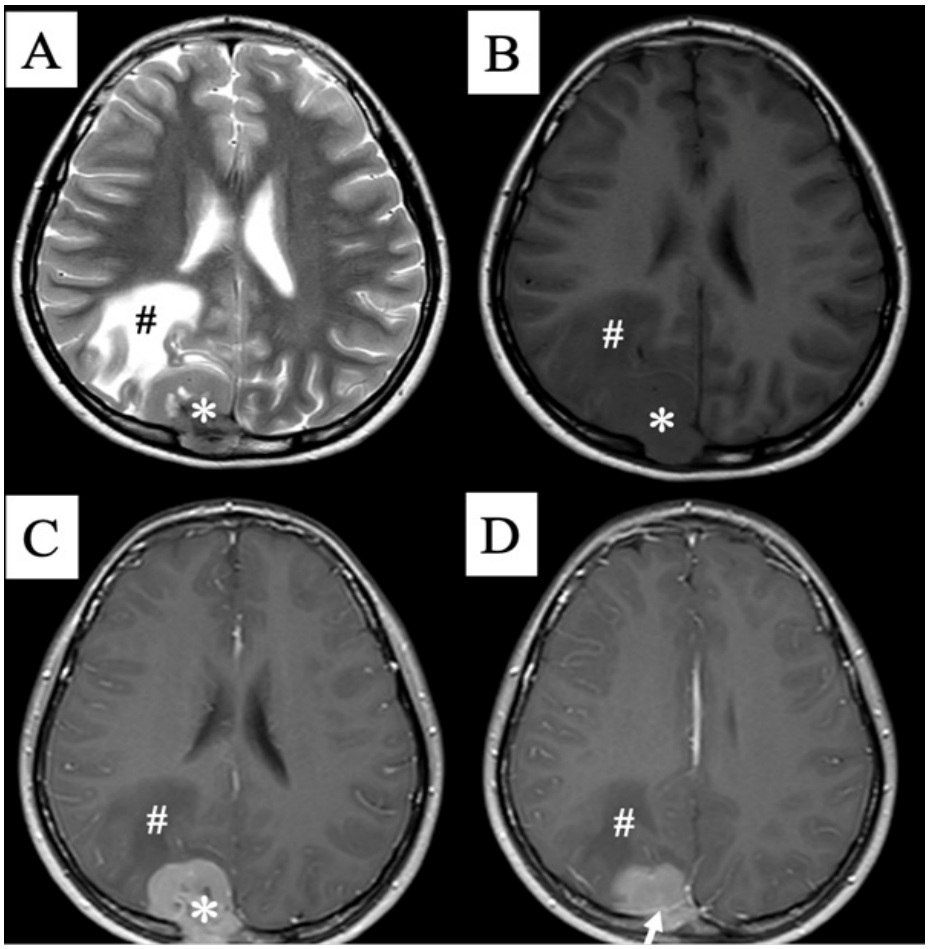

Figure 2: Pre-operative axial MR images of the brain. (A) T2-weighted and (B) pre-contrast enhanced T1-weighted images depicted an isointense right occipital extra-axial mass (asterisk) with adjacent cerebral vasogenic oedema (hashtag). (C, D) Post-contrast enhanced T1-weighted images showed the mass to be heterogeneously enhancing, associated with dural enhancement (arrow).

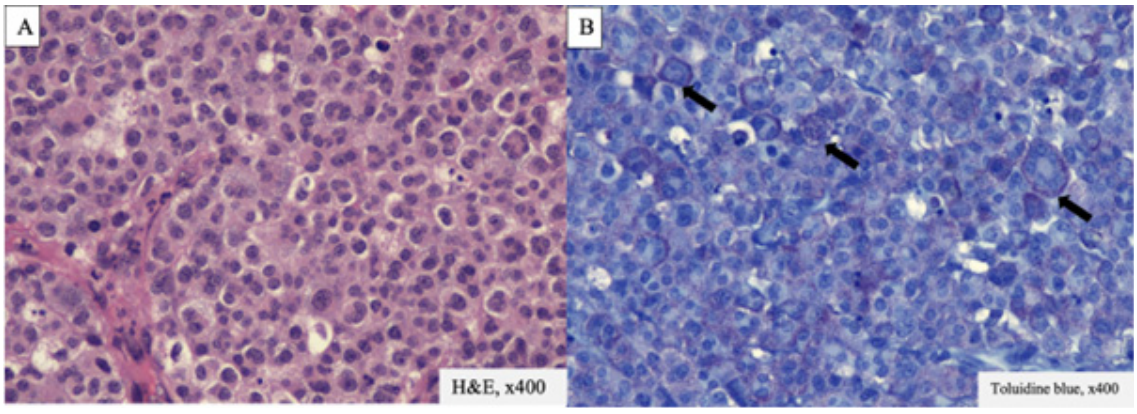

Figure 3: Light Microscopy High power view x400 magnification. (A) Haematoxylin and eosin staining (H&E) of extra-axial mass depicted hypercellular sheets of neoplastic cells displaying variable round, oval, and reniform nuclei with scattered interspersed multinucleated foms. (B) Toludine blue highlighted metachromatic granules (arrows) in the neoplastic cells.

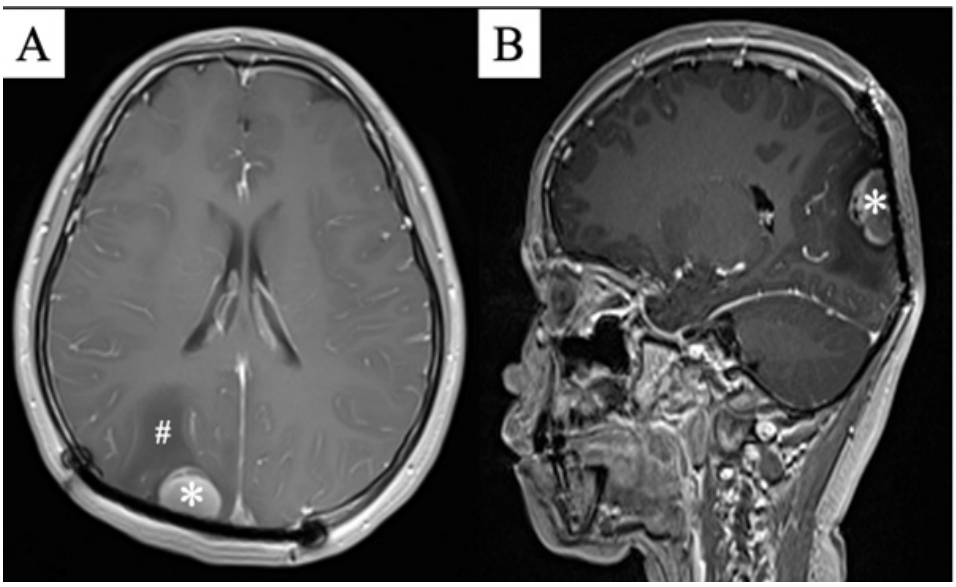

Figure 4: Post-operative contrast-enhanced MR images of the brain. (A) Axial and (B) Sagittal plane showed tumour recurrence (asterisk) with cerebral vasogenic oedema (hashtag).

pediatric mastocytosis cases. Most follow a benign course, often exhibiting spontaneous improvement or resolution before reaching the prepubescent stage (Carter et al., 2015). The majority of children with SM tend to have indolent SM, with the more aggressive or advanced forms of the disease being rare. Additionally, in comparison to adult mastocytosis, the pediatric disease is less likely to be associated with haematological, bone marrow or gastrointestinal involvement; similar as noted in this case report (Cooper et al., 1982; Horan et al., 1991; Parker, 2000).
Meanwhile, mastocytosis in adults tends to present in the 5th decade of life or later (Arber et al., 2016) and persist throughout life. Bone abnormalities are prevalent in approximately 50% of adult patients with systemic mastocytosis (Barete et al., 2010). These abnormalities can manifest in various forms, including diffuse or focal, lytic, sclerotic or mixed patterns (Rossini et al., 2011; Van der Veer et al., 2012). Unlike adult mastocytosis, bone involvement in childhood-onset mastocytosis is rare, with only a few reported cases (Castells, 2006; Guenther, 2001). Most of them do not meet the criteria for SM and are instead described as solitary mast cell neoplasms with lytic bone lesions.

The 2022 WHO diagnosis of SM needs the presence of one major and one minor criterion, OR three minor criteria for confirmation:

a.The major diagnostic criterion for SM is the presence of multifocal mast cell aggregates (15 or more mast cells) in the bone marrow or other extracutaneous organs.
b.The minor criteria for SM include the presence of atypical mast cells of more than 25 per cent, the activation of KIT codon 816 mutations, the expression of one or more surface markers (CD2, CD25, CD30), and the elevation in serum tryptase levels exceeding 20 ng/mL.

The patient in this case report met the diagnostic criteria for systemic mastocytosis, based on histopathological analysis. The specimen exhibited one major criterion and two minor criteria, characterized by multifocal dense aggregates of mast cells exceeding 15, with more than 25% of all mast cells being of the atypical type II variety and expressing CD2 and CD25 antigens.

CONCLUSION

Paediatric-onset systemic mastocytosis is a sporadic condition with distinctive and often

atypical presentation compared to its adult counterpart. Clinicians, radiologists, and pathologists must recognise that solitary mast cell neoplasm may indicate an underlying systemic disease. Multidisciplinary team collaboration integrating clinical, radiographic, and immunophenotypic correlations is vital in the diagnosis and management of this condition.

CONFLICT OF INTEREST

All authors affirm that they have no affiliations with or involvement in any organisation or entity that may have financial or non-financial interests in the subject matter or materials discussed in this manuscript.

CONSENTS

Written informed consent was acquired from the child's father.

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