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Borneo Journal of Medical Sciences

Volume 19, Issue 3, September 2025

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Borneo Journal of Medical Sciences
Volume 19, Issue 3, September 2025
ISSN 1985-1758 E-ISSN 2710-7353

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Borneo Journal of Medical Sciences

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2024
A Member of the Malaysian Scholarly Publishing Council (MAPIM)

BJMS
Borneo Journal of Medical Sciences
Volume 19, Issue 3, September 2025
Journal of the Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah

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Universiti Malaysia Sabah
Jalan UMS
88400 Kota Kinabalu
Sabah, Malaysia
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88400 Kota Kinabalu
Sabah, Malaysia
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EDITORIAL

Clouds of Harm: The Health Impact of Youth Vaping in Malaysia

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Received: 4 August 2025

Accepted: 6 August 2025

Published : 2 September 2025

DOI: https://doi.org/10.51200/bjms.v19i3.6686

Keywords: *E-cigarettes, Vaping, Youth, Health, Malaysia*

E-cigarettes (EC), also known as vape pens, e-cigars, or vaping devices, produce an aerosolised mixture that contains flavoured liquids and nicotine, which users inhale. These electronic nicotine-delivery systems come in a wide variety due to differences in nicotine concentrations, e-liquid volumes, carrier compounds, additives, flavours, and battery voltages. Each EC device typically operates using a standard system, which includes a rechargeable lithium battery, a vaporisation chamber, and a cartridge. The lithium battery powers the vaporisation chamber, which contains the atomiser. Users inhale through a mouthpiece, and the airflow activates a sensor, initiating the atomiser to deliver nicotine to the lungs. The liquid nicotine stored in a small cartridge is then vaporised and inhaled.

The number of e-cigarette users has significantly increased, mainly due to the perception that they are a healthier alternative to traditional tobacco consumption, minimal regulation on use, and the appealing design of the devices. Over the past decade, e-cigarette use among young adults in Malaysia has risen dramatically. In 2011, the prevalence of EC use among individuals aged 15 and older was 0.8%. By 2016, this number had grown to 3.2% for Malaysians aged 18 and older, and by 2019, EC use among those aged 15 and above had reached 4.9%. Among Malaysian youth aged 15–19, the usage was reported at 7.5%, and for young adults aged 20–24, it was 14.7%. In contrast, less than 5% of adults aged 30 and older used e-cigarettes.

Usage is particularly prevalent among

younger age groups, with a 2023 survey showing that EC use among individuals aged 15–24 rose from 1.1% in 2011 to 8.6%. Demographically, e-cigarette users in Malaysia are more likely to be male, younger, and possess higher education levels. A study at Universiti Malaysia Sabah (UMS) revealed that 27.2% of students reported using e-cigarettes, with male students aged 18 to 21 being more likely to use EC than those aged 22 to 24. Peer influence was a significant factor in the decision to use EC, as accepting an offer to vape from friends significantly increased the likelihood of usage. Additionally, individuals with a history of smoking combustible cigarettes were found to be more inclined to use e-cigarettes.

Nationally, the prevalence of EC use among young adults aged 20–24 years was recorded at 14.7%. A nationwide study highlighted that young adults, particularly males and those identifying as Malays, Bumiputera from Sabah, and Bumiputera from Sarawak, are more susceptible to EC usage. This demographic data indicates a higher prevalence of e-cigarette use among young adults in Sabah compared to other regions, emphasising the need for targeted public health interventions and policies to tackle this growing concern.

The health impact of e-cigarettes raises significant issues. Research indicates that both short-term and long-term effects on lung function exist.

Short-Term Effects on Lung Function

Some studies suggest that short-term inhalation of e-cigarette vapour may not cause substantial changes in lung function among healthy individuals. A meta-analysis revealed no significant changes in lung function parameters following acute exposure. However, many participants reported experiencing an acute cough following short-term use. Furthermore, short-term use of nicotine e-cigarettes has been linked to decreased oxygen levels, increased airway resistance, and reduced specific airway conductance in healthy users. Other studies have noted significantly lower blood oxygenation levels (SpO2) after vaping for just 20 minutes.

Long-Term Effects on Lung Function

Concerns have emerged regarding long-term respiratory effects, which have demonstrated measurable adverse biological impacts on respiratory health, including inflammation and impaired immune responses. This could potentially result in chronic respiratory conditions. A study focusing on young adults revealed that both vapers and smokers exhibited significantly lower peak exercise capacities and oxygen intake compared to non-smokers, indicating compromised physical fitness and potential lung function impairment.

Nicotine-Free E-Cigarettes. It is worth noting that even nicotine-free e-cigarettes can negatively affect lung function. Research indicates that vaping, regardless of nicotine content, can lead to decreased oxygen saturation levels, signifying reduced oxygen intake by the lungs.

Cardiovascular Effects

Vaping has been associated with adverse effects on the cardiovascular system. Users may experience cardiac arrhythmia, hypertension, acute coronary syndromes, and heart failure, which show a modest increase in incidence and mortality among vapers. The underlying mechanisms that contribute to these harmful effects are believed to include inflammation, endothelial dysfunction, atherosclerosis, oxidative stress, and hemodynamic changes. However, the exact mechanisms remain unclear.

A meta-analysis suggested that while e-cigarettes (EC) have adverse acute effects on heart rate, beneficial changes may occur in blood pressure regulation when individuals switch from traditional tobacco smoking to long-term EC use. Conversely, some

researchers reported that blood pressure remained unchanged or did not decrease in vaping participants compared to their pre-vape status. It was also indicated that vaping might hinder the anticipated reduction in blood pressure experienced during periods of relaxation. These findings align with other studies observing variable correlations between nicotine use and elevated blood pressure. After using a vape, increased heart rate and blood pressure are common immediate physiological responses.

Effects of E-Cigarettes on Bone Mineral Density (BMD)

Research on the impact of e-cigarette use on bone health is limited. Some studies suggest that exposure to e-cigarette vapour may negatively affect bone cell function. It has been documented that e-cigarette vapour condensate can reduce the viability and impair the function of osteoblasts. Additionally, the impact on bone remodelling, characterised by reduced viability and impaired functions of osteoblasts and osteoclasts, is associated with high concentrations of nicotine.

Impact on Muscle Function

Nicotine, a primary component of many e-cigarettes, can interfere with muscle protein synthesis. Research indicates that nicotine may suppress genes and cellular pathways essential for muscle repair and growth, which can hinder muscle development. Furthermore, nicotine has been shown to elevate cortisol levels, a stress hormone that can promote muscle breakdown, further impeding muscle growth and function.

Effects on Brain Development

The human brain continues to develop until around the age of 25, particularly the prefrontal cortex, which is responsible for decision-making, impulse control, and emotional regulation. Nicotine, the main addictive substance in e-cigarettes, disrupts this developmental process. Research indicates that nicotine exposure during adolescence alters synaptic plasticity and neurotransmitter pathways. It is associated with reduced cognitive performance, including poor attention span, learning difficulties, and memory deficits. Some animal studies have found that adolescent rats exposed to nicotine exhibited long-term changes in brain circuits, increased risk-taking behaviour, and a heightened reward response to other addictive substances. Studies from Universiti Malaya and USM (2021–2023) revealed that students who vape heavily reported lower academic performance and difficulties in focusing. Additionally, some experienced irritability, poor sleep, and increased symptoms of dependency.

Mental Health Effects

Mental health issues may lead youth to vape, and vaping can exacerbate existing anxiety, depression, and stress. Young vapers are 2 to 3 times more likely to experience depression, anxiety, and mood disorders. Frequent vaping is linked to low self-esteem and emotional dysregulation. Many young people use vaping as a coping mechanism, which increases the risk of addiction. Research from Universiti Kebangsaan Malaysia (2022) found a higher prevalence of depressive symptoms among university students who vape regularly. Feelings of loneliness and peer rejection were also more common among vapers. Some participants described vaping as a "temporary relief" for stress, leading to overuse.

Withdrawal symptoms such as anxiety, irritability, and restlessness when not vaping can negatively affect mental well-being.

Reproductive Health Effects

These effects are becoming a growing concern but are less commonly discussed. Nicotine and other chemicals in e-cigarettes can influence reproductive hormones, blood flow, and sexual performance. The American Journal of Preventive Medicine (2021) reported a link between nicotine and erectile dysfunction (ED) in young males, even among those without

a smoking history. E-cigarettes can impair endothelial function, reducing blood flow to the genitals. Young male vapers are beginning to report early signs of ED. The Journal of Adolescent Health (2009) also published findings that female users experienced increased menstrual irregularities and reduced libido. Toxic chemicals, such as formaldehyde and diacetyl, may impact sperm quality and testosterone levels, though more research is needed. Malaysian health professionals have raised concerns about reproductive side effects, but there is limited peer-reviewed local data available.

Vaping among young people in Malaysia has become a serious public health concern. Research shows that e-cigarette use can harm brain development, worsen mental health, impair respiratory and cardiovascular function, negatively affect bone and muscle health, and even impact sexual health in young adults. Despite being marketed as a safer alternative to smoking, vaping exposes users to nicotine addiction and other harmful chemicals. In response to this growing issue, the Malaysian government has recently (1st August, 2025) announced a ban on vaping, particularly targeting products that contain nicotine or appealing flavours, as well as the use of addictive drugs and chemicals that attract youth. This is a significant and timely step to protect young Malaysians from the harmful effects of e-cigarettes.

However, the ban alone is insufficient. It must be supported by rigorous enforcement, education in schools, awareness campaigns, and support for those wanting to quit. Malaysia now has a critical opportunity to reverse the vaping trend and prevent long-term health consequences for its young population. With continued action and collaboration, we can clear the clouds of harm and protect the next generation.

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ORIGINAL ARTICLE

Association of Smoking, Alcohol, BMI, and Physical Activity with Colorectal Cancer Risk in North Borneo's Multiethnic Population

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Received: 14 October 2024

Accepted: 12 March 2025

Published: 2 September 2025

DOI: https://doi.org/10.51200/bjms.v19i3.5493

Keywords: *Body mass index, Borneo, Colorectal Carcinoma, Lifestyle, Non-communicable Disease*

ABSTRACT

The onset of colorectal cancer (CRC) the third most prevalent malignancy worldwide, results from the interactions between inherited and lifestyle factors. Therefore, there is ample opportunity to prevent the incidence of colorectal cancer by addressing the modifiable risk factors, which are still inconsistent in the Asian population. This study aims to determine the association between smoking, alcohol consumption, BMI, and physical activities in North Borneo. This is matched case-control research with a ratio of 1:2, and the sample size was matched to two controls (103:206) regarding age, gender, and ethnicity. Statistical significance was $p<0.05$, which is significant using SPSS. The frequencies, chi-square, and univariate logistic regression were used. The mean age of respondents is 54.47±11.8 years on average. Major indigenous ethnicities contributed more than 20% in the case group, such as Bajau, Kadazan, and Dusun. Other Indigenous ethnicities are less than 20% (Bugis, Brunei, Murut, Sungai, Bisaya, Jawa, Lundayeh, and Rungus). Although there is no correlation between physical activities, alcohol, and smoking, there is evidence that certain factors like smoking have a weaker relationship (OR= 2.209; 95% CI =1.144-4.264) and more significant or enhanced risk of colorectal incidence. We discovered that a strong association exists between BMI and colorectal Cancer. The implication or consideration of this research is that it might

be beneficial in lowering the incidence of colorectal cancer, provided that the public health system devises strategies to engage and empower primary care providers by providing substantial resources or by emphasizing the significance of Indigenous populations for a more significant influence on the incidence and prevention of Cancer.

INTRODUCTION

The onset of colorectal Cancer (CRC), like the Development of other multifactorial diseases, results from a complicated interaction involving lifestyle variables and hereditary factors (Veettil et al., 2017). Vast established research studies' comparability is constrained because they employ distinct lifestyle variables and assessments, define adherence differently, and approach lifestyle research methodologically in unique ways (Botteri et al., 2020; Liang et al., 2009). However, colorectal cancer in Asian populations appears to be inconsistent because the majority of colorectal cancers take 15 years to develop (Akter et al., 2021; Chiu et al., 2017) and progress slowly (Bagnardi et al., 2015; Forde, 2018; Ganapathy et al., 2019; Mutalip et al., 2011; NHMS 2015; WHO, 2019). Meta-analysis research publishes the correlation between smoking and CRC (Terry et al., 2001; Chen et al.,2003; San Joaquin, 2004). Other reviews indicate a 30%–70% greater risk connected with lifestyle and CRC (Frezza, Wachtel & Chiriva, 2006; Bardou; Barkun & Martel, 2013; Morrison et al.,2013; Chen et al., 2015). Therefore, this study aims to determine the association between smoking, alcohol consumption, body mass index (BMI), and physical activities in North Borneo multi-ethnicities.

MATERIALS AND METHODS

Study design

This case-control study applied a multi-level research approach and a 1:2 ratio to minimize bias.

Study setting

All colorectal cases notified from the four tertiary hospitals in Sabah are gathered in the research case group. The control group is from the health clinic in the same district as the hospital cases group.

Population and Sample Size

The study's target population consists of individuals diagnosed with colorectal cancer (CRC) between 2019 and 2021 and applied to any gender. These individuals must have recorded their information in the Sabah Cancer Registry or the National Cancer Registry. Participants in the control group with 206 were matched up with CRC patients (103) in Sabah who were the same age (within five years), gender, and significant Indigenous North Borneo ethnicity, achieving a power of 80% and detect odds ratios more than 2.0 or lower than 0.6. These patients were also from the same district and indigenous group. The size of the sample was decided upon by taking into account the risk of CRC (odds ratio [OR] =1.78, 95% confidence interval [CI], P2= 0.546 based on the study by Ulaganathan, Kandiah & Mohd Shariff 2018.

Data collection procedure

Data collection started from March 2020 until December 2021 in hospitals and communities. Additional assistance from the respective or selected hospitals, clinics, and Sabah State Health Departments to access cancer registry lists, hospital records of diagnoses, and medical records of subject matter or patients. The cases were selected using a technique known as convenience sampling, while the control subjects were selected using a method known as simple random sampling. The control subjects were assigned to mirror the respondents of the community cases and the health clinic chosen. The Medical Review and Ethics Committee (MREC) of the Malaysian Ministry of Health endorsed the study protocol. All qualified participants provided written informed consent before the interview.

Inclusion and exclusion

A confirmed CRC patient diagnosed with HPE in 3 tertiary hospitals within three years (2019 to 2022) registered with the Sabah State and still alive is the subject for the selected cases. The respondent must be over 18 years old, of North Borneo ethnicity) or Malaysian, have lived in the area for five years, and be willing to participate in the study. Control groups indicated to persons with no disease symptoms or family history of cancers and screened for CRC using the fecal immunochemical blood test (iFOBT). The iFOBT is an earlier screening stool-based method used for the initial screening of CRC. Both samples cannot comprehend or respond to the questionnaire without written consent.

Assessment of sociodemographic, risk of tobacco, alcohol, and physical activities

Sociodemographic data

At first, the survey included questionnaires about sociodemographics, such as age, gender, ethnicity (Sabah ethnicity), religion, marital status, educational status (non-formal education, primary school, secondary school, high education level), monthly income (< RM 1000, RM 1000-RM 3000,>RM 3000), occupational status (International Labor Organization).

Smoking Status

The smoking status of individuals was categorized into three distinct groups based on the number of cigarettes they inhaled per day: current or present smokers, ex-smokers (those who had ceased smoking), and non-smokers who had not smoked (Malaysian National Health Morbidity Survey 2015). The information about smoking history or smoking intensity, such as for current smokers, acquired about the age at first smoking (≤16 years old and >16 years old); the specific number of cigarettes smoked daily (1-10/day, 11-20/day, and >20/day): the total number of years of cigarette smoking (1-10 years, 11-30 years and > 30 years); cigarette pack years (20 pack years, 20-39 and 40) (Sasco et al., 2004: America Tobacco Atlas, 2019). For ex-smokers, the smoking duration was calculated by subtracting the age at which they first started smoking regularly (initiation) from the age at which they quit smoking. It is a self-administered adapted questionnaire (Mutalip et al., 2011; Ganapathy et al., 2019). The risk of tobacco is quantified by documenting the number of pack years a person has smoked. It is calculated by taking the average number of cigarettes smoked in a day, dividing that number by 20, and multiplying that result by the number of years that person has smoked cigarettes.

Alcohol status

The term or category for alcohol consumption is "current drinker," which refers to any respondents who have consumed alcohol-containing drinks in the 12 months before the study. The ex-drinker was one of those people who had given up consuming alcoholic beverages during the previous year. Never drinkers are described as people who never have drunk alcoholic beverages (Lim et al.,2018).The prevalence of heavy episodic drinking (HED) for monitoring hazardous alcohol use or weekly consumption of pure alcohol amounting to or exceeding 60 grams to six standard beverages (World Health Organization, 2019). Moderate drinkers engage in binge drinking of 50g or less or consume six or more standard drinks in one sitting. Heavy drinkers are those who consume 50g or more of alcohol daily or consume six or more standard drinks in one sitting at least once a week (Malaysian National Health Morbidity Survey 2015).

Body mass index (BMI)

Body mass index (BMI) is directly measured using various measuring instruments. The subject's body mass was determined using a digital SECA scale (model seca clara 803, seca gmbh & co. kg., Hamburg, Germany) per the protocols generally followed. BMI is a formula that uses a person's weight in kilograms divided by their height in square meters.

This formula determines whether a person is underweight, normal, overweight, or obese. All of the participants were classified into one of four groups according to their body mass index (Asian): BMI between 18.5 and 24.9 kg/m2 (standard), BMI between 25 and 29.9 kg/m2 (overweight), and obesity was defined in this study as BMI >30 kg/m2 (Zainuddin et al., 2011; NHMS 2015).

Physical activities

All participants self-reported their physical activities on the validated, abbreviated International Physical Activity Questionnaire (IPAQ). A well-established questionnaire of IPAQ assesses past physical history activities over the last seven related to vigorous, moderate, walking, sitting, and sleeping activities. (Forde, 2018). The Metabolic Equivalent of Task (MET) computes the intensity of an activity using the MET value derived from the activity's metabolic equivalent. To determine an individual's level of physical activity, the sum of the durations of walking, moderate-intensity, and vigorous-intensity activities performed throughout one week. METs are classified into three categories: vigorous intensity (more than 3,000 MET minutes per week) or walking for at least seven days a week or three thousand metabolic equivalent minutes per week; moderate intensity (600–3,000 MET minutes per week) engaging in intense effort activities for five days or more a week, accruing at least 600 minutes of MET time per week; and low intensity is with less than 600 MET minutes per week (Forde, 2018). Nil activities are called the unsure answer, and there are no MET minutes to count. Sedentary behavior is the cumulative amount of time spent daily in a stationary position except sleep or an individual who spends more than four hours a day in one of the following positions: sitting, lying down, or standing (Sigmundova, 2015: Nunez et al., 2017).

Ethical consideration

The Medical Research Ethics Committee of the Ministry of Health in Malaysia (NMRR: 19-3905-52394) and the University of Malaysia Sabah Research Ethics Committee (UMS/FPSK 6.9/100-6/1/95) cleared the study to be conducted according to ethical standards. The patient's privacy and confidentiality were protected.

Statistical analysis

IBM SPSS statistics version 28.0 was utilized. The sociodemographic data were presented descriptively and frequently (percentage, %), and simple logistic regression or univariable conditional logistic regression was conducted to the association between lifestyle (tobacco, alcohol, physical activities, BMI) and CRC. Variables were included in the analysis if their p-values were less than 0.05. The results were reported with unadjusted and adjusted odds ratios (OR), 95% confidence intervals (CI), and p-values corresponding to each ratio.

RESULT

Characteristics of Study Population

The baseline characteristics of the case-control study are presented in Table 1. The mean age of respondents is 54.47±11.8 years on average. Major indigenous ethnicities contributed more than 20% in the case group, such as Bajau, Kadazan, and Dusun. Other Indigenous ethnicities are less than 20% (Bugis, Brunei, Murut, Sungai, Bisaya, Jawa, Lundayeh, and Rungus). The average age of the participants was 68.7 years. In contrast with females, current smokers' prevalence was around ten times lower among males (28.1%, 95% CI 24.8-31.6 vs 2.9%, 95% CI 1.9-4.4). Furthermore, the percentages of Malays (19.7%, 95% CI 17.1-22.6) and other Bumiputras residing in Sabah and Sarawak (21.3%) who were current smokers were significantly higher than those of Chinese (9.0%, 95% CI 6.9-11.7) and Indians (7.1%, 95% CI 3.8-14.3).

Smoking cigarettes, Alcohol consumption, and Physical activities

As shown in Table 2, no significant difference was found between CRC with the smoking,

ex-smoking, and never-smoking groups (P-value=0.037). However, there is a risk of having CRC when the respondent started smoking <18 years old (OR= 1.288; 95% CI =0.556-2.985) and started smoking>18 years old (OR=0.407; 95% CI=0.134-1232). Respondents who smoked >10 cigarettes per day (OR=1.718; 95% CI=0.641-4.605) had a higher risk than respondent smoke <10 cigarettes per day (OR=0.464; 95% CI=0.184-

Table 1: Demographic characteristics of participants (n=309)

Variables	Case	Control	OR	95% CI		
	(n=103) n (%)	(n=206) n (%)		Lower	Upper	P-value
Age of respondent						0.911
25-44	17(16.5%)	36(17.5%)	0.472	0.061	3.643	
45-65	61(59.2%)	122(59.2%)	0.5	0.69	3.636	
>65	23(22.3%)	46(22.3%)	0.5	0.66	3.78	
18- 24	2 (1.9%)	2(1.0%)	Referent			
Gender						1
Female	66(64.1%)	132(64.1%)	1	0.611	1.637	
Male	37 (35.9%)	74(35.9%)	Referent			
North Borneo Indigenous						1
Kadazan	21 (20/4%)	39(18.9%)	0.977	0.47	2.029	
Dusun	21(21.3%)	43(20.9%)	1	0.371	2.694	
Bajau	22(21.4%)	44(21.4%)	1.077	0.515	2.251	
Brunei	6(5.8%)	14(6.8%)	0.857	0.29	2.585	
*Other North Borneo Indige-nous	16(15.5%)	32(15.5%)	1	0.454	2.536	
**Others Ethnicity	9(8.7%)	18(8.7%)	1	0.384	2.585	
Bugis	8(7.8%)	16(7.8%)				
Marital status						0.465
Divorce	8(7.8%)	10(4.9%)	0.633	0.24	1.668	
Widow	9(8.7%)	16(7.8%)	0.9	0.381	2.13	
Single	8(7.8%)	26(12.6%)	1.646	0.72	3.805	
Married	78(75.7%)	154(74.8%)	Referent			
Education						0.309
Primary	22(21.4%)	41(19.9)	0.47	0.15	1.467	
Secondary	52(50.5%)	105(51.0%)	0.433	0.149	1.26	
Higher	21(20.4%)	53(25.7%)	0.347	0.112	1.077	
None	8(7.8%)	7(3.4%)	Referent			
Income						0.22
RM1000-3000	32(31.1%)	83(40.3%)	0.405	0.258	0.837	
>RM3000	32(31.1%)	76(36.9%)	0.507	0.281	0.917	
<RM 1000	39(37.9%)	47(22.8%)	Referent			
Occupation						0.15
Professional	4(3.9%)	6(2.9%)	0.967	0.256	3.647	
Manager	3 (2.9%)	6(2.9%)	0.725	0.171	3.07	
Technician and associate pro-fessional	10(9.7%)	41(19.9%)	0.354	0.159	0.787	
Clerical support workers	4(3.9%)	11(5.3%)	0.527	0.157	1.774	
Service and Sales worker	5(8.7%)	21(10.2%)	0.345	0.12	0.992	
Skilled in agricultural, forestry, and fishery worker	7(6.8%)	4(1.9%)	2.538	0.697	9.244	
Craft and related trades work-ers	4(3.9%)	4(1.9%)	1.45	0.342	6.14	
Plant and machine operators and assemblers	3(2.9%)	1(0.5%)	4.35	0.437	43.333	
Elementary occupation	2(1.9%)	16(7.8%)	0.181	0.039	0.832	
Armed force	0	2(1.0%)	0	0	0	
Pensioner	39(37.9%)	58(28.2%)	0.846	0.432	1.657	
Not working working	22(21.4%)	36(17.5%)	Referent			

*(Murut, sungai, Bisaya, Jawa, Lundayeh, Rungus,Suluk,Irranun,Cocos, Kegayan, Tidung)

** (Chinese, Malay)

1.172) especially those who smoked 10-20 packs a year with (OR=1.955; 95% CI=0.613-6.237) and smoked > 20 packs (OR=1.676; 95% CI=0.574-5.136).

Smoking cigarettes, Alcohol consumption, and Physical activities

As shown in Table 2, no significant difference was found between CRC with the smoking, ex-smoking, and never-smoking groups (P-value=0.037). However, there is a risk of having CRC when the respondent started smoking <18 years old (OR= 1.288; 95% CI =0.556-2.985) and started smoking>18 years old (OR=0.407; 95% CI=0.134-1232). Respondents who smoked >10 cigarettes per day (OR=1.718; 95% CI=0.641-4.605) had a higher risk than respondent smoke <10 cigarettes per day (OR=0.464; 95% CI=0.184-1.172) especially those who smoked 10-20 packs a year with (OR=1.955; 95% CI=0.613-6.237) and smoked > 20 packs (OR=1.676; 95% CI=0.574-5.136).

Table 3 shows that former drinkers of alcohol have a higher risk of colorectal cancer than drinkers of alcohol (OR=1.361; 95% CI=0.613-4.022). This risk is higher than colorectal Cancer among drinkers of alcohol (OR=1.803; 95% CI=0.900-3.612). Those who began consuming alcohol before the age of 18, at a younger age, have a higher risk of developing colorectal Cancer (OR = 1.947; 95% CI=0.796-4.760) than those who began drinking alcohol after the age of 18 years old (OR = 1.318; 95% CI = 0.526-3.298). Consuming alcohol for 30 years or longer is not exempt from the heightened risk of colorectal Cancer (OR=2.129; 95% CI=0.947-4.791).

The physical activities of the respondent are demonstrated in Table 4. BMI was positively associated with the risks of CRC. Overall, respondents who were overweight had a significantly lower incidence of colorectal Cancer (CRC) than those who were obese (OR=4.444; 95% CI=1.231-16.04; P-value <0.001), even though obese individuals were nearly twice as likely to receive a CRC diagnosis (OR=4.444; 95% CI=1.231-16.04). The physical activity levels indicated that those with high

Table 2: Odds ratio and 95% CI of colorectal cancer risk according to tobacco users (n=309)

Variables	Case (n=103) n (%)	Control (n=206) n (%)	OR	95% CI		P-value
				Lower	Upper	
Smoking status						0.037*
Smoker	14(13.6%)	36(17.5%)	0.859	0.435	1.698	
Ex-smoker	22(21.4%)	22(10.7%)	2.209	1.144	4.264	
Never smoker	67(65.0%)	148(71.8%)	Referent			
Age started smoking						0.202
< 18	10(9.7%)	15(7.3%)	1.288	0.556	2.985	
>18	4(7.7%)	19(9.2%)	0.407	0.134	1.232	
Never smoker	89(86.4%)	172(83.5%)	Referent			
Typical no of cigarettes daily						0.12
<10	6(5.8%)	25(12.1%)	0.464	0.184	1.172	
>10	8(7.8%)	9(4.4%)	1.718	0.641	4.605	
Never smoker	89(86.4%)	172(83.5%)	Referent			
Cigarettes pack a year						0.52
1-9	2(1.9%)	17(8.3%)	0.230	0.052	1.018	
10-20	6(5.8%)	6(2.9%)	1.955	0.613	6.237	
>20	6(5.8%)	7(3.4%)	1.676	0.574	5.136	
Never smoker	89(86.4%)	174(85.3%)	Referent			
Total of years of cigarette smoking						0.502
<30	6(5.8%)	11(5.3%)	0.611	0.265	1.411	
>30	25(12.1%)	8(7.8%)	1.042	0.373	2.910	
Never smoker	89(86.3%)	170(82.5%)	Referent			

*level of significance p<0.05

activity levels had a lower likelihood of being diagnosed with CRC (OR=0.863; 95% CI=0.402-1.850), showing an 18% difference from the case group compared to individuals with no physical activity.

DISCUSSION

CRC in Asian populations is scarce and inconsistent (Ganapathy et al., 2019). Therefore, this study represented the risk factors of modifiable lifestyles of individuals from major Indigenous North Borneo, such as tobacco use, alcohol consumption, and physical activity.

Sociodemographic

Table 3: Odds ratio and 95% CI of colorectal cancer risk about alcohol consumption (n=309)

Variables	Case (n=103) n (%)	Control (n=206) n (%)	OR	95% CI		
				Lower	Upper	P-value
Drinking status						0.213
Drinker	17(16.5%)	21(10.2%)	1.803	0.9	3.612	
Ex-drinker	11(10.7%)	18(8.7%)	1.361	0.613	3.022	
Never drink	75(72.8%)	167(81.1%)	Referent			
Age drink started						0.299
< 18	10(9.7%)	11(5.3%)	1.947	0.299	0.166	
>18	8(7.8%)	13(6.3%)	1.318	0.796	4.76	
Never drink	85(82.5%)	182(88.3%)	Referent			
Drinking duration						0.166
<30	5(4.9%)	12(5.8%)	0.887	0.303	2.599	
>30	13(12.6%)	13(6.3%)	2.129	0.947	4.791	
Never drink	85(82.5%)	181(87.9%)	Referent			
Drinker level						0.616
Moderate	5(4.9%)	6(2.9%)	1.734	0.515	5.838	
Heavy drinker	11(10.7%)	19(9.2%)	1.204	0.549	2.642	
Never drink	87(84.5%	181(87.9%)	Referent			

*level of significance p<0.05

Table 4: Odds ratios and CI of CRC according to BMI, PA levels, and Sedentary Levels

Odds ratio (95% CI)						
BMI						P-value <0.001*
Underweight	Ca/Co (%)	Overweight	Ca/Co (%)	Obese	Ca/Co(%)	
1	55(53.4%)	2.296	45(43.7%)	4.444	3(2.9%)	
(Referent)	66(32.0%)	(1.401-3.765)	124(60.2%)	(1.231-16.049)	16(7.8%)	
Physical activities levels						P-value 0.267
Low	Ca/Co(%)	Moderate	Ca/Co(%)	High	Ca/Co(%)	Nil activity
1	41(39.8%)	0.642	30(29.1%)	0.863	18(17.5%)	1.178
(Referent)	62(30.1%)	(0.306-1.344)	61(29.6%)	(0.402-1.850)	50(24.3%)	(0.516-2.690)
Sedentary activities level						P-value 0.87
Not sure	Ca/CO (%)	<4 hours	Ca/Co(%)	>4 hours	Ca/Co (%)	
1	50(48.5%)	0.624	36(35.0%)	1.295	17(16.5%)	
(Referent)	109(52.9%)	(0.362-1.077)	49(23.8%)	(0.678-2.473)	48(23.3%)	
Ca (case) Co(control)		BMI (Body Mass Index)		PA (Physical activities)		

*level of significance p<0.05

Data indicated that Indigenous ethnic groups reported the most significant incidence of CRC in Sabah. Similar disparities exist in other studies regarding cancer incidence and survival between Indigenous and non-Indigenous people (De Moor et al., 2015; Sigmundova et al., 2015). Females registered as the majority in cases registered as CRC. Similar to the global finding, CRC placed second among women and third among males in 2018 in Asian countries (Jung et al., 2011; Sekeras et al., 2011). The respondent mean age (SD) is 54.47± years, about the same as the mean age found in a study in Pondicherry, India, which was 54.1± years with 11.5 years of difference. Although age has a significant role in how quickly colorectal cancer spreads, males in China have a greater incidence rate than women of all ages (Liang et al., 2009; Siegal et al., 2020).

Smoking

Our research results indicate that those who used to smoke are more likely at risk to develop CRC when respondents started smoking <18 years old with >10 cigarettes per day, especially those who smoked 10-20 packs a year. The meta-analysis risk estimates on the effect of cigarette smoking from 188 research published from 1958-2018 show that smoking increases the risk of CRC incidence with duration and intensity (Botteri et al., 2020). This relationship's strength is weaker than that found for adenomas (OR= 2.209; 95% CI =1.144-4.264) than for current smokers (OR=0.859; 95% CI=0.435-1.698). This study indicates that increased tobacco use among individuals under 18 elevates the risk of CRC (OR=1.288; 95% CI=0.556-2.985), consistent with findings from the National Health Morbidity Survey 2015. Smokers who consume over ten cigarettes daily (OR=1.718; 95% CI=0.641-4.605), 10-20 packs annually (OR=1.955; 95% CI=0.613-6.237), and individuals smoking more than 20 packs per year (OR=1.676; 95% CI=0.574-5.136) exhibit an increased risk for CRC.

The risk of CRC is substantially elevated in individuals who are exposed and smoke over 20 cigarettes daily or for a minimum of 30 years (30 packs/year) (Liang et al.,2009; Myint et al.,2016). This evidence was observed and provides strong support for risk increase with the intensity and duration of smoking by 25%–30% in smokers of 40 cigarettes per day or in those who smoke for 50–60 years (Botteri et al., 2020). However, wide variation in age at initiation and duration of smoking complicates the identification of the warning signs in the association between smoking and CRC (Tsoi et al., 2009).

Alcohol

North Borneo Indigenous people tend to prepare homemade alcoholic beverages (Mutalip et al., 2014), but this study demonstrated that they are not statistically associated with CRC. This is like other case-control studies from Thailand, Canada, and Egypt (Mahfouz et al.,2014). In contrast with other cohort and case studies, there is an association between alcohol consumption and CRC in both genders (Marmot et al., 2007). However, there is a risk of CRC occurrence Drinker (OR=1.803; 95% CI=0.9-3.612) and ex-drinker (OR=1.361; 95% CI=0.613-3.022) increased when started to drink before 18 years old (OR=1.947; 95% CI=0.299-0.166) and less risk when began to drink after 18 years old (OR=1.318; 95% CI=0.796-4.76).

The Morbidity Survey of 2014 indicated that the age of drinking started as late as 21 years old and still, we found that as young as 16 years old or younger, as observed in other nations. predicts lifetime alcohol-related problems and alcohol disorders in later life (Gomez et al., 2011). Lifetime exposure to alcohol is seen as a higher risk with CRC respondents who drink alcohol for more than 30 years (OR=2.129; 95% CI=0.947-4.791). In contrast, it stated there is no strong association between lifetime exposure to alcohol, frequency of drinking, and age at starting to drink alcohol (Loomis et al., 2018). Our finding on alcohol risk to

colorectal cancer is consistent with existing evidence studies, which indicated that there was no correlation between the quantity of alcohol consumed during one's life and the probability of survival (Phipps et al., 2017). The drinker level, whether moderate or heavy drink, shows the risk of CRC (Moderate drinker: OR=1.737; 95% CI=0.515-5.838 and Heavy drinker: OR=1.204; 95% CI=0.549-2.642). CRC mortality rate was found to be positively correlated with excessive alcohol consumption (>50 g/day) (Hamid et al., 2009; Bagnardi et al., 2015; Ben et al.,2015; Abar et al., 2018). Similar to the findings of other studies from India and (Iswarya et al., 2016), Our study did not identify a statistically significant association between smoking habits or alcohol consumption and the likelihood of developing CRC. This could be the possibility of potential underreporting by respondents because the exposure to the risk factors is predictable in the self-report questionnaire, which also introduces a recall bias.

Body Mass Index

Our findings show that regardless of gender, the obese (respondent intends to have a higher risk of CRC (OR= 4.444; 95% CI=1.231-16.049) than the overweight respondent (OR=2.296; 95% CI=1.401-3.765) but both are statistically significant correlation between BMI with the colorectal cancer risk with P-value of 0.001. The results from 13 distinct meta-analytical cohort studies indicated that weight gain or BMI is associated with an increased risk of colon cancer (WCRF & AICR, 2007; Karahalios et al., 2015; Veettil et al., 2017). Excess weight (body mass index (BMI) of 25 kg/m2 or higher) and obesity (BMI of 30 kg/m2 or higher) are two highly changeable risk variables that have consistently been linked to an elevated risk of CRC up to 9% to 19% and have a substantial impact on the occurrence and death rate of CRC in both sexes (Huu et al., 2009). According to a 2017 study on CRC and obesity conducted in Malaysia, Malaysia had a lower population attributable fraction (PAF) for overweight compared to Korea and Brazil. However, the negative impacts it may have on multiracial countries like Malaysia are still not fully understood. Further study into the underlying understanding of biological mechanisms and pathways relating to obesity to CRC is required.

Physical Activities

This case-control study did not find any significant association between the level of physical activity (PA) and CRC with a P-value of 0.267 and support by the odds ratio on high-level PA/vigorous level (≥3.000 MET minutes a week) OR= 0.863;95% CI= 0.402-1.850 and moderate PA level or 600 3.000 MET minutes per week (OR= 0.642;95% CI= 0.306-1.344) but slightly risk to CRC with Not sure answer from the respondent (OR=1.178;95% CI=0.516-2.690) were 13.6% from pre-diagnosis or case group and 16.0 % from the control groups. Consistent with the conclusion reached by the American Institute for Cancer Research and the World Cancer Research Fund, physical activity does not provide any correlation with the risk of developing rectal Cancer (Schmid et al., 2014).

However, emerging evidence reported an association between moderate and higher physical activity levels and CRC risk (Golshiri et al., 2016). The CRC risk of individuals who engaged in moderate to vigorous exercise (16.6 Met-h/week) was found to be 31% lower in a cohort study from Norway Rangul 2018 [95% confidence interval (95% CI), 1.00–1.70] than in those who exercised less than 8.3 Met-h/week (Schmid et al., 2014; Rangul et al., 2018). Vigorous physical activity may have an even more significant beneficial effect, but low physical activity is significantly associated with an increased risk of CRC (Golshiri et al., 2016; Alsheridah et al., 2018).

Subsequently, we also observed that respondents who engaged in sedentary behaviour for more than 4 hours were at a higher risk of colorectal Cancer (OR=1.295; 95% CI=0.678-2.473) than those who practised less than 4 hours (OR=0.624; 95% CI=0.362-1.077).

This outcome was in line with the conclusions of other studies that identify sedentary behaviour as a growingly acknowledged risk element for CRC occurrence and death, regardless of physical activity (Cao et al., 2015; Morris et al., 2018). In this current study, we cannot compare our results with those studies because sedentary behaviour is unable to be explicitly assessed as associated with CRC risk, and it is similar to the study by (Morris et al., 2018). Further research is required in a wide range. Additional studies on the trends linking Indigenous features toward CRC are essential to successfully applying the evidence-based guidelines in Malaysia.

CONCLUSION

Our research has shown that adopting unhealthy lifestyles, such as smoking, drinking alcohol, and engaging in physical activities, differs from other country Indigenous peoples. Proven by Smokers have a weaker risk association to developing CRC started smoking at <18 years old with >10 cigarettes per day, especially those who smoked 10-20 packs a year. On the other hand, we also discovered that a strong association exists between BMI and CRC. Empowerment primary care providers by emphasizing the significance of Indigenous populations for a more significant influence on the incidence and prevention of Cancer.

CONFLICT OF INTEREST

This study was fully self-funded and had no conflicts of interest

ACKNOWLEDGEMENTS

Nhe authors thank everyone involved and the Ministry of Health Malaysia for permission to conduct this research.

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BJMS
Borneo Journal of Medical Sciences

ORIGINAL ARTICLE

Health Empowerment Program Among Security Personnel at A Public University

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Received: 26 October 2024

Accepted: 14 March 2025

Published: 2 September 2025

DOI: https://doi.org/10.51200/bjms.v19i3.5534

ABSTRACT

The shift in the national health focus from curative towards prevention and wellness has sustained the importance of health-promoting activities, such as health empowerment programs which have been an important element in contributing to developing health-prioritizing mindsets in due respect with myriads of occupational factors. This has justified the need for frontlines type of work, especially security personnel to be continuously instilled with health and safety related information. Thus, three series of health empowerment programs were conducted among security personnel at the Universiti Malaysia Sabah. The health empowerment program aimed to compare the knowledge, attitude and practice scores, before and after the series of programs had been duly conducted. This intervention study was conducted over three consecutive weeks, which involved pre- and post-evaluation of the knowledge, attitude and practice elements of three domains of topics, which were Occupational Safety and Health awareness, noncommunicable and communicable diseases. Data analysis was conducted by using SPSS version 29 and a paired T-test was conducted to determine the mean score outcomes and its significant differences. Overall, this study has been pioneered among small numbers of security personnel due to duty constraints. In a 90% response rate, there were significant differences in the

Keywords: *Security Personnel, Occupational Health, OSH awareness, Noncommunicable Diseases, Communicable Diseases*

pre-and post-test mean score outcomes of knowledge and attitude elements in the series of noncommunicable diseases and practice elements in the series of communicable diseases. The health empowerment program was deemed significant instead of being treated as a non-pivotal element in ordinary health-related courses.

INTRODUCTION

Every security personnel who was on duty would be predisposed to a plethora of threats (Manandhar et. al., 2021; OSHA 3335-10N 2007; WHO Europe 2002). The potentially occurring Occupational Health (OH) hazards within the study population area of protection included road accidents and sudden emergencies related to zoonoses such as dog bites, bee stings, spider venoms and even snake bites which had also been described by Hussain et. al., 2020. This occasionally rendered them the ones to lead the scene while waiting for appropriate aids to come over, such as the ambulance and firefighters. They would be the ones to whom everyone within their area of protection to be reached whenever an emergency occurred. Apart from that, several types of OH hazards were associated with security personnel. The OH hazards can be classified into a few types, which are physical, biological, chemical, ergonomic and psychological (Manandhar et. al., 2021).

There were significant influences of occupational factors among occupants in various broad occupations including the security duty natures. Occupants of different sectors tended to be developing or inculcating various modes of dietary patterns, socializing norms and within-society adaptation (Parkash et. al., 2019). Epidemics of NCDs and CDs in every locality of origin could have been continuously widespread in societies if preventive measures were conducted.

The above-mentioned factors suggested the need for the security personnel to be equipped with health educational information for mutual benefits among the employer and employees to prevent subsequent losses due to sickness and mishaps and to promote health (WHO Europe 2002; OSHA 3335-10N 2007). Health empowerment activities within workplaces would be an example of good OH practices that should be conducted to improve the quality of life among employees. The improvement in a healthier workforce would be reflected through decreased absenteeism, indirectly increasing workers' working performances (International Well-Being Insights 2019; OSHA 3335-10N 2007; WHO Europe 2002). It would also lead to changes at both individual and organizational levels (International Well-Being Insights 2019; OSHA 3335-10N 2007; WHO Europe 2002).

Due to this, three series of train the trainer (TTT) health empowerment programs were conducted, which started with the Occupational Safety and Health (OSH) awareness series, followed by non-communicable (NCD) and communicable diseases (CD). All three series of health empowerment programs were to inseminate the knowledge, attitude and practice (KAP) information against minimizing the risk of OH hazards among the security personnel of a public university setting.

Meanwhile, the pre-and post-evaluation of outcomes of the health empowerment program were conducted. The knowledge, attitude and practice (KAP) scores in the three series of health empowerment programs were evaluated and compared, before and after each series of programs.

MATERIALS AND METHODS

Study Design, Setting & Participants

The health empowerment program has served to be an intervention study among security personnel at the Universiti Malaysia Sabah. The health empowerment program involved three main series, which were the OSH awareness,

the NCDs and CDs. The three series of health empowerment were pioneered in a train-of-trainer program. The health empowerment program fulfilment would be based on modules developed specifically meant for the targeted study participants. During the series of health empowerment activities, data scoring for knowledge (K), practice (P) and attitudes (A) were also conducted before and after each main subject of the health empowerment talks. Questionnaires were adapted from similar literature. The KAP elements in the three series of health empowerment programs were assessed among the participants through the pre- and post-questionnaires, during the intervention study. The questionnaires in the three series of health empowerment programs, contained three main elements, as the following: (a) knowledge (10 items), (b) attitude (10 items) and (c) practice (10 items). There were two different types of questions namely, 'Yes' or 'No' questions for knowledge questions and 'Likert Scale' for attitude and practice questions. The scoring scales for the main elements were listed as follows:

Knowledge Scales

For knowledge questions, 1 point was given for correct answers, and 0 points were given for wrong answers. A total of 23 scores were given for knowledge questions. The score ranges for knowledge (Paul et. al., 2022) were categorised as the following:

- High Knowledge: 7 – 12 (85% -100%
- Medium Knowledge: 5 – 6 (60% - 84%)
- Low Knowledge: ≤4 (≤59%)

Attitude Scales

For attitude questions, 0 points were given for those who answered, 'Strongly Disagree', 1 point for 'Disagree', and 2 points for 'Agree' and 'Strongly Agree'. A total of 50 scores were given for practice questions. The score ranges for attitude (Paul et. al., 2022) were categorized into:

- Positive Attitude: 17 – 25 (70% - 100%)
- Negative Attitude: ≤16 (≤69%)

Practice Scales

For practice questions, 0 points were given for those who answered, 'Strongly Disagree', 1 point for 'Disagree', 2 points for 'Agree' and 3 points for 'Strongly Agree'. A total of 60 scores were given for practice questions. The score ranges for practice (Paul et. al., 2022) were categorized into:

- Good Practice: 27 – 30 (70% - 100%)
- Poor Practice: ≤26 (≤69%)

Dependent Variables

The pre-and post-KAP scores were generated by every participant in the three series of health empowerment programs.

Independent Variables

Module developed by every speaker in the three series of health empowerment programs and mode of presentation conducted by every speaker during the entire intervention study.

Sample Size Calculation & Sampling Technique

The sample size was determined based on Krejcie and Morgan (1970) sample size formulae. With a population of 10, the sample size is 10.

Data Analysis

The knowledge, attitude and practice (KAP) scores were obtained by total addition of every score as given in the health empowerment scales (as shown above). Scores for each element were compiled, and mean score and significance differences were identified by paired T-tests, SPSS version 29.0. P-value <.05 was considered statistically significant.

Ethical Approval

The approval code was JKEtika 1/23 (13) given by the Faculty of Medicine and Health Sciences of the Universiti Malaysia Sabah. In addition, research activity consent was also submitted and approved by the public university setting

security division.

Table 1: The Paired Sample Test of Mean Knowledge, Attitude and Practice Scores of OSH Awareness Series (n=10)

Variable	Mean (SD)		Mean Diff. (95% CI)	*t*-statistics (*df*)	p-value
	Pre	Post			
OSH Awareness Knowledge Scores	8.63 (.518)	6.75 (4.166)	1.875 (-1.570, 5.320)	1.287 (7)	.239
OSH Awareness Attitude Scores	17.75 (.707)	17.00 (2.828)	.750 (-1.768, 3.268)	.704 (7)	.504
OSH Awareness Practice Scores	20.56 (3.087)	21.67 (3.775)	-1.111 (-5.001, 2.779)	-.659 (8)	.529

*Paired sample t-test, significant if p<0.05.

Table 2: The Paired Sample Test of Mean Knowledge, Attitude and Practice Scores of NCD Series (n=10)

Variable	Mean (SD)		Mean Diff. (95% CI)	*t*-statistics (*df*)	p-value
	Pre	Post			
NCD Knowledge Scores	6.13 (2.100)	8.13 (1.246)	-2.000 (-3.341, -.659)	-3.528 (7)	.010
NCD Atti-tude Scores	14.13 (4.086)	18.38 (3.335)	-4.250 (-7.465, -1.035)	-3.126 (7)	.017
NCD Prac-tice Scores	14.75 (1.753)	16.63 (1.923)	-1.875 (-4.216, .466)	-1.894 (7)	.100

*Paired sample t-test, significant if p<0.05.

Table 3: The Paired Sample Test of Mean Knowledge, Attitude and Practice Scores of CD Series (n=10)

Variable	Mean (SD)		Mean Diff. (95% CI)	*t*-statistics (*df*)	p-value
	Pre	Post			
CD Knowledge Scores	9.67 (.707)	9.44 (.527)	.222 (-.290, .735)	1.000 (8)	.347
CD Attitude Scores	13.33 (1.500)	12.89 (1.537)	.444 (-1.403, 2.292)	.555 (8)	.594
CD Practice Scores	14.56 (3.005)	18.44 (3.609)	-3.889 (-7.400, -.378)	-2.554 (8)	.034

*Paired sample t-test, significant if p<0.05.

RESULTS

There were no significant differences in the pre-and post-mean knowledge (p=.239), attitude, (p=.504) and practice scores (p=.529) in the series of OSH awareness health empowerment programs. This is shown in Table 1.

Alternately, there were significant differences in the pre-and post-mean knowledge (p=.010) and attitude (p=.017) scores in the series of NCDs' health empowerment programs. However, there were no significant differences in the pre-and post-mean-practice (p=.100) scores in the series of NCDs health empowerment programs. This is shown in Table 2.

On the other hand, there were no significant differences in the pre-and post-mean knowledge (p=.347) and attitude (p=.594) scores in the series of CD health empowerment programs. However, there were significant differences in the pre-and post-mean practice (p=.034) scores in the series of CD's health empowerment program. This is shown in Table 3.

DISCUSSION

The conflict in health empowerment of programs if not thoroughly tackled, would otherwise resemble the teacher-class conventional activities (O'Connor et. al., 2015). However, it would be rather difficult to simply reach out to big communities in tremendous moves such as having big and wide-scale health empowerment activities. Potential barriers might exist on a big scale, and among two and possibly multiple ways of interaction most probably among the presenter and the participants. Thus, training the trainer's health empowerment program would surpass the setbacks that might occur during the process (Brendsetter et. al., 2015; O'Connor et. al., 2015). The idea would be that, through peer power, every health-related information could be shared, circulated and multiplied within their working community (O'Connor et. al., 2015).

The duty nature and shortage of manpower of the current setting security personnel have served to be the limiting factors for the entire security division participation. Thus, the three series of health empowerment programs were pioneered among a small sample size of participants, in a train-of-trainer mode of intervention study. However, due to exclusion factors during the implementation of the intervention study, there have been inconsistencies in the attendance of participants on day one and day two in each series of topics. The overall rate of response is 90%.

A coordinated and comprehensive training module, which included activities to disseminate health and safety information, was designed to meet the occupational health and safety needs of the study population. The integration and coordination between OH and health promotion were needed at every organizational level to reach the public community with a blend of stipulated working sector relevant OH information. The OH scope to be emphasized should not be restricted only to the prevention of NCDs but should be expanded to improve the quality of total health among them.

This study assessed the KAP components about awareness of the risk of OSH among security personnel, in the first series of the program. The knowledge of OSH would be to assess the security personnel's uptakes on self-responsibility in protecting themselves against safety and health hazards. Whereas attitude towards OSH would likely be positive about any safety-related activities or training, and compliance with safety policies and regulations at work. Meanwhile, the practice of OSH at work includes an action that can prevent any accident from occurring (Mohd et. al., 2019). Of such, questions assessed in the pre and post-test were related to the awareness of their duty roles as to follow the Standard Operating Procedure (SOP), the awareness to abide by the rules to protect themselves and peer colleagues against health hazards and risk factors, the interest of attending the supplementing OSH and emergency aids, types of technical and theory seminars and importance of applying personal protective equipment (PPE) when getting exposed to hazardous material (Mohd et. al., 2019; My et. al., 2012; Paul et. al., 2022).

In the second series, the risk factors, and rate of incidences of global and Malaysian region's NCDs were discussed. The knowledge elements being assessed were the risk factors that lead to the development of NCDs such as heart disease and diabetes mellitus. The

attitude elements are inferred with the perceptions towards maintaining good health, through health screenings, having the ideal body mass index (BMI) by avoiding fast and processed food, the priority of selecting nutritious contents when doing groceries and preferences of active over lame lifestyles. Apart from that, practice elements assessed in the series of NCDs were preferences in living healthy lifestyles by having a balanced diet and maintaining physical activities (Mohammad et. al., 2018).

The third series of health empowerment programs was the CD topics which comprised Tuberculosis (TB), AIDS and Sexual Transmitted Infections (STIs). The knowledge elements of CDs being assessed were the respondents to know the causative agents of TB and STIs, in terms of bacteria causing its inflictions. The knowledge of how TB affects the human bodily organs and HIV invasions to human immunity system (Poudel et. al., 2015), the symptoms of TB and STIs, and know how AIDS and STIs (Al-Batanony, 2016; Das et. al., 2015; Demis et. al., 2017; Poudel et. al., 2015) can be contacted. In addition, to assess the knowledge on the importance of BCG vaccination in the prevention of TB. The attitude elements were to assess the behaviours of respondents in getting relevant information on TB, STI and AIDS, which in the meantime to avoid the wrong information about the diseases being stigmatized and circulated in the societies. The attitude also inferred the desire to share the knowledge of the CDs among their families and friends, and that themselves to promote good ventilation in secluded spaces to prevent transmission of airway diseases such as TB and to avoid random sexual activities, drug abuse and homosexual activities to prevent themselves from being contracted with HIV and STI. The practice elements of CDs being assessed were the respondents to have the correct knowledge of the facts of TB, AIDS and STIs. The fact that TB could be treated by medication if detected earlier, and aware of the symptoms of TB, have insights into how HIV (Poudel et. al., 2015), is spread in the community and the risk factors of STIs and wearing condoms in preventing contraction of STIs (Al-Batanony, 2016; Das et. al, 2015; Demis et. al., 2017; Poudel et. al., 2015).

Literature findings on separate studies of OSH awareness, NCDs and CD interventions were quite numerous, and KAP assessments simultaneously conducted with intervention research activities were relatively few in recent years. Inherently, a health empowerment program among security personnel of a public university, comprising OH-related topics would be a preponderance for innovation in module production of the health empowerment program. This study could be regarded as a pioneer study. This alternately provides room for extensive exploration and creativity of other studies bearing similar interests.

CONCLUSION

Having a good understanding of OH-associated predisposing health and safety concerns would contribute to targeting public health concerns regarding general and work-related diseases. Beyond that, it was hoped that working performances among the security personnel would be alleviated by promoting health qualities.

CONFLICT INTEREST

The authors have no conflicts of interest.

ACKNOWLEDGEMENTS

Warmest thanks and deepest feelings of gratefulness to our research project leader and co-supervisors who made our work possible. Finally, very heartfelt gratitude to the university for having funded this research project. This work was supported by the Research Fund provided by the University Malaysia Sabah, Research Grant SDK 0108-2019.

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BJMS
Borneo Journal of Medical Sciences

ORIGINAL ARTICLE

Prevalence and Characteristics of Undiagnosed Hemoglobinopathies Among Adolescents in a High Beta-Thalassemia Prevalence Area: A Cross-Sectional Study

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Received: 13 November 2024

Accepted: 19 February 2025

Published : 2 September 2025

DOI: https://doi.org/10.51200/bjms.v19i3.5598

Keywords: *Hemoglobinopathies, Thalassemia, Prevalence, Disease attributes, Adolescent*

ABSTRACT

Research on hemoglobinopathies mainly targets school-aged and adult groups, underscoring a lack of studies on adolescents nearing reproductive age. The primary objective was to determine the prevalence of hemoglobinopathies among adolescents who had not been previously screened. Additional objectives were to explore possible associations between undiagnosed hemoglobinopathies, socio-demographic factors, and specific characteristics of these disorders. This cross-sectional observational study included 149 adolescents aged 10 to 24. All participants underwent physical examinations and hematological analyses. The collected data were analyzed using established statistical methods. Among the 149 adolescents studied, 8.7% (13 individuals) had hemoglobinopathies, with the majority being Kadazandusun (92.3%). Specific findings included two cases of hemoglobin E trait and eleven of beta-thalassemia trait. Those with hemoglobinopathies were typically 1.5 years younger than those without. Statistically, they had a higher prevalence of microcytes (61.5% vs. 27.2%, p=0.024) and hypochromic red cells (61.5% vs. 27.9%, p=0.028), increased red cell counts (mean difference of 0.92, p<0.01), decreased hemoglobin levels (mean difference of -1.3, p=0.016), and elevated platelet counts (mean difference of 54.28, p=0.01). Hemoglobin electrophoresis showed higher hemoglobin A2 (mean difference of 9.47%, p=0.004) and fetal hemoglobin levels

(mean difference of 1.16%, p=0.009). Even in a highly prevalent area with thalassemia, where the true prevalence of undiagnosed hemoglobinopathies in adolescent age groups was unknown, the actual prevalence was high at 8.7% thus proving the need to increase more screening in this group of apparently healthy adolescents to prevent potential development of new cases of beta-thalassemia major.

INTRODUCTION

Background

Hemoglobinopathies encompass a group of genetic disorders characterized by abnormalities in hemoglobin structure or production. These disorders are divided into qualitative defects, like sickle cell anemia, which involves issues with hemoglobin structure; and quantitative defects, like thalassemia, which pertains to hemoglobin production (Shrestha & karki, 2013).

Thalassemia is one of the most common autosomal recessive disorders and is highly prevalent in countries within the tropical belt, including Malaysia (Cao & Kan, 2013 & Weatherall, 2018). Malaysia, a diverse multi-ethnic country, comprises Malays and other indigenous groups making up 67.4% of the population, Chinese at 24.6%, Indians at 7.3%, and others at 0.7%. In this ethnically varied landscape (Alwi & Syed-Hassan, 2022), thalassemia, including both alpha- and beta-thalassemia, emerges as one of the most prevalent genetic diseases in the nation.

As of 28 November 2018, 8,681 patients with thalassemia had been registered in the Malaysian Thalassemia Registry (MTR). Out of these, 7,984 (91.97%) were alive, with 130 (1.63%) reported as cured by stem cell transplantation. Another 614 patients (7.7%) were lost to follow-up, while the remaining 697 patients (8.03%) had passed away (Ibrahim et al., 2020). Sabah, a state in East Malaysia located on Borneo Island, has a diverse population around of 3.2 million people, encompassing 33 ethnic groups. According to the latest national census, the main indigenous ethnic groups include Kadazandusuns, Bajau, Malays, and Muruts" (Tangit, 2017). A study on Indigenous people revealed that 30% (193/645) of the sample tested positive for the following: beta-thalassemia trait (78%; 151/193), HbE trait (10%; 20/193), Homozygous HbE (2%; 4/193) and other hemoglobinopathies (7%; 13/193). The remaining 3% (5/193) of the abnormal results were inconclusive, necessitating further molecular analysis (Pauzy et al., 2018).

Study Rationale

The National Thalassemia Prevention and Control Program in Malaysia was established in 2004 to reduce the prevalence of thalassemia and improve the management of affected individuals in the country. This program focuses on the early detection of thalassemia carriers and other hemoglobinopathies, targeting couples before marriage and pregnant women. In 2016, a school-based screening initiative was implemented under this program, targeting Form 4 students (typically aged 16) to identify carriers early (Ministry of Health Malaysia, 2020).

While many studies focus on school-based and adult populations, further attention on adolescents is still required as this age group represents an important group that will soon enter the reproductive phase of life, thus detection needs to be more thorough and widespread screening should be conducted. Additionally, there is evidence that pockets of adolescents missed the National Thalassemia Prevention and Control Program in a study showing that the lack of knowledge and misconceptions about the disease including fear of social stigma or discrimination (Wong et al.,2011) were among the factors leading to refusal to the program. A study in 2020 also showed that parents refused screening for their children, believing that their children are not at risk of thalassemia as there were no thalassemia major or carrier in their family (Che Mat et al.,2020).

By focusing on adolescents, adolescents' awareness and understanding of their carrier status can influence community health behaviors, fostering a generation that is more knowledgeable and proactive. Accurate data backed by widespread screening in this age range will serve as the cornerstone for successful public health initiatives, allowing stakeholders and governments to more strategically allocate resources. Future generations' healthcare costs related to treating thalassemia and other hemoglobinopathies may be decreased in the long run by early intervention through adolescent screening.

The primary objective of this study was to determine the true prevalence of hemoglobinopathy in apparently healthy, undiagnosed adolescents in a high-prevalence area for beta-thalassemia major in Sabah. Additional objectives include examining the association between undiagnosed hemoglobinopathy and sociodemographic factors, clinical findings from physical examination, hematological parameters, serum iron level and hemoglobin electrophoresis.

MATERIALS AND METHODS

This was a cross-sectional observational study conducted in Kota Kinabalu, Sabah focusing on adolescents in the community, defined as aged between 10 to 24 years (Sawyer et al., 2018). The study was conducted by invitation for adolescents who fulfilled the inclusion criteria of the age range stated above, who may or may not have a family history but never underwent any screening for hemoglobinopathy and were willing to participate in the study by providing informed consent.

Participants were selected via simple random sampling and invited to participate in the study. Once recruited and informed consent was obtained, baseline demographics information was taken such as age, gender, ethnicity, family history of blood disorders, and family history of consanguinity. Anthropometric measurements of height and weight were taken, and body mass index (BMI) was calculated. A clinical examination was performed to assess symptoms of headache and frequency of headache if present, signs of anemia, jaundice, oedema, and measurement of vital signs of systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate were taken. Disease-specific questionnaires are reliable and validated to estimate disease burden and these questionnaires were adopted (Thein et al., 2009). The questionnaire was translated into Malay by the researchers who are proficient in both English and Malay using the forward-backward translation method. Pilot testing was done on 30 participants from the target study population and reliability metrics were assessed, with Cronbach's alpha value of 0.85, indicating strong internal consistency.

In addition, 4 ml of venous blood was collected in ethylene diamine tetraacetate (EDTA) vials, and hematological analysis of hemoglobin level, red cells count, total and differential white cells count, platelets counts was performed with automated cell counter (ABBOT CELL-DYN Ruby Hematology Analyzer) for complete blood counts. The microscopic examination and full blood count results were co-interpreted together with the automated cell counter results by the principal investigator. Serum iron level and reticulocyte counts were measured. The blood was also sent for hemoglobin electrophoresis, which was performed using BIORAD D10 High Performance Liquid Chromatography (HPLC) system. Due to budget limitations, additional tests like DNA analysis and the Isoelectric Focusing (IEF) method to confirm the Hb E and other hemoglobin variants could not be performed.

Sample size was calculated at 130 participants, with a confidence is 95%, expected prevalence was 0.175 and precision

was 0.05 (Naing et al., 2006) as the minimum number of participants. Accounting for a 10% dropout the number was raised to 143 so that if dropout or missing data occurred, the minimum required number for the sample size would still be achieved.

Relevant data were collected which included demographic data, hematological parameters and peripheral blood smear finding were correlated with interpretation of HPLC. Data collected were then transferred to IBM SPSS version 27 for data analysis. Categorical variables were presented as proportions while numerical variables were described as either mean or median depending on the normality of the data distribution. Pearson chi-square or Fisher Exact test was used to compare categorical data variables between normal hemoglobin patients and those with hemoglobinopathies, while independent t-test was used for normally distributed data variables or Mann-Whitney U test was performed if the data were not normally distributed.

RESULTS

A total of 149 adolescents were recruited in this study with 96 out of 149 (64.4%) being females.

Table 1: Baseline demographics and related family information between the two groups of normal hemoglobin and those with hemoglobinopathies.

Description	Normal Hemoglobin (n = 136)		Hemoglobinopathies (n = 13)		p-value
	Mean	(S.D)	Mean	(S.D)	
Age (years old)	21.5	(2.15)	20.0	(3.21)	0.02#
	n	(%)	n	(%)	
Female Gender	87	(90.6)	9	(9.4)	0.94
Ethnicity					0.013
Dusun/Kadazan	71	(52.2)	12	(92.3)	
Others	65	(47.8)	1	(7.7)	
Parental Consanguinity					1.00
Yes	9	(90.0)	1	(10.0)	
No	127	(91.4)	12	(8.6)	
Family history of blood-related diseases					0.16
Yes	17	(81.0)	4	(19.0)	
No	119	(93.0)	9	(7.0)	
Family history of Anemia					0.39
Yes	23	(85.2)	4	(14.8)	
No	13	(92.6)	9	(7.4)	

Note: All comparative analysis were performed using Pearson Chi-Square statistical test except for # was done using independent t-test.

126 individuals (84.5%) were aged between 20 and 24 years and 46.9% of the participants held a diploma degree. All participants never had any screening for hemoglobinopathy previously and upon hemoglobin electrophoresis performed for all participants, the prevalence of hemoglobinopathies was found to be 8.7% (13 out of 149) among adolescents recruited for this study. Two out of 13 were diagnosed with hemoglobin E trait while the other 11 were diagnosed as having beta-thalassemia trait.

Baseline demographic and related family history information on hemoglobinopathy are presented in Table 1, together with comparative analysis using appropriate statistical tools. Between the two groups, those with hemoglobinopathies were younger by 1.5 years than adolescents with normal hemoglobin and 12 out of 13 of those with hemoglobinopathies were of Dusun ethnicity (92.3%, p-value 0.013).

Anthropometry and clinical characterization differences between both groups depicted in Table 2 such as weight, height and BMI were taken and calculated. Clinical examination was performed to look for presence of anemia, jaundice, and organ enlargement, as well as physiological vital signs such as systolic blood pressure, diastolic blood pressure and heart rate. There were no statistically significant differences observed when comparing both groups in terms of anthropometry, clinical examination, and vital signs measurement.

Table 2: Comparative analysis between adolescents with normal hemoglobin and those hemoglobinopathies in term of anthropometric measurements, important clinical findings, and vital signs measurements.

Description	Normal Hemoglobin (n = 136)		Hemoglobinopathies (n = 13)		p-value
Anthropometric Measurements	Mean	(S.D)	Mean	(S.D)	
Height (meters)	1.60	(0.09)	1.57	(0.72)	0.22
Weight (kg)	58.4	(14.4)	55.3	(7.27)	0.20
BMI	22.5	(4.4)	22.4	(3.26)	0.91
Clinical Examination	n	(%)	n	(%)	
Presence of Anemia	27	(87.1)	4	(12.9)	0.57
Presence of Jaundice	0	(0)	0	(0)	
Presence of Oedema	0	(0)	0	(0)	
Presence of Headache	7	(87.5)	1	(12.5)	1.00
Vital Signs Measurement	Mean	(S.D)	Mean	(S.D)	
Systolic Blood Pressure (mm Hg)	113.68	(9.86)	111.54	(5.54)	0.44
Diastolic Blood Pressure (mm Hg)	75.04	(5.62)	73.08	(4.80)	0.23
Mean Arterial Pressure (mm Hg)	87.92	(6.32)	85.90	(4.74)	0.26
Heart Rate (beats/min)	85.16	(11.5)	84.31	(6.42)	0.68

Note: All comparative analysis were performed using independent t-test except for * which was done using Pearson Chi-Square.

For biochemical characterization and differences, all participants had their blood investigations taken for peripheral blood film examination and hematological analysis including hemoglobin level, red cell counts, white blood cell counts, platelets counts, reticulocyte counts, serum iron and

Table 3: Univariate comparative analysis showing differences in terms of peripheral blood film morphology, hematological analysis, and hemoglobin electrophoresis between the two groups having normal hemoglobin and those with hemoglobinopathies.

Description	**Normal (n = 136)**		**Abnormal (n = 13)**		**p-value**
Peripheral Blood Film	n (%)		n (%)		
Microcytic Red Cells					0.022*
Yes	37 (27.2)		8 (61.5)		
No	99 (72.8)		5 (38.5)		
Hypochromic Red Cells					0.023*
Yes	38 (27.9)		8 (61.5)		
No	98 (72.1)		5 (38.5)		
Anisopoikilocytosis					0.06*
Yes	99 (72.8)		7 (46.2)		
No	37 (27.2)		6 (53.8)		
Hematological Analysis	***Mean (S.D)***	***Mean (S.D)***	***Mean diff (95% CI)***	***t-statistic (df)***	
Hemoglobin (g/dL)	13.56 (1.83)	12.26 (1.83)	1.30 (0.24, 2.35)	2.437 (147)	0.016
Red Cell Counts (10^9/L)	4.98 (0.57)	5.91 (0.70)	-0.92 (-1.27, -0.59)	-0.548 (147)	<0.001
Serum Iron Level (µmol/L)	13.24 (6.93)	11.84 (5.58)	1.4 (-2.51, 5.31)	0.705 (147)	0.482
White Cell Counts (10^9/L)	7.89 (1.93)	8.82 (1.80)	-0.93 (-2.03, 0.18)	-1.662 (147)	0.099
Platelets Counts (10^9/L)	299.72 (69.3)	354.00 (80.8)	-54.28 (-94.6, -13.9)	-2.658 (147)	0.009
Reticulocyte Counts (10^9/L)	1.57 (0.43)	1.75 (0.38)	-0.18 (-0.42, 0.06)	-1.491 (147)	0.138
Hemoglobin Electrophoresis					
Hemoglobin A2	3.046 (0.38)	12.52 (9.65)	-9.47 (-11.1, -7.87)	-3.536 (12)	0.004
Fetal Hemoglobin	0.719 (0.18)	1.88 (1.32)	-1.16 (-1.39, -0.91)	-3.139 (12)	0.009

Note: All comparative analysis were performed using independent t-test except for * which was done using Fisher's Exact Test.

hemoglobin electrophoresis to measure the types of hemoglobin and identify abnormal types of hemoglobin including fetal hemoglobin level and hemoglobin A2 level as depicted in Table 3.

Adolescents diagnosed with hemoglobinopathies showed higher microcytes (61.5% v 27.2%, df(1), F(5.1), p-value 0.024) and hypochromic red cells (61.5% v 27.9%, df(1), F(4.8), p-value 0.028) when compared to those with normal hemoglobin. However, there was no statistically significant difference in terms of anisopoikilocytosis appearance between the two groups.

Adolescents with hemoglobinopathies also showed lower hemoglobin level (mean difference 1.30 g/dL, df(147), t(2.437), p-value 0.016), higher red cell counts (mean difference 0.9 x109/L, df(147), t(-0.548), p-value <0.001) and higher platelets counts (mean difference 54.28 x109/L, df(147), t(-2.658), p-value <0.001). Results from hemoglobin electrophoresis showed that those with Hemoglobinopathies had significantly higher hemoglobin A2 proportion (mean difference 9.47%, df(12), t(-3.536), p-value 0.004) and significantly higher fetal hemoglobin proportion (mean difference 1.16%, df(12), t(-3.139), p-value 0.009).

DISCUSSION

In this study, hemoglobinopathies were identified in 8.7% (13 out of 149) of adolescents aged 10 to 24 in Kota Kinabalu, Sabah, showing a higher prevalence in an area with a high prevalence of beta-thalassemia. The prevalence of thalassemia trait among students from Sabah and Sarawak at UiTM Selangor was found to be 7.5% (3 out of 40 volunteers) (Ali et al., 2023). This also indicates a high prevalence of thalassemia trait in this study population.

A cross-sectional observational study in Indonesia assessed knowledge, attitude, and practice using an online questionnaire targeted at youth aged 15–24. Of 906 responses, 878 respondents had poor knowledge (62.1%), a positive attitude (83.3%), and poor practice (54.4%) regarding thalassemia (Wahidiyat et al., 2021). To accurately determine the prevalence of hemoglobinopathies among adolescents, comprehensive studies employing both qualitative and quantitative approaches with larger sample sizes are necessary.

A cross-sectional observational study among anemic patients at Kathmandu Pathlab revealed a hemoglobinopathy prevalence of 47.3% (77 out of 163), with a mean age of 20.45 ± 11.98 years and a slight female predominance (KC & Gyawali, 2017). Although the age range of participants was similar to our study, their population was anemic patients, resulting in a higher prevalence than our findings.

The World Health Organization has advocated for improved education and screening programs, especially in regions with high occurrences of hemoglobinopathies, to facilitate rapid interventions and prevent severe complications (World Health Organization, 2008).

In our study, hemoglobinopathies were more frequently detected in younger adolescents, with those diagnosed being on average 1.5 years younger than those without hemoglobinopathies. This suggests that younger individuals with hemoglobinopathies tend to show symptoms at an earlier age, making routine screenings essential for early identification. This highlights the need for healthcare systems to incorporate genetic testing and comprehensive educational programs to improve early detection and overall healthcare outcomes for affected adolescents. Proactive measures can greatly reduce the impact of these genetic disorders (Cao & Galanello, 2010).

In our study, 12 out of 13 individuals with hemoglobinopathies were of Kadazandusun ethnicity (92.3%, p-value 0.013). One research

indicated that among indigenous groups screened, Kadazandusuns had the highest prevalence of hemoglobinopathies at 35% (87/250), followed by Muruts at 33% (15/45), Malays at 29% (19/65), other races at 26% (46/180), and Bajau at 23% (19/84). This study involved collecting peripheral blood samples from various health clinics and hospitals across Sabah, with participants aged 1 to 73 years from all ethnicities undergoing the same screening procedures (Pauzy et al., 2018). These findings support our finding that a higher number of hemoglobinopathies were detected among Indigenous ethnic communities.

A high prevalence of hemoglobinopathies was reported that 46% of the indigenous population was affected, it was a higher rate than that found in the non-indigenous community (KC & Gyawali, 2017). Approximately 1.5% of the global population are carriers of β-thalassemia. While the global carrier frequencies are generally known, detailed micromapping has seldom been performed. When such mapping has been done, significant variations in carrier rates have been observed within small geographical areas (Colah et al., 2010). The global epidemiology of hemoglobinopathies highlighting the influence of ethnic and genetic backgrounds on the prevalence and clinical presentation of these disorders (Fucharoen & Weatherall, 2012).

In our cohort, 2 out of 13 individuals were identified with hemoglobin E trait, while 11 were diagnosed with beta-thalassemia traits. This aligns with findings from similar studies conducted in Asia and globally, highlighting the significant public health challenge these disorders pose. In Southeast Asia, the most common combination of beta-thalassemia with an abnormal hemoglobin or structural variant showing thalassemic traits is Hb E/β-thalassemia, with a carrier frequency of around 50 percent (Galanello & Origa, 2010). According to the Malaysian Thalassemia Registry, 5,712 thalassemia patients were recorded in 2013, with 1,847 diagnosed with Hb E/β-thalassemia and 2,329 with β-thalassemia major (β-TM) (Alwi & Syed-Hassan, 2022).

A high prevalence of thalassemia in the Sabah population was reported with 23% of those screened having beta-thalassemia trait and 3.1% exhibiting hemoglobin E trait (Pauzy et al., 2018). Another study in Malaysia estimated the β-thalassemia carrier rate to be between 3-5% of the population (Ibrahim, 2009). In contrast, our study focused on adolescents, and found that 11 out of 13 cases were beta-thalassemia traits, indicating a significantly higher prevalence of beta-thalassemia traits in our study group.

A community-based cross-sectional study was conducted in Shan State, Myanmar, among high school adolescents found a prevalence of hemoglobin E trait and hemoglobin E disease at 15.5% (45 out of 290 participants), with 19 cases in males (42.2%) and 26 in females (57.8%) (Aung et al., 2021). The sample size and the prevalence of hemoglobin E traits and diseases were notably higher compared to those reported in our study.

Hemoglobinopathy is a major contributor to anemia and remains a significant health challenge among adolescents. Our study highlights the vital need for early detection and effective management of hemoglobinopathies, presenting new opportunities for tackling this pressing health issue.

Diagnosing hemoglobinopathies involves various methods, including evaluating clinical and family histories, conducting complete blood counts (CBC), assessing red cell indices, and measuring levels of hemoglobin A2 (HbA2), fetal hemoglobin (HbF), the sickling test and hemoglobin electrophoresis. For beta-thalassemia heterozygotes, the hemoglobin pattern typically shows 92–95% HbA, over 3.8% HbA2, and variable amounts of HbF ranging

from 0.5% to 4% (Cao & Galanello, 2010). In our study, hemoglobin electrophoresis played a crucial role in identifying hemoglobinopathies by detecting elevated levels of HbA2 and HbF.

Elevated HbA2 levels play a crucial role in diagnosing beta-thalassemia, a condition marked by an imbalance in globin chain production. Carriers of beta-thalassemia generally exhibit HbA2 levels above 3.5%. They are easily detected through routine hematological methods, often showing microcytosis (small red blood cells) and occasionally mild anemia (Wonke et al., 2007).

While some laboratories consider HbA2 levels of 4.0% or higher diagnostic for β-thalassemia, others use thresholds of 3.3% or 3.5%. Levels below these thresholds are often classified as "borderline." Accurate detection of borderline beta-thalassemia carriers requires a comprehensive molecular analysis of the β-globin gene, ensuring precise identification where standard cut-offs may not be sufficient (Colaco & Nadkarni, 2021).

In HbE/β-thalassemia and other β-thalassemia syndromes, high levels of fetal hemoglobin (HbF) are generally due to increased erythropoietin levels, leading to bone marrow expansion and potentially enhanced F-cell production. This, combined with ineffective erythropoiesis, provides a survival advantage to F-cells, allowing them to persist and function under these conditions (Rees et al.,1999).

The presence of microcytes and hypochromic red cells in blood films is a key indicator of hemoglobinopathies, including thalassemia and other variants. These red blood cell morphologies indicate abnormalities in hemoglobin synthesis and serve as diagnostic markers for these conditions. In our study, adolescents with hemoglobinopathies showed reduced hemoglobin levels, increased red blood cell counts, and elevated platelet counts. A descriptive cross-sectional study that screened students for beta-thalassemia found that affected individuals typically exhibited microcytic hypochromic red blood cells, including the presence of target cells (Qazi et al., 2014). Reactive thrombocytosis can result from conditions such as acute hemorrhage, malignancy, chronic inflammation, iron deficiency anemia, and hemolytic anemia (Tailor et al., 2015). Additionally, β-thalassemia is associated with anemia and hypercoagulability, increasing the risk of thromboembolic events and underscoring the need for early identification and management of this state (Vasilopoulou et al., 2022).

Our study is limited by a relatively small sample size of 149 adolescents, which may impact the generalizability of the carrier frequency of hemoglobinopathies. Additionally, the absence of molecular analysis limits the ability to achieve detailed genetic characterization and confirm hemoglobinopathies or thalassemia traits, which may be overlooked during mass screening. We adopted the questionnaire as described but did not include a cross-validation component. This study directed to the prevalence of hemoglobinopathy and did not aim to explore absenteeism in the National Thalassemia Screening Program.

CONCLUSION

In regions with a high prevalence of beta-thalassemia, such as Kota Kinabalu, Sabah, the prevalence of hemoglobinopathies among adolescents is significant, particularly among genetically predisposed ethnic groups like the Kadazandusuns. Those identified with hemoglobinopathies were generally younger. Our findings underscore the critical importance of comprehensive screening and counseling programs to improve adolescents' awareness of their carrier status. That will minimize missed cases in the National Thalassemia Prevention and Control Program. Moreover, we plan to extend the research to include molecular studies in the future to enhance the

accuracy of diagnosing hemoglobinopathies, particularly for differentiating variants and confirming specific traits that may not be fully resolved through HPLC alone.

CONFLICT OF INTEREST

The authors declare no conflict of interest regarding the publication of this manuscript. All authors have reviewed and approved the final version of the manuscript, and there are no financial, personal, or professional relationships that could inappropriately influence or appear to influence the content of this research.

ACKNOWLEDGMENT

We would like to express our sincere gratitude to Prof Mohammad Saffree Bin Jeffree (Former Dean of FPSK) for allowing us to conduct this research and to Universiti Malaysia Sabah for the financial support. We also thank all Medical Laboratory Technicians and participants involved in this study.

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BJMS
Borneo Journal of Medical Sciences

ORIGINAL ARTICLE

Prospective Evaluation of CT Parameters as a Predictive Value of Impacted Stone and Ureteric Stricture Post Ureteroscopy (PRECIOUS Study)

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Received: 19 November 2024

Accepted: 18 February 2025

Published: 2 September 2025

DOI: https://doi.org/10.51200/bjms.v19i3.5632

ABSTRACT

Impacted ureteric stones present significant challenges in urological procedures, often leading to complications such as ureteral strictures. This prospective cohort study primarily aimed to evaluate preoperative CT parameters, particularly ureteral wall thickness (UWT) and the Hounsfield Unit Attenuation Ratio (HAB ratio), as predictors of stone impaction and ureteric stricture formation in patients undergoing elective primary ureteroscopy. A total of 24 patients with ureteric stones (18 impacted, 6 non-impacted) underwent primary ureteroscopic lithotripsy (URSL) between August 2023 and August 2024. Results indicated that impacted stones were associated with a significantly higher UWT (2.79 mm vs. 1.97 mm, $p = 0.018$). ROC curve analysis revealed that UWT had strong predictive value for stone impaction, with an area under the curve (AUC) of 0.824 at a threshold of 2.69 mm. UWT and HAB ratio did not predict postoperative ureteric strictures, which occurred 16.7% in impacted stones. These findings suggest that UWT is a valuable predictor for assessing stone impaction but has limited utility in predicting ureteric stricture formation. This study also found that moderate hydronephrosis demonstrated a strong predictive value for impacted stones ($p < 0.001$). and its combination with UWT further enhanced diagnostic accuracy. These results highlight the importance of preoperative UWT assessment in predicting stone impaction and

Keywords: *Ureteral wall thickness, Hounsfield Unit Attenuation Ratio, Impacted Ureteral Stone, Ureteral Stricture*

guiding treatment decisions, such as choosing between extracorporeal shockwave therapy (ESWL) and primary URSL. Due to the small sample size, additional research with larger cohorts and alternative parameters should be explored to improve the prediction of ureteric strictures following surgical intervention.

INTRODUCTION

Impacted ureteric stones occur when a stone becomes lodged within the ureter, obstructing the flow of urine and impeding its natural passage.They are frequently associated with intraoperative difficulty in stone removal, lower stone-free rates with possibility of long-term ureteric strictures (Roberts et al., 1998, Brito et al., 2006).Treatment options such as ureteroscopy (URS) and shock wave lithotripsy (SWL) depend on the characteristics of the stone observed on computed tomography (CT) scans and patient-specific factors. Each treatment modality offers different success rate and associated complications however to date no predictive CT parameters have been incorporated as part of treatment guideline to recommend urologist one treatment to another. In our clinical practice, perioperative parameters and postoperative results differ for impacted and non-impacted ureteral stones. Identification of factors that can accurately stone impaction preoperative accurately helps surgeons to plan better pre-operatively, counselling patients on the outcomes of operation, risks, failure rate, and need for ancillary procedures (Rasheed et al., 2023). Impacted stones cause persistent irritation to the ureteral mucosa at the impaction site resulting in adhesion of stone to the ureteral wall, epithelial hypertrophy, local inflammation and oedema leading to an increase in the ureteral wall thickness (UWT) with resultant susceptibility to fibrosis and stricture formation (Ozbit et al., 2020).

CT attenuation of ureter above and below ureteral stone (HAB ratio) was also reported to be useful to predict impacted stones (Ozbit et al., 2020). HU values measured above the stone are more likely to be lower, closer to liquid density because of urine, whereas HU values below the stones are higher, closer to tissue density due to the lack of urine caused by impaction. As a result impaction stone is expected to have a lower HAB ratio than non-impacted stone.Many retrospective studies have been carried out to predict stone impaction based on preoperative CT characteristics but none studied the relationship between UWT and HAB ratio together to predict stone impaction and subsequent ureteric stricture rate post endourologic treatment prospectively (Legemate et al., 2017, Ozbit et al., 2020). These parameters are useful adjuncts to daily clinical practise to provide better information and tailored treatment modalities to both surgeon and patients during index clinic visit with aims of achieving least complications, complete stone free-rate and need for subsequent auxillary treatments. Our primary objectives include preoperative ureteric wall thickness (UWT) and ratio of Hounsfield Unit above and below (HAB ratio) ureteric stone on pre-operative non-contrasted CT imaging (NCCT) as a predictor of impacted stone and ureteric stricture rate. Secondary objectives includes exploring stone impaction status with degree of hydronephrosis, stone free-rate, length of operative time, length of hospital stay, need for ancillary procedures and complications.

MATERIALS AND METHODS

This was a prospective cohort study conducted between 1st August 2023 – 31st August 2024, involving 24 adults (13 males, 11 Females). A minimal sample size 24 was calculated using OpenEpi software, taking mean difference of in UWT between population of having impacted and non-impacted stones to achieve 95% power at an alpha of 0.5 (Rasheed et al., 2023). All urological patients age >18 years old with evidence of a single ureteric stone with size 5mm to 15mm undergoing elective primary ureteroscopic procedures with semi-rigid

URS size 6/7.5Fr Wolf are recruited. Diagnosis and assessment of stones were confirmed with non-contrasted computed tomography urogram, employing 1.25mm slices axial and coronal images. The degree and severity of hydronephrosis were graded according to the Society for Fetal Urology grading system. Demographic data including HU of the stones are recorded.

The definition of impacted calculi requires at least one of the following criteria to be met (Fam et al., 2015): 1. Difficulty encounter in passing standard guidewire or ureteral catheter passed level of calculi in the first attempt ; 2. Moderate to severe hydronephrosis proximal to level of calculi from NCCT ; 3. Stone remain at the same location in the ureter for more than 2 months ; 4. Endoscopic findings of impacted stones, kinks in the ureter, ureteral edema, polyp, and stricture(Yoshida et al., 2017). HU above and below stone measured by calculating the HU from the centre of the ureter, one slice proximal and distal to the stone on axial NCCT image. HAB ratio is calculated as HU above (HA) divided by HU below (HB) (Figure 1-3). UWT measures from the point of highest soft-tissue ureteral wall/ inflammatory oedema surrounding ureteral stone on axial image soft tissue window setting. Retrograde semi-rigid ureteroscopy size 6/7.5Fr Wolf with holmium:YAG 365um laser to assist in fragmentation of the stones. Operations were performed by urologists or trainees at our centre. Laser frequency is set at 6-12Hz and energy limited to 800mJ for all cases (4.8-9.6 Watts). Intra operative ureteral complications will be recorded as per the post ureteroscopic lesion scale (PULS) grade 1 to grade 5. Postoperative complications were recorded using the modified Clavien grading scale, grades 1 through 5.

Stone free is classified based on intraoperative endoscopic findings, KUB x-ray performed post operatively 4 weeks for radiopaque stones. Follow up KUB ultrasound arranged at 3 months post removal of stent if inserted initially to look for presence of moderate to severe hydronephrosis. If present, a follow up CT-IVU will be used for further assessment to confirm formation of ureteric strictures. Children and pregnant ladies, multiple stones within a single ureter, bilateral ureteric stones, patients with preoperative nephrostomy/ stenting, calculus with Hounsfield unit (HU) >1000, renal impairment and sepsis were excluded from this study. The data were recorded and processed using Microsoft Excel. Data analysis done using the SPSS version 22. Categorical data will be analyzed using Chi-square or Mann-Whitney U tests according to impaction status. Univariate analysis and multivariate logistic regression models will be used to identify predictors of stone passage. A value of $P < 0.05$ is considered statistically significant. Ethical MREC permission for pilot research NMRR ID-23-02443-BY7 was granted on 19 October 2023.

RESULTS

A total of 24 patients underwent elective primary ureterolithotripsy during this 1-year study period, stratifying CT parameters and clinical outcomes according to impaction status. A total of 18 patients with impacted stones and 6 with non-impacted stones were analyzed (Table 1).

The average ureteral wall thickness (UWT) was significantly higher in the impacted group 2.79 mm [1.49–4.0] compared to the non-impacted group 1.97 mm [1.45–2.59] , with a p-value of 0.018. The degree of hydronephrosis differed significantly between the impacted and non-impacted groups ($p < 0.001$). In the impacted group, 66.7% of patients exhibited moderate hydronephrosis, while 33.3% had severe hydronephrosis. Conversely, in the non-impacted group, 66.7% had mild hydronephrosis, with only 16.7% showing severe hydronephrosis and 16.7% moderate hydronephrosis. These findings highlight that impacted stones are associated

Table 1: Patient characteristics, CT Parameters and operative outcomes stratified by impaction status

	Impacted Stone (n=18)	Non-Impacted (n=6)	P-value
BMI	27.1, (17.8 - 43.0)	27.5, (18.3 - 35.0)	0.887[a]
UWT	2.79 (1.49 - 4.0)	1.97 (1.45 - 2.59)	0.018[a]
HA	9.61 (1.83 - 23.0)	6.52 (1.7 - 14.6)	0.280[a]
HB	31.76 (10.0 - 45.1)	19.58 (6.10 - 47.3)	0.052[a]
HAB	0.31 (0.06-0.72)	0.40 (0.08 - 0.66)	0.387[a]
Stone Size (mm)	10.4 (0.7-16.3)	10.8 (6.82-13.1)	
Stone density (HU)	918.1 (660 - 998)	794.7 (379 - 989)	0.194[a]
Degree of hydronephrosis, n (%)			< 0.00[b]
Mild	-	4 (66.7)	
Moderate	12 (70.6)	1 (16.7)	
Severe	6 (33.3)	1 (16.7)	
Location of stone, n (%)			0.600[b]
Proximal	7 (38.9)	3 (50.0)	
Middle	7 (38.9)	1 (16.7)	
Distal	4 (22.2)	2 (33.3%)	
Operative Times (mins)	53.2 (25 - 73)	37.3 (17 - 67)	0.102[a]
Post Ureteric Lesion Scale (PULS)			0.449[b]
1	14	6	
2	2	-	
3	2	-	
Duration of Impaction (Days)	145.4 (10-514)	83.8 (24-233)	
Mean stone free rate, n (%)	18 (77.8)	6 (66.7)	0.625[a]
Stricture, n (%)	3 (16.7)	-	
Length of stay, days	2.17	2.00	0.323[a]
Modified Clavien-Dindo			1.000[b]
I	17	6	
II	1	-	

a : Mann-Whitney U Test
b : Chi-square test

BMI = Body Mass index, UWT = Ureteral Wall Thickness, HA = Hounsfield unit above,
HB = Hounsfield unit below, PULS = Post Ureteric Lesion Scale
Data presented as no. (%) or mean(range)

with more severe degrees of hydronephrosis and increased UWT compared to non-impacted stones.

Receiver operating characteristic (ROC) curve analysis demonstrated strong predictive value for both ureteral wall thickness (UWT) and hydronephrosis in determining stone impaction, with UWT cutoff value of 2.69mm (AUC, 0.824; sensitivity,55.6%; specificity 100%) and grade 2 hydronephrosis (AUC, 0.806; sensitivity, 100%; specificity, 66.7%) (Figure 3,4). Average HA (9.61 vs. 6.52) and HB (31.76 vs. 19.58) were greater in the impacted group than in the non-impacted group; however, these differences were not statistically significant (p = 0.280 and p = 0.052, respectively). Similar, HAB ratio were lower in impacted group (0.31 vs. 0.40), but there was no discernible difference (p = 0.387). Separate univariate logistic regression analyses were conducted on other preoperative CT parameters to predict impaction and ureteral strictures.. Among all variables analyzed for stone impaction, only degree of hydronephrosis showed a statistically significant association (p = 0.028). A higher degree of hydronephrosis increases the odds of stone impaction by approximately 13 times. None of the variables analyzed were significantly associated with ureteric stricture (Table 2).

The impacted group had a longer average operative time compared to the non-impacted group (53.2 minutes vs. 37.3 minutes, p = 0.102) and also higher stone-free rate (77.8% vs. 66.7%, p = 0.625). Our reduced stone-free rate in the non-impacted group can be attributable to stone repulsion during ureterolithotripsy, which require adjunct treatments (n = 6). A greater number and higher severity of post-ureteric lesion scales were observed in the impacted group, as expected (p = 0.449). Ureteric stent was placed for all patients undergone primary URSL and the average length of hospital stay is 2.13 days. There was no difference in overall highest Clavien-Dindo complications between the groups (p = 1.000).

Follow-up ultrasound was performed 3 months post-stent removal (ROS) to assess

Table 2: Multivariable Logistic Regression Analysis of factors affecting stone impaction and ureteric strictures.

Variables	Stone Impaction			Ureteric Stricture		
	OR	95% CI	P-value	OR	95% CI	P-value
UWT	8.97	2.35 - 83.10	0.0535	0.997	0.989 - 1.006	0.554
Degree of Hydronephrosis	13.61	1.33 - 139.48	0.028	4.040	0.56 - 29.07	0.166
HAB ratio	0.11	0.001 - 13.88	0.372	0.198	0.001 - 62.444	0.581
Stone Density	1.01	0.999 - 1.012	0.122	1.000	0.994 - 1.007	0.88
Operative times	1.05	0.993 - 1.118	0.083	1.046	0.971 - 1.126	0.24
Stone size	0.97	0.726 - 1.291	0.825	1.058	0.674 - 1.662	0.806

OR = Odd Ratio, CI = Confidence Interval
UWT = Ureteral Wall Thickness, HAB = Hounsfield above and below calculi

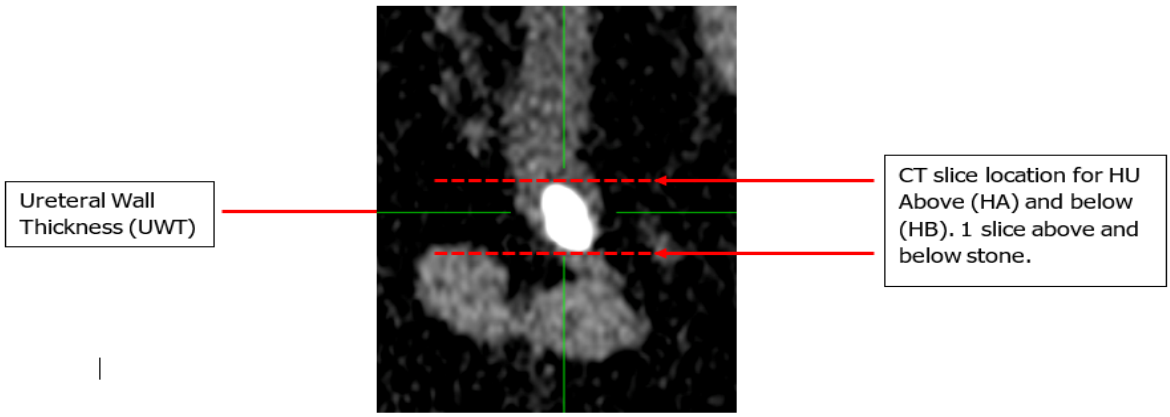

Figure 1: NCCT scan coronal view to depict points of measurement.

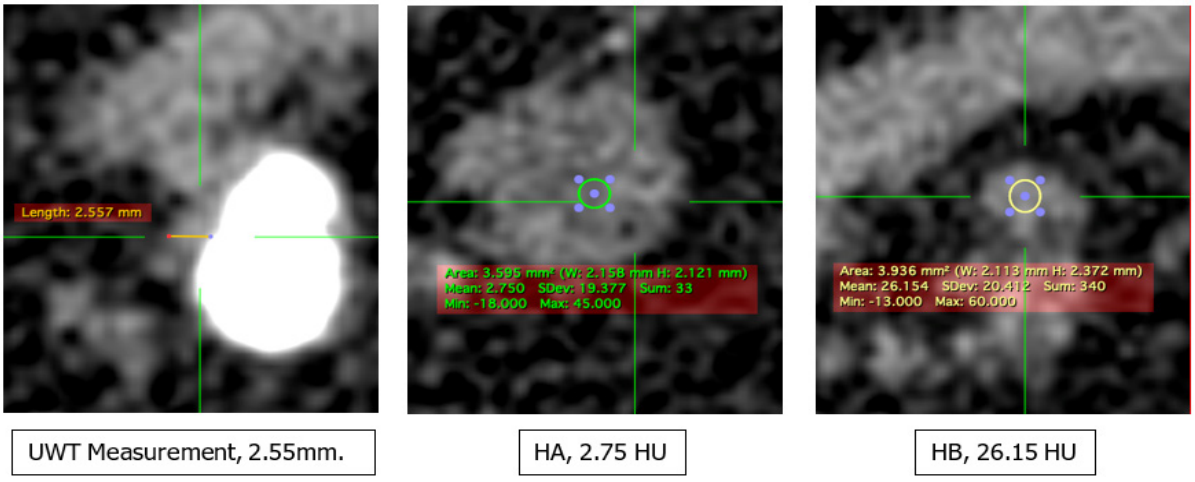

Figure 2: NCCT scan axial view depicting ureteral wall thickness measurement, Hounsfield unit 1 slice above and below stone measured on center of ureter.

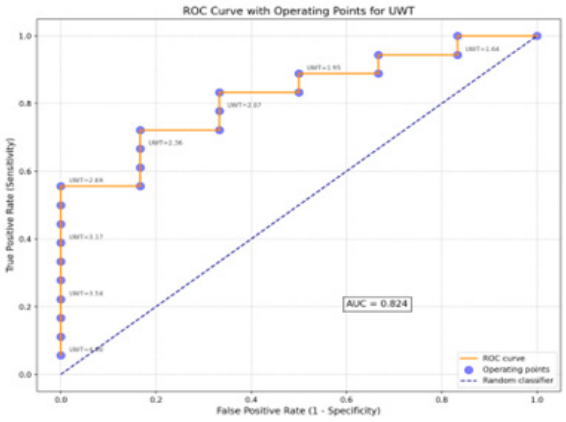

Figure 3: ROC Curves for UWT

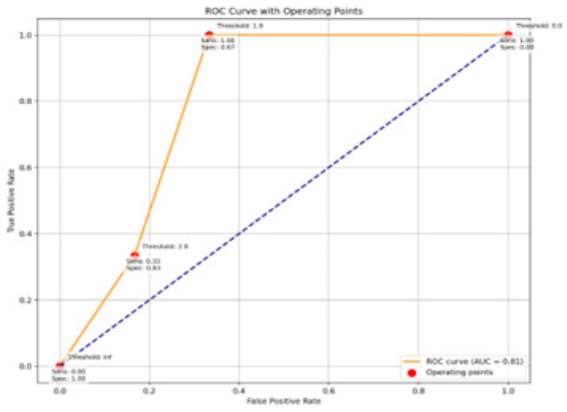

Figure 4: ROC Curves for Degree of Hydronephrosis

hydronephrosis (HN), followed by CT IVU to confirm ureteric strictures. 6 patients were excluded from the follow-up ultrasound assessment as they required additional treatment i.e repeat ureterolithotripsy (URSL). These patients were excluded as this cohort of patients may significantly influence the final study of stricture formation resulting from repeated endoscopic interventions.

Out of 18 cases, 4 patients (22.2%) had neither a stricture nor an impacted stone identified intraoperatively. In 11 patients (61.1%), an impacted stone was observed during surgery, but no stricture was present. Additionally, 3 patients (16.7%) had both an impacted stone and a stricture intraoperatively. Three patients (16.7%) who underwent ultrasonography (USG) assessment three months after retrograde intrarenal surgery (ROS) showed moderate to severe hydronephrosis, with confirmatory CT scans revealing ureteric strictures at the previous stone impaction sites. Similarly, a previous retrospective study by Brito et al. (2006) reported a 14.2% incidence of ureteric strictures in 42 patients treated for impacted ureteral calculi.

The duration of stone impaction was significantly longer in the impacted group compared to the non-impacted group (145 days vs. 83 days). Similarly, the mean stone density was higher in the impacted group (918.1 vs. 794.7), though this difference was not statistically significant ($p = 0.194$). The multivariable logistic regression analysis revealed that stone density had no statistically significant association with either stone impaction or ureteric stricture. For stone impaction, the odds ratio (OR) was 1.01 (95% CI: 0.999–1.012, $p = 0.122$). Similarly, for ureteric stricture, the OR was 1.000 (95% CI: 0.994–1.007, $p = 0.88$) (Table 2).

DISCUSSION

The primary objective of this prospective study involved prediction of stone impaction and ureteric stricture post-primary ureterolithotripsy using preoperative CT parameters. Our prospective study found that higher UWT and grade of hydronephrosis (moderate) are significantly associated with impacted stones found intraoperatively, resulting in longer operative times (53.2 minutes vs. 37.3 minutes) ($p = 0.102$). Our cohort noted a lower HAB within the impacted group compared with the non-impacted group, however not statistically significant (0.31 vs. 0.40, p-value = 0.387).

In previous retrospective study, thicker UWT, a higher grade of hydronephrosis, and a lower HAB ratio are frequently found in stone-impacted groups (Deguichi et al., 2022). HAB ratio was also an independent predictor of stone impaction with an optimal cutoff value of 0.3. One study also reported the equivalent of HAB ratio to UWT in terms of prediction of stone impaction (Özbir et al., 2020). Impacted stones are known to cause chronic inflammation of the ureteric mucosa, interstitial fibrosis, and thickening of the urothelium. The longer operative durations observed in the affected group may result from multiple attempts at guidewire placement beyond the impacted stone prior to initiating primary ureteroscopy (URS). Additionally, significant lasering time was required to fragment stones from altered mucosa caused by edema, polyps, kinking, or adherence. Preoperatively, a higher degree of hydronephrosis also concurred with our intraoperative findings of stone impaction and was consistent with previous findings (Tran et.al., 2019, Iwahashi et al., 2019). This is expected due to poor urinary passage by the obstructing calculi.

With the average ureteral wall thickness (UWT) cut-off value of 2.69 mm and moderate hydronephrosis, the combined logistic regression model incorporating both parameters achieved an overall accuracy of 88%, with particularly strong performance in identifying impacted stones (sensitivity

94%, specificity 89%). These findings suggest that while both parameters independently provide robust prediction of stone impaction, their combined use offers superior diagnostic accuracy, with UWT excelling at ruling in impaction (high specificity) and hydronephrosis at ruling out impaction (high sensitivity).

Notably, there were no cases where patients had stricture without stone impaction. All patients with stricture (n=3) had impacted stone intraoperatively suggesting a potential relationship between these conditions. Stricture only occurs in conjunction with stone impaction (100% of stricture cases had impaction. Subgroup analysis for those who developed stricture revealed longer mean operative time (59mins vs 46 mins, p-value=0.102), ureteral edema, kinking and angulation. Univariate logistic regression analysis did not find statistically significant (OR 1.046, 95% CI 0.971 - 1.126, p-value = 0.24). Limited working space due to impacted stone and ureteral factors i.e edema, kinking and angulation may lead to higher chance of ureteral mucosal injury during initial guidewire advancement and prolong lasering time contributing development of ureteral stricture long term. Long-term stone impaction often leads to ureteral lesions, including inflammatory polyps and strictures (Mugiya et al., 2004; Xi et al., 2009). Changes occurring within the ureter as a result of stone impaction causing decreased blood flow due to the pressure exerted and long period of impaction resulting ureteral tortuosity above the stone. Edematous ureter, in conjunction with the shape and dimensions of the obstructing stone, leads to inadequate saline irrigation flow and increases the risk of ureteral perforation during manipulation and fragmentation of the stone.

While the large majority of patients (N=11) had impacted stones but no ureteral stricture, these cohort of patients have shorter mean operative time (53mins), combination of smaller ureteroscope size 6/7.5Fr and lasering energy restricted to maximum of 9.6 Watts may have contributed to lower risk of ureteral stricture formation. Although stone impaction is not a causation for ureteral stricture in our study, stone impaction, severe hydronephrosis and ureteric angulation/kinking resulted in one patient failure to stent requiring nephrostomy and another had ureteric perforation (<50%, PULS 3) complication post primary URSL. Primary URSL was performed to create channel in aiding stent placement, subsequently requiring another repeat URSL to clear of residual stone fragments. Ureteral perforations have 75-80% risk of developing ureteral strictures (Brito et al., 2006, Robert et al., 1998). Systemic literature review reported ureteral perforation and mucosal damage are main predictors of ureteral strictures after ureteroscopic treatment of impacted stones (Tonyali et al., 2023).

This study has a number of limitations. This prospective study has a relatively small cohort in to draw broad conclusion. We only collected 24 patients in the duration 1 year which was the minimal sample required to achieve 95% power at an alpha of 0.5 (Rasheed et al., 2023). The limited sample size was due to the stringent inclusion criteria that focused on CT characteristics to avoid potential influence. While this approach minimized confounding factors, it also reduced the diversity of the sample and limited the applicability of the findings to a wider range of clinical scenarios. We also acknowledged this study involved procedures performed by both urologist and trainees. Variability in surgical expertise and technique could influence outcomes such as operative time, complications, and stone-free rates, introducing potential bias. Larger multi-institutional cohort might result in more representative results. The duration of stone impaction was calculated based on the date of diagnosis from preoperative non-contrasted CT scans rather than the date of symptom onset. This may not accurately reflect the true duration of impaction, potentially affecting

the analysis of its impact on outcomes such as ureteric stricture formation. Lastly, long follow-up period might provide better insight in the long-term risk of stricture formation albeit no specific timeframe has been recommended.

CONCLUSION

This investigation emphasises the significance of preoperative CT parameters, specifically hydronephrosis grading and ureteral wall thickness (UWT), in the prediction stone impaction in patients undergoing primary ureterolithotripsy. The combined use of UWT (cut-off value 2.69 mm) and moderate hydronephrosis demonstrated high diagnostic accuracy for identifying impacted stones but was not effective in predicting ureteral stricture formation. The clinical relevance of these preoperative markers was further substantiated by the discovery that all cases of ureteric strictures were associated with impacted stones in the study. CT imaging parameters serve as a valuable tool for urologist in determining the appropriate treatment modality during the initial consultation, enabling them to offer patients informed counsel regarding the potential complications associated with elective endoscopic treatment for ureteral calculi. This includes the prediction of stone impaction and its possible subsequent complications, such as ureteral perforation, strictures, stent failure necessitating nephrostomy insertion, and the potential need for secondary treatment. If primary ureterolithotriopsy were chosen as a treatment modality for impacted stone, we recommend limited lasering energy to a maximum of 9.6W, short operative time <60mins, and use of smaller URS scope 6/7.5Fr to reduce stricture rate. Alternatively, extracorporeal shock wave lithotripsy (ESWL) could be offered to disimpact and followed by URS later possibly lower down complications rate. Nevertheless, this pilot study requires an additional follow up research with larger cohorts is required to verify these findings and enhance predictive models for long-term outcomes, including stricture formation.

CONFLICT INTEREST

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

FUNDING

This research did not receive any specific funding.

ACKNOWLEDGEMENTS

We would like to thank the patients from the Department of Urology, Hospital Queen Elizabeth for their participation in this study.

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BJMS
Borneo Journal of Medical Sciences

ORIGINAL ARTICLE

Quality of Life Among Prostate Cancer Patients in Sarawak, Malaysia: A Cross-sectional Analysis of Demographic, Clinical and Treatment Factors

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Received: 9 October 2024

Accepted: 18 December 2024

Published: 2 September 2025

DOI: https://doi.org/10.51200/bjms.v19i3.5469

ABSTRACT

Advancements in prostate cancer management improves survival but each treatment modality has its side effects. Quality of life (QOL) among survivors is equally important as survival. There is currently limited data regarding QOL among prostate cancer patients in Malaysia. The aim of this study was to determine the overall QOL among prostate cancer patients in Sarawak and to explore the relationship between socio-demographic factors, clinical factors and patients' QOL. A cross-sectional study conducted across 4 major hospitals in Sarawak with 205 patients recruited via consecutive sampling. QOL was assessed with validated questionnaires consisted of European Organization for Research and Treatment of Cancer QLQ-C30 and QLQ-PR25 module in Malay and English versions. The mean age of patients was 73.4 years (SD 6.8), majority comprised of Chinese ethnic (55.6%), secondary educational level (45.9%), married (92.2%), unemployed (86.3%) and had no difficulties in medical accessibility (92.7%). About 45.9% of the cohort were of metastatic disease state, 18.5% experienced disease progression, 69.8% were on ongoing active treatment, 74.6% was under androgen deprivation and 81.5% underwent non-surgical management. The mean global health status score was 73.6 (SD 19.9). From the QLQ-C30, the highest functioning and symptom scale were social functioning 83.2 (SD 22.5) and fatigue 32 (SD 22.8). As for QLQ-

Keywords: *Prostate, Prostatic neoplasms, Quality of life, Malaysia*

PR25, highest functional and symptom scale were sexual functioning 72.1 (SD 31.6) and urinary symptoms 31.0 (SD 20.2). Our study concludes that men below 80-year-old, Malay ethnicity, unmarried or widowed, employed, higher education level, and have access to medical care reported a better QOL. Factors such as advanced disease, usage of androgen deprivation therapy, presence of disease progression, and ongoing treatment are associated with a lower QOL.

INTRODUCTION

Prostate cancer ranks as the third most prevalent malignancy globally and the second most frequently diagnosed cancer among males with around 1.4 million cases reported worldwide in 2020. Prostate cancer is the third most prevalent cancer among males in Malaysia, with 2146 new cases recorded in 2020. It constitutes 9.3% of all cancer cases in the country, following pulmonary and colorectal cancer and the prevalence of prostate cancer is increasing in a steady trend (Sung et al., 2021).

With advancements of management options of prostate cancer and the improvement in quality and access to medical care, mortality among prostate cancer patients were significantly improved. However, living longer with prostate cancer does not necessarily equate to living well, and quality of life (QOL) among cancer patients may be affected by physical, emotional, social function and financial constraints. Various treatment modalities are available for prostate cancer, but each modality comes with its own set of side effect profile. Treatment modality is generally determined by the stage of the disease, health status and life expectancy of the affected individual.

Shrestha et al. (2019) emphasised the significance of variations in QOL and survival among cancer patients. Elderly people prioritise QOL over longevity, potentially due to their deteriorating physical condition with age. In contrast, younger patients are more inclined to pursue intensive treatments aimed at extending their lifespan (Shrestha et al., 2019). Prostate cancer is typically associated with older individuals and has a relatively favourable median survival time of 58.02 months (95% CI 56.62–61.73), as reported by the Malaysian study on cancer survival (MySCan). This stresses the importance of QOL among prostate cancer survivors.

The notion of QOL is inherently subjective, varying in interpretation among patients at different phases of life. However, there are shared characteristics that may be identified among all cancer patients. Based on these shared characteristics, patient reported outcome measures (PROMs) have been developed and validated for men with prostate cancer. Tools with best evidence for psychometric properties and feasibility for use in daily practice to assess PROMs were European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 and QLQ-PR25 for patients with prostate cancer (Ratti et al., 2022). Both the EORTC QLQ-C30 and QLQ-PR25 were also validated to be used among prostate cancer patients in Malaysia (Ismail et al., 2020).

Currently, there is a scarcity of data regarding the QOL among prostate cancer patients in Malaysia. This is the first study evaluating QOL among prostate cancer survivors in Sarawak with validated questionnaires. The only study evaluating QOL among prostate cancer patients in Malaysia at the time of literature review was the validation of EORTC QLQ-C30 and QLQ-PR25 by Ismail et al (Ismail et al., 2020). It is worth noting that Sarawak, which is the largest state in Malaysia, accounts for 8.7% of the total population of 31.7 million Malaysians (Department of Statistics Malaysia, 2024). The purpose of this study was to assess the QOL ratings among prostate cancer patients in Sarawak, Malaysia and aims to fill the gaps in knowledge regarding the

relationship between socio-demographic factors, clinical factors and patients' QOL.

MATERIALS AND METHODS

A cross-sectional study was conducted between January 2023 till September 2023 across 4 major hospitals in Sarawak with urological services (Sarawak General Hospital, Sarawak Heart Centre, Hospital Sibu, and Hospital Miri). Figure 1 illustrates the hospitals located in the state of Sarawak which provides urological care and urological visiting services. Ethics approval to conduct this study was obtained from the Medical Research and Ethics Committee. The study was registered in National Medical Research Register with the registration number, NMRR ID-22-01337-K3X (IIR).

Figure 1: Major hospitals located in the state of Sarawak which provides urological care and urological visiting services.

A total of 205 patients were recruited via consecutive sampling. The recruitment sites of this study are the main follow up centres for prostate cancer patients in Sarawak where participants are encountered consecutively. The inclusion criteria for this study were patients from the state of Sarawak with confirmed diagnosis of prostate cancer and who were above 18 years old. Patients with dual malignancy were excluded from this study. Written informed consent was obtained from the patients. Socio-demographic details, diagnosis, and disease stage and treatment modality received were obtained from the case report form to ensure the authenticity of patient's information.

Prostate cancer patients attending the urology outpatient clinic who consented to participate in this study were each given the EORTC self-administered questionnaires which consists of QLQ-C30 and QLQ-PR25 module with the option of English or Malay version. The EORTC QLQ-C30 set consists of 30 items with three main domains consisted of functional scale, symptom scale and global health status while EORTC QLQ-PR25 consists of 25 questions with both functional and symptom scales. Breakdown of the items of the questionnaires are as per Figure 2. Completion of the questionnaires were ensured as all the participants were assisted to answer the missing questions and were asked for their comment on understanding of the

Domain	Number of Questions
EORTC QLQ-C30	
Global Health Status	2
Functional Scales	
Physical Functioning	5
Role Functioning	2
Emotional Functioning	4
Cognitive Functioning	2
Social Functioning	2
Symptom Scales	
Fatigue	3
Nausea and vomiting	2
Pain	2
Dyspnea	1
Insomnia	1
Appetite loss	1
Constipation	1
Diarrhea	1
Financial difficulties	1
EORTC QLQ-PR25	
Functional Scales	
Sexual activity	2
Sexual functioning	4
Symptom Scales	
Urinary symptoms	8
Incontinence Aid	4
Bowel symptoms	6
Hormonal treatment related symptoms	1

Figure 2: EORTC QLQ-C30 and QLQ-PR25 questionnaire domains and items.

questionnaires by medical doctors and allied health professionals.

All raw data were linearly transformed to give a score between 0-100. A high score for a functional scale represents a healthy level of functioning whereas a high score for a symptom scale represents a high level of symptomatology or problems. An exception for the "sexual activity" variable of the functional scale of QLQ-PR25 where a higher score represents poor level of functioning. High scores on the global and functional scales indicate good QOL, on the symptom scales low scores represent less intense symptom experience, hence higher QOL and vice versa (Fayers & Bottomley, 2002; van Andel et al., 2008).

Sample Size

For this study, the sample size was estimated using the rule of thumb to determine the factors associated with the Global health status score (GHS-S) for multiple linear regression analysis as suggested by Tabachnick and Fidell (2013). The sample size calculation 50 + 8 (p) was used as a guideline, where p equals to the number of predictor variables, assuming an error 0.05 and 0.80 for power of the study. Since this study had 12 factors, therefore, the minimal required sample of 146 was determined based on the for a medium-sized relationship. The final sample of this study was 205.

Statistical Analysis

Descriptive data will be expressed as mean and standard deviation (SD) or frequencies and percentages unless otherwise stated for socio-demographic characteristics of the respondents and the scales in the EORTC questionnaires. Normality analysis was carried out for continuous variables. For comparison between the QOL scores and categorical data, Kruskal-Wallis or Mann Whitney U tests will be utilised. Simple and multiple linear regression was used to identify the associated factors (i.e., age, ethnicity, education level, marital status, employment status, difficulty in seeking medical care, current disease stage, disease progression, treatment modality, ongoing androgen deprivation therapy (ADT) and ongoing treatment) and GHS-S. For multiple linear regression analysis (MLR), a significance level of $P<0.25$ for factors in simple linear regression (SLR) was chosen to produce a model of best fit, parsimonious, and biological plausibility in multivariate analysis process (i.e., variable selection steps).

The study used a cutoff of $P<0.25$ in univariate analysis to ensure important variables were not excluded, as some variables might become significant when analysed alongside others in multivariable analysis. For the final multivariate model, a stricter cutoff of $P<0.05$ was applied to determine statistical significance, consistent with prior studies (Bursac et al., 2008; Mohammad Ziaul Islam & Tanvir, 2020). All tests were performed using IBM SPSS Statistics 28.0.

RESULTS

The study involved a cohort of 205 participants diagnosed with prostate cancer. Table 1 and Figures 3-5 present the socio-demographic and disease characteristics of the patients. The mean age of the participants in this study was 73.4 years (SD 6.8). Majority of participants, accounting for 56.6%, were in the age range of 70-80 years. The youngest patient was 52 years, whilst the eldest of the participants was 92 years. Majority of the cohort were of Chinese ethnicity (55.6%) followed by others (Local Sarawak ethnics, 24.9%), Malay (19%) and Indian (0.5%). Most common educational level among the cohort were secondary level (45.9%) followed by primary (29.8), tertiary (16.6%) and no formal education (7.8%). 92.2% of the cohort were married and majority of the cohort were unemployed (86.3%). 92.7% of the patients had no difficulties in terms of accessibility to medical care.

During the trial, 45.9% of the patients were in metastatic disease state, localised

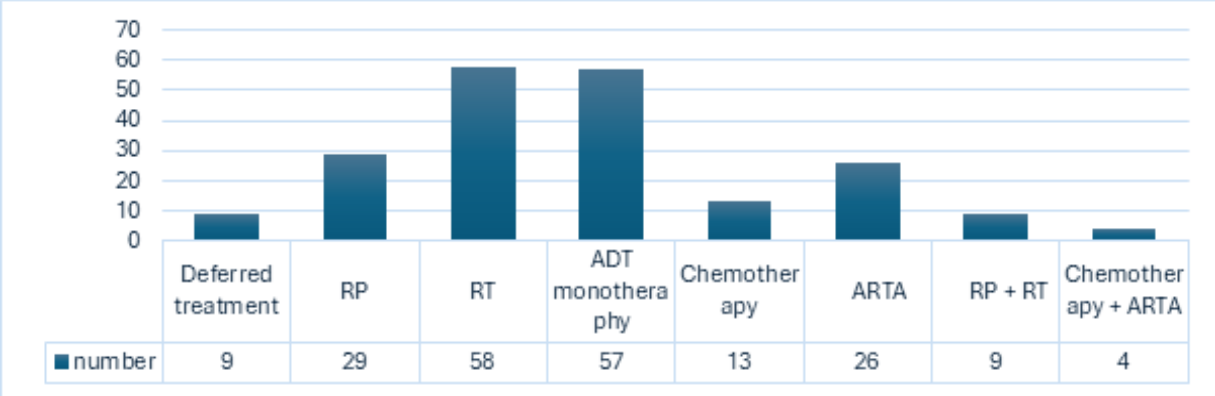
Table 1: Socio-demographic and disease characteristics of responde

Characteristics	Number	%
Age group (years)		
< 70	58	28.3
70 - 80	116	56.6
> 80	31	15.1
Ethnic		
Malay	39	19.0
Chinese	114	55.6
Indian	1	0.5
Others	51	24.9
Education		
Primary	61	29.8
Secondary	94	45.9
Tertiary	34	16.6
None	16	7.8
Marital status		
Single	7	3.4
Married	189	92.2
Widow	9	4.4
Employment status		
Yes	28	13.7
No	177	86.3
Difficulty seeking medical care		
Yes	15	7.3
No	190	92.7
Current disease stage		
Localized	86	42.0
Locally advanced	25	12.2
Metastatic	94	45.9
Disease progression		
Yes	38	18.5
No	167	81.5

disease (42%) followed by locally advanced disease (12.2%). 18.5% of the cohort experienced disease progression during the treatment period. About 69.8% (143 patients) were ongoing active treatment at the time of the study. Moreover, 74.6% of the cohort was under androgen deprivation therapy which included patients underwent orchidectomy. Patients in this cross-sectional study predominantly underwent non-surgical treatment (81.5%) whereas surgical treatment consisted of 18.5%.

Table 2 displays the QOL scores across various domains in the EORTC questionnaires. The mean global health status of the 205 participants was 73.6 (SD 19.9). The QLQ-C30 questionnaire revealed that the highest mean score in the functioning scale was observed for social and emotional functioning, with scores of 83.2 (SD 22.5) and 82.8 (SD 20.0), respectively. On the other hand, the lowest mean score in the functioning scale was found in role functioning, with a score of 77.5 (SD 26.8). In terms of the symptom scale, the highest mean score was observed for the fatigue symptom, with a score of 32 (SD 22.8), while the lowest mean score was found in the nausea and vomiting symptom scale, with a score of 6.3 (SD 13.3). In relation to QOL ratings related to prostate cancer using the prostate cancer module (QLQ-PR25), the group exhibited a generally low level of sexual activity, with an average score of 85.3 (SD 24.1). Out of the 63 individuals (30.7% of the total participants) who reported being sexually active, the average score on the sexual functioning scale was 72.1 (SD 31.6). The urinary symptoms were the most troublesome, with a mean score of 31 (SD 20.2), while the requirement of incontinence help was the least troublesome, with a score of 5.5 (SD 20.7).

Table 3 displays the median QOL scores based on patient demographics categorised by age, ethnicity and employment status. Prostate cancer patients below the age of 80 exhibited a greater overall global health status, which corresponds to an improved QOL. Notable disparities were observed in the functioning scales, including physical, emotional, and cognitive aspects, as well as in the symptom scales, such as constipation, diarrhoea, and sexual activity. The Malay patients had a higher QOL compared to the other patients, with notable disparities observed in the functional scale (physical, role, and social functioning) and



Notes: RP = Radical prostatectomy, RT = Radiotherapy, ADT = Androgen deprivation therapy, ARTA = Androgen receptor targeting agents.

Figure 3: Treatment modality of respondents, n=205.

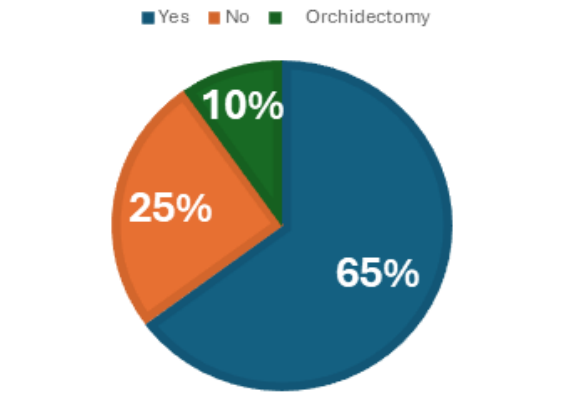


Figure 4: Ongoing androgen deprivation status of respondents, n=205.

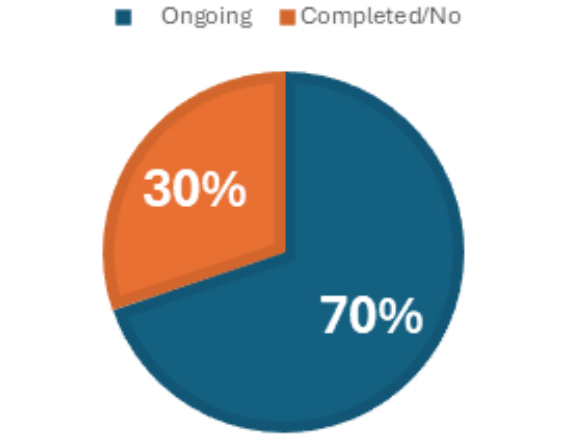


Figure 5: Treatment status of respondents, n=205.

symptom scale (pain, dyspnoea, constipation, and symptoms associated to hormonal treatment). Single and widowed patients reported a higher QOL, but no significant differences were observed on the functioning and symptom scale. Employed patients exhibited a superior QOL in comparison to unemployed patients. Statistically significant disparities were observed in the domains of role functioning and symptoms, namely in the areas of constipation, diarrhoea, and sexual activity. Patients who did not encounter any obstacles in accessing medical care reported a greater QOL, particularly in terms of physical functioning. Additionally, patients with a tertiary education level and those with no formal education also reported a better QOL.

Tables 4-6 display the median QOL scores based on disease characteristics, including the access to medical care respectively, current stage of the disease, ongoing androgen deprivation therapy, ongoing treatment, and the modality of prostate cancer treatment. When comparing patients at different stages of prostate cancer, those with metastatic illness experienced a lower QOL. This difference was particularly evident in symptom scales, namely in terms of financial issues and sexual activity. Patients who experienced disease progression during the course of treatment also reported a decrease in their QOL score. QOL was better among patients who were not

Table 3: QOL scores stratified by age group, ethnicity, and employment status.

QOL domains	Age group (years)				Ethnicity					Employment status		
	< 70	70 - 80	> 80	P[b]	Chinese	Malay	Indian	Others	P[b]	Yes	No	P[c]
GHS S	83.3 (25.0)	83.3 (16.7)	66.7 (16.7)	0.108	79.2 (16.7)	83.3 (16.7)	25.0 (0.0)	75.0 (16.7)	0.238	83.3 (20.8)	75.0 (16.7)	0.099
PF S	86.7 (33.3)	80.0 (20.0)	66.7 (40.0)	0.009	86.7 (20.0)	86.7 (20.0)	86.7 (0.0)	73.3 (20.0)	0.049	86.7 (13.3)	80.0 (26.7)	0.073
RF S	83.3 (33.3)	83.3 (50.0)	66.7 (33.3)	0.534	100.0 (33.3)	83.3 (33.3)	100.0 (0.0)	66.7 (50.0)	< 0.001	100.0 (16.7)	83.3 (33.3)	0.024
EF S	100.0 (16.7)	83.3 (33.3)	83.3 (25.0)	0.009	91.7 (33.3)	91.7 (25.0)	66.7 (0.0)	83.3 (33.3)	0.423	91.7 (29.2)	91.7 (33.3)	0.597
CF S	83.3 (16.7)	83.3 (33.3)	66.7 (16.7)	0.002	83.3 (33.3)	83.3 (33.3)	50.0 (0.0)	83.3 (33.3)	0.100	83.3 (33.3)	83.3 (33.3)	0.833
SF S	100.0 (33.3)	100.0 (16.7)	66.7 (16.7)	0.263	100.0 (33.3)	100.0 (16.7)	66.7 (0.0)	83.3 (50.0)	0.021	100.0 (25.0)	100.0 (33.3)	0.982
Fatigue S	22.2 (22.2)	22.2 (33.3)	33.3 (33.3)	0.076	27.8 (33.3)	33.3 (22.2)	33.3 (0.0)	33.3 (33.3)	0.104	27.8 (27.8)	33.3 (22.2)	0.311
NauseaV S	0.0 (0.0)	0.0 (16.7)	0.0 (16.7)	0.280	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (16.7)	0.808	0.0 (8.3)	0.0 (0.0)	0.892
Pain S	16.7 (33.3)	16.7 (33.3)	33.3 (16.7)	0.970	0.0 (33.3)	16.7 (33.3)	50.0 (0.0)	16.7 (50.0)	0.013	16.7 (33.3)	16.7 (33.3)	0.467
Dyspnea S	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.157	0.0 (0.0)	0.0 (33.3)	33.3 (0.0)	0.0 (33.3)	0.039	0.0 (0.0)	0.0 (33.3)	0.239
Insomnia S	33.3 (33.3)	0.0 (66.7)	33.3 (0.0)	0.075	33.3 (33.3)	0.0 (33.3)	0.0 (0.0)	33.3 (66.7)	0.069	16.7 (33.3)	33.3 (66.7)	0.358
Appetite S	0.0 (0.0)	0.0 (0.0)	33.3 (0.0)	0.156	0.0 (33.3)	0.0 (33.3)	0.0 (0.0)	0.0 (33.3)	0.579	0.0 (33.3)	0.0 (33.3)	0.676
Constipation S	0.0 (33.3)	0.0 (33.3)	33.3 (0.0)	0.048	0.0 (33.3)	0.0 (33.3)	66.7 (0.0)	0.0 (33.3)	0.023	0.0 (16.7)	0.0 (33.3)	0.041
Diarrhea S	0.0 (0.0)	0.0 (33.3)	33.3 (33.3)	0.049	0.0 (0.0)	0.0 (0.0)	33.3 (0.0)	0.0 (33.3)	0.090	0.0 (0.0)	0.0 (33.3)	0.035

Table 3: *Continued.*

QOL domains	Age group (years)				Ethnicity					Employment status		
	< 70	70 - 80	> 80	P[b]	Chinese	Malay	Indian	Others	P[b]	Yes	No	P[c]
FI S	33.3 (33.3)	0.0 (33.3)	33.3 (0.0)	0.359	0.0 (33.3)	0.0 (33.3)	33.3 (0.0)	33.3 (66.7)	0.158	0.0 (33.3)	0.0 (33.3)	0.351
URI S	20.8 (20.8)	29.2 (25.0)	37.5 (16.7)	0.369	27.1 (29.2)	29.2 (25.0)	29.2 (0.0)	33.3 (25.0)	0.064	29.2 (39.6)	29.2 (29.2)	0.365
AID S	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.056	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.895	0.0 (0.0)	0.0 (0.0)	0.638
BOW S	0.0 (16.7)	8.3 (8.3)	25.0 (8.3)	0.983	8.3 (16.7)	0.0 (8.3)	16.7 (0.0)	8.3 (16.7)	0.388	8.3 (16.7)	8.3 (16.7)	0.657
HTR S	11.1 (11.1)	11.1 (11.1)	11.1 (5.6)	0.984	5.6 (11.1)	11.1 (16.7)	16.7 (0.0)	11.1 (22.2)	0.006	5.6 (13.9)	11.1 (11.1)	0.208
SA S	66.7 (66.7)	100.0 (33.3)	100.0 (33.3)	0.022	100.0 (16.7)	100.0 (16.7)	83.3 (0.0)	100.0 (33.3)	0.122	83.3 (33.3)	100.0 (16.7)	0.030
SF S[a]	83.3 (50.0)	83.3 (50.0)	100.0 (33.3)	0.550	75.0 (41.7)	91.7 (16.7)	Nil	83.3 (66.7)	0.508	70.8 (33.3)	83.3 (50.0)	0.702

Table 4: QOL scores stratified by accessibility to medical care and current disease stage.

QOL domains	Accessibility to medical care			Current disease stage			
	Yes	No	P[c]	Localized	Locally advanced	Metastatic	P[b]
GHS S	66.7 (33.3)	75.0 (16.7)	0.474	75.0 (25.0)	83.3 (25.0)	75.0 (16.7)	0.052
PF S	73.3 (33.3)	86.7 (20.0)	0.028	86.7 (20.0)	80.0 (20.0)	83.3 (26.7)	0.813
RF S	100.0 (33.3)	83.3 (33.3)	0.608	83.3 (33.3)	83.3 (33.3)	83.3 (33.3)	0.899
EF S	75.0 (33.3)	91.7 (33.3)	0.143	87.5 (33.3)	83.3 (33.3)	91.7 (25.0)	0.558
CF S	66.7 (33.3)	83.3 (33.3)	0.206	83.3 (33.3)	83.3 (33.3)	83.3 (33.3)	0.316
SF S	100.0 (33.3)	100.0 (33.3)	0.931	100.0 (33.3)	100.0 (33.3)	100.0 (33.3)	0.998
Fatigue S	33.3 (33.3)	33.3 (33.3)	0.543	33.3 (33.3)	33.3 (33.3)	33.3 (22.2)	0.594
NauseaV S	0.0 (0.0)	0.0 (16.7)	0.247	0.0 (16.7)	0.0 (0.0)	0.0 (16.7)	0.833
Pain S	16.7 (33.3)	16.7 (33.3)	0.691	16.7 (33.3)	16.7 (33.3)	16.7 (33.3)	0.224
Dyspnea S	0.0 (33.3)	0.0 (0.0)	0.068	0.0 (33.3)	0.0 (0.0)	0.0 (0.0)	0.420
Insomnia S	0.0 (66.7)	33.3 (66.7)	0.873	33.3 (66.7)	33.3 (33.3)	33.3 (66.7)	0.929
Appetite S	0.0 (33.3)	0.0 (33.3)	0.627	0.0 (33.3)	0.0 (0.0)	0.0 (33.3)	0.342
Constipation S	0.0 (33.3)	0.0 (33.3)	0.723	0.0 (33.3)	0.0 (33.3)	0.0 (33.3)	0.467
Diarrhea S	0.0 (33.3)	0.0 (33.3)	0.409	0.0 (33.3)	0.0 (33.3)	0.0 (0.0)	0.658
FI S	33.3 (66.7)	0.0 (33.3)	0.078	0.0 (33.3)	0.0 (33.3)	33.3 (33.3)	0.043
URI S	33.3 (33.3)	29.2 (29.2)	0.186	29.2 (29.2)	37.5 (37.5)	29.2 (25.0)	0.123
AID S	0.0 (0.0)	0.0 (0.0)	0.559	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.656
BOW S	8.3 (25.0)	8.3 (8.3)	0.102	8.3 (16.7)	8.3 (16.7)	0.0 (8.3)	0.280
HTR S	11.1 (22.2)	11.1 (11.1)	0.185	5.6 (16.7)	11.1 (16.7)	11.1 (11.1)	0.846
SA S	100.0 (33.3)	100.0 (33.3)	0.480	100.0 (33.3)	100.0 (16.7)	100.0 (16.7)	0.032
SF Sa	45.8 (8.3)	83.3 (41.7)	0.163	66.7 (62.5)	83.3 (41.7)	95.8 (29.2)	0.184

Notes: an = 63, [b]Kruskal Wallis test, [c]Mann Whitney U test, QOL = Quality of life, Significant P in bold, Data presented as median and interquartile range.

Table 5: QOL scores stratified by ongoing androgen deprivation therapy and ongoing treatment.

QOL domains	Accessibility to medical care				Current disease stage		
	Yes	No	Orchidectomy	P[b]	Ongoing	Completed/No	P[c]
GHS S	75.0 (16.7)	83.3 (20.8)	70.8 (33.3)	0.153	75.0 (16.7)	83.3 (16.7)	0.172
PF S	80.0 (26.7)	86.7 (20.0)	76.7 (30.0)	0.067	80.0 (26.7)	86.7 (20.0)	0.088
RF S	83.3 (33.3)	100.0 (33.3)	100.0 (41.7)	0.171	83.3 (33.3)	100.0 (33.3)	0.081
EF S	91.7 (33.3)	95.8 (25.0)	83.3 (33.3)	0.263	83.3 (33.3)	95.8 (33.3)	0.183
CF S	83.3 (33.3)	83.3 (33.3)	83.3 (33.3)	0.399	83.3 (33.3)	83.3 (33.3)	0.184
SF S	100.0 (33.3)	100.0 (33.3)	100.0 (33.3)	0.602	100.0 (33.3)	100.0 (33.3)	0.349
Fatigue S	33.3 (22.2)	22.2 (27.8)	27.8 (38.9)	< 0.001	33.3 (22.2)	22.2 (22.2)	< 0.001
NauseaV S	0.0 (16.7)	0.0 (0.0)	0.0 (16.7)	0.225	0.0 (16.7)	0.0 (0.0)	0.180
Pain S	16.7 (33.3)	0.0 (16.7)	16.7 (41.7)	0.006	16.7 (33.3)	0.0 (16.7)	0.003
Dyspnea S	0.0 (33.3)	0.0 (33.3)	0.0 (0.0)	0.731	0.0 (33.3)	0.0 (33.3)	0.743
Insomnia S	33.3 (66.7)	0.0 (33.3)	33.3 (66.7)	0.173	33.3 (66.7)	0.0 (33.3)	0.146
Appetite S	0.0 (33.3)	0.0 (0.0)	0.0 (33.3)	0.001	0.0 (33.3)	0.0 (0.0)	0.007
Constipation S	0.0 (33.3)	0.0 (33.3)	16.7 (33.3)	0.331	0.0 (33.3)	0.0 (33.3)	0.253
Diarrhea S	0.0 (33.3)	0.0 (0.0)	0.0 (0.0)	0.026	0.0 (33.3)	0.0 (0.0)	0.027
FI S	0.0 (33.3)	0.0 (33.3)	33.3 (50.0)	0.043	0.0 (33.3)	0.0 (33.3)	0.200
URI S	33.3 (29.2)	22.9 (31.3)	33.3 (22.9)	0.079	33.3 (29.2)	25.0 (33.3)	0.049
AID S	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.084	0.0 (0.0)	0.0 (0.0)	0.035
BOW S	8.3 (16.7)	8.3 (12.5)	0.0 (8.3)	0.140	8.3 (16.7)	8.3 (8.3)	0.906
HTR S	11.1 (16.7)	5.6 (11.1)	5.6 (13.9)	< 0.001	11.1 (16.7)	5.6 (11.1)	< 0.001
SA S	100.0 (16.7)	100.0 (33.3)	100.0 (0.0)	0.049	100.0 (16.7)	100.0 (33.3)	0.197
SF Sa	91.7 (41.7)	66.7 (41.7)	83.3 (25.0)	0.313	91.7 (41.7)	66.7 (41.7)	0.116

Notes: an = 63, [b]Kruskal Wallis test, [c]Mann Whitney U test, QOL = Quality of life, Significant P in bold, Data presented as median and interquartile range.

Table 6: QOL scores stratified by treatment modalities.

QOL domains	Treatment modalities								
	Deferred treatment	R^P	R^T	ADT mono-therapy	Chemother-apy	ARTA	RP+RT	Chemother-apy + ARTA	P^b
GHS S	75.0 (16.7)	83.3 (25.0)	83.3 (16.7)	66.7 (25.0)	75.0 (16.7)	83.3 (16.7)	58.3 (16.7)	66.7 (20.8)	0.317
PF S	86.7 (20.0)	93.3 (20.0)	86.7 (20.0)	73.3 (33.3)	86.7 (20.0)	80.0 (26.7)	86.7 (6.7)	66.7 (50.0)	0.096
RF S	83.3 (33.3)	100.0 (33.3)	100.0 (33.3)	66.7 (50.0)	66.7 (50.0)	100.0 (33.3)	83.3 (33.3)	58.3 (66.7)	0.127
EF S	83.3 (33.3)	100.0 (25.0)	91.7 (33.3)	83.3 (33.3)	91.7 (16.7)	91.7 (33.3)	75.0 (25.0)	100.0 (20.8)	0.581
CF S	83.3 (33.3)	83.3 (33.3)	83.3 (33.3)	83.3 (33.3)	83.3 (16.7)	83.3 (33.3)	66.7 (50.0)	75.0 (33.3)	0.370
SF S	100.0 (33.3)	100.0 (33.3)	100.0 (33.3)	100.0 (33.3)	100.0 (16.7)	91.7 (33.3)	83.3 (33.3)	75.0 (66.7)	0.960
Fatigue S	33.3 (22.2)	22.2 (22.2)	27.8 (22.2)	33.3 (22.2)	33.3 (22.2)	33.3 (44.4)	33.3 (11.1)	38.9 (50.0)	0.151
NauseaV S	0.0 (0.0)	0.0 (16.7)	0.0 (0.0)	0.0 (16.7)	0.0 (0.0)	0.0 (16.7)	0.0 (0.0)	16.7 (33.3)	0.332
Pain S	16.7 (16.7)	0.0 (16.7)	16.7 (33.3)	16.7 (50.0)	16.7 (0.0)	16.7 (33.3)	16.7 (33.3)	16.7 (66.7)	0.271
Dyspnea S	0.0 (33.3)	0.0 (33.3)	0.0 (0.0)	0.0 (33.3)	0.0 (0.0)	0.0 (0.0)	0.0 (33.3)	0.0 (16.7)	0.858
Insomnia S	33.3 (66.7)	0.0 (33.3)	33.3 (33.3)	33.3 (66.7)	0.0 (33.3)	33.3 (66.7)	33.3 (66.7)	0.0 (16.7)	0.103
Appetite S	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (33.3)	0.0 (33.3)	0.0 (33.3)	0.0 (0.0)	16.7 (50.0)	0.137
Constipation S	0.0 (33.3)	0.0 (33.3)	0.0 (33.3)	33.3 (33.3)	0.0 (33.3)	0.0 (33.3)	0.0 (33.3)	16.7 (66.7)	0.559
Diarrhea S	0.0 (0.0)	0.0 (0.0)	0.0 (33.3)	0.0 (33.3)	0.0 (33.3)	0.0 (33.3)	0.0 (33.3)	0.0 (0.0)	0.495
FI S	0.0 (33.3)	33.3 (33.3)	0.0 (33.3)	0.0 (33.3)	33.3 (66.7)	33.3 (66.7)	0.0 933.3)	0.0 (33.3)	0.257
URI S	25.0 (41.7)	25.0 (25.0)	33.3 (29.2)	29.2 (29.2)	20.8 (16.7)	31.3 (29.2)	37.5 (20.8)	8.3 (37.5)	0.505
AID S	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (50.0)	0.018
BOW S	8.3 (8.3)	8.3 (16.7)	8.3 (16.7)	0.0 (8.3)	0.0 (8.3)	4.2 (8.3)	8.3 (8.3)	0.0 (4.2)	0.165
HTR S	5.6 (5.6)	5.6 (11.1)	11.1 (16.7)	11.1 (16.7)	5.6 (5.6)	8.3 (11.1)	22.2 (22.2)	13.9 (19.4)	0.096
SA S	83.3 (33.3)	83.3 (33.3)	100.0 (33.3)	100.0 (16.7)	100.0 (33.3)	100.0 (0.0)	66.7 (33.3)	100.0 (16.7)	0.058
SF Sa	91.7 (0.0)	66.7 (41.7)	79.2 (41.7)	100.0 (50.0)	100.0 (100.0)	100.0 (16.7)	66.7 (58.3)	Nil	0.412

Notes: an = 63, [b]Kruskal Wallis test, QOL = Quality of life, Significant P in bold, Data presented as median and interquartile range, Nil = Not available, RP = Radical prostatectomy, RT = Radiotherapy, ADT = Androgen deprivation therapy, ARTA = Androgen receptor targeting agents.

on androgen deprivation therapy. Significant differences were associated with symptoms scale (fatigue, pain, appetite loss, diarrhoea, financial difficulties, hormone treatment related symptoms and sexual activity). Similarly, patients who had completed their treatment reported an improved QOL, with notable disparities in symptoms such as weariness, discomfort, decreased appetite, diarrhoea, urinary symptoms, reliance on incontinence aids, and side effects associated to hormones. Comparison among patients who underwent different treatment modalities, patients among the surgical intervention group (radical prostatectomy), radiotherapy, androgen receptor targeted agents (ARTA) group reported a better QOL. Patients who received a combination of treatments due to disease progression such as adjuvant radiotherapy post-surgery and 2nd line ARTA post chemotherapy reported a worse QOL. Only the symptom scale (usage of incontinence aid) was found to be significantly different. Marital status, education level and disease progression tables are not included in this article.

Table 7 displays the results of the single linear regression analyses conducted to examine the relationship between independent variables and the global health status score. The only significant factor linked with GHS-S was the locally advanced stage (b=9.972, P=0.019). The multivariate analysis in this study did not yield any statistically significant predictors.

DISCUSSION

The Malaysian Study on Cancer Survival (MySCan) reported the median survival time of prostate cancer was 58.02 months (95% CI 56.62–61.73), whilst the 5-year relative survival of stages I, II, III and IV prostate cancer was 97.3%, 92.1%, 93.0% and 43.2%, respectively (National Cancer Registry Malaysia, 2018). Our study shows that majority of the patients (45.8%) were in the advanced stages of prostate cancer where it is consistent with the finding of the Malaysia Prostate Cancer Study (M-CaP) where multi-ethnic Asian men are more likely to present at a later stage of prostate cancer (Lim et al., 2021). With the evolving landscape of the management of prostate cancer where treatment improves overall survival, it is imperative to understand more about the effect of prostate cancer therapies on QOL among prostate cancer survivors.

This study identified factors that contribute to a good QOL among prostate cancer patients. Socio-demographic factors that contributed good QOL are patients below 80 years old, Malay ethnicity, single or widowed, being in employment, higher education level and convenience to medical access. It is known that age strongly influences treatment decision making. Older men are also more likely to be diagnosed with advanced disease and face a higher risk of cancer-specific mortality (Konety et al., 2008). A lower QOL among older men may indicate that they may have a lower baseline QOL score to begin with. Patients <80 years old from our study has better functioning and lower symptom score in all domains as compared to men <80 years old except for the insomnia symptom scale. Religiousness such as seeking God's love or protection, seeking help in religious literature and prayers were positively associated with better QOL and low level of psychological distress (Idler et al., 2009). This could contribute to the higher QOL among the Malay ethnic shown in this study. Married men in this study reported a poorer QOL compared to single or widowed men. This may be a personal reflection that prostate cancer is a burden to their spouse. According to Swedish population-based register study, partners of patients with cancer (n=10353) suffer from significantly more mood disorders, poorer reactions to severe stress and ischaemic heart disease during the year after the cancer diagnosis (Möllerberg et al., 2016). Employed cancer patients reported better QOL (Tamminga et al., 2020). Employment may enhance QOL but a certain level of requirement

Table 7: Factors associated with global health status using

Variables	Simple linear regression (SLR)		
	Crude b	95% CI	P
Age	-0.329	-0.731, 0.074	0.109*
Ethnic			
Indian (ref)	0	Nil	Nil
Malay	3.076	-3.921, 10.074	0.387
Chinese	0.406	-5.132, 5.943	0.885
Employment			
No (ref)	0	Nil	Nil
Yes	5.784	-2.188, 13.757	0.154*
Difficulty to seek medical care			
No (ref)	0	Nil	Nil
Yes	-4.459	-15.007, 6.089	0.406
Marital status			
Single (ref)	0	Nil	Nil
Married	-8.887	-19.071, 1.296	0.087*
Widow	5.362	-8.048, 18.772	0.431
Education			
None (ref)	0	Nil	Nil
Primary	-3.615	-9.612, 2.383	0.236*
Secondary	-0.647	-6.168, 4.874	0.818
Tertiary	4.056	-3.320, 11.433	0.280
Current disease stage[c]			
Metastatic (ref)	0	Nil	Nil
Localized	-3.391	-8.948, 2.165	0.230*
Locally advanced	9.972	1.678, 18.267	0.019*
Progression of disease			
No (ref)	0	Nil	Nil
Yes	-2.830	-9.900, 4.240	0.431
Treatment modalities			
Deferred (ref)	0	Nil	Nil
RP	6.861	-0.156, 13.878	0.055*
RT	1.559	-4.303, 7.421	0.601
ADT monotherapy	-4.233	-10.093, 1.627	0.156*
Chemotherapy	-1.801	-10.687, 7.086	0.690
ARTA	2.577	-4.727, 9.881	0.487
RP+RT	-4.023	-13.730, 5.683	0.415
Chemotherapy + ARTA	0.835	-10.455, 12.125	0.884
Ongoing ADT			
No (ref)	0	Nil	Nil
Yes	-3.977	-9.715, 1.761	0.173*
Orchidectomy	-3.502	-12.763, 5.758	0.457
Ongoing treatment			
No (ref)	0	Nil	Nil
Yes	-3.774	-9.742, 2.194	0.214*

Notes: b = regression coefficient, CI = confidence interval, ref = reference group, Nil = Not available, RP = Radical prostatectomy, RT = Radiotherapy, ADT = Androgen deprivation therapy, ARTA = Androgen receptor targeting agents, *Variables in SLR with P < 0.250 were included in MLR analyses to avoid from losing of important variables. During the MLR steps, none of the factors were found significant.

of functioning may be needed to be able to continue with work. It is evident in our study that employed men have better functioning status in all domains hence it translates to a better QOL. Group educational interventions based on the rationale that providing emotional support adjusting to patients' knowledge, attitude and expectations about cancer can have a positive effect on QOL. Eton et al. (2001) reported that a higher educational level correlates with a better QOL among prostate cancer patients when engaged in group interventions. Although patients from this study were not involved in any formal educational interventions, our results showed better QOL among the patients with tertiary education qualification which may reflect a better understanding of the disease and better management of self-expectations.

The disease's characteristics that positively influenced the QOL included having localised prostate cancer, not being on ADT, no evidence of disease progression, having completed prostate cancer treatment, and not requiring additional treatment due to disease progression. Clinically localised prostate cancer is usually asymptomatic (Thompson et al., 2007). However, in advanced prostate cancer, it commonly metastasizes to the bone leading to bone pain and fractures. Other symptoms associated with metastatic prostate cancer are fatigue and problems with urinary and sexual functioning which correlates with our study population. In the present study, around 74.7% of the study population received ADT therapy, either alone or in combination with other therapies (radiotherapy, chemotherapy, or ARTA), highlighting the importance of evaluating the effects of ADT on the QOL among prostate cancer survivors. QOL among the patients on ADT fair worse compared to patients without ADT (Huang et al., 2019). Patients on ADT reported worse symptoms of fatigue, pain, appetite loss, diarrhoea, financial difficulties, hormone treatment related symptoms and sexual activity. Poorer QOL in the ADT group compared with the non-ADT group may also be due to that patients who require ADT are usually at a more advanced state of prostate cancer be it from progression or diagnosed de-novo.

About 42.4% of our study population underwent localised treatment (radical prostatectomy/radiotherapy) and they reported the best QOL among all other treatment modalities. Adam et al. (2019) reported that patients treated with radical prostatectomy or radiotherapy alone reported the best QOL and the lowest symptom burden based on a population-based study in Germany. Patients fit for curative management are at early stages of the disease with 5-year relative survival rate of > 90% and ADT side effects are negated in the radical prostatectomy group and only short-term ADT of 6-24 months is required in combination with radiotherapy depending on the risk of prostate cancer. Patients in the follow-up phase (not on active treatment or ADT) of this study reported higher QOL scores compared to patients in treatment phase. Median time to testosterone recovery after ADT use ranges from 1.5 to 5.1 years depending on age and duration of ADT (Nabid et al., 2023). Our results showed significant lower symptoms score of fatigue, pain, and hormone treatment related symptoms for the follow-up phase patients.

This cross-sectional study gives an overall insight of the overall QOL of prostate cancer patients in Sarawak, Malaysia. It is to date the first survey on QOL among prostate cancer patients using validated questionnaires namely the EORTC QLQ-C30 and QLQ-PR24 questionnaires among Sarawakians. This study is inclusive of the majority prostate cancer patients treated in the public hospitals in Sarawak thus providing valuable decision-making information for healthcare providers and patients. Treatment landscape of prostate cancer varies according to the disease stage and with the large armamentarium of treatment options, health care providers and patients need to be aware of the benefits and

risks of the different treatment modalities. While survival outcome is the key objective of prostate cancer treatment, QOL among survivors is equally important which it turns has significant public health implications. Limitations of this study are namely that this study was an observational study and hypothesis generating. Consecutive sampling was adopted to overcome patients' accessibility issues due to geographical constraints and the short time frame of this study. While sample size of this study was enhanced to improve the power of statistical test, potential sampling bias was inadvertent. A prospective study with probability sampling and a larger sample size assessing the QOL before and after prostate cancer treatment would be advantageous in the study of treatment impact on QOL. Participants may have provided inaccurate responses to certain questionnaire items, particularly those related to sexual activity and sexual functioning as these domains are subjected to recall bias and social desirability bias where social and gender norms create different expectations about socially acceptable sexual behaviour. Translation assistance from doctors and allied health professionals were provided to patients with linguistic challenges as only the English and Malay versions of the questionnaires were validated for the Malaysian population at the time of this study. Conducting a validation study on the Chinese version of the questionnaires could be advantageous for the Malaysian population. While the multivariate analysis conducted in this study did not find any significant predictors of QOL, our study confirmed strong independent link between patients' self-reported global health status and current disease stage in simple linear regression. Thus, collecting EORTC QLQ-C30 and QLQ-PR25 data in routine clinical practice to achieve a bigger dataset could offer additional useful information for future clinical decision-making and it would be advantageous to explore other socio-demographic and illness factors not considered in this study.

CONCLUSION

Overall, our study provides a comprehensive analysis of the QOL in prostate cancer patients at various stages of the disease who underwent different treatment methods. The QOL of prostate cancer patients was better in those who were below the age of 80, of Malay ethnicity, unmarried or widowed, employed, had a higher level of education, and had convenient access to medical care. Factors such as advanced disease, usage of androgen deprivation therapy, presence of disease progression, and ongoing treatment were associated with a lower QOL. The multivariate analysis in this study did not yield any statistically significant predictors of QOL. Future studies exploring local socio-demographic challenges and disease related factors in relation to QOL is paramount in optimising QOL improvements alongside survival outcomes for prostate cancer patients in Malaysia.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ACKNOWLEDGEMENTS

The authors would like to acknowledge all the participants for their support and cooperation throughout the data collection and Director-General of Health for the permission to publish the article.

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BJMS
Borneo Journal of Medical Sciences

REVIEW ARTICLE

Macrophages: Cells That Are More Than Just Scavengers

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Received: 11 October 2024

Accepted: 8 January 2025

Published: 2 September 2025

DOI: https://doi.org/10.51200/bjms.v19i3.5479

ABSTRACT

Macrophages are a part of the mononuclear phagocyte system, which not only phagocytose the invading microorganisms but also as serve as antigen-presenting cells (APC) that process protein antigens to be presented to T cells. Macrophages also contribute to cell-mediated immunity and humoral immunity after they are activated by cytokines. Macrophages also serve to maintain the homeostasis of organs and systems. In addition to these immune-related and physiological functions, macrophages play a pivotal role in creating the tumour microenvironment by polarizing themselves into pro-tumour or anti-tumour phenotypes. Functions of macrophages are beyond the scope of innate immunity and immune regulation. As they contribute their role in tumour evolution, several studies documented that reprogramming the macrophages may have a therapeutic role in inflammation and tumorigenesis.

Keywords: *Emacrophages, Scavengers,Macrophage polarization, Tumourigenesis, Atherosclerosis*

INTRODUCTION

During normal homeostatic states, macrophages are transformed from blood monocytes and they are present as tissue-resident macrophages. Macrophages normally exist in different tissues namely alveolar macrophages in lung alveoli, Kupffer cells in liver sinusoids, sinus histiocytes in lymph nodes, microglia in the brain, Langerhans cells in the skin and osteoclasts in bones (Park et al., 2022). Developmental processes and physiological functionality such as angiogenesis, neuronal development, adipogenesis and ageing are

also orchestrated by macrophages (Mass et al., 2023). Macrophages act in the first step of the immune response as antigen-presenting cells (APC) during exposure to a foreign antigen in a particular tissue. They have the phagocytic property and are mainly described as scavenger cells of the immune system which remove dying or dead cells, microorganisms and other cell debris. Their actions in immune mechanisms are augmented by producing growth factors and signalling molecules to further protect the body. As the disease process begins, cell signals induce the influx of diseases-associated macrophages (M-0 macrophages) to the sites of pathologic lesions. Studies have shown that in addition to their role in immune reactions, macrophages are important for the pathogenesis of metabolic diseases such as atherosclerosis. Moreover, macrophages possess tumouricidal properties aiding the management of malignancy (Mantovani et al., 2022). Macrophages in solid tumours known as tumour-associated macrophages (TAMs) express inhibitory surface receptors that can suppress adaptive immune responses which aid in checkpoint blockade immunotherapy (Duan & Luo, 2021). This article reviewed the functions of macrophages in physiology and the process of essential functions of macrophages in various pathological aspects that will help to understand more about their potential therapeutic aspect in macrophage-related diseases.

Development of macrophages and their markers

Macrophages are components of the mononuclear phagocyte system and are derived from blood monocytes. Monocytes developed from colony-forming unit granulocytes/monocytes (CFU-G/M) which are derived from common myeloid stem cells of bone marrow called M-0 macrophages and they circulate in the blood. The functional core programme of macrophages enhances physiological adaptation important for organ homeostasis (Hussell, 2016). Ly6C or CD-16 is a marker for an inflammatory population of monocytes. Ly6Chi monocytes develop into M1 cells under low inflammatory conditions in the tissues and some of these differentiate into Ly6Clo monocytes or M2 cells (Miyake et al., 2024). Ly6C+ macrophages invade tissue by interaction with CCR2/CCL2 (MPC-1) via a VLA-1/VCAM1 and are activated by interferon-√ (IFN-√), LPS and GM-CSF. Ly6C- macrophages are also recruited to tissue and differentiate into M2 macrophages by the action of cytokines such as interleukins (IL)-4, 6 and 13, TLR ligands (Wculek et al., 2022). The process of transforming into two distinct macrophage functional phenotypes based on specific signals is called polarization.

M1 cells augment NADPH oxidase isoform 2 (NOX2), inducible nitric oxide synthase (iNOS), synaptotagmin-binding cytoplasmic RNA interacting protein (SYNCRIP), and tumour necrosis factor receptor-associated factor 6 and increases oxygen and nitrogen reactive species (Pérez and Rius-Pérez, 2022). These M1 cells are known for their properties such as pro-inflammatory, phagocytosis and cytotoxicity. M2 macrophages down-regulate NOX2, and iNOS, upregulate superoxide dismutase type 1 and counteract oxidative and nitrosative stress. These cells have immunosuppressive and tissue reparative properties (Pérez and Rius-Pérez, 2022, Wynn & Vannella, 2016). Polarization of M1 to M2 is controlled by galectin-1 (Gal-1), Gal-2 and interferon (IFN)-β resulting in the resolution of inflammation (Kane et al., 2022). In inflammation, if the M1 infiltration phase continues it will produce tissue damage so that in the later phase, M2 cells replace the injured area.

Macrophages are commonly identified by specific markers such as CD11b/Integrin alpha M, CD14, CD169, and CD68 in humans (Hume, 2015), in the forms of surface markers and intracellular markers. The formers are F4/80, CCR2, CD169, CX3CR1, CD206, CD163, Lyve1, CD9, TREM2, and MHCII and CD68, iNOS, Arg-1, and Gal-3 are intracellular (Wei et al., 2023). M1 gene markers are CD-38, G-protein

coupled receptor 18 (Gpr-18), and fomyl peptide receptor-2 (Fpr2). M2 exclusive gene markers are early growth response protein 2 (Egr2) and c-Myc (Jablonski et al., 2015) which are useful for immunotherapy.

A glance at functions of tissue macrophages

Macrophage functions are seen in early development including the maintenance of placental function in pregnancy. Macrophages function as prominent decidual immune cells which constitute 36% until the second and third trimester (Krop et al., 2023). Early decidual macrophages remove apoptotic vascular smooth muscle cells (Lash et al., 2016) and endothelial cells to remodel the maternal spiral arteries (Krop et al., 2023) and trophoblast-derived galectin-9 activates macrophages to suppress the remodelling (Li et al., 2024). In the decidua, natural killer (NK) cells and macrophages produce galectin-1 to induce apoptosis of CD3+ T cells and galectin-2 to inhibit apoptosis of Treg for immune homeostasis and regulate apoptosis (Chen et al., 2024). The normal function of immune cells at the maternal-fetal interface is important for normal uterine artery remodelling (SAR) to prevent circulatory dysfunction and preeclampsia.

In addition to involvement in placental homeostasis, macrophages perform the remodelling process in skeletal tissues. The coordination of functions between osteoblasts and osteoclasts is an essential role in the bone remodelling process to maintain bone mass. Cytokines produced by macrophages such as IFN-√, TNF-α and IL-6 promote proliferation of pre-osteoclasts and differentiation of osteoclasts (Weivoda and Bradley, 2023).

Kupffer cells (KCs) are macrophages that exist in liver sinusoids. In normal conditions, they have immunosuppressive functions engulfing the gut-derived foreign substances and apoptotic cells preventing the excessive inflammation in the liver and restoring the liver architecture. KCs also have a function in acute and chronic liver diseases In acute liver injury, KCs initiate the tissue repair response by secreting IL-10 and promote hepatocyte regeneration. They also release matrix metalloproteinases (MMPs) such as MMP12 and ADAM to induce remodelling of extracellular matrix (ECM) (Li et al., 2022). In chronic liver injury, KCs can differentiate into fibroblasts contributing to ECM deposition, and regulating haemopoietic stem cell (HSC) activity and survival via TGFB1 and EGFR signaling (Terkelsen et al., 2020).

Similarly, microglia are macrophages of the brain parenchyma. Microglia not only protect from pathogens but also maintain homeostasis. Microglia express high mitochondrial oxidative phosphorylation (OXPHOS)–related genes to adjust brain glucose levels by switching to the use of glutamine as the main fuel to meet the energy demands (Bernier et al., 2020). As components of the neurovascular unit (NVU), they regulate cerebral blood flow (CBF) by producing vasoactive mediators such as IL-1β, TNF-α, NO, PGE2, or ROS (Zhao et al., 2018). P2Y12R-positive microglia regulate CBF response by signalling somatosensory pathways (Császár. et al., 2022). Survival of microglia is supported in the nervous system by central and peripheral neurons through growth factors like MCSF and IL-34 (Kana et al., 2019).

Macrophages act to maintain the metabolic homeostasis of humans (Sreejit et al., 2020). Alveolar macrophages regulate the lipid catabolism and clearance of pulmonary surfactant proteins. Dysfunction of activated macrophages caused by disruption of signals of granulocyte-macrophage colony-stimulating factor (GM-CSF) leads to pulmonary alveolar proteinosis (Nakamura et al., 2013).

Aging and macrophage functions

Macrophages play an essential function in ageing when they have adaptive changes. Age-related changes are seen in their effector functions. Long-lived macrophages are integrated into a programme of high self-

renewing capacity to change their behaviour to react to micro-environmental signals (Mass, 2023). Short-lived macrophages are replenished by monocytes and these ontogenetically distinct macrophages can have different effector functions for tissue structure changes and stiffness of extracellular matrix in ageing (Selman & Pardo, 2021, Zahalka et al., 2022). Events of mild inflammation induced by lipopolysaccharides enhance long-lived macrophages to be reinforced with proinflammatory and reparative abilities (Zahalka et al., 2022).

There is a decrease in secretion or altered function of tumour necrosis factor (TNF), IL-6 and IL-1β in aged macrophages in pro-inflammatory settings (Hirano, 2021) and phagocytic and chemotactic functions of macrophages regulated by transcription factors MYC and USF-1 decline with ageing (Moss et al., 2024). This immunosenescence affects the progression of age-related diseases such as tumours and the repair process after injury.

Macrophages in tumour microenvironment

The tumour microenvironment (TME) is a complex ecosystem surrounding the tumour and it consists of a matrix, tumour cells, stroma, carcinoma-associated fibroblasts, endothelial undergoing mesenchymal transition, network of blood vessels, and immune cells (Yang et al., 2023). Macrophages are most abundant and play a key role in tumour immunity and tumourigenesis.

Hypoxic TME controls the infiltration of tumour-associated macrophages (TAMs) in cervical and hepatocellular carcinomas (Fernández-Palanca et al., 2023). TAMs undergo polarization to M1-macrophages under the influence of interferon (IFN), TNF, LPS and other growth factors like GM-CSF (Cencini et al., 2021). Increased expression of neuropilins (nrp) which are receptors for mononuclear phagocyte chemotaxis and co-receptors for epidermal growth factor (EGF), are seen in tumour hypoxic areas with associated increased infiltration of M2 macrophages (Chen, 2019). nrp-2 expression is associated with increased angiogenesis and infiltration of macrophages in tumours (Fernández-Palanca et al., 2023). TME infused with M-CSF, IL-4, IL-10, and IL-13 polarizes the macrophages into M2 macrophages with protumour and inflammatory effects (Hwang et al., 2020). TAMs readapt metabolic needs to favour tumour support and immune evasion. Such metabolic changes are acidosis, hypoxia and dysregulated lipid metabolism contributing to tumour survival and aggressiveness (Bian et al., 2021). Dendritic cells in TME present the tumour antigen to T cells and achieve T cell-mediated immunity. After metabolic adaptation, dendritic cells uptake lipid droplets through Msr1 receptors resulting in in defective translocation of major histocompatibility complex (MHC) to the cell surface thus impairing the antigen presentation and anti-tumour immunity (Jiang et al., 2018).

Macrophages can be used as a diagnostic marker as well as prognostic predictors (Bied, 2023). Tumour cells secrete cytokines such as CCL2 and CXCL12 to transform M1 into M2. A high M1/M2 ratio is associated with ovarian cancer survival (Zheng et al., 2014). CD68 can be used as a pan macrophage marker and CD163 is used to identify M-2 in the solid tumours (Svensson et al., 2022). Leukaemia cells can polarize M-1 macrophages and help in tumour immunity by phagocytosis and mediating cytolysis of tumour cells (Mantovani et al., 2022). M-2 macrophages are involved in growth and metastasis. TAM towards a pro-tumour type and M2 TAM can determine disease progression and drug resistance (Cencini, 2021).

In a primary tumour, TAMs favour tumourigenesis by creating a pro-tumoral immune environment. It occurs by inactivating cytotoxic T cells through PD-L1 expression and producing cytokines to create

an inflammatory milieu. M2 macrophages favour tumour growth by the production of tumour cell proliferating growth factors such as EGF and FGF and angiogenetic factors VEGF, PDDGF, TGFβ, MMPs, and CXCL8. TAM favours distant metastasis by increased epithelial-mesenchymal transition (EMT) and extracellular matrix remodelling by releasing factors such as matrix metalloproteinase, CCL18, TGFβ, MMPs, and TNFα, which ultimately causes metastasis and secondary tumour formation (Bied et al., 2023).

TAMs can negatively affect the functions of NK cells, dendritic cells and cytotoxic T cells. They promote immunosuppression by actively playing a role in the recruitment of Treg cells in the TME (Basak et al., 2023). TAMs also secrete cytokine and growth factors to induce T cells to release immune inhibitory checkpoint protein to form immunosuppressive TME to accept seedlings of circulating tumour cells (Lin et al., 2019). TREM2+ m0-macs are considered to be both pathogenic and protective potential. TREM2 deficiency is associated with the growth of murine HCC, suggesting that the TREM2 program is linked with pathogenic and protective potential (Esparza-Baquer et al., 2021). Various signals in TME activated the recruited macrophages to exhibit important steps in tumour initiation, metastasis, tumour surveillance and angiogenesis.

Tumour angiogenesis is essential for tumour growth and survival. Angiogenesis is induced by hypoxia-inducible factor (HIF) and HIF expression is significant in TAMs. Knockout of the HIF-1α gene enhances M2 polarization and attenuates their pro-angiogenic responses (Werno et al., 2010). Hypoxic stress in TME M2 polarization induces tumour angiogenesis by producing angiogenic factors such as VEGF-A, EGF, IL-1 beta, IL-8, CCL2 and CXCL12 (Hughes et al., 2015). TAM-induced matrix metalloproteinase (MMPs) from macrophages degrades the basement membrane and the extracellular matrix favours metastasis (Niland et al., 2022). Researchers target TAMs in the treatment of cancer which are based on inhibition and genetic manipulation of TAMs (Mantovani et al., 2022).

Macrophages and atherosclerosis

Atherosclerosis is caused by the accumulation of lipids in the vascular wall. Tissue-resident and monocyte-derived macrophages contribute to the formation and regression of atheromas. Monocytes infiltrate the subendothelium and transform themselves into macrophages. Macrophages as APCs present oxidized LDL (ox-LDL) to T cells to accelerate the inflammation. In normal steady states, Ly6Clo monocytes protect the endothelium and arterial vasculature by engulfing lipid particles, cellular debris and necrotic cells. Their numbers increased in hyperlipidemic and atherosclerotic conditions. Ly6Clo monocyte activity is partly stimulated by CCR5 and their signalling and lifespan are controlled by Lck/yes tyrosine kinases (Miyake et al., 2024).

Chemokine induces Ly6C+/ Ly6Chi macrophages to M1 polarization in the plaque shoulder. These M1cells which have pro-inflammatory, phagocytic and cytotoxic properties are responsible for matrix degradation and necrotic core formation (Lin et al., 2021). They phagocytose lipids including low-density lipoproteins (LDL) complexes to clear the inciting stimuli (Theofilis et al., 2023). M1 cells have increased expression of lipid–processing genes and also interact with other immune cells in the progression of atherosclerosis and sustained inflammation.
Ly6C- /Ly6Clo monocytes which normally patrol the endothelium stability differentiate into M2 subtypes when induced by IL-4, IL-13, toll-like receptor (TLR) agonists and other soluble factors in the later phase at the core of atheroma. They maintain the tissue homeostasis and resolution of inflammation by inhibiting pro-inflammatory cytokines and inducing secretion of anti-inflammatory cytokines such as IL-10 and IL-12 (Theofilis et al., 2023). M2 cells promote angiogenesis

and fibroblast formation and aid in tissue repair at the site of atheroma. Inflammatory macrophages with up-regulated inflammatory genes are key contributors to atherosclerosis. As Gal-1 and Gal-2 induce reprogramming from pro-inflammatory into anti-inflammatory types, treatment with anti-Gal nanobodies reduces atherosclerotic burden (Kane et al., 2022). The diversity of macrophages accumulation in atheromatous plaque and their metabolic characterization determine the type of atheromatous plaques. Stable plaques characterized by slow growth can give rise to progressive stenosis of arteries with low embolic sequelae. Unstable plaques have higher risks of thromboembolic manifestations.

Macrophages and infections

Macrophages are key members of the immune system against infection. They detect the infective agents and engulf and kill them. They present antigens to T and B lymphocytes after recruiting them by secreting cytokines and chemokines to assist the immune reaction. Macrophages possess specific pattern recognition receptors to detect pathogen-associated molecular patterns (PAMPs). After being detected, pathogens are engulfed and fused with lysosomes, phagosomes mature and pathogens are degraded (Pandey et al., 2022). Intracellular microorganisms such as Mycobacterium can survive inside macrophages as latent state and reactivate when the host immune systems weakened (WHO, 2015). Macrophage proteins such as Slc11a1 mediate resistance to certain intracellular microorganisms by promoting the transport of Fe+2 into phagosome and iron-mediated toxicity to the microbes (Blanc-Potard and Groisma, 2020) and polymorphism of protein results in susceptibility to microbes (Liu et al., 2017). Pathogen-induced macrophage intracellular microenvironment affects the nutrients and growth factors required for bacterial intracellular survival. Micronutrients are required for the regulation of virulence factors for example, magnesium for PhoP/PhoQ two-component system in Salmonella, iron for Shiga toxin in Shigella, and calcium for Yersinia. Macrophages undergo polarization and secrete cytokine towards pro or anti-inflammatory actions in the presence of infection by Staphylococcus aureus. Bacteria may be killed by intracellular or extracellular mechanisms. Alternatively, bacteria may escape antimicrobial killing and survive intracellularly by ROS and RNS, phagosome acidification, nutrient restriction and release of degradative enzymes (Pidwill et al., 2021). Reactive oxygen species (ROS) are molecules with oxidizing properties and they are produced as a result of cell metabolism. ROS induce oxidative stress in bacteria and kills them by breaking the DNA strands or modification of lipids and proteins (Vaishampayan and Grohmann, 2021). Some bacteria adapt themselves by developing genes required for anti-oxidant defence. For example, S aureus survives the killing by their enzyme property of superoxide dismutase A (SodA) and superoxide dismutase M (SodM) which can dysfunctional the superoxide radicals (Pidwell et al., 2021). Reactive nitrogen species (RNS) are nitrogenous products such as nitric oxide (NO) produced by nitric oxide synthase (NOS). Formation of inducible NOS (iNOS) occurs mainly in macrophage phagolysosomes when macrophages are stimulated by immune reactions. RNS impairs microbial growth by inhibiting bacterial respiration and DNA replications (Fang and Vázquez-Torres, 2019). Successful microorganism develops virulence-associated genes to survive nutrient restriction and phagolysosome toxicity (Pandey et al, 2022). The ability of Salmonella typhimurium to survive inside macrophages needs the two-component virulence regulatory system, PhoP/PhoQ which consists of sensor PhoQ and regulator PhoP. These genes regulate the magnesium concentration in the salmonella-containing vacuoles inside macrophages thus promoting the virulence of bacteria in low magnesium concentration. Mildly acidic pH in macrophages also activates the PhoP/PhoQ system and increases bacterial virulence

(Choi and Groisman, 2016). Nutritional immunity refers to how host factors restrict bacterial growth by changing the nutritional status in the microenvironment of host cells and bacteria. Acidification of macrophage phagosomes is important in killing engulfed bacteria since bacterial growth is reduced at pH4.5 (Bore et al., 2007). Methicillin-resistant S aureus (MRSA) overcomes the killing by Kupffer cells of the liver survives intracellularly and spreads through circulation. Liposomal formulation of vancomycin targets the source of reservoirs of bacteria without attacking liver toxicity and dissemination to other organs (Surewaard et al., 2016).

Macrophage and immune disorders

Macrophages Macrophage activation syndrome (MAS) is an acute and severe inflammatory syndrome triggered by various factors such as infections, immune disorders, malignancy and drugs. It is also known as secondary haemophagocytic lymphohistiocytosis which is a potentially harmful immune disorder. MAS is usually associated with the expression of markers namely increased levels of cytokines such as IL-1, IL-6, TNF-α, INF-γ, high levels of ferritin and complicated by multiple organ failure (Wynn, 2022). In the bone marrow, activation of macrophages leads to secondary haemophagocytic lymphohistiocytosis which results in phagocytosis of haemopoietic cells including red cells, lymphocytes and other haemopoietic precursors and enlarged extramedullary haemopoietic organs such as liver and spleen (Nguyen et al., 2022).

Macrophages are major cells in the development of type IV hypersensitivity reaction which is useful for immune reaction against intracellular microorganisms such as mycobacteria, fungi parasite infections and other granulomatous inflammations. Macrophages act as APCs that present antigens to CD4+ T cells, in association with class II MHC molecules. Macrophages also produce cytokines namely interleukin (IL)- 12, a critical cytokine, for induction of TH1 lymphocyte response leading to production of other cytokines such as tumour necrosis factor (TNF) and interferon (IFN) -√ which induce further differentiation of TH1cells to augment the delayed hypersensitivity. Due to their property to function as APCs in both transplanted grafts and recipients, macrophages induce local delayed hypersensitivity reactions on kidney allografts leading to the destruction of histocompatible grafts (Lackner et al., 2023).

The age-related functional decline of macrophages may represent a starting innate immune functional decline associated with ageing and age-related diseases (Moss et al., 2024). Identifying downstream targets of macrophage functionality in ageing is a future therapy for geriatric diseases. Modern genome editing technologies mediate the alteration, addition and ablation of genes (Dunbar et al., 2018). Genetic alteration in macrophage genes is associated with bone mass abnormality. Clusters of inflammatory macrophages expressing CD209, CCl4, IL-1B, CD14 and MMP9 are expanded in patients with inflammatory bowel disease. ETS2 signalling through MEK1/2 inhibition affects cytokines such as TNF and IL-23 which can be used as targets for inflammation-related diseases. This pathway is also related to IL-1β which is linked to therapy resistance cases (Stankey et al., 2024).

Based on the knowledge of the polarization of macrophages into M1 and M2 phenotypes and their distinctive functions in inflammatory and tumourigenesis, the macrophage-based therapeutic approach is a hopeful future for anticancer therapy. Anti-cancer therapy possibly uses depletion of TAMs by inhibitors of colony-stimulating factor-1 receptor (CSF 1R) (Cassetta & Pollard, 2018) and targeting TAM is a future novel approach. Gene therapy targeting to modulate the macrophage function through the nucleic acid modification is a future hope for precision cancer Medicine. Nucleic acid therapeutics

such as plasmid DNA (pDNA), messenger RNA (mRNA), small hairpin RNA (shRNA) and microRNA (miRNA) are delivered through gene delivery vectors (Dunbar, 2018) to alter their TAM's phenotypes or expression of receptors or release of cytokines and chemokines (Huang et al., 2023). DNA nanoparticles combined with peptides or hyaluronic acids repolarize the macrophages to reverse tumour immunoresistance (He et al., 2018).

Together with clinical and morphological parameters, measuring baseline TAM content in malignancies may be useful for the prediction of disease prognosis and identifying high-risk groups in leukaemia, lymphoma and myeloma patients (Cencini et al., 2021). The use of CD163 as a marker for TAM was proposed as a useful marker for predictor of clinical outcome in classical Hodgkin lymphoma patients in general and advanced-stage groups (Klein et al., 2014, Nam et al., 2014). Dysregulation of the metabolic system can bring up polarization of anti-tumour M1 and pro-tumour M2 phenotypic changes in the immune milieu of TME. Reprogramming of immunometabolism in macrophage polarization can be applied in the modification of tumour environment (Leon, 2020) and inflammatory lesions (O'Neill et al., 2016).

Immunotherapy is a major choice of treatment in non-small cell lung cancer (NSCLC). The evolution of tumour cell mutation with resultant increased tumour mutational burden is a major concern in the failure of response to immunotherapy. Lung cancer activation module (LCAMhi), a cellular module which consists of SPP1+ macrophages and other immune cells, is enriched in NSCLC lesions. Baseline data of abundant LCAMhi score is closely related to NSCLC clinical response to immunotherapy proven in patients with high TMB (Leader et al., 2021). TAMs possess receptors with collagenous structure (MARCO). In therapy using the antibodies to block these receptors, TAMs can be changed into pro-inflammatory effectors with a resultant anti-tumour immune response (Georgoudaki et al., 2016). Cytokine and chemokines are produced in TME to both recruit and polarize tumour-promoting myeloid cells and anti-tumour and immunostimulating functions. Trials use mechanisms that inhibit these cytokines to control the regulators of myeloid cell functions. Macrophages can be candidate cell therapy with chimeric antigen receptor effector cells (Mantovani et al., 2022). Chemokine with receptor-ligand CCL-5 and vascular endothelial growth factor (VEGF) regulate the macrophage recruitment in tumour TME. Monoclonal antibodies or receptor antagonists can reduce the tumour growth rate and macrophage density in TME (Beltraminelli & De Palma, 2020). As TAMs uptake lipids through MARCO, studies showed that genetic modification and inhibition of MARCO results in reduced lipid accumulation in TAMs and redirect TAMs towards an anti-tumour profile (Masetti et al., 2022). Genetic deletion of CD36 stops lipid scavenging by TAMs and renders anti-tumour efficacy in haematological malignancies (Su et al., 2020). As dysregulated lipid metabolism of TAMs promotes tumour survival and progression, targeting therapy at changing lipid metabolism in TAMs is also a hopeful approach in cancer therapy (Ren et al., 2024).

CONCLUSION

TUnderstanding through past knowledge of macrophages is they are part of the mononuclear phagocyte system which functions as scavengers in inflammation. Moreover, macrophages also have their roles in the induction of cell-mediated immune responses by processing antigens and presenting peptide fragments to T cells. They also serve as effector cells in immune responses such as delayed hypersensitivity reactions. After being activated by T cell-released cytokines, macrophages are enhanced to perform the killing of microbes and tumour cells. Recent and upcoming advances suggest there are many more functions of macrophages other than scavenger functions. Based on the

knowledge of macrophage biodiversity and immune functions, scientists try to modify macrophages to use them as candidates for treating inflammation-related diseases as well as malignant diseases as a modality of immunotherapy and markers for predicting prognosis.

CONFLICT INTEREST

The authors do not have any conflict of interest.

ACKNOWLEDGEMENTS

The authors would like to thank researchers who are dedicated to their research work on macrophage biology and tumour immunology.

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Borneo Journal of Medical Sciences

REVIEW ARTICLE

[Correction] Exploring the Bacteriophage in Malaysia: An Overview of Applications and Challenges

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Received: 8 March 2024

Accepted: 9 October 2024

Published : 2 September 2025

DOI: https://doi.org/10.51200/bjms.v19i3.6760

Keywords: *Bacteriophages, applications, Antimicrobial-resistant, AMR, Malaysia*

In the published version of this article (Mastor et al., 2025), several inaccuracies in Table 1 concerning reference alignment and supporting information were identified. The authors have provided a corrected version of Table 1 here.

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Mastor, N. N. I., Hoque, M. Z., & Subbiah, V. K. (2025). Exploring the Bacteriophage in Malaysia: An Overview of Applications and Challenges. Borneo Journal of Medical Sciences, 19(2), 110–122. https://doi.org/10.51200/bjms.v19i2.6172

Table 1: The list of bacteriophages studies in Malaysia included in this article.

Phage Application	Phage strain	Phage family	Isolation source	Host pathogen	Reference
Clinical	vB_ZEFP	*Podoviridae*	Hospital wastewater plant	*Enterococcus faecalis*	(El-Telbany et al., 2021)
Clinical	k2a, k2b, k2w5,k2w6, kP99,k9w6, k9coc	*Podoviridae*	Sewage water and cockles	*Klebsiella pneumonia*	(Baqer et al., 2021)
	k9w5,k8coc	*Myoviridae*			
	k7w9	*Siphoviridae*			
Clinical	C34	*Myoviridae*	Sea water	*Burkholderia pseudomallei*	(Guang-Han et al., 2016)
Clinical	ΦNUSA-1	*Myoviridae*	Raw sewage wate	*Staphylococcus aureus*	(Tan et al., 2020)
	ΦNUSA-10	*Siphoviridae*			
Agriculture	No strain name	Not reported	Sewage and soil sample	*Escherichia coli*	(Tan and Tony, 2014)
Clinical	pPM_01	*Siphoviridae*	Sewage treatment facility	*Proteus mirabilis*	(Wirjon et al., 2016)
Agriculture	NΦ-1 and NΦ-3	*Podoviridae*	Termite infected rice	*Xanthomonas oryzae* In rice	(Liu et al., 2021)
Clinical	ΦKpaV04 ΦKpaV08 ΦKpaV12	*Myoviridae*	Domestic sewage facility	*Klebsiella pneumoniae*	(Paran et al., 2020)
	ΦKpaV03 ΦKpaVa10	*Podoviridae*			
Livestock	SE07	*Podoviridae*	Retail chicken meat	*Salmonella Enteritidis*	(Thung et al., 2017)
Livestock	SE01-SE14 ST01-ST04 CJ01-CJ04 VP01 and VP02 EC01-EC05	Not reported	Various food types and sewage water	*Salmonella Enteritidis SalmonellaTyphimurium Camphylobacter Jejuni Vibrio parahymolyticus Escherichia coli*	(Thung et al., 2020)
Livestock	ΦLM2, ΦLM3 ΦLM6, ΦLM4 ΦLM05	Not reported	Animal based food (Beef, chicken, seafoods and shrimps) and environmental samples (water and sewage)	*Camphylobacter jejuni, Escherichia coli, Staphylococcus aureus, Listeria monocytogenes*	(Premarathne et al., 2017)
	ΦEC1, ΦEC2, ΦEC3				
	ΦSA1, ΦSA2				
	ΦMRSA1				
	ΦCj1, ΦCj2, ΦCj3, ΦCj4, ΦCj5				
Livestock	EC1	*Not reported*	Chicken faeces	*Escherichia coli*	(Lau et al., 2010)
Aquaculture	VPUSM	*Myoviridae*	Environmental water samples: rivers, lakes, sewage, fish farms, ditches, ponds	*Vibrio cholerae*	(Al-Fendi et al., 2014)
Livestock	CJ01	*Myoviridae*	Retail chicken meat	*Camphylobacter jejuni and Camphylobacter lari*	(Thung et al., 2020)
Aquaculture	Vp33, Vp22, Vp21, Vp02	*Podoviridae*	Seafood samples	*Vibrio parahaemolyticus*	(Tan et al., 2021)
	Vp08 and Vp11	*Siphoviridae*			
Aquaculture	vB_Sags-UPM1	*Siphoviridae*	Infected tilapia	*S. agalactiae*	(Megat et al., 2023)
Aquaculture	VpKK5	*Siphoviridae*	Coastal sand sediment	*Vibrio parahaemolyticus*	(Lal et al., 2016)
Aquaculture	VpKM4	*Myoviridae*	A dieases culture Barramundi Perch Lates calcarifer	*Vibrio harvevi and Vibrio parahaemolyticus*	(Lal et al., 2017)

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CASE REPORT

Rare Calyceal Diverticulum in a 10-year-old Child: A Case Report

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Received: 11 October 2024

Accepted: 7 January 2024

Published: 2 September 2025

DOI: https://doi.org/10.51200/bjms.v19i3.5482

Keywords: *Calyceal diverticulum, Urinary tract infection, CT abdomen*

ABSTRACT

A calyceal diverticulum is an outpouching of the collecting system into the renal parenchyma. A 10-year-old obese child was presented with on and off fever associated with polyuria for 2 months. Initial ultrasound showed complex cysts at the upper pole of right kidney. Computed tomography (CT) abdomen in excretory phase revealed passive filling of the "cysts". The patient was treated conservatively with antibiotics and was discharged. Calyceal diverticulum is rare, happening in only 0.21 to 0.6% of intravenous urograms of both adults and children. Underlying chronic phimosis and recurrent urinary tract infection could have contributed to the formation of calyceal diverticulum. Calyceal diverticulum should be considered as a possible diagnosis in children when the patient is presented with urinary tract symptoms and multiple cysts are found on ultrasound. CT abdomen in excretory phase is required to diagnose this condition although it gives higher radiation dose to the child.

INTRODUCTION

A calyceal diverticulum is the outpouching of the upper collecting system into renal parenchyma rather than confined within the renal pelvis. It connects with the main collecting system through a narrow channel and is covered with transitional cell epithelium (Waingankar et al., 2014). It may be difficult to differentiate calyceal diverticulum from renal pelvis, simple renal cysts, parapelvic cysts, hydrocalyx, cystic renal tumours, early presentation of autosomal dominant

polycystic kidney diseases or other renal cystic diseases (Alaygut et al., 2020; Bombinski et al., 2015; Zhao et al., 2022). Calyceal diverticulum is rare, happening in only 0.21 to 0.6% of intravenous urograms of both adults and children. In 48.9% of the cases, it occurs in both upper poles of the kidneys, and in 29.7% and 21.4%, it happens in lower poles of the kidneys (Waingankar et al., 2014). Calyceal diverticulum affects women more commonly than men with incidence of 63% and 37% respectively. Sizes of diverticulum ranges from 0.5 to 7.5cm, with average size of 1.72cm. Stones are found in 9.5% to 50% of the cases with sizes ranging from 0.1cm to 3.0cm, averaging at 1.2cm (Waingankar et al., 2014). Several factors have been proposed as the causes of calyceal diverticulum, such as congenital causes, obstruction, infection, neuromuscular (dysfunction of sphincter around the calyces), traumatic, and fibrotic causes (Waingankar et al., 2014). Calyceal diverticulum can be classified into two types namely Type I (communicating with an infundibulum or minor calyx) and Type II (communicating with a major calyx or renal pelvis) (Waingankar et al., 2014).

There are no history, physical examination, or laboratory findings that are diagnostic of calyceal diverticula. Some of the symptoms presented maybe flank pain, symptoms of urinary tract infection, or haematuria (Waingankar et al., 2014). Asymptomatic patients usually do not require any treatment. However, several cases suggested that the diverticulum may close off and become a cyst, abscess, or may cause symptomatic enlargement, stones, and urinary tract infections (Estrada et al., 2009; Nicholas, 1975; Siegel & McAlister, 1979; Zhang et al., 2019). If complications of the calyceal diverticulum arises, either open excision or minimally invasive methods such as ureterorenoscopy, percutaneous puncture, laparoscopy can also be performed during surgical intervention (Alaygut et al., 2020; Chattopadhyay et al., 2021). In this case report, we presented a case of a 10-year-old boy with urinary urgency. Calyceal diverticulum was diagnosed upon computer tomography (CT) abdomen scan in excretory phase. The patient was treated conservatively with antibiotics and was well upon discharge and one year follow-up.

CASE PRESENTATION

We presented a case of 10-year-old boy who had underlying obesity weighing 57.9 kg. He presented with an increase in frequency of urination for 2 months and worsening for 2 weeks. He also had fever for 2 weeks with on and off chills. Otherwise, there was no dribbling or straining during urination, no dysuria, haematuria, abdominal pain or loin tenderness. Initial blood investigation noted white cell count at 29.7 x 103/uL. Meanwhile,

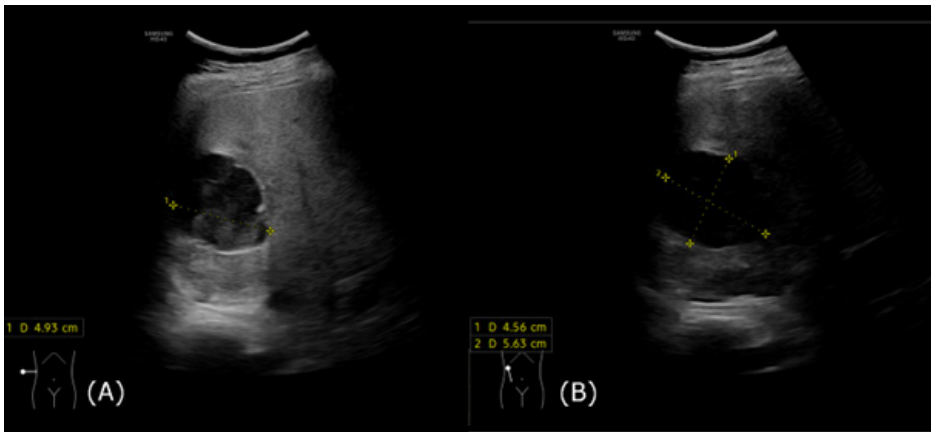
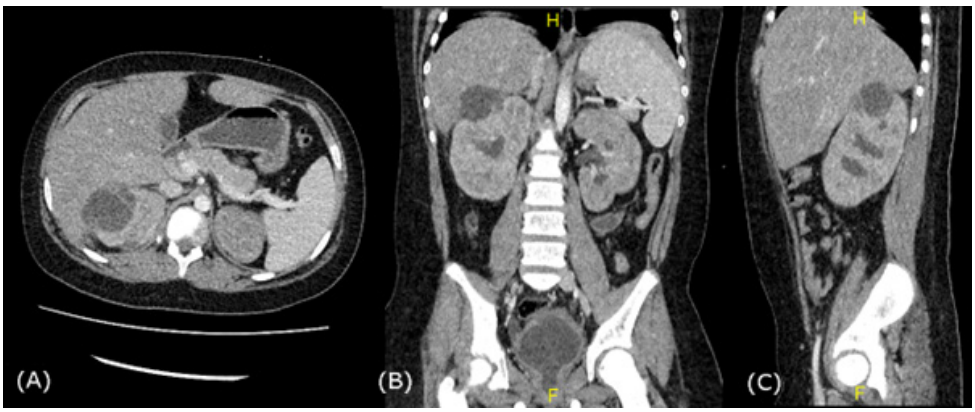
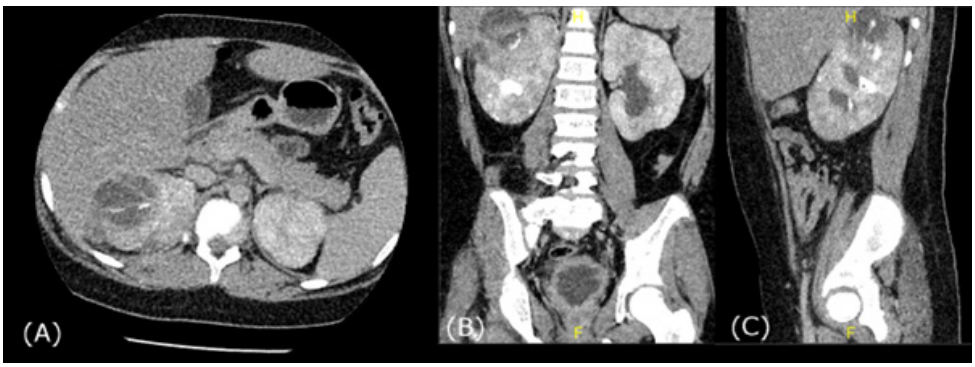


Figure 1A and 1B: show a well-defined, anechoic, lobulated right upper pole calyceal diverticulum as seen on ultrasound.



Figures 2A, 2B, and 2C : Show the well-defined, round, lobulated, hypodense right upper pole calyceal diverticulum with septation within on



Figures 3A, 3B, and 3C : Show the passive filling of the calyceal diverticulum during excretory phase on CT abdomen. portal venous phase of

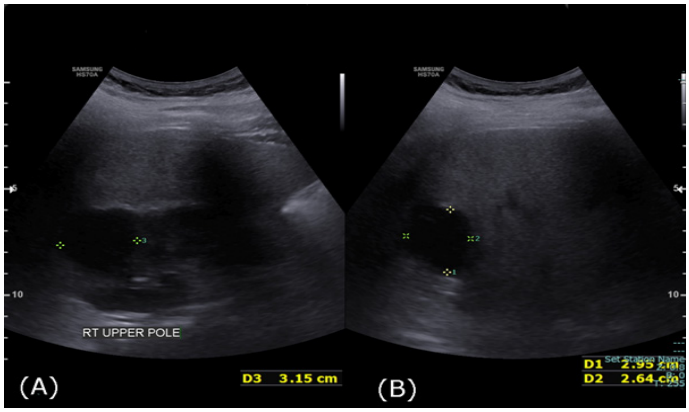


Figure 4A and 4B : Show a repeat ultrasound at day-14 after admission revealing a right upper pole cystic lesion had become smaller in size. CT

urea was at 26.5 mmol/L and creatinine level at 313 umol/L. The patient had acute kidney failure.

Ultrasound kidney, ureter, bladder (KUB) (Figure 1) was done on day 1 of admission. It showed a multiseptated cystic lesion with debris within the upper pole of right kidney with bilateral mild hydronephrosis. There was loss of corticomedullary differentiation of the bilateral kidneys which could be suggestive of infective or pyelonephritic changes. In view of the complex renal cystic lesion, the patient proceeded with contrasted CT abdomen (Figure 2) on day 3 of admission. A well-defined lobulated cystic lesion (HU range from

+1 to +20) was noted at the upper pole of right kidney, measured 4.5x4.7x6.7 cm (APxWxCC) with few internal septa but no calcification. The patient proceeded with excretory phase in view of complex nature of the cyst. In the excretory phase at 8 minutes (Figure 3), passive filling and layering of contrast within the cyst was noted. There was also a small tract with length of 8mm that communicates the cyst with the upper pole calyx. Both the kidneys appear swollen with poor nephrogram and bilateral moderate hydronephrosis and hydroureters. The diagnosis was changed to right upper calyceal diverticulum secondary to sequala from recurrent infection in view of the CT abdomen findings as described above.

Ultrasound was repeated at 14 days after admission (Figure 4). The right upper pole cystic lesion had become smaller in size, measuring 3.0x2.6x3.2 cm (APxWxCC). However, another new exophytic hypoechoic lesion appeared at the right upper pole, measuring 1.4x2.0x2.2 cm (APxWxCC). Irregular renal margins may represent scarring due to residual infective changes. There was also irregular thickening of the urinary bladder wall, in keeping with cystitis.

Initial venous blood gas noted compensated metabolic acidosis (pH at 7.35, bicarbonate at 13.9 mmol/L and base excess at -11.3 mmol/L). At day 4 of admission, there was difficult urinary catheter insertion because the child had a buried penis with phimosis. Pus was noted to come out from meatus. The urinary catheter was eventually inserted, releasing the phimosis. Penile swab culture and sensitivity (C&S) and urine C&S repeated showed the growth of E. coli which was sensitive to meropenem and intermediate sensitivity to amoxicillin/clavulanic acid. The patient undergone conservative antibiotics treatment and completed a total of 9 days of antibiotics. Upon discharge, his serum urea level was improved to 5.0 mmol/L and creatinine level improved to 66 umol/L. The white cell count was improved to 13.87x 103/uL upon discharge. Phimosis was noted when it was decided patient will be readmitted later for circumcision. Further investigations such as micturating cystourethrogram (MCUG) were not conducted unless patient has recurrent symptoms because phimosis is a known cause of vesicoureteral reflux which would lead to recurrent urinary tract infections (UTI).

The patient was later electively readmitted for circumcision for phimosis and repair of buried penis. During the operation buried penis and glandular hypospadias was noted. The patient was well during 3 months follow-up.

DISCUSSION

On ultrasound, calyceal diverticulum appears as anechoic cysts unless filled with hyperechoic stones. The stones will change position according to the body habitus of the patient (Waingankar et al., 2014). Heterogeneously echogenic sediments forming a fluid level is indicative of infection. However, this feature is not helpful in differentiating calyceal diverticulum from renal cyst (Bombinski et al., 2015). Calyceal diverticulum may also be suspected if a connection is demonstrated between renal cyst with the collecting system on ultrasound but this feature may not be always demonstrable (Alaygut et al., 2020). On CT scans, calyceal diverticulum can be seen during excretory phase of the CT abdomen when there is passive filling of the diverticulum from the renal pelvis (Waingankar et al., 2014). CT abdomen in excretory phase is necessary to diagnose calyceal diverticulum despite increased radiation dose to a child. This is because slight increase in density within the diverticular content during the renal parenchymal phase is not specific and may be mistaken as renal tumour enhancement (Bombinski et al., 2015).

A study conducted by Alaygut D et al. in 2020 found that 9 out of 40 children follow-up for renal cysts or parapelvic cysts have calyceal diverticulum. These children were

aged from 1 to 17 years old. Two children had renal stones while three children had recurrent urinary tract symptoms (Alaygut et al., 2020). Ningshu Lin et al., in a study conducted in 2013 on adolescents and adults, showed that by applying compression bands on the abdomen [similar to intravenous urogram (IVU)] and excretory image acquisition of computed tomography urography (CTU) at 60 minutes after contrast administration may increase sensitivity and specificity in identifying calyceal diverticulum (Lin et al., 2013). However, such a measure is impractical to perform in a busy hospital setting.

In our case, the calyceal diverticulum was round, located at the upper pole of right kidney measuring 4.5cm in size, and showed incomplete filling during excretory phase of CT renal at 8 minutes. Underlying chronic phimosis and recurrent urinary tract infection could contribute to the formation of calyceal diverticulum in this child.

CONCLUSION

Calyceal diverticulum should be considered as a possible diagnosis in children with urinary tract infection and multiple cysts found on ultrasound. Recurrent urinary tract infections could have contributed to the formation calyceal diverticulum in children. The condition can be diagnosed by excretory phase in CT abdomen although it gives higher radiation dose in children.

CONFLICT INTEREST

No funding was received for the preparation of this article. No financial competing interests declared.

CONSENTS

Written consent was taken from the mother to publish this case report. A copy of the written consent is available for review by Chief Editor.

ACKNOWLEDGEMENTS

None

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CASE REPORT

Rare Ileal Inflammatory Fibroid Polyp Causing Intussusception: A Case Report

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Received: 9 March 2024

Accepted: 25 June 2024

Published: 2 September 2025

DOI: https://doi.org/10.51200/bjms.v19i3.5548

ABSTRACT

An inflammatory fibroid polyp (IFP) is a rare, benign tumor most commonly presenting in the gastric antrum (60–70%), followed by the intestines (18–20%). We present a case of intussusception due to an IFP. A middle-aged female was admitted with right iliac fossa pain and abdominal distention. A CT of the abdomen showed a 5 cm smooth, oval, fluid-like (24 HU), simple hypoattenuating lesion at the terminal ileum complicated with intussusception. An open laparotomy and end-to-end anastomosis were performed. The tumor was resected. Histopathological results showed an IFP. IFP can be identified on CT abdomen as oval, hypoattenuating, fluid like lesion, However, it is not specific and other differential diagnoses of bowel lesions should be considered. Histopathologically, it is rare that this lesion extends into the muscularis propria and subserosa.

Keywords: *Inflammatory fibroid polyp, Intussusception, CT abdomen*

INTRODUCTION

Intussusception is a condition whereby a proximal bowel slides into the distal portion of the bowel, thus blocking food particles or fluid from passing through the bowel. Intussusception can also cuts off blood supply to the affected bowel loop. Intussusception is rare in adults, affecting 1 in 1,000,000 patients per year worldwide. About 90% of those who had intussusception have an underlying lesion that caused it, where half of the lesions were malignant (Guerci et al., 2022). Benign causes of intussusception are gastrointestinal stromal

tumours (GISTs), polyps, Meckel's diverticulum, inflammatory lesions and trauma (Choi et al., 2004).

Inflammatory fibroid polyp (IFP) is a rare, benign tumor that most commonly presents in the gastric antrum (66 to 75%), followed by the small intestine (18 to 20%) (Akbulut, 2012) and the large intestine and rectum (4 to 7%) (Sugawara et al., 2018). The tumor is present in those aged 4 to 80 years old (Akbulut, 2012; Garmpis et al., 2021). Rarely it happens in the gall bladder, esophagus, duodenum, or appendix (Akbulut, 2012). Females have a slightly higher chance of getting an IFP with a female-to-male ratio of 1.3:1 (Garmpis et al., 2021).

IFPs usually do not cause symptoms and are found incidentally during endoscopic procedures or laparotomy. In the small bowel, it can cause intussusception or intestinal obstruction (Akbulut, 2012). The size of an IFP is usually 2 to 5 cm, but some may reach up to 20 cm. They originate from the submucosa and grow into the intestinal lumen. IFPs originate from the mesenchymal cells of the intestinal tract (Akbulut, 2012). Initially, the presence of eosinophils within the lesion suggests it is of inflammatory origin, thus, the name "inflammatory fibroid polyp" is conceptualized. However, later studies showed mutations in platelet-derived growth factor receptor alpha (PDGFRA), causing its development to be in favor of a neoplastic origin (Rais et al., 2017). In terms of immunohistochemistry, an IFP stains positive for CD 34 and vimentin and stains negative for CD 117, S100, and DOG-1 (Akbulut, 2012).

Due to the rarity of this tumor, epidemiological data has been sparse. Since the attenuation of IFP is similar to surrounding intestinal mucosa, it is often missed during CT scans as a potential lead point for intussusception. Besides, small size of the polyp (< 1cm) and collapsed bowel also makes the detection of the polyp difficult on CT. We present a case report of a 51-year-old female who presented with IFP terminal ileum intussusception. We also performed a literature review on its imaging features.

CASE PRESENTATION

A 51-year-old female presented with right iliac fossa pain for one week, which was colicky and non-radiating in nature, with a pain score of 6. She had abdominal distention for 2 days, vomiting for one day, and loose stools for one week. She did not have a fever, and her vital signs were stable. Blood pressure was recorded to be 130/83 mmHg with a pulse rate of 93/min and normal oxygen saturation on room air.

On admission, full blood count showed a hemoglobin level of 10.9 g/dL, a white cell count of 10.1x 103/uL, and a platelet count of 609 x 103/uL. -rayA peripheral blood film (PBF) was performed because the patient was mildly anemic. The PBF showed mild normocytic normochromic anemia with thrombocytosis.

An abdominal radiograph (Figure 1) showed small bowel dilatation. Next, a contrast-

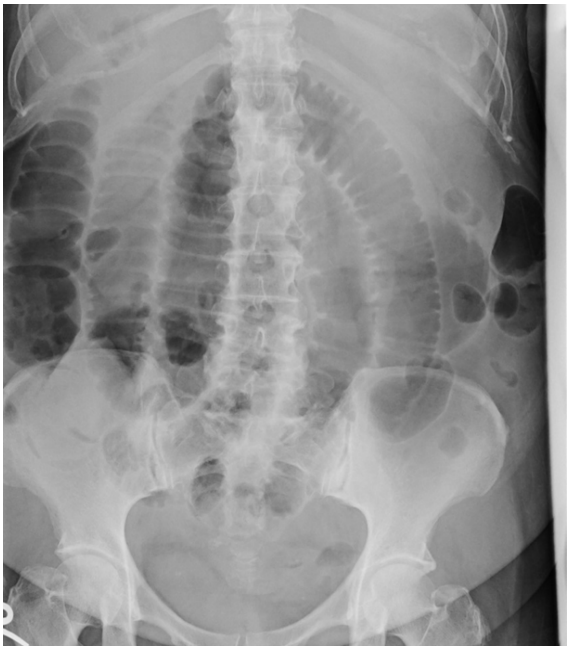

Figure 1: Abdominal radiograph showed small bowel dilatation.

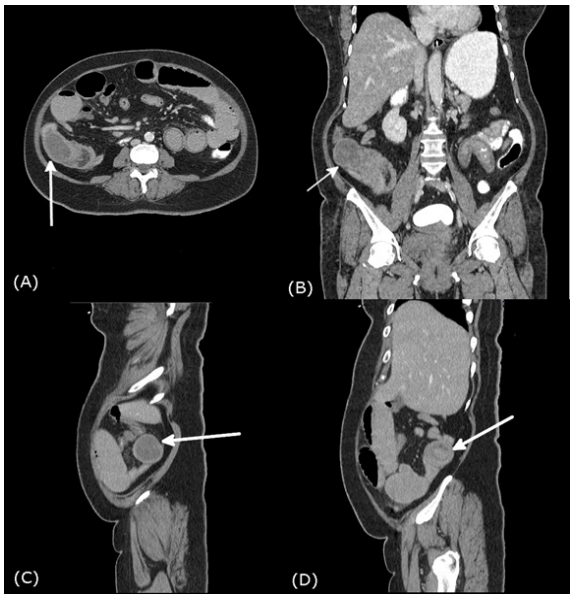

Figure 2: CECT abdomen pelvis in (A) axial, (B) coronal, (C and D) sagittal views. Figures 2A, 2B, and 2C showed the position of the cross-sections of the inflammatory fibroid polyp at the terminal ileum. Figure 2D showed the target appearance of the bowel, in keeping with intussusception.

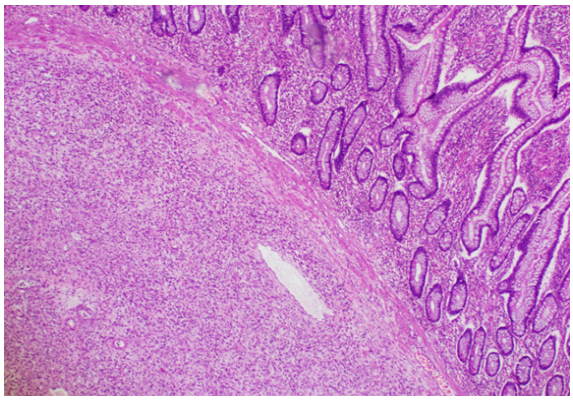

Figure 3: Haematoxylin & Eosin stain, 100x magnification. Submucosal lesion composed of a proliferation of haphazardly arranged short spindled and stellate cells. Small and intermediate-size blood vessels are seen within the lesion.

enhanced CT of the abdomen was performed to find the cause of the bowel obstruction. Both oral and rectal positive contrasts were administered. The abdominal CT (Figure 2) showed a dilated small bowel from the distal jejunum to the distal ileum. The terminal

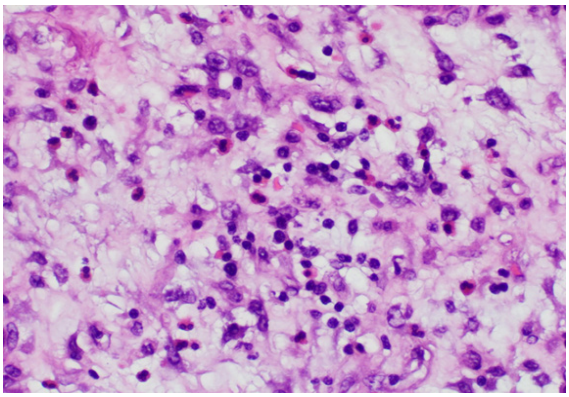

Figure 4: Haematoxylin &Eosin stain, 400x magnification. IFP cells have fine chromatin, indistinct nucleoli, and scant eosinophilic cytoplasm. The stroma is edematous to myxoid with prominent eosinophils, lymphocytes, and plasma cells.

ileum was also distended. The ascending and transverse colon colon werecollapsed while the descending colon was partially distended with contrast. A well-defined, oval, hypodense lesion measuring 4.7 x 3.0 x 4.1 cm (AP x W x CC) with mucosal hyperenhancement was seen at the terminal ileum. The lesion showed hypoattenuation, measuring +24 Hounsefield Units (HUs).

An exploratory laparotomy was performed. Intra-operatively, the proximal small bowel was dilated. An ileal intussusception was found 50 cm from the ileocecal valve. The small bowel collapsed distal to the intussusception. The intussusception was reduced, and a polypoidal tumor, sized at 5 x 3 x 3 cm (AP x W x CC), was found. The tumor was resected, and a primary end-to-end anastomosis was performed. The postoperative recovery was uneventful. The patient was discharged on day 5 post-operation. The resected tumor was sent for histopathological examination.

Gross pathology showed a hemorrhagic and tan-cut surface. Microscopy examination shows a poorly marginated, hypocellular lesion in the submucosa, extending into the muscularis propria and subserosa. It contained spindle-shaped cells and stellate cells with fine chromatin, (Figure 3) indistinct nucleoli, and

scant eosinophilic cytoplasm. Additionally, the stroma of the tumor was myxoid to edematous in appearance, containing eosinophils, lymphocytes, and plasma cells (Figure 4). There are also some small to intermediate-sized blood vessels with concentric fibrosis. Immunohistochemistry stains were positive for CD 34 and had multifocal positivity for SMA. It tested negative for CKAE1/AE3, CD 117, DOG-1, S100, ALK 1, and Desmin.

DISCUSSION

CT scan has a 58 to 100% accuracy in diagnosing intussusception (Akbulut, 2012). Small bowel tumors, whether benign or malignant, account for no more than 2% of all gastrointestinal tumors (Gill et al., 2001). Ivanis N et al. reported 77 cases of IFP in the English literature from 1976 to 2019 (Ivanis et al., 2020). In all the IFPs that were imaged by CT, only 46–50% of the cases could a lead point be found (Han et al., 2015; Lee & Yuen, 2014). However, CT scan is the standard diagnostic tool not only for polyp, but also for any lead point in the abdomen, whether intussusception is present or not because of its wide availability and fast diagnosis

Two research articles systematically explored the imaging features of IFP on CT. Han G et al. characterized the imaging features of IFP based on size, shape, margins, contour, growth patterns, mucosal hyperenhancement, homogeneity, and degree of enhancement in a case series of 27 patients from a single institution. The majority of IFP lesions appear as round or oval, hypoattenuating, smooth masses (Han et al., 2015). Mucosal ulceration is associated with hyperenhancement of the mucosa on a CT scan (Han et al., 2015). Meanwhile, Lee CY et al. performed a literature search from 1990 to 2013, focusing on the size, shape, margin, and attenuation of the lesion with HU values, if available. They showed similar results as Han G et al. Meanwhile, the HUs for IFP for these cases range from 16 to 17 (Lee & Yuen, 2014). Our case agreed closely with these two articles on the general imaging features of IFP. The density IFP in our case was fluid-like with an attenuation of 24 HUs. However, other gastrointestinal tumours may show similar features on CT scans such as gastrointestinal stromal tumour (GIST), plexiform myxofibroma, and schwannoma, thus should be included as differential diagnoses for IFP (Mocellin, 2021). In addition, our sample showed a hemorrhagic cut surface, which may be associated with the small and intermediate sized blood vessels found in histopathological study as shown in Figure 3. Proliferation of blood vessels in tumours are commonly due to neovascularization. When brittle blood vessels ruptured, they may contribute to chronic blood loss in the patient, causingmild anemia.

Other authors came across the imaging features of IFP on endoscopic ultrasound, abdominal ultrasound and MRI, On endoscopic ultrasound, IFP is presented as a homogenous, hypoechoic lesion (Inayat et al., 2018)..On transabdominal ultrasound, IFP is described as round, hypopechoic soft tissue mass (Akbulut, 2012; Bhutia et al., 2016). In MRI abdomen, IFP is described as homogenously T1-weighted isointense soft tissue mass when compared to surrounding muscles; central hypointensity with peripheral ring on T2-weighted sequence. While on DWI sequence, IFP resembles a “target” sign (Feldis et al., 2015). However, endoscopic ultrasound can only reach until duodenum; Bowel lesion is not normally seen on transabdominal ultrasound unless the bowels are distended and fluid filled. Meanwhile, MRI has limited availability and time consuming. Therefore, CT scan is still the best modality in finding lead point or small bowel lesion in emergency setting.

In this case, the IFP stroma is oedematous to myxoid based on histopatholoical study. The infiltration of the tumor into the muscularis propria and subserosa, which is found in our case, is a rare feature of IFP. However, it is impossible to differentiate between the IFP

subtype and the degree of mucosal invasion on CT scan.

CONCLUSION

CT scan is the most practical modality for the diagnosis of IFP in case of intussusception. The CT of the abdomen shows a smooth, oval, fluid-like, hypoattenuating lesion. However, such features are not specific and other types of bowel lesions should also be considered. It is also rare that such lesions can extend into the muscularis propria and subserosa on histopathological study

CONFLICT INTEREST

No funding was received for the preparation of this article. No financial competing interests declared.

CONSENTS

Written consent was obtained from the patient to publish this case report. A copy of the written consent is available for review by the Chief Editor.

ACKNOWLEDGEMENTS

None

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BJMS
Borneo Journal of Medical Sciences

SHORT COMMUNICATION

Traumatic Injuries from Suicidal Attempts: The Unseen Impact of COVID-19

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Received: 3 December 2024

Accepted: 20 May 2025

Published: 2 September 2025

DOI: https://doi.org/10.51200/bjms.v19i3.5686

Keywords: *Suicide, Trauma, Surgery, COVID 19, Polytrauma*

ABSTRACT

The COVID-19 pandemic in Malaysia imposed a strict lockdown that led to an increase in non-accidental suicidal attempts. This retrospective study examines 12 cases of suicidal attempts resulting in traumatic injuries treated at the General Surgery Department of Hospital Sultanah Aminah, Malaysia, between June and September 2021. The cohort predominantly comprised male patients (median age: 27.5 years), with penetrating injuries, particularly stab wounds, being the most frequent mechanism. A high mortality rate (41.7%) was observed, attributed primarily to hypoxic brain injury, severe burns, and visceral organ perforation. The findings underscore the potential influence of the COVID-19 pandemic on mental health crises, emphasising the critical need for integrated psychological support in trauma care. While trauma surgeons play a pivotal role in managing acute life-threatening injuries, early psychiatric intervention is essential to mitigate fatalities and address underlying psychosocial stressors.

INTRODUCTION

The COVID-19 pandemic in Malaysia led to a series of lockdowns, resulting in the third movement control order that occurred in Jun 2021. This had led to an enormous financial constraint on the community and the country's economy. Due to strict restrictions, there was a significant drop in accidental traumatic injuries. Albeit, there was a reciprocal increase in non-accidental suicidal attempts treated at

our institution (Tan Chor Lip, 2020). Concerns over mental health deterioration due to psychological distress in the general public were reported by various local mental health groups (Moni, 2021; Shanmugam, 2020). Adding on to the concern, during the peak of COVID-19-related deaths in August and September 2021, there were concomitant reports of an increasing number of suicidal cases (Pizaro, 2021). This is described as dual mortality during the pandemic due to suicide and COVID-19 by the psychiatric experts (Banerjee, 2021). A local publication reported an alarming rate of 11.1% among health care workers who had suicidal ideation during the pandemic (Sahimi, 2021). Owing to the rising suicidal cases and sequelae of life-threatening injuries, we describe a case series of suicidal attempts with injuries to different body regions, management strategies and the eventual outcome of these patients.

MATERIALS AND METHODS

All patients who were treated for non-accidental attempted suicide injuries by the General Surgery Department of Hospital Sultanah Aminah, Malaysia, from June to Sept 2021 were included. This is a retrospective cohort study on all cases of traumatic suicidal injuries. All patients had psychiatric referral for assessment and psychosocial intervention; these cases were reported to the police. Demographic data, mechanism of injury, organ involved, hemodynamic parameters, blood investigations and operative details were retrieved. Patient outcomes after treatment were recorded and tabulated. The case details were retrieved from medical records and the trauma registry.

Table 1: Demography, mechanism, injuries, treatment and outcome of all patients with suicidal attempts

Age Race Gender	Mechanism	Injury sustained	Surgery performed/ treatment given	Outcome (function/ alive)
43 years, Chinese, man	Alleged suicidal attempt by slashing his throat.	Penetrating neck injury cuts through the superficial strap muscle, exposing the hyoid bone.	Exploration, debridement, muscle repair, toilet and suturing.	Survive
25 years, Chinese male	Alleged suicidal attempt by jumping from the 2nd floor	Tile C pelvis fracture with left zone 2 and 3 retroperitoneal hematoma, L2 compression fracture with paraplegia	Laparotomy and extra peritoneal pelvic packing, Left sacroiliac joint screw fixation, left anterior column screw fixation and Posterolateral spine fusion of T12 to L3	Death
27 years, Malay male	Stabbed himself in the right chest wall region after arguing with his wife	Stab wound over the right thorax region with minimal right hemothorax	Chest tube	Survive
28 years, Malay male	Alleged suicidal attempt by hanging in a drug centre	Hypoxic brain injury and minor Cortical C1 fracture	Conservative management	Death
60 years, Indian male	Stabbed himself on the left lower abdominal wall after arguing with the children	Stab injury with evisceration of the bowel	Exploratory laparotomy, peritoneal lavage and underrunning of bleeders	Survive
27 years, Chinese male	Alleged suicidal attempt by slashing his throat	Penetrating Neck injury with Right internal Jugular Vein injury with Hypoxic Ischemic Encephalopathy	Neck Exploration and ligation of the proper internal Jugular Vein ligation	Death

32 years, Indian female	Alleged suicidal attempt due to depression. Found by a passerby, the patient's body was on fire.	Sustained 52% burn over face, neck, anterior trunk, posterior trunk, right upper limb, bilateral anterior thigh (deep dermal), left upper limb (full thickness)	*Wound debridement*	Death
57 years, Indian male	Alleged suicidal attempt by shooting himself with a nail gun	Nail gun penetrating injury over the abdomen, skull and left axilla. Left frontal lobe nail with tip on corona radiata, bilateral abdominal wall nails, left anterior chest wall nail	*Craniotomy, laparotomy, Wound exploration and Nail Removal*	Survive
64 years, Malay male	Alleged suicidal attempt by stabbing himself in the umbilical region	Penetrating injury of the abdomen	*Laparotomy and Small Bowel Repair.*	Survive
26-year-old Chinese male	Alleged suicidal attempt by ingesting corrosive fluid, 100mls of Nitric acid	burning sensation over the throat, epigastric pain, vomiting, hoarseness of voice. Peritonitis. Severe metabolic acidosis, pH 6.9	Alkaline diuresis Intubation	Death
24-year-old Burmese male	Suicidal attempt fell from 3 3-story height	Minimal Subarachnoid haemorrhage in Rt parietal lobe and a slight contusional bleed in the left occipital lobe. Bilateral lung contusion with left first rib fracture. T7 Chance fracture, L1-L5 transverse process fracture. Multiple pelvic bone fractures involving the ilium and superior pubic ramus. Right femur fracture	Immobilisation of the fracture, internal fixation of the femur fracture.	Survive
24-year-old Nepalese male	Stab injury to the abdomen	Stab Injury to the abdomen	Diagnostic laparoscopy	Survive

RESULTS

We identified 12 cases of suicidal attempts with varying patterns of traumatic injuries. The median age is 27.5 years (24 to 64) and male predominant. Penetrating injuries (stabbings) were the most common mechanism of injury, with knives and nails being more frequently used. These penetrating injuries involved the abdomen, neck, chest and head. Other reported mechanisms of self-inflicted injuries were hanging, burns, corrosive ingestion and fall from height. A high mortality rate of 41.7%, with five deaths recorded from the total of 12 patients, was recorded (Table 1). The non-survivors have shown a trend of younger patients, injury related to a fall from height, corrosive ingestion or flame burn. The survivors are more often older and due to stab injuries (Table 2).

DISCUSSION

Within developed nations, self-inflicted traumatic injuries leading to death have been reported and discussed widely. Due to that, established feedback systems for traumatic injuries and mental health have been set up to identify and prevent suicidal attempts. (Schecter, 2005). In contrast to high-income nations, low to middle-income nations contribute 78% of suicidal traumatic injuries due to a lack of an adequate feedback system. With the lockdown due to COVID-19, there

were increasing cases of suicidal and traumatic injuries, which are not reported regionally. This study reports a cohort of patients with suicidal traumatic injuries treated by a general surgical department. In concordance with the previous report, the age groups and gender involved in our series were similar in the 2nd to third decades of age and male predominant (Bachmann, 2018).

over 10 years with injuries from suicidal attempts. The demographic pattern is similar to the current series, which was seen more often in males and the younger age group. The patient pool includes a portion of expatriates from South Asia (55%), and more than half had psychiatric consultations. Like the current series, the injury patterns were mainly related to cutting or piercing. The mortality rate was

Table 2: Table summarising key differences between survivors and non-survivors (arranged in sequence following their age)

Survivors	Non-survivors
A 24-year-old Burmese man fell from a 3-storey height, with intracranial bleeding, lung contusion, spine and femur fracture.	25 years old, Chinese man jumping from the 2nd floor, pelvis fracture, retroperito-neal hematoma, spine compression fracture with paraplegia
A 24-year-old Nepalese man, with a stab inju-ry to the abdomen	26 26-year-old Chinese man, ingesting cor-rosive fluid, 100mls of Nitric acid
27 years old, Malay man, Stab over right chest wall, minimal right haemothorax	27 years old, a Chinese man slashing his throat Penetrating Neck injury with Right internal Jugu-lar Vein injury
43 years, Chinese, man, slashing his throat. Penetrating neck injury	28 years, Malay man, hanging, hypoxic brain injury and minor Cortical C1 fracture
57 57-year-old Indian man is shooting himself with a nail gun. Nail gun penetrat-ing injury over the abdomen, skull and left axilla.	32 years, Indian lady, 52% burn
60 years old, an Indian man, stabbed him-self on the left lower abdominal wall after having Stab injury with evisceration of the bowel	
64 years old, a Malay man, stabbing himself at the umbilical region. Penetrating injury of the abdomen	
Based on the comparison between cases of death and survivors, the deceased are usually younger patients, fall from height, corrosive ingestion, or flame burn. The survivors are more often older and have the mechanism of stab injuries.	

Commonly reported attempted suicides were by hanging, self-poisoning and firearms. In this current series, there were a higher number of stab injuries as the data were collected from the surgery unit alone. A trauma surgery unit in Qatar reported 206 patients

only 8%, far lower than our series (Al-Thani, 2020). This may be due to underreporting of minor suicidal injuries, as they may be discharged home directly from our emergency department, and the current reported series only included patients who are admitted to

the general surgery department. This cohort may have a higher severity of injury as they are referred with a possible need for surgical intervention (Tan Chor Lip, 2020).

During the movement restriction order due to the COVID-19 pandemic, Data in Malaysia records a rise in suicidal attempts. (Pizaro, 2021). This trend is also seen in other nations due to the distress caused by a restriction on movement. (Fayed & Sharif, 2021; Shields, 2021). The current series reporting 12 cases of suicidal attempts with serious injuries and death highlights the need for psychological intervention for the entire nation. Nonetheless, the collaboration of the emergency department, surgical unit, psychiatry, and public health plays an important role in this extreme spectrum of issues. (Al-Thani, 2020)

CONCLUSION

Rising suicidal injury and death are evident in this pandemic era. Death by suicide highlights the need for early psychiatric intervention. Trauma surgeons played the role at the end of the spectrum, where the outcome may not be changed if the injuries were too severe. Further research is needed to determine the psychiatric interventions on trauma-related suicide attempts.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

ACKNOWLEDGEMENT

The authors obtained institutional approval from Hospital Sultanah Aminah to publish this study. We gratefully acknowledge the Director of Hospital Sultanah Aminah for granting permission.

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