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Editorial

Confronting Antimicrobial Resistance: The Change Starts with Us

Sathiadas MG

Antimicrobial resistance (AMR) poses a major threat to human health worldwide. Bacterial antimicrobial resistance occurs when changes in bacteria cause the drugs used to treat infections to become less effective and has emerged as one of the leading public health threats of the 21st century. Estimates suggest that bacterial AMR is a health problem whose magnitude is at least as significant as major diseases such as HIV and malaria. It is crucial to identify the leading pathogens and drug combinations that contribute to the bacterial AMR burden. If left unchecked, the spread of AMR could make many bacterial pathogens much more lethal in the future than they are today

An estimated 4.95 million (3.62–6.57) deaths were associated with bacterial AMR in 2019. At the regional level, the death rate attributable to resistance was highest in western sub-Saharan Africa, at 27.3 deaths per 100,000 (20.9–35.3), and lowest in Australasia, at 6.5 deaths (4.3–9.4) per 100,000. Lower respiratory infections accounted for more than 1.5 million deaths associated with resistance in 2019. The pathogen–drug combination of methicillin-resistant *S. aureus* caused more than 100,000 deaths attributable to AMR in 2019, while six other combinations—multidrug-resistant, third-generation cephalosporin-resistant *E. coli*; carbapenem-resistant *A. baumannii*; fluoroquinolone-resistant *E. coli*; carbapenem-resistant *K. pneumoniae*; and third-generation cephalosporin-resistant *K. pneumoniae*—caused 50,000–100,000 deaths each. (1)

Resistance to fluoroquinolones and β-lactam antibiotics (i.e., carbapenems, cephalosporins, and penicillins), which are often considered first-line treatments for the empirical therapy of severe infections, accounted for more than 70% of deaths attributable to AMR. In 2017, the WHO published a priority list for developing new and effective antibiotic treatments. The aim was "to guide and promote research and development of new antibiotics, as part of WHO's efforts to address growing global resistance to antimicrobial medicines." The microbes were divided into three categories: critical, high priority, and medium priority. The critical category included the carbapenem-resistant pathogens *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and Enterobacteriaceae. *Vancomycin-resistant Enterococcus faecium* and *clarithromycin-resistant Helicobacter pylori* were among the high-priority pathogens, whereas *penicillin-non-susceptible Streptococcus pneumoniae* and *ampicillin-resistant Haemophilus influenzae* were classified as medium priority. Notably, multidrug-resistant *Mycobacterium tuberculosis* was not included in the list. It is worth noting that these medium-priority and excluded microorganisms cause the highest burden of disease in low- and middle-income countries (LMICs). We cannot expect the authority to deal with AMR but it has to come within ourselves.

Intervention strategies to overcome AMR are the prevention of infection. Preventing healthcare-acquired infections, and community-based programmes focused on water, sanitation, and hygiene are key to overcoming AMR. Vaccinations are paramount for reducing the need for antibiotics. Minimizing the use of antibiotics unrelated to human disease treatment is a crucial strategy for reducing risk. The increased use of antibiotics in agriculture has been recognized as a significant contributor to antimicrobial resistance (AMR) in humans. Minimising the use of antibiotics should be prioritized especially when they are not necessary to improve human health such as treating viral infections.

Building infrastructure that allows clinicians to diagnose infection accurately and rapidly is crucial so that antimicrobial use can be narrowed or stopped when appropriate. Investment in research to develop new antibiotics must be initiated. Inappropriate use of

antibiotics driven by insufficient regulations and ease of acquisition are the areas that need change. Access to second-line antibiotics in locations without widespread access is essential. (2)

Antibiotic stewardship remains a core strategy in most national and international AMR management plans, although barriers to implementing stewardship programmes in LMICs should be addressed.

Individual behavior and personal responsibility as AMR interventions are strongly influenced by personal attitudes and, in consequence, the behavior and the choices made, which is known as the 'ABC' paradigm for social change. (3)

Multisectoral approaches are also important as most microorganisms dwell in animals as well. Microorganisms that affect human, animal, food, and environmental systems are crucial, highlighting the need for multisectoral approaches to address antimicrobial resistance (AMR) from a 'One Health' perspective.

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Review Article

Anatomy Education in Sri Lanka. Do we need unclaimed bodies?

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Abstract

Cadaver-based education is accommodated by medical institutions with the hope of producing medical practitioners with essential knowledge in anatomy which is deemed fundamental to manage the clinical problems in their day-to-day clinical practice. It appears that the contemporary anatomy education of many countries is in need of unclaimed bodies, despite controversies in their usage, to meet the educational standards prescribed by the medical institutions and national authorities. Medical institutions in Sri Lanka procure dead bodies for anatomical studies primarily, if not wholly, through voluntary body donation programmes. However, the Transplantation of Human Tissues Act (THTA) of 1987, a Sri Lankan legislative act, permits the use of unclaimed bodies for anatomical research. This manuscript aims to review the procurement of unclaimed bodies for anatomy education in historical contexts, as well as regulatory and ethical dilemmas associated with using them for anatomical studies, particularly in the case of cadaveric dissection.

Key words: unclaimed bodies, anatomy, body donation

Introduction

Cadaver-based education enables the future generation of medical practitioners to learn essential anatomy which is fundamental to manage the clinical problems in their day-to-day clinical practice. The lessons learned from studying a formerly living human being are indeed more than learning authentic anatomy, for example, they also introduce the reality of death to medical students in an early non-clinical setting. The anatomical dissection of cadavers, despite legal and ethical dilemmas in their procurement in both the past and present, has retained its popularity as an efficacious method of teaching/learning macroscopic anatomy in many countries. However, there were medical institutions commenced their medical education without using cadavers (1, 2) and, medical institutions in certain countries, for example, Fiji, Samoa and Solomon Islands do not employ cadaveric dissections at all (3).

The dissection room experience is undoubtedly beyond learning macroscopic anatomy. It can be used to impart lessons of medical professionalism among undergraduate medical students early in the medical curriculum. Learning the ethical integrity of procedures related to handling the cadavers, from acceptance to disposal of their remains, would enable the medical students to acquire values of the medical profession and principles of medical ethics in the freshman years of medical education. Learnt values and principles would form a strong foundation in medical students which is fundamental to their future ethical based clinical practice. Knowledge on practice of high standards in the setting of anatomical dissection at multiple levels would certainly enhance the ethical viewpoint of the medical students (4).

The two common methods of acquisition of dead bodies for anatomical studies by medical institutions at present are the body donations and procurement of unclaimed bodies. The term "body donation" usually refers to the voluntary (body) donation made by the deceased while living by his/her informed consent for medical education and/or research. However, body donations made after death by the next-of-kin or other family members may be accommodated in this category.

Unclaimed bodies significantly contribute to anatomy education. An unclaimed body can be described as the body of a deceased individual whose body has not been claimed within a certain period of time as stipulated by

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the legislation of the country. Recently, Habicht J.L. et al (2018) reported that 45 out of 68 countries (66%) that used cadavers for anatomy teaching purposes in the undergraduate medical curricula procured unclaimed bodies. Among these 45 countries, the unclaimed bodies were the exclusive source in 21 countries (31%) whereas they served as the main source of cadavers in 18 countries (26%) (3). This data clearly highlights that medical institutions in many countries are in obvious need of unclaimed bodies for the successful implementation of their medical programme.

A brief historical viewpoint

Cadaveric dissection is widely used for anatomy education despite the introduction of new teaching methods for learning macroscopic anatomy. The earlier sources of cadavers include dead bodies obtained from executions, grave robbing, slave owners, and even through murders. Grave robbing was an illegal and unethical method of acquisition of bodies for which the economically and socially least privileged portion of the society was the most vulnerable (5). Grave robbing resulted in public outcry that prompted countries to enact legislation against such immoral activity and/or to search for alternative sources. For example, in 1789, the United States passed legislation against grave-robbing. At the same time, the judges were permitted "to sentence dissection to those being hanged for arson and burglary in addition to murder" (6).

In 1830 and 1833, Massachusetts (a state of the United States) enacted the laws, permitting unclaimed bodies to be used for anatomical dissection. Later, many other states of that country followed the suit and enacted that "unclaimed bodies of people who died in hospitals, asylums, and prisons would be allocated to that state's medical schools for the purpose of anatomical dissection" (6). In Britain, the 1832 Anatomy Act, permitted the use of unclaimed bodies for anatomical dissection. This act was successful in ending the era of bodysnatching (7). However, evidence suggests that the unclaimed bodies were legally available for anatomy education since the late seventeenth century (8). In summary, unclaimed bodies have served as a legal source of cadavers for anatomy education over centuries, and their role in contemporary anatomy education cannot be underestimated.

Source of unclaimed bodies in modern era

A dead body is deemed unclaimed if it qualifies one or more of the four scenarios: In the first category, the deceased individual does not have any relatives (next-of-kin or other family members), non-related legal guardian, or friends who could accept the dead body for conducting a decent funeral. In the second category, the deceased individual does have relatives or friends, but they refuse to accept his or her dead body due to many reasons, for example, financial difficulties to organize a proper funeral, family disputes, social concerns, etc. In the third category, the identity of the deceased person could not be revealed even after extensive search. As a result, relevant authorities are prevented from informing the relatives, non-related legal guardian or friends of the deceased individual for their further action. In the final category, the deceased individual has relatives or friends willing to claim the body but they couldn't do so within the stipulated period of time as prescribed by the legislation of the country. Unacceptance of dead bodies within the stipulated time results in disposal of such bodies as per the law of a country set in place.

Why unclaimed bodies are considered for anatomy education

The use of unclaimed bodies for anatomical studies can be viewed as a win-win situation for a country as it is beneficial for both the advancement of medical education and to solve the issue of limited spaces in the morgues, and likely in the graveyards. In a way it is also beneficial for the family members of the deceased individual as they are exempted from funeral expenses.

There are significant cultural limitations towards body donation in some societies (9). In such a situation, medical education may rely, at least partly on, unclaimed bodies.

Concerns and constraints of handling unclaimed bodies

Impact on learning values of professionalism

Cadavers are regarded as "great teachers" (10). The scope of "their teaching" is beyond anatomical sciences if they are obtained through voluntary body donation. For example, understanding the ethical principles,

procedures, and legislative requirements of body donation provides an opportunity for medical students to appreciate the importance of obtaining informed consent for healthcare procedures and respecting the differences of opinion of the patients (11). It is not realistic to expect that the use of unclaimed bodies in anatomical studies would contribute in the development of such qualities to the medical students. Instead, by knowing the fact that they dissect a once-lived person without his or her consent, the medical students may become stressful, and would perceive the cadaver as an object.

The cadavers are viewed as "first patients" (12) of the medical students. When the students learn that the dead bodies provided for their anatomy education are obtained through body bequests, they are impelled to think about the altruism and generosity of the donors and / or their family members that driven them to donate this greatest gift to medical education. The selfless act of body donation establishes a social bond with the medical students which heartens them to provide a safe, effective, and efficient patient care in their future clinical practice and always reminds them to handle their patients with kindness, empathy and due respect.

In contrast, one may argue that the utilization of unclaimed bodies would lead to moral distress for the students and is less likely to create a social bond between medical students and society as these bodies are obtained without the consent of the deceased individual and his or her family members.

Ethical concerns and conflicts

The ethical question arises if the deceased person is considered as an individual or at least a once-lived moral agent rather than an object or property. The main ethical concerns in using unclaimed bodies for anatomical studies are *disrespect* and *injustice* to the deceased person.

The use of an unclaimed body for anatomical dissection (i.e. without informed consent) could be viewed as a *disrespect* to the deceased person as his or her personal, religious, cultural beliefs with which he or she had lived are not considered before subjecting him or her to anatomical studies. As the wishes of the deceased person regarding his or her end-of-life treatment is not known, one may argue that it could be contradictory to being subjected to anatomical dissection. In this manner, respect for a person is deemed not respected. The recommendations of the International Federation of Associations of Anatomists (IFAA) published in 2012 excludes the use of unclaimed bodies for the "donation and study of human bodies and tissues for anatomical examination". It precisely indicates that "Informed consent from donors must be obtained in writing before any bequest can be accepted" (13). Johns DG and Whitaker MI (2012) viewed the use of unclaimed bodies as a form of exploitation since the bodies primarily of the poor and marginalized end up in this state (9). Especially, the use of dead bodies in anatomical studies that were left as unclaimed due to financial burden can be seen as an *injustice* to the deceased person. It becomes a sensitive issue to the family members of the deceased person when they realize their financial difficulties prevent them from claiming the body of the deceased. In addition, they may be prevented from expressing their views on the dissection and other procedures, and unable to speak on behalf of the deceased individual on his or her known beliefs and postmortem preferences.

The medical institutions that had obtained an unclaimed body through legal procedures may also face an ethical concern. For example, in certain instances, the family become aware of the death of a person after his or her body was declared as an unclaimed body and handed over to a medical institution. In this case, they may request the legal authorities and/or medical institutions for permission to give their last respect or even to conduct a proper funeral. In this scenario, the medical institutions face ethical dilemmas in handling the issue.

Unclaimed bodies - Sri Lankan context

Use of unclaimed bodies was common in Sri Lanka in the 1940's before independence. Body bequests gradually increased (14) but dependence on unclaimed bodies for medical education continued. Evidence indicates their usage in the 1960's at a Sri Lankan University (15). Thereafter, from the 1970's onwards, body donations became the only source of cadavers for medical education (14). Subasinghe SK and Johns DG, (2015) deliberated that all the medical institutions in

Sri Lanka procure dead bodies by donation, and most of the medical institutions in the country obtain more donated bodies than they actually need to deliver their medical course (14).

Sri Lanka, at present, legitimately permits the use of both donated and unclaimed bodies for medical education. The Sri Lankan legislation, the Transplantation Of Human Tissues Act (No. 48 of 1987) (THTA, 1987), states under the title "Power to authorize the removal of unclaimed bodies, for post-mortem examinations and anatomical research" as follows "Where any dead body is lying unclaimed in any hospital or other institution for over seven days from the date of death, the prescribed officer in such hospital or other institution may authorize the removal of such dead body for any post-mortem examination, and thereafter to any prescribed institution for any anatomical research" (THTA, 1987. Sect. 12) (16).

At present, most medical institutions in Sri Lanka exhibit information on body donation in their websites (17, 18, 19, 20, 21, 22, 23, 24, 25). In addition, the whole-body donation programme has been established in the Faculty of Dental Sciences, University of Peradeniya (26) as well. It is notable that information of another legitimate source of cadavers, the unclaimed bodies, is not generally available in the institutional websites. Thus, it is instructive to consider that the medical institutions in Sri Lanka encourage or endorse (or at least in favour of) obtaining bodies through bequest probably due to its ethical superiority. In a way, by requesting the details of next-of-kin/legal guardian/executor during provisional registration (during the lifetime of the owner) (17, 20, 23) and/or at the time, when the dead body is handed over to the institution (17, 19, 20, 23, 18), the medical institutions may ensure what they receive is not an unclaimed body. However, in a purely legal viewpoint, it is not clear whether an institution operating in the country has an option to refuse an unclaimed body, otherwise acceptable, when it is handed over through the legal procedures.

Regulatory concerns

Generally medical institutions have their own criteria for body donation in accordance with the legislation of a country. The Sri Lankan legislation directs (any) postmortem examination prior to handing over the unclaimed dead body for any anatomical research (THTA, 1987. Sect.12) (16). It is indeed helpful to determine the cause of death and to detect any pathological conditions that may be present in the dead body. However, the body donation programmes of the medical institutions in the same country do not accept body donations if the dead bodies were subjected to autopsy or postmortem examinations (17, 19, 20), or their acceptance is subject to approval of the Head of the Department of Anatomy (18). The reason behind the decision of the medical institution is likely to ensure that all the organs and structures of the body are intact for anatomical studies. However, the discrepancy between the legislation (for procurement of unclaimed bodies) and the guidelines of medical institutions (for body donation) may confuse the stakeholders and may affect the procurement of unclaimed bodies (if any) for medical education.

One of the criteria followed by certain medical institutions for considering acceptance of a dead body for medical education is "body can be donated only after a natural death" (19, 20). However, it appears that the relevant legislation of Sri Lanka (16) remains silent on this matter.

Conclusion and recommendations

Sri Lanka, a country with long-held cultural, moral, and religious values, would take an initial step towards abolishing the provision for legitimate use of unclaimed bodies in the revision of the relevant Act. Moreover, the revised legislation could ensure that the informed consent of the donor given voluntarily during his or her lifetime is a mandatory requirement for acceptance of body donation. It would set an example in place for other countries to avoid procuring unclaimed bodies in the name of medical education and/or eliminate its legality in the relevant countries. However, as the information pertaining to the current usage of unclaimed bodies in the medical institutions of the country is lacking, one may argue that attaining the pre-defined scientific goals of dissection can be affected by eliminating the use of unclaimed bodies. This argument can be viewed undeniable on a purely scientific ground in light of increasing number of state medical institutions (20%

[from 10 to 12]), and number of students admitted to those institutions (40.498% [from 1484 to 2085) in the country (from academic year 2017/2018 to 2022/2023 [proposed number]) in order to produce sufficient number of doctors to serve the country (27, 28).

In this context, until the actual requirement of unclaimed bodies is properly audited, the following strategies are useful to consider. 1. Minimizing the refusal of acceptable donated bodies (for example, due to inadequate storage facilities) 2. Promoting the concepts of body donation at the community level (having open dialogues with stakeholders).

A practical recommendation for enhancing body donations (and minimizing the use of unclaimed bodies) would be launching a national database for body donation. In Sri Lanka, establishing a national database for body donation with limited access to ensure confidentiality by interconnecting all medical institutions would be an important strategy to minimize the refusal of bodies due to inadequate storage facilities. In this case, the donated cadavers in excess can be directed to nearby institutions where there is a shortage of cadavers. However, successful implementation of this strategy requires legal framework, proper planning, timely coordination, and necessary documentation. In this regard, the Anatomical Society of Sri Lanka (ASSL) (29) may play a pivotal role by initiating discussions among anatomists to examine the feasibility of implementing such a notion.

Body donations are based on public trust. Therefore, establishing an independent advisory committee at the University level for the purpose of ensuring transparency in procedures from acceptance of a dead body to respectful disposal of its remains would enhance the public trust, thereby likely to succeed the body donation programme.

Moving towards a meaningful humanistic cadaver-based learning, originating from the body donation, would culminate in a competent and, more importantly, compassionate medical practitioner. The ethical principles and values that the medical students had learned by handling the donated bodies in the early stage of curriculum would be expected to reflect in their actions in patient care in the clinical appointments in the subsequent years of studentship and thereafter, as a medical practitioner

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Original Article

Association Between Acanthosis Nigricans and Cardiometabolic Risk Among Overweight and Obese Patients Admitted to the Teaching Hospital Jaffna

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Abstract

Acanthosis nigricans is strongly associated with obesity and insulin resistance. This cross-sectional analytical hospital-based study is conducted to access the Association Between Acanthosis Nigricans (AN) and cardiometabolic risk among overweight and obese patients aged 18 and above admitted to medical wards of Teaching Hospital Jaffna. Data were entered and analysed using Statistical Packages for social sciences (SPSS) version 21.

Out of the 230 overweight and obese patients 74.8% had AN. Patients with AN had a higher mean BMI value of 29.65 suggesting that significant percentage of patients with AN are obese rather than being overweight. Higher prevalence of AN among females were noted. Presence of skin tags revealed an important association with AN. Most of the participants had central obesity regardless whether they were overweight or obese.

Even though statistically insignificant, individuals with AN had increased likelihood of having metabolic syndrome and associated with smokers. A significant association between Sagittal Abdominal Diameter(SAD) and presence of AN were noted. The mean of sagittal circumference in those with AN and those without respectively are 22.02 and 20.43. In conclusion AN is strongly associated with higher BMI (Obesity), higher waist circumference and higher sagittal abdominal diameter and metabolic syndrome and smoking demonstrated a strong association with AN.

Introduction

Acanthosis nigricans is a common dermatological condition characterized by velvety, hyperpigmented and hyperkeratotic plaques on skin (1). It is commonly encountered over the intertriginous areas such as back of the neck, axilla and groin. But it can occur over the other body parts like elbows, knees and mucus membranes as well but its spares the palms and soles. Presence of acanthosis nigricans over the neck as the commonest site is clinically important because of easy accessibility to diagnose (2). Two most common medical disorders associated with acanthosis nigricans are obesity and diabetes mellitus. (3,4,5) Insulin resistance is the key factor in the pathogenesis of acanthosis nigricans in these patients (6).

Obesity is considered as a chronic disease which is increasing in prevalence globally (7). Rise in obesity prevalence is associated with a significant increase in morbidity (including diabetes mellitus, hypertension, dyslipidaemia, heart disease, stroke etc) and mortality globally (6,8). Most of the metabolic complications of obesity are driven by insulin resistance which is commonly associated with acanthosis nigricans and skin tags irrespective of the cause for insulin resistance (9). Jaffna is believed to be a land of traditional values and healthy lifestyle practices in view of active lifestyle, farming and healthy dietary practices (10). This study aims to determine the association between acanthosis nigricans and cardiometabolic risk among overweight and obese patients admitted to Teaching Hospital Jaffna.

Methodology

It is a hospital-based cross-sectional analytical study as hypothesis testing was performed using cross-sectional data. The study was designed to be conducted in the medical wards of Teaching Hospital Jaffna for four months from March 2022. Overweight and obese

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patients with and without acanthosis nigricans above the age of 18 years admitted to the Teaching Hospital of Jaffna were recruited for this study. The adult population above the age of 18 years is selected because studies had shown that acanthosis nigricans are commoner among the adult population. Since this study was designed to evaluate the features of obesity-related insulin resistance, the study population selected were overweight and obese patients.

Data were entered in Statistical Packages for social sciences (SPSS) version 21 was used for statistical analysis. Descriptive statistics were performed using mean (±SD) and/or median (interquartile range) for numerical variables and numbers and percentages for categorical variables. Appropriate graphs were used to present the distribution of data. The significance of the association was assessed at a 5% critical level. Unadjusted measures of risk were obtained using a chi-squared test or t-test or one-way ANOVA or non-parametric tests depending on the type of variables compared and the distribution of data. Logistic regression was performed to obtain the adjusted measures of risk. Cut off p-value to consider adding a variable to the logistic regression model is a 5% level of significance.

Results

This study recruited 230 patients in the medical wards of Teaching Hospital, Jaffna from March 2022 to June 2022. Among all the participants, 74.8% were with Acanthosis nigricans (AN+) and the remaining were without Acanthosis nigricans (AN-). Patients' age ranged from 30 to 80 years with a mean age of 56.08 ± 11.85 years. The gender ratio between males and female is 1: 1.23. The majority (95.2%) of the participants are Tamil. Around 78% of them were married and 15.7% were widowed. 78.7% of the participants completed their secondary education and 14.8% completed their primary education level. All the participants were obese and overweight with a mean BMI of 29.17 (SD = 3.7) [Table 1].

According to the statistical analysis of anthropometric data, there is a significant difference between the groups AN+ and AN- as to BMI (p=0.0001), sagittal diameter (p=0.034), and skin tags (p=0.0001), which shows that patients with AN are mostly obese [Table 1].

Table 1: Distribution of socio-demographic factors and anthropometric measurements.

Parame-ters	Types	Total	AN+	AN-	P value
N		230	172	58	
Mean age		56.08 ± 11.85 years	55.36 ± 12.39 years	58.22 ±1.41 years	0.112
Male: female		1: 1.23	1:1.49	1: 0.7	0.014
Ethnicity	Tamil	95.2%	93.6%	100%	0.054
	Muslim		4.1%		
	burgher		2.3%		
Marital status	Married	78%	74.1%	89.7%	0.032
	Unmarried		5.9%		
	Divorced		0.6%	5.1%	
	Widowed	15.7%	19.4%	5.2%	
Educa-tion	No schooling		2.3%		0.719
	Primary	14.8%	14.5%	15.5%	
	Secondary	78.7%	76.7%	84.5%	
	Higher		6.4%		
Income	<50000		89.5%	98.3%	0.053
	50000-100000		8.1%	1.7%	
	>200000		2.3%		
Smoking	Yes		5.4%	13.8%	0.031
	no		94.6%	86.2%	
Height in cm			158.65 ± 8.8	161.26 ± 6.9	0.055
Weight in kg			74.93 ± 13.7	72.11 ± 8.5	0.107
Waist circumference in cm			100.37 ± 9.4	98.96 ± 5.3	0.323
Sagittal diameter in cm			22.02 ± 5.2	20.43 ± 3.6	0.034
Neck circumference in cm			42.17 ± 32.07	40.97 ± 13.9	0.768
BMI			29.65 ± 3.9	27.7 ± 2.5	0.0001
Skin tags	Presence		53.0%	7.4%	0.0001
	Absence		21.7%	17.8%	

Physical activity among the participants was calculated according to the IPAQ and the physical activity profile was categorized according to the score. Figure 1 showed the trend of the profile of physical activity with and without acanthosis nigricans.

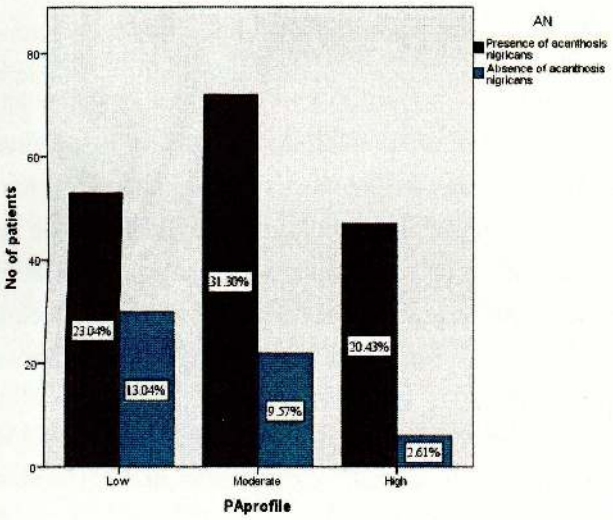

Figure 1: Illustration of physical activity profile

Table 2: Likelihood ratio of clinical features with acanthosis nigricans

Effect	Model Fitting Criteria	Likelihood Ratio Tests	
	-2 Log Likelihood of Reduced Model	Chi-Square	p-value
Age	182.470	.311	.577
Waist circumference	182.859	.700	.403
M1	182.956	.797	.372
M2	183.174	1.015	.314
M3	182.358	.199	.656
M4	183.226	1.067	.302
M5	182.253	.094	.759
Metabolic syndrome	183.139	.980	.322
Physical activity profile	200.723	18.564	.000
Skintags	211.499	29.340	.000

The likelihood ratio tests conducted to determine the association between clinical features of obesity-related insulin resistance (IR) and acanthosis nigricans (AN) yielded several notable results:

1. **Physical Activity Profile and Skintags**: These variables showed a significant association with AN, as indicated by their low p-values ($p < .001$). Participants with higher levels of physical activity and those with skintags were more likely to exhibit AN. (Table 2)

2. **Male Gender**: The variable "Male" also showed a significant association with AN ($p = .003$), suggesting that males were more likely to have AN compared to females in the sample population. (Table 3)

3. **Other Clinical Features**: Variables such as Age, Waist Circumference, BMI of more than 35, and Neck Circumference of more than 40cm did not show a significant association with AN, as their p-values were greater than the conventional threshold of .05.

4. **Metabolic Syndrome**: Although not statistically significant ($p > .05$),"Metabolic Syndrome" showed some degree of association with AN, with p-values close to the significance threshold.

Overall, the findings suggest that certain clinical features, including high physical activity profile, skintags, and male gender, are associated with the presence of AN among individuals with obesity-related IR. However, other factors such as age, waist circumference, BMI, and neck circumference do not appear to have a significant independent association with AN in this model.

Table 3: Association between cardiometabolic risk factors and the presence of acanthosis nigricans

Cardio metabolic risk factor	AN + (N=172)	AN- (N=58)	P value
DM	47.7%	62.1%	0.069
HT	75.9%	77.6%	0.693
DL	64.5%	68.4%	0.710
Metabolic syndrome	80.2%	91.4%	0.05
Smoking	94.8%	86.2%	0.031

The chi-square test results provide insights into the association between cardiometabolic risk factors and the presence of acanthosis nigricans (AN) among the study population.

1. **Diabetes Mellitus (DM)**: While there was a trend towards a lower prevalence of DM among individuals with AN compared to those without AN (47.7% vs. 62.1%), the difference was not statistically significant ($p = 0.069$).

2. **Hypertension (HT), Dyslipidaemia (DL)** : The prevalence rates of these cardiometabolic risk factors were comparable between individuals with

and without AN, as indicated by non-significant p-values (> 0.05).

3. **Metabolic Syndrome**: A significantly higher proportion of individuals with AN had metabolic syndrome compared to those without AN (80.2% vs. 91.4%, p = 0.05), suggesting a potential association between AN and metabolic syndrome.

4. **Smoking**: The prevalence of smoking was significantly higher among individuals with AN compared to those without AN (94.8% vs. 86.2%, p = 0.031), indicating a possible association between smoking and the presence of AN.

Overall, while some cardiometabolic risk factors such as diabetes mellitus, hypertension, and dyslipidaemia did not show significant associations with AN, there were significant associations observed with metabolic syndrome and smoking. These findings suggest that individuals with AN may have an increased likelihood of having metabolic syndrome and being smokers, highlighting the potential importance of addressing these factors in the management and prevention of AN and associated cardiometabolic complications.

Table 4: Logistic regression of cardiometabolic risk factors with anthropometric measurements

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
(Constant)	2.086	.363		5.741	.000
Sagittal	-.007	.006	-.075	-1.045	.297
BMI	-.034	.013	-.290	-2.678	.008
Waist circumference	.001	.004	.029	.403	.687
Neck circumference	.000	.001	-.028	-.433	.666

In the logistic regression analysis, the coefficients provide insights into the association between cardiometabolic risk factors and anthropometric measures among overweight and obese patients.

BMI: The coefficient for BMI is -0.034, with a standardized coefficient (Beta) of -0.290. This suggests that for each unit increase in BMI, the log odds of having cardiometabolic risk factors decrease by 0.034 units after controlling for other variables. The standardized coefficient indicates that BMI has a relatively strong negative association with cardiometabolic risk factors.

Sagittal Abdominal Diameter, Waist Circumference, and Neck Circumference: These variables (Sagittal, Waist circumference, and Neck circumference) do not appear to have a statistically significant association with cardiometabolic risk factors among overweight and obese patients, as indicated by their non-significant p-values (>.05). The coefficients for these variables are close to zero, indicating minimal impact on the log odds of cardiometabolic risk factors after accounting for other variables. (Table 4)

Overall, these findings suggest that among overweight and obese patients, BMI is a significant predictor of cardiometabolic risk factors, with higher BMI values associated with lower odds of having these risk factors. However, sagittal abdominal diameter, waist circumference, and neck circumference do not seem to have a significant independent association with cardiometabolic risk factors in this model. It's important to consider additional factors and conduct further research to fully understand the relationship between anthropometric measures and cardiometabolic health in this population.

Discussion

Acanthosis nigricans and skin tags are commonly associated with insulin resistance regardless of its cause. Insulin resistance is defined as subnormal glucose response to endogenous and/ exogenous insulin. Though the causes for insulin resistance are numerous such as obesity, stress, pregnancy, lipodystrophy, insulin antibodies and medications like HAART, oral contraceptives, and steroids, insulin resistance most commonly observed in association with obesity. In this study, among 230 overweight and obese patients' majority of the patients had acanthosis nigricans. (74.8%). Patients with the presence of acanthosis nigricans have a higher mean BMI value of 29.65 suggesting that significant percentage of patients with acanthosis nigricans are obese rather than being overweight. There is a significant association between gender and acanthosis nigricans also noted in this study with the higher prevalence of acanthosis nigricans among females compared to males.

Clinical detection of acanthosis nigricans is very important because it is associated with various systemic metabolic abnormalities. Two most common medical disorders associated with acanthosis nigricans are obesity and diabetes mellitus. The consequences of obesity – related insulin resistance are diabetes mellitus, coronary artery disease and metabolic syndrome. To date there are several studies which have evaluated the prevalence of acanthosis nigricans among different population from various parts of the world. They have also evaluated the association between acanthosis nigricans and type 2 diabetes mellitus, its risk factors, atherosclerosis, and metabolic derangements. This study differs in particular from the other studies done previously is that its direct correlation with Acanthosis Nigricans and selected cardiometabolic risk factors namely Diabetes Mellitus, Hypertension, Metabolic syndrome. The selected study population is a previously unevaluated different ethnic group. Smoking and sedentary lifestyle with acanthosis nigricans also was studied. In this study we could be able to demonstrate that individuals with AN may have an increased likelihood of having metabolic syndrome and being smokers, highlighting the potential importance of addressing these factors in the management and prevention of AN and associated cardiometabolic complications. Unfortunately, we were unable to prove a statistically significant association of other cardiometabolic risk factors named Diabetes Mellitus, Hypertension, and low physical activity profile as a marker of sedentary lifestyle with presence of acanthosis nigricans.

Sagittal abdominal diameter, a novel anthropometric measure is a reliable indicator of visceral adiposity and shows a stronger correlation to cardiovascular risk and other risk factors in metabolic syndrome than other traditional anthropometric measures such BMI and waist circumference. (11) (6). We found a significant association between sagittal diameter and presence of acanthosis nigricans. The mean of sagittal circumference in those with acanthosis nigricans is 22.02 and 20.43 in those without acanthosis nigricans. But in our study, we could not be able to demonstrate a statistically significant association of sagittal abdominal diameter (SAD) with cardiometabolic risk factors as listed. It could be explained to the fact that studies have shown that when sagittal abdominal diameter is >30cm, it is significantly associated with cardiometabolic risk factors. But our study population demonstrated an overall low SAD value, lesser than 30cm.

The results for BMI and large neck circumference are the same for other anthropometric measurements suggesting no statistically significant correlation to cardiometabolic risk factors.

Further studies required to evaluate the significance of the association between anthropometric measurements and cardiometabolic risk factors.

Conclusion

Acanthosis Nigricans is strongly associated with higher BMI (Obesity), higher waist circumference and higher sagittal abdominal diameter.

Among all the cardiometabolic risk factors tested, metabolic syndrome and smoking demonstrate a strong association with acanthosis nigricans. However statistically significant correlations between acanthosis nigricans were not made with other cardiometabolic risk factors such as diabetes mellitus, dyslipidemia, hypertension, and sedentary lifestyle. These results could be explained because this study was conducted in a subset of overweight and obese patients as opposed to a general population.

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Original Article

Clinical profile and outcome of symptomatic COVID 19 infection among vaccinated patients admitted to Teaching Hospital Jaffna

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Abstract

COVID-19 (Corona Virus Disease) was a pandemic disease affecting the world leading to a large number of morbidity and mortality all over the world. The introduction of vaccines for this disease has been the cornerstone to fight this disease. In this study, we analyzed the clinical profile and outcome of symptomatic COVID-19 infection among vaccinated patients admitted to Teaching Hospital Jaffna.

We conducted a population-based descriptive type of observational study on symptomatic COVID-19 patients admitted to teaching hospital Jaffna who had taken at least one dose of the COVID-19 vaccine. A total number of 349 Symptomatic COVID-19 patients admitted to teaching hospital Jaffna who had taken at least one dose of COVID-19 vaccine were recruited to the study from December 2021 to March 2022. An interviewer-administered questionnaire was used to get the general information of the participants including age, gender, area of residence, and prevailing medical conditions. To decide the severity of infection and complications a data sheet was used. This was filled by checking the bedhead ticket. Data were entered into an Excel data sheet and descriptive statistics and chi-square tests were analyzed using Statistical Package for Social Sciences (SPSS) version 21.

According to the study the patients who had taken both doses had less severe illness (79.8%) compared to those who had taken a single dose (33.3%) and there was a reduction in severity with the duration of vaccination. There was no association between severity of the disease and gender but there was an increase in severity of illness and death with increasing age. Our study also demonstrates that, with an increased number of comorbidities there is an increase in the severity of infection

In our study, all the vaccines were effective in reducing the severity of the illness. However, there are a number of patients who had severe illness despite taking the full vaccination. There are factors such as advancing age and the number of comorbidities also influence the severity of illness. There was no association between the severity of the disease and gender.

Introduction

COVID-19 affecting all parts of the world leading to more than 83 million known cases by the end of 2020 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, the deployment of vaccines and antibody therapies has led to tremendous progress in the management of this disease. Targeting the viral spike protein is the main strategy used in the production of vaccines. However, the viral variants and mutations that occur along with these vaccines, reduce the efficacy of these vaccines. [1]

Vaccine effectiveness (VE) is the term used to describe the effectiveness of the vaccine against the virus. This vaccine's effectiveness varies from vaccine to vaccine. This is estimated to be 60-90% for preventing COVID-19 infection 2 weeks after receiving the second dose of Pfizer, Moderna, or AstraZeneca vaccines. [2,3] Although there is a higher degree of protection provided against COVID-19 infection by vaccines, no vaccine is 100% effective. So it is expected that a small proportion of vaccinated individuals may become infected with COVID-19 disease. When COVID-19 cases occur following vaccination, there is

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evidence that vaccines reduce symptomatic infection, the severity of illness, as well as transmission.[4,5] The vaccine effectiveness in the prevention of serious outcomes such as hospitalizations and intensive care unit (ICU) admissions and death ranges between 70-90%. Vaccine effectiveness also may be impacted by COVID-19 variants of concern. Evidence has shown that the B.1.1.7 (Alpha) variant has less significant impact on vaccine effectiveness. [6] However, the B.1.617.2 (Delta) variant, has been shown to impact vaccine effectiveness against symptomatic infection, especially for individuals who have only had one dose of vaccine.[7]

In Sri Lanka, we had a huge spread of infection and there were a large number of oxygen-dependent patients due to the spread of delta variants throughout the country. Even patients who are vaccinated are admitted to hospital due to illness related to COVID-19 disease.

If the vaccine reduces symptomatic infections, it can lead to ignorance of symptoms and carelessness among people. Ultimately it can increase the spread of infection. Therefore, symptoms of COVID-19 infection among vaccinated patients and the severity of these symptoms must be explored. However, up to now, there are no studies available in Sri Lanka regarding post-vaccination COVID-19 infection. Therefore this study aimed to assess the symptomatic infection among patients who have at least received the first dose of vaccination.

Methodology

We conducted a population-based descriptive type of observational study. A total of 349 symptomatic COVID-19 patients admitted to teaching hospital Jaffna who had taken at least one dose of COVID-19 vaccine were recruited to the study from December 2021 to March 2022. An interviewer-administered questionnaire was used to get the information from the participants. To decide the severity of infection and complications a data sheet was used. This was filled by checking the bedhead ticket. Data were entered into an Excel data sheet and descriptive statistics and chi-square tests were analyzed using Statistical Package for Social Sciences (SPSS) version 21.

Results

There were 349 symptomatic test-positive participants admitted to Teaching Hospital, Jaffna enrolled in the study. These participants were from all the MOH areas from Jaffna but the majority of participants were from the Jaffna MOH area.

In the study, we have analyzed the preexisting medical comorbidities of the symptomatic COVID-19 patients. In that analysis, 212 participants had at least a single comorbidity and 137 participants didn't have any comorbidity. The majority of participants had Diabetes mellitus and hypertension.

In our study, 172 participants (49.28%) were fully vaccinated and among them, 23 had their 3rd booster dose as well, rest of the 144 participants were partially vaccinated, among them, 41 had received both doses but received their 2nd dose less than 14 days of infection and another 103 only received one dose of vaccine but they developed the illness after 14 days of vaccination. 33 participants were under the category of 'Not protected from the vaccine' since they had not completed 14 days following the 1st dose of vaccine.

The commonest symptoms associated with illness were fever, cough and shortness of breath, which accounts for 75.4%, 61.9% and 37.8%. The other symptoms such as sore throat (17.2%) and diarrhea (13.2%) also were present in a number of participants. There were 78 patients who presented with fever with cough and 35 participants presented with fever, cough and shortness of breath.

In our study around 200 (57.3%) participants did not develop any other complications. There were 78(22.4%) participants who developed secondary bacterial pneumonia and 69 (19.8%) participants developed acute kidney injury. Another 78(22.4%) participants developed hepatic impairment and cardiac and CNS involvement were less in number. Complications the participants developed during the illness *are* demonstrated below (*Table* 1).

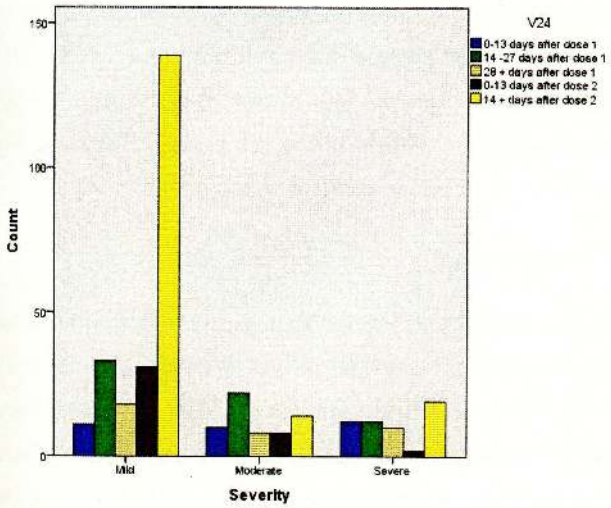
Table 1: Number of complications the participants developed during the illness

No complications	200 (57.3%)
Secondary bacterial pneumonia	29 (8.3%)
Acute kidney injury	23 (6.6%)
Cardiac problems	1 (0.3%)
Hepatic impairment	30 (8.6%)
CNS involvement	1 (0.3%)
Secondary bacterial pneumonia + Acute kidney injury	13 (3.7%)
Secondary bacterial pneumonia + Acute kidney injury + Cardiac problems	2 (0.6%)
Secondary bacterial pneumonia + Acute kidney injury + Hepatic impairment	15 (4.3%)
Secondary bacterial pneumonia + Cardiac problems	2 (0.6%)
Secondary bacterial pneumonia + Hepatic impairment	17 (4.9%)
Acute kidney injury + Hepatic impairment	16 (4.6%)

The association between severity of illness with the duration and dose of vaccination is demonstrated below (*Figure 1*). This analysis shows reduction in severity with the duration of vaccination. According to the Chi square test, the participants those who had completed the 2nd dose of vaccine had less severity of illness. analyzed the duration of vaccination with the severity of the disease.

Figure 1 : Association between severity of illness with the duration and dose of vaccination

Severity	1st dose	1st and 2nd dose	Chi square p value
Mild	57	175	0.0001
Moderate	39	23	
Severe	32	23	



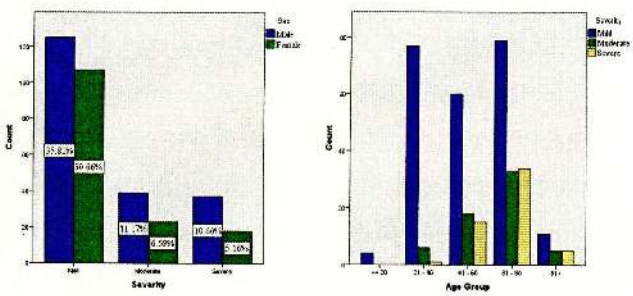
The association between the severity of illness with the type of vaccination demonstrated below (*Table 3*). According to Fisher's Exact test all four types of vaccine are effective in reducing the severity. At the same time sinopharm which includes all categories of patients shows more mild symptomatic patients that show the effectiveness of vaccines in reducing the severity.

Table 2 : Association between the severity of illness with the type of vaccination

Severity	AstraZeneca	Sinopharm	Pfizer	Moderna	Fisher's Exact Test P value
Mild	39	190	3	0	0.0014
Moderate	2	59	0	1	
Severe	2	53	0	0	
Total	43	302	3	1	

The association between the severity of illness and age and gender is demonstrated below (*Figure 2*).

Figure 2: Association between the severity of illness and age and gender



In the study, we have analyzed the number of comorbidities with the severity of disease. This shows with an increased number of comorbidities there is an increase in the severity of the disease. The association between the number of comorbidities with the severity of illness demonstrated below (*Table 4*).

Table 4 : Association between the number of comorbidities with the severity of illness

	Mild	Moderate	Severe	P value
No comorbidity	112	12	11	0.010
One comorbidity	37	11	10	
Two comorbidities	39	12	12	
Three comorbidities	31	16	17	
Four or more comorbidities	13	7	9	

Discussion

In our study most symptomatic COVID-19 participants at least had a single medical comorbidity which accounted for 60.7% and 39.3% didn't have any medical comorbidity. In those comorbidities, most of the participants had Diabetes mellitus and hypertension which account for 42.7% and 38.4% respectively. Among them, 16.1% had a single medical condition and 44.7% had multiple medical conditions. A significant number of participants had other comorbidities such as Dyslipidemia, Ischemic heart disease, and chronic kidney disease which account for 18.9%, 16%, and 12.9% respectively.

According to our study, those who completed the 2nd dose of the vaccine had less severity. Out of 232 participants who have developed mild disease, 175 participants (75.4%) have taken both doses and 57 (24.6%) have taken only the first dose. Of 62 participants who had developed the moderate disease 23 (37%) had taken both doses and 39(63%) had only taken the first dose. The number of participants who had developed severe diseases is 55. Among them, 23 (41.8%) took both doses, and 32 patients took only one dose. This shows the participants who have taken both doses had a less severe illness which was demonstrated by Chi-square test. In our study, 23 participants had their 3rd booster dose, in those participants all of them had mild disease and none of them had ICU admissions.

We compared the duration of vaccination with the severity of illness, participants who had taken only 1 dose and developed symptoms within 0 to 13 days had mild disease in 11(33.3%) participants, moderate disease in 10(30.3%), and severe disease in 12(36.4%) participants. Participants who had taken only 1 dose and developed symptoms after 14 days had mild disease in 51(49.5%) participants, moderate disease in 28(27.2%) and severe disease in 24(23.3%) participants who had taken both doses and developed symptoms, had mild disease in 170(79.8%) participants, moderate disease in 20(9.4%) and severe disease in 23(10.8%) participants. This shows a reduction in severity with the duration of vaccination.

Most of the participants had the Sinopharm vaccine which accounts for 302 participants and another 43 participants had the Astra Zeneca vaccine. In those who had taken the Sinopharm vaccine, the majority of participants (62.91%) had developed only mild symptoms another 19.5% of participants developed moderate symptoms and 17.6% of participants developed severe symptoms. 43 participants had taken the Astra Zeneca vaccine and 90.7% of participants developed mild symptoms, 4.7% developed moderate symptoms and 4.7% of participants developed severe symptoms. This shows these vaccines are quite effective in reducing the severity of the illness.

In our study, we have compared the number of comorbidities with the severity of illness. Of those who did not have any comorbidities, 112(82.2%) had mild disease, 12 (8.9%) had moderate disease and 11 (8.1%) had severe disease. Of those who had one comorbidity 37 (63.8%) had mild disease, 11 (19%) had moderate disease and 10 (17.2%) had severe disease. Of those who had two comorbidities 39 (61.9%) had mild disease, 12 (19%) had moderate disease and 12 (19%) had severe disease. Of those who had three comorbidities 31 (48.4%) had mild disease, 16 (25%) had moderate disease and 17 (26.6%) had severe disease. Of those who had more than four comorbidities, 13 (44.8%) had mild disease, 7 (24.1%) had moderate disease and 9 (31%) had severe disease. This shows with an increased number of comorbidities there is an increase in the severity of infections.

Almost all of these patients had multiple comorbidities and especially 9 patients had chronic kidney disease and transplant recipients who were on multiple immunosuppressive. This shows that chronic kidney disease and immunosuppressive therapy, increase the severity of illness and cause more deaths.

Conclusion

In the study the patients who have taken both doses had less severe illness and there was a reduction in severity with the duration of vaccination. The vaccines were effective in reducing the severity of the illness. There was no association between the severity of the disease

and gender. Our study has demonstrated a significant increase in the severity of illness and death with the increasing age and increasing number of comorbidities.

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Original Article

Antibiotic sensitivity patterns of uropathogens in hospitalized patients at Teaching Hospital Jaffna

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Abstract

Indiscriminate use of antibiotics has led to the emergence of antibiotic resistance in hospital settings. Awareness of local antimicrobial resistance patterns is essential for prudent empirical therapy of urinary tract infections.

This study describes the uropathogens isolated, their antibiotic sensitivity patterns and associated factors in adult inpatients with a positive urine culture at Teaching Hospital Jaffna.

All positive urine culture reports and relevant request forms of adult inpatients (≥18years) investigated at the Microbiological Unit of Teaching Hospital Jaffna during a three-month period (October 1st to December 31st 2020) were analyzed retrospectively with SPSS v27. Standard descriptive statistics and the chi square test were used (critical value 0.05).

Data were extracted from 426 culture reports. Mean age of the sample was 53.2 years (SD 19.9); 47.2% (n=201) of the reports belonged to patients ≥60 years and 60.1% (n=256) were of females. Antibiotics prescribed prior to culture were documented in 183 (43%) reports. The most commonly prescribed empirical antibiotic was co-amoxiclav (24%, n=183). Coliforms were the commonest isolate (63.4%, n=270) and showed resistance to several commonly prescribed antibiotics; antibiotic sensitivity was relatively low to ampicillin (9.5%), ceftriaxone (40%) and amoxicillin (48.1%); highest susceptibility was to meropenem (87.6%). Age group and gender were significantly associated with the type of uropathogen isolated ($p \leq 0.05$).

Prior antibiotic therapy was common among inpatients with urinary tract infection at the Teaching Hospital Jaffna. Sensitivity patterns suggest that antibiotic resistance is a major concern. Empirical therapy needs to be guided by institutional policies and local sensitivity patterns.

Keywords: Uropathogens, Urinary tract infection, Antimicrobial resistance, Antibiotic therapy, Coliforms

Introduction

Urinary tract infection (UTI), which refers to the invasion and growth of microorganisms in the urinary tract, is a common problem in clinical practice (1) The most common uropathogens are *Escherichia coli*. Other common causative organisms include *Enterococcus* spp., *Klebsiella* spp., *Proteus* spp., *Staphylococcus aureus* and *Staphylococcus saprophyticus* (2).

In Sri Lanka, nitrofurantoin, norfloxacin, cefuroxime, co-trimoxazole, and co-amoxiclav are recommended as empirical antibiotics for uncomplicated UTIs in adults. For complicated UTIs, such as UTIs in men/pyelonephritis, intravenous antibiotics like co-amoxiclav, ceftriaxone, ceftazidime, meropenem, or piperacillin-tazobactam are usually recommended (3).

A urine culture should be performed before commencing antibiotic treatment, and continuing antibiotic therapy should be based on an antibiotic sensitivity test (ABST) (4, 5). An ABST can identify the effective antibiotic(s) against specific uropathogens and guide the prescription of the most appropriate antibiotic (5,6).

Inappropriate antibiotic therapy has led to the emergence and spread of antimicrobial resistance (AMR) throughout the world, including in Sri Lanka(1) antibiotic susceptibility rates, association between(7).

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Though AMR is a concern in community-acquired UTIs, it is especially worrying in hospital settings where UTI is a common hospital-acquired infection(8). Although retrospective studies have described antibiotic sensitivity patterns of uropathogens in several outpatient settings in Sri Lanka. Less is known about the problem among hospitalized patients, particularly in Jaffna. (9,10).

Teaching Hospital Jaffna is the biggest tertiary care centre in the Northern Province serving a population of about 1.2 million. The hospital has a Microbiology Unit operating under a Consultant Microbiologist. Although healthcare facilities should have their own antibiotic policies based on the local sensitivity patterns (11). Such policies are yet to be developed for the Teaching Hospital Jaffna.

This study aims to describe the uropathogens isolated, their antibiotic sensitivity patterns and associated factors among adult inpatients (≥18 years) with a positive urine culture investigated at the Microbiology Unit of the Teaching Hospital Jaffna.

Methods

This institution-based cross-sectional study based on secondary data was carried out at the Microbiology Unit of Teaching Hospital Jaffna. Data were extracted from all positive urine culture reports and relevant request forms of adult inward patients (≥18 years) investigated at the Microbiology Unit between October 1, 2020 and December 31, 2020. Data were analyzed with the Statistical Package for Social Sciences (SPSS v27). Standard descriptive statistics were used to describe patient characteristics, uropathogens and antibiotic sensitivity patterns. The association between age and sex and the type of uropathogen was determined using chi square test with the critical level set at 0.05.

Ethics approval for this study was obtained from the Ethics Review Committee, Faculty of Medicine, University of Jaffna.

Results

Data were extracted from a total of 426 positive urine culture reports and relevant request forms. The mean age of the patients was 53.2 years (SD 19.9) with a median of 58 years (IQR 35-70). Just under half the reports belonged to patients who were 60 years of age or above (47.2%, n=201), and the majority were females (60.1%, n=256; Table 1).

Table 1. Age and sex distribution of patients with a positive urine culture (n=426)

Demographic details		n	%
Age (years)	<40	132	31.0
	40-59	93	21.8
	≥60	201	47.2
Gender	Male	170	39.9
	Female	256	60.1
Total		426	100.0

Table 2 describes the uropathogens documented in positive urine culture reports of inpatients. Coliforms were the most common (63.4%, n=270) followed by *Candida* spp. (19.2%, n=82), *Pseudomonas* spp. (8.2%, n=35), *Acinetobacter* spp. (4.2%, n=18) and *Enterococcus* spp. (4.2%, n=18). *Staphylococcus aureus* was the least common (0.7%, n=3).

Table 2. Uropathogens isolated from positive urine cultures (n=426)

Uropathogen	n	%
Coliforms	270	63.4
Candida spp	82	19.2
Pseudomonas spp.	35	8.2
Acinetobacter spp.	18	4.2
Enterococcus spp.	18	4.2
Staphylococcus aureus	3	0.7
Total	426	100.0

Antibiotic therapy given before culture was documented in 183 (43%) inpatients. Details of prior antibiotic therapy were not documented in 36 request forms (8.5%) whereas the remainder (48.5%, n=207) had not received prior antibiotic therapy. Based on documented prior antibiotic therapy among 183 patients, the most commonly prescribed antibiotic was co-amoxiclav (24%, n=44), followed by ceftriaxone (19.7%, n=36), and ciprofloxacin (15.8%, n=29) (Figure 1).

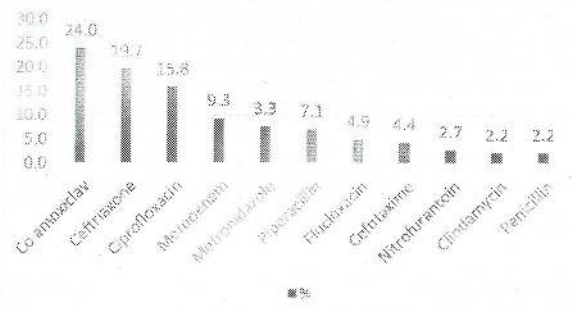

Figure 1. Antibiotic used prior to culture (n=183)

Our analysis of antibiotic sensitivity patterns showed that a large proportion of coliform isolates showed resistance to ampicillin (90.5%), ceftriaxone (60%), amoxicillin (41.1%), norfloxacin (42.8%), and ciprofloxacin (39.9%), while comparatively greater proportion of coliform isolates showed susceptibility to amikacin (83.1%), gentamicin (77.6%) and nitrofurantoin (76.3%). Meropenem resistance was seen in 9.3 % of the coliforms (Table 3).

Table 3. Antibiotic sensitivity patterns of uropathogens

Antibiotics	CF			PA			EC			A			SA		
	S	I	R	S	I	R	S	I	R	S	I	R	S	I	R
Meropenem	87.6	3.1	9.3	66.7	0	33.3	-	-	-	75	0	25	-	-	-
Amikacin	95.9	4.2	17.7	70	0	30.0	-	-	-	23.1	0	76.9	-	-	-
Gentamicin	77.6	3.6	20.8	69.7	0	30.3	-	-	-	44.4	0	55.6	-	-	-
Nitrofurantoin	76.3	10.5	13.2	-	-	-	88.9	0	11.1	0	0	100	100	0	0
Piperacillin	66.7	1.6	31.7	40	10	50.0	-	-	-	36.4	0	63.6	-	-	-
Tazobactam															
Gatrimaxazole	36.5	0.6	40.5	50	0	50.0	0	0	100	57.1	14.3	28.6	100	0	0
Ciprofloxacin	58.5	1.6	39.9	67.6	0	32.4	50	0	50	37.5	0	62.5	0	50	50
Cefotaxime	58.5	1.7	39.8	-	-	-	-	-	-	0	0	100	-	-	-
Norfloxacin	56.4	0.8	42.8	61.1	0	38.9	38.2	19.2	61.6	28.6	0	71.4	0	0	100
Ceforoxime	52.5	2.5	44.8	-	-	-	-	-	-	33.3	0	66.7	-	-	-
Cephalexin	49.2	1.2	50.4	-	-	-	-	-	-	0	0	100	-	-	-
Amoxicillin	48.1	10.9	41.1	0	0	100	-	-	-	0	50	50			
Nalidixic acid	44	9	56	100	0	0	50	0	50	66.7	0	33.3	-	-	-
Ceftriaxone	40	0	60				-	-	-	-	-	-	-	-	-
Ceftazidime	33.5	0	66.7	78.8	3	18.2	-	-	-	50	13.3	46.7			
Aztreonam	24.3	7.1	68.4	33.3	11.1	55.6	-	-	-	100	0	0			
Ticarcillin	12.1	0	87.9	-	-	-				-	-	-			
Clavulanic acid															
Ampicillin	9.5	0	90.5	-	-	-	38.9	0	61.1	-	-	-	0	0	100
Imipenem	0	0	100	66.7	0	33.3	-	-	-	36.4	0	63.6	-	-	-
Vancomycin	-	-	-	-	-	-	23.1	15.4	61.5	-	-	-	100	0	0

CF- Coliforms, PA- Pseudomonas aeruginosa, A-Acinetobacter, EC-Enterococcus, SA- Staphylococcus aureus, S- Sensitive, I-Intermediate, R- Resistant

A comparatively higher proportion of *Pseudomonas* isolates were sensitive to ceftazidime (78.8%), amikacin (70%) and gentamicin (69.7%), while only 40% were sensitive to piperacillin-tazobactam. Meropenem resistance was seen in 33.3% of the *Pseudomonas* isolates. Only 23.1% of *Acinetobacter* isolates were sensitive to amikacin and 36.4% to piperacillin-tazobactam. Meropenem sensitivity was seen in 75% of the *Acinetobacter* isolates. *Enterococcus* isolates showed good sensitivity to nitrofurantoin (88.9%) with a lower proportion showing sensitivity to ampicillin (38.9%) and norfloxacin (18.2%). Only 23.1% of the Enterococci were sensitive to vancomycin. *Staphylococcus aureus* showed 100% sensitivity to nitrofurantoin, cotrimoxazole and vancomycin, while 50 % of the isolates showed resistance to ciprofloxacin (Table 3).

Overall, 75.7% of all isolates were susceptible to nitrofurantoin. Overall susceptibility of uropathogens to ciprofloxacin was 57.8 % and to ceftriaxone 40% and meropenem 87.2%.

We found evidence of an association between the uropathogen isolated and age (X^2=18.89, df=10, p value=0.042) and sex (X^2=12.35, df=5, p value=0.030) of the patients (Table 4).

Table 4: Association of age and sex with uropathogen isolated

		n	CF	PA	A	EC	C	SA	p value
Age	<40	132	84 63.6%	12 9.1%	11 8.3%	4 3.0%	20 15.2%	1 0.8%	0.042
	40-59	93	63 67.7%	6 6.5%	4 4.3%	4 4.3%	14 15.1%	2 2.2%	
	≥60	201	123 61.2%	17 8.5%	3 1.5%	10 5.0%	48 23.9%	0 0%	
Sex	Male	170	102 60%	21 12.4%	3 1.8%	10 5.9%	33 19.4%	1 0.6%	0.03
	Female	256	168 65.6%	14 5.5%	15 5.9%	8 3.1%	49 19.1%	2 0.8%	

CF- *Coliforms*, PA- *Pseudomonas aeruginosa*, A-*Acinetobacter*, EC-*Enterococcus*, C- *Candida* spp, SA- *Staphylococcus aureus*

Discussion

Among the organisms causing UTI in the present study, coliforms (63.5%) stand at the top of the list as has been previously described in several studies (1,2,6,13) followed by *Candida* spp., *Pseudomonas* spp., *Enterococcus* spp. (4.2%), *Acinetobacter* spp. and *Staphylococcus aureus*. The high percentage of *Candida* isolated in the present study indicates the need to consider whether they are an important cause of UTI among inpatients in our settings. This high proportion may be due to poorly controlled diabetes and/or immunocompromised status(12), given the high community prevalence of type 2 diabetes mellitus in Jaffna(13). However, another reason for *Candida* in urine could be contamination of urine samples due to indwelling catheters (14).

A substantial proportion of hospitalized patients with UTI had received antibiotics prior to culture, perhaps because the study focused on inpatients who are more likely to have been treated prior to admission. It is

noteworthy that whether antibiotics were given prior to culture was not documented in 8.5% of the request forms, signaling the need for improved investigation requisition practices in ward settings.

The most commonly prescribed antibiotic in the present study was co-amoxiclav, followed by ceftriaxone, ciprofloxacin and meropenem (Figure 1). It is encouraging to know that the most commonly prescribed antibiotic for inpatients with UTI was co-amoxiclav in our study as it is the recommended first-choice antibiotic for complicated UTIs and pyelonephritis. However, we could not describe its sensitivity pattern from the data available owing to the unavailability of co-amoxiclav discs at the Microbiology Unit during the period under study. Parenteral antibiotics such as ceftriaxone and meropenem may have been prescribed before culture to these patients because they had recurrent UTI with pathogens resistant to oral antibiotics or because they were treated for acute pyelonephritis/complicated UTI. This pattern of prescription differs from that described in a study among inpatients at Colombo North Teaching Hospital, where the most frequently prescribed empirical antimicrobial was ciprofloxacin (54.6%), followed by cefuroxime (12.3%) and nitrofurantoin (9.2%)(1). This difference might be due to the varying spectrum of clinical conditions for which antibiotics were prescribed in the two studies which we cannot confirm in our study as the indication for antibiotic prescription was not documented in the request forms.

The sensitivity pattern of coliforms to nitrofurantoin (76.3%) in our study was similar to that of a Colombo North Teaching Hospital study (74.8%), whereas a higher percentage of susceptibility was seen in India (90%) and in the United Kingdom (93.9%)(1) In the present study, coliforms had higher resistance to antibiotics such as co-trimoxazole (40.9%) and norfloxacin (42.8%), which can be used in the empirical treatment of uncomplicated cystitis than the Colombo North Teaching Hospital study (1). The large proportion of coliform isolates resistant to amoxicillin (41.1%), ceftriaxone (60%) and ceftazidime (66.7%)—the latter which is recommended in the treatment of complicated UTI and pyelonephritis(4)(5)—is comparable to that of the Colombo North study(1). Though sensitivity of coliform isolates to ciprofloxacin, the third most commonly prescribed empirical antibiotic in the present study, was only 58%, susceptibility was notably greater than that reported in the Colombo North Teaching Hospital study where only 37.7% of coliform isolates were susceptible to ciprofloxacin(1). A higher proportion of coliforms were sensitive to amikacin in Colombo North Teaching Hospital study (93.1%) compared to that of ours (83.1%). However, gentamicin sensitivity to coliforms was higher (77.6%) in the present study than in the Colombo North Teaching Hospital study (63.0%).

We found a higher percentage of coliforms (9.3%) in the present study showed resistance to meropenem, an antibiotic that has been the ultimate option for several drug resistant uropathogens, including extended spectrum beta-lactamase (ESBL) producers. This result is similar to that of the study carried out at Colombo North Teaching Hospital (10.4%). According to the authors of the latter study, the ampicillin susceptibility reported in their study (13.4%) was one of the lowest reported in the literature (1). However, our study elicited an even lower susceptibility to ampicillin (9.5%).

More than 65% of the Pseudomonas isolates were sensitive to ciprofloxacin, gentamicin and ceftazidime in our study which is higher than the sensitivity pattern seen in the Colombo North study(1). although susceptibility to amikacin and meropenem was comparatively lower in our study. It is noteworthy that a high percentage of resistance (50%) was seen to piperacillin-tazobactam among Pseudomonas isolates and an even higher percentage of resistance (63.6%) to piperacillin-tazobactam among *Acinetobacter* isolates in the current study. Indeed, more than 60% of Acinetobacter in our study showed resistance to most of the antibiotics tested, including amikacin (76.9%) and a quarter were resistant to meropenem.

Enterococcus spp. showed higher resistance to norfloxacin (63.6%), vancomycin (61.5%) and ampicillin (61.1%) and good sensitivity to nitrofurantoin (88.9%). The high percentage of vancomycin-resistant Enterococci seen in our study is of great concern. It is much higher than the colonization seen in ICU patients

at the National Hospital of Sri Lanka in 2012 (18). All *Staphylococcus aureus* in our study were resistant to ciprofloxacin, whereas around 40% were sensitive in the Colombo North study.

According to a recent study in China by Wei Zhang *et al*, piperacillin-tazobactam is an effective, safe, and definite treatment option for complicated UTIs by ESBL-producing Enterobacteriaceae (19). However, piperacillin-tazobactam resistance was high among the uropathogens documented in our study, with resistance among *Pseudomonas spp*, 50%, *Acinetobacter* spp., 63.6% and even coliforms, 31.7%. These findings question its use in the empirical treatment of complicated UTI in patients exposed to antibiotics or hospitalized recently.

In our study, *Pseudomonas* and *Enterococcus* isolates were seen more in male patients, while females had more *Acinetobacter*. *Candida* and *Enterococcus* were isolated more in the age group of more than 60 years, whereas *Acinetobacter* was isolated among the younger group of less than 40 years. These results are consistent with the Colombo North study, which found that Pseudomonas and *Candida* isolates were seen more in male patients and elderly patients, respectively (1). In a China study, *Pseudomonas*, *Enterococcus* and *Acinetobacter* isolates were seen more in female patients and *Enterococcus* and *Acinetobacter* displayed an age-related increase in prevalence.(20).

High resistance among the uropathogens seen in our study to most antibiotics tested, including empirical antibiotics, can lead to treatment failure and possible sepsis. Further, it will demand the use of more toxic and expensive antibiotics and more hospital admissions. These findings highlight the need for urgent measures to address antimicrobial resistance in the hospital setting. An initial step would be to develop and implement an institutional policy to ensure the collection of urine samples for culture prior to empirical therapy and to continue antibiotic therapy according to local sensitivity patterns(21). Of course, it is essential to ensure education and pre- and in-service training regarding the basics of urine collection and catheter care for healthcare professionals and adherence to infection prevention and control measures during urine collection for culture (22). As irrational use of antibiotics is a major contributor to antibiotic resistance (23), measures to incentivise adherence to institutional guidelines on antibiotic therapy and strict infection control measures are needed.

This study has some limitations. We relied solely on the request forms and culture and ABST reports for data. Therefore, we were unable to find adequate clinical data and the type of UTI, which are likely to be important factors associated with the uropathogens isolated from inpatients with UTI. Further, although co-amoxiclav was the most commonly prescribed empirical antibiotic, we could not describe the sensitivity patterns of uropathogens to co-amoxiclav due to the unavailability of discs at the Microbiology Unit during the period under study.

Conclusion

A high proportion of isolates from adult inpatients at Teaching Hospital Jaffna were found to be resistant to several commonly prescribed antibiotics. These findings indicate the need for regular surveillance of uropathogens and their antibiotic sensitivity patterns, institutional policies to guide antibiotic prescription, and in-service training on strict infection prevention and control measures. Efforts should be made to perform co-amoxiclav sensitivity tests on uropathogens as it is the recommended first-choice antibiotic for complicated UTIs and pyelonephritis. The prevalence of vancomycin-resistant enterococci (VRE) in our setup should be studied further. Piperacillin-tazobactam should be used with caution as an empirical antibiotic for complicated UTI in our setting. A substantial proportion of hospitalized patients with UTI received antibiotics prior to culture, and a sizeable proportion of urine culture request forms did not contain details of prior antibiotic therapy. Therefore, improved investigation requisition practices in ward settings should be encouraged.

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Conflicts of interest

The authors have no conflicts of interests to declare.

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Original Article

The correlation between global longitudinal strain by speckle tracking echocardiography and coronary angiogram finding in patients with suspected chronic stable angina pectoris

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Abstract

The objective of this study was to evaluate and forecast the significance of Global Longitudinal Strain (GLS) measured at rest and its correlation with the presence and severity of coronary artery disease (CAD) in individuals with suspected stable angina pectoris in the Sri Lankan population

Patients diagnosed with chronic stable angina and normal left ventricular function (EF ≥ 50%) were included in the study and underwent coronary angiography, followed by speckle-tracking echocardiography. The study measured the global longitudinal strain and analyzed its correlation with the coronary angiography findings for each patient.

A total of 78 participants were included in this study, 44(56.5%) were diagnosed with coronary artery disease. Significant differences between CAD and non-CAD groups were observed in terms of age (P - 0.003), diabetes mellitus (P - 0.02), hypertension (P - 0.004) and family history of premature CAD (P - 0.01). There was a notable decrease in GLS values among CAD patients (-17.97 ±0.85) compared to non-CAD patients (-20.26 ±1.03), with a significant decrease observed as the count of affected vessels rose (P = 0.0001). A GLS cutoff value of -19 demonstrated promising sensitivity (72.7%) and specificity (70.6%) in predicting significant CAD, supported by an AUC of 0.717 (P = 0.001). In regression analysis, only diabetes showed a significant association with reduced GLS. GLS demonstrated a significant p-value of less than 0.001 (β -2.292 CI [-3.6594, -0.9246]) establishing it as an independent and significant predictor of the presence of significant coronary artery disease.

Assessing global longitudinal strain at rest demonstrates excellent diagnostic accuracy for detecting coronary artery disease in patients with chronic stable angina and normal systolic function.

Keywords

Chronic stable angina, Echocardiography, Kandy Sri Lanka

Introduction

Coronary artery disease (CAD) is a significant cardiac issue in the world that contributes to high morbidity and mortality. A common initial presentation of coronary artery disease (CAD) is chronic stable angina (CSA) which is approximately 50% of cardiovascular disease patients [1].

Non-invasive investigations such as functional imaging to detect ischemia or anatomical imaging via CT coronary angiography (CTCA) are recommended as the primary diagnostic approaches for stable coronary artery disease [2]. CTCA, myocardial perfusion imaging or stress magnetic resonance imaging are giving high diagnostic accuracy. However, the major limitations are lesser availability, exposure to radiation, and additional expense. Exercise electrocardiography, while cost-effective, demonstrates lower diagnostic accuracy compared to imaging tests and has restricted capability to rule in or rule out coronary artery disease [2]. Dobutamine stress echocardiography is another noninvasive investigation with relatively inexpensive and free of radiation exposure, but it requires expertise and has infrequent arrhythmogenic complications [3].

Speckle Tracking Echocardiography is an ultrasound imaging technique utilized to identify cardiac tissue

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motion by analyzing speckle patterns within the heart muscles. Specifically, it focuses on detecting the motion of longitudinally oriented myocardial fibers, primarily situated in the subendocardial region. This technique proves valuable in identifying areas prone to ischemia, where intermittent ischemic events can lead to myocardial stunning. Strain measurement via speckle tracking enables the detection of such myocardial abnormalities [4-6]. Longitudinal motion and deformation measurements particularly left ventricular global longitudinal strain (GLS) obtained via two-dimensional speckle-tracking echocardiography, have emerged as highly sensitive indicators for detecting CAD. This technique has shown efficacy in predicting significant CAD in acute or sub-acute ischemic events. [7-9]

The objective of this study was to evaluate and forecast the significance of GLS measured at rest and its correlation with the presence, and severity of CAD in individuals with suspected stable angina pectoris and normal left ventricular function in the Sri Lankan population.

Materials and methods

Study design and study population

This prospective observational study was conducted at National Hospital Kandy between September 2020 and February 2021. The study included patients diagnosed with chronic stable angina who had normal left ventricular function (ejection fraction ≥ 50%). Approval for the study was obtained from the institutional ethics committee (NHK/ERC/28/2020) and informed consent was obtained from all participants. Patients meeting the inclusion and exclusion criteria were selected for the study after the purpose of the research was explained to them, and their informed consent was obtained. The study's stream chart is delineated in Figure 1.

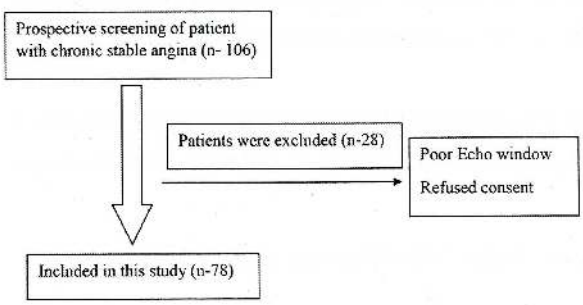

Figure 1: The study's flow chart

Inclusion criteria was patients aged 18 years and above, presenting with symptoms and medical history indicative of suspected stable angina and possessing normal left ventricular function (≥ 50%), were included in the study.

Exclusion criteria was patients with left ventricular systolic dysfunction (ejection fraction < 50%), patients with acute coronary syndrome, a prior history of CABG or myocardial infarction, ECG shows left bundle-branch block or any territory pathological Qwaves or atrial fibrillation, any valvular disease, congestive heart failure, individuals with poor acoustic window, and those undergoing cytotoxic drug therapy.

Each patient underwent a comprehensive clinical examination, including a detailed evaluation of clinical symptoms, risk factors, past medical history, physical examination, and assessment of cardiovascular disease. The findings were documented in a pre-designed data collection form. Moreover, all patient-related information was treated with utmost confidentiality.

Echocardiographic assessment

Standard echocardiographic examination was performed within 24 hours of admission using the Philips® cardiovascular ultrasound system, and the EPIQ 7® scanner. Apical four-chamber, three-chamber and two-chamber views were recorded for three consecutive heart cycles image loops and stored digitally for offline analysis by Q lab software. The left ventricular ejection fraction was assessed by the biplane a2DQ method.

The investigator performed a two-dimensional speckle tracking analysis using software (EPiq 7 c, aCMQ, version 1.5.8). The average of all segmental peak systolic strain values was calculated as GLS.

All offline image loops were analyzed by an investigator blinded to clinical data and before coronary angiography. GLS was assessed using aCMQ strain analysis, involving semi-automatic tracking of acoustic markers frame-by-frame throughout the cardiac cycle. Endocardial borders were delineated at end-systole in 2D images,

and longitudinal strains for all myocardial layers were derived from three apical views. Any poorly tracked segments were manually adjusted by the investigator. Segments that remained sub-optimally tracked after manual correction were excluded from the analysis.

Coronary angiography

A coronary angiogram was performed by SEIMONS AXIOM Sensis XP - Digital Cardio Imaging system. Experienced interventional cardiologists who were blinded to patients' data were assessed the coronary angiograms. Significant lesions of the major coronary arteries were inspected in two orthogonal planes. If patients have ≥70% stenosis in the left anterior descending artery, left circumflex artery and right coronary artery with its major branches and ≥50% stenosis in the left main stem would be considered as positive CAD.

Statistical analysis

Statistical analyses were conducted using the SPSS version 17. Quantitative variables were reported as mean ± standard deviation, while qualitative variables were presented as numbers and percentages. The independent sample t-test was used to compare values between two groups for continuous variables, and the chi-square test was employed for categorical variables. Receiver operating characteristic (ROC) curves were used to evaluate the predictive diagnostic value of GLS for the presence of coronary artery disease. Regression analysis was utilized to predict various risk factors associated with coronary artery disease. A P value < 0.05 was considered statistically significant.

Result

A total of 78 participants were included in this study, 44(56.5%) were diagnosed with coronary artery disease (CAD), with those affected being older (60.54 ±2.48) compared to those without CAD (58.67 ±2.9). Among CAD patients, 25(56.8%) had single-vessel disease (SVD), 12 (27.3%) had double-vessel disease (DVD), and 7 (15.9%) had Multi-vessel disease (MVD). Notably, the male-to-female ratio among CAD patients was 2.4:1. Significant differences between CAD and non-CAD groups were observed in terms of age (P - 0.003), diabetes mellitus (P - 0.02), hypertension (P - 0.004) and family history of premature CAD (P - 0.01), while other baseline variables were evenly distributed between the two groups. Details of the baseline variables are provided in Table 1.

Table 1: Details of the baseline variables

Variables	CAD absent (N = 34)	CAD Present (N = 44)	*P* value
Age group	58.67 ±2.91	60.54 ±2.48	0.0032
Male	15 (44.1%)	31 (70.5%)	0.0190
Diabetes mellitus	6 (17.6%)	18 (40.9%)	0.0272
Hypertension	13 (38.2%)	23 (52.2%)	0.0043
Dyslipidemia	7 (20.5%)	13 (29.5%)	0.3689
Family history	2 (6%)	12 (27.2%)	0 .0146
Smoking	4 (11.7%)	7 (15.9%)	0.6020
Ejection fraction	60.38 ±1.6	59.95 ±1.12	0.167

Table 2 presents the mean GLS in both CAD and non-CAD groups, There was a notable decrease in GLS values among CAD patients compared to non-CAD patients (P = 0.0001), with a significant decrease observed as the count of affected vessels rose. Furthermore, figure 1 presents the ROC curve depicting the relationship between GLS values and the severity of coronary artery disease. .A GLS cutoff value of -19 demonstrated promising sensitivity (72.7%) and specificity (70.6%) in predicting significant CAD, supported by an AUC of 0.717 (P = 0.001) and cutoff value of -18 shows sensitivity of 56.8%) and specificity of 79.4% in predicting significant CAD (AUC of 0.681).

Table 2: The mean global longitudinal strain (GLS) value varies depending on the number of vessels blocked in patients.

	CAD absent	CAD present	*P* value
GLS mean	-20.26 ±1.03	-17.97 ±0.85	0.0001
Single vessel disease GLS	-20.26 ±1.03	-18.63 ±1.195	0.0001
Double vessel disease GLS	-20.26 ±1.03	-17.75 ±1.32	0.0001
Multi-vessel disease GLS	-20.26 ±1.03	-15.98 ±1.51	0.0001

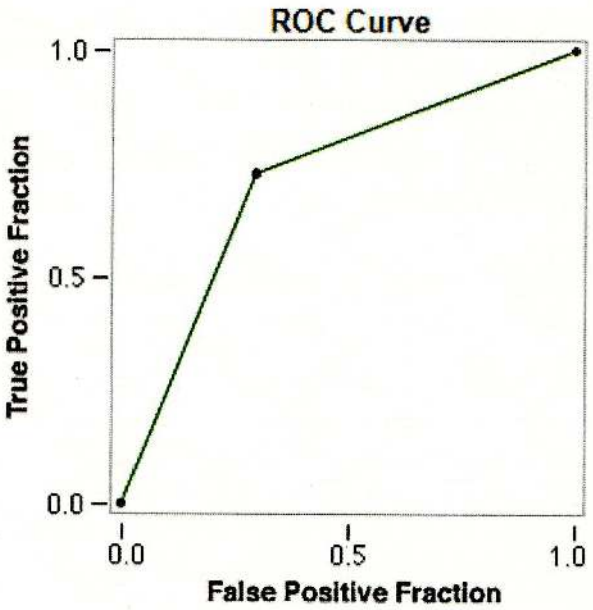

Figure 1: ROC curve depicting the GLS values to predict the significant CAD

In regression analysis, only diabetes showed a significant association with reduced GLS. Other risk factors, significantly difference in two groups such as age, hypertension, and family history of CAD did not predict abnormal GLS. GLS demonstrated a significant p-value of less than 0.001 (β -2.292 CI [-3.6594, -0.9246]) establishing it as an independent and significant predictor of the presence of significant coronary artery disease. (See Table 3)

Table 4: Regression analysis for prediction of CAD

	Standardized coefficients (β)	*P* value	95.0% CI for β Lower	Upper
Age	0 .096	0.832	-0.810	1.002
Diabetes Mellitus	0.13	0.001	0.098	0.153
Hypertension	0.011	0.682	-0.042	0.064
Family history	0.022	0.069	0.349	0.025
GLS	-2.29	.001	-3.659	-0.924

Discussion

This study aimed to assess the predictive value of GLS measured by speckle tracking echocardiography in determining the presence and severity of CAD among stable coronary angina patients. Results revealed a negative correlation between GLS values and the severity of CAD, indicating that lower GLS values were associated with more severe CAD.

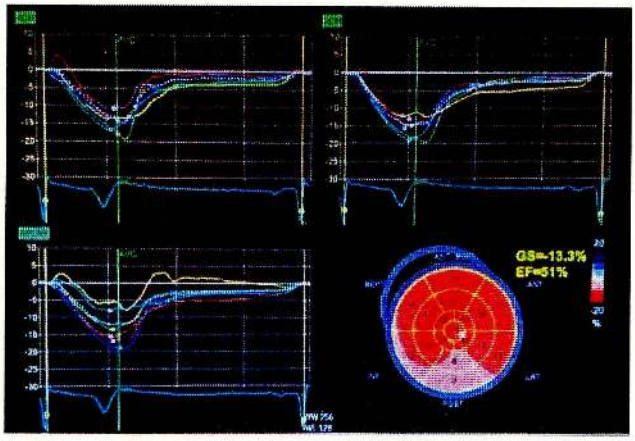

Figure 2

Figure 3

Figure 2 displays the echocardiographic image illustrating GLS, while Figure 3 depicts the coronary angiography of the same patient.

In our study, the mean age group observed was 59.73 ±1.9years, comparable to the population mean age of 60 ± 12 documented by Montgomery et al [10]. We noted a significantly higher prevalence of diabetes mellitus, advanced age, hypertension, smoking, and male gender among patients in the CAD group compared to those in the non-CAD group, consistent with findings reported in previous studies [10-11].

A significant difference ($P < 0.0001$) in GLS was observed between Non-CAD (-20.26 ±1.03) and CAD (-17.97 ±0.85) groups, aligning closely with findings reported by Montgomery et al. [10] and Bakhoum et al. [12].

In our study, we observed a mean GLS value of -18.63 ±1.195 in patients with single-vessel disease (SVD), -17.7 ±1.32 in patients with double vessel disease

(DVD), and -15.98 ±1.51 in patients with multi-vessel disease. These findings align with previous studies by Yadav et al. [13] as well as Radwan et al. [14].. These consistent trends support an inverse relationship between GLS values and the severity of coronary artery disease in our study.

In our study, we determined the optimal cutoff for global longitudinal strain (GLS) in identifying CAD to be -19 (Sensitivity- 72.7%, Specificity- 70.6%, AUC of 0.717 and $P < 0.001$). Furthermore, we observed a decrease in GLS values with increasing severity of CAD, consistent with previous research on longitudinal strain in patients with CSA. Although the optimal diagnostic cutoff for abnormal GLS may vary across studies, our findings align with existing literature. For instance, Liou et al[15]. conducted a meta-analysis involving 10 studies with 1385 patients, reporting pooled sensitivity, specificity, of 74.4% and 72.1% for GLS accuracy in detecting moderate-to-severe CAD.

In our regression analysis, only diabetes showed a significant association with reduced GLS. Notably, other risk factors such as age, hypertension and family history did not emerge as predictors of abnormal GLS, aligning closely with findings reported by Bala et al [11].

The limitations of our study must be acknowledged, including the relatively small and non-randomized patient sample. We solely relied on coronary angiography for comparing GLS values with the presence and severity of disease. Additionally, our study utilized a single type of echocardiography equipment (EPiq 7 c, aCMQ, version 1.5.8), which may introduce variability in GLS measurements influenced by factors such as software type, left ventricular mass and hemodynamic variables. These factors might potentially confound our results. Moreover, we did not assess radial, transverse, circumferential strain, or synchrony analysis, which could provide further insights into myocardial function. Finally, the findings of the coronary angiogram rely on the visual assessment rather than the invasive fractional flow reserve on coronary angiography.

Conclusion

Incorporating GLS measurements from echocardiography may improve the prediction of severe CAD in patients suspected of having it, potentially reducing the need for invasive procedures. However, further validation in larger studies is necessary. Additionally, GLS assessment at rest shows promising diagnostic accuracy for CAD in patients with CSA and normal systolic function, but more research is needed to determine if longitudinal strain analysis alone is sufficient for diagnosing ischemia in CSA patients.

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Original Article

Quality of Life of Children with Asthma and Their Caregivers: A Study at a Single Tertiary Care Centre in Northern Sri Lanka

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Abstract

Asthma is the most prevalent chronic disease among children, representing a leading cause of paediatric morbidity and healthcare utilisation. It profoundly impacts various aspects of children's quality of life and the quality of life of their caregivers. This study aims to assess the quality of life experienced by children with asthma and their caregivers and to determine the association between asthma control and quality of life.

The children aged 6 to 16 years with asthma under the care of paediatric clinics at Teaching Hospital Jaffna and their caregivers were recruited. Data were collected through an interviewer-administered questionnaire. Pearson correlation coefficient was used to assess the correlations between asthma score and quality of life, and a linear regression was done to identify whether the asthma score can predict the child's quality of life.

Ninety-nine children and their caregivers participated in the study. Asthma was more prevalent among boys (54.5%). The mean age of children was 115.5± 31.6 months. The mean score on the childhood asthma control test was 19 ±4.05. The child-reported mean quality of life score was 74.47±10.05. Overall quality of life score was significantly diminished in children with uncontrolled asthma (p=0.003). There was a weak, positive correlation between the child's total quality of life score and the asthma score. (r=0.25, p=0.006)

In conclusion, this study highlights that asthma exerts a significant impact on children's quality of life, particularly when the condition remains uncontrolled. The weak, positive correlation between the child's asthma control score and total QoL score indicates that while asthma severity affects QoL, it is not the sole determinant

Keywords

Asthma, Quality of life, Children, PedsQL, Caregivers

Introduction

Asthma is a chronic, heterogeneous, complex inflammatory disease of the respiratory system, characterized by recurrent symptoms such as cough, wheezing, chest tightness, and difficulty in breathing. It is the most common chronic disease of childhood and adolescence.

Asthma affected an estimated 262 million people and caused 455 000 deaths in 2019 [1] Globally, according to the Phase III International Study of Asthma and Allergies in Childhood, the prevalence of current asthma in the 13-14-year age group and the 6-7-year age group was 14.1% and 11.7%, respectively. [2] In Sri Lankan children, the prevalence of current wheeze in the age group of 13-14 years is 17.5%, and in the 6–7-year age group, it is 18.1%. [3] A recent report by the World Health Organization (WHO) indicates that one in 10 children has asthma symptoms [4]

Quality of life (QOL), defined by the World Health Organization, is "an individual's perception of their position in life in the context of the culture and value systems in which they live and to their goals, expectations, standards, and concerns." [5] Measuring the quality of life of children with chronic diseases such as asthma is essential because it provides a comprehensive view of a person's overall well-being rather than just their disease status. The importance of understanding the impact of disease and treatment on the Quality of Life of children is now recognized.

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Asthma significantly affects many aspects of children's quality of life. Recurrent symptoms like coughing, wheezing, and breathlessness limit physical activity, disrupt sleep, and impair academic performance, all of which impact overall well-being. Additionally, the psychosocial effects of living with a chronic condition—including anxiety, social isolation, and stigma—add further challenges for children with asthma.

Asthma can affect children's and caregivers' Quality of Life (QOL).[6] Care for a child with asthma is a difficult and complex task. This involves monitoring of symptoms, medication supplementation, and visits to healthcare facilities for follow-up and in emergencies. Due to the chronicity of asthma, caregivers could suffer from long-term stressors that affect their decision-making, work responsibilities and productivity[7] Moreover, caregivers frequently suffer from poor quality sleep because they need to be vigilant to observe any child's symptoms, especially at midnight. They easily get stressed and wake many times to check on the child and provide care if needed[8]

Health-related quality of life (HRQoL) is a complex, multidimensional concept that includes social, emotional, and physical functioning or well-being and is related to the patient's health state [9]. This increased recognition has increased the use of child self-report and proxy-report instruments in paediatric clinical practice.

There are several well-documented and validated generic HRQoL questionnaires available for use with children and proxies, such as the Paediatric Quality of Life Inventory (PedsQL) [10], the Child Health Questionnaire (CHQ) [11], or the Quality-of-Life Scale for Children (QOL-C) [12].

The asthma caregivers' quality of life is commonly assessed using the Paediatric asthma caregiver's quality of life questionnaire (PACQLQ), which is a validated questionnaire available in multiple languages.[13]

This research aimed to explore the quality of life of children with asthma and their caregivers and to determine the correlation between asthma control and quality of life.

Methodology

Study design and setting

An institution-based cross-sectional descriptive study was conducted at the pediatric clinics of Teaching Hospital Jaffna. This tertiary care hospital, located in the Northern Province of Sri Lanka, serves a population of 1.3 million across an area of 8,890.07 square kilometres, approximately 13.5% of Sri Lanka's total land area. The hospital operates five pediatric clinics each week, with an attendance of 50 to 60 children per clinic.

Study population

Children and their caregivers were recruited when the children fulfilled the following criteria: Diagnosed with asthma by a consultant paediatrician, aged between 6-16 years, on long-term inhaled corticosteroids for at least 3 months, and attending the paediatric clinics at Teaching Hospital Jaffna. Children who had other comorbidities like congenital heart disease, chronic kidney diseases, liver diseases, or bronchiectasis were excluded from the study.

Sample size

The sample size was calculated using the formula; $n = Z^2 \sigma^2/d^2$ (σ pooled standard deviation 11.05 [14] The acceptable margin of error is considered as 2.5 thus, the total sample required is 75. Considering the 15% non-respondence, the needed sample is 99.

Study instrument

The study instrument was an interviewer-administered questionnaire that included details regarding baseline characteristics of the study participants such as child age, sex residence and other sociodemographic factors, family history of asthma, asthma control, and quality of life of the child and the caregiver.

Asthma control

Asthma control was evaluated using the Childhood Asthma Control Test (C-ACT), a validated tool for assessing asthma control [15]. The test consists of two sections: questions 1-4 are answered by the child, while questions 5-7 are completed by the caregiver. The

C-ACT score ranges from 0 to 27, with scores above 20 indicating well-controlled asthma, scores between 12 and 19 indicating partially controlled asthma, and scores below 12 indicating poorly controlled asthma.

Quality of Life Assessment

The child's quality of life was assessed using the Pediatric Quality of Life Questionnaire (PedsQL Tamil version for India 4.0). This modular instrument measures health-related quality of life in children and adolescents aged 2 to 18 years. The PedsQL 4.0 Generic Core Scales include multidimensional child self-report and parent proxy-report scales, with 23 items relevant to healthy school and community populations, as well as pediatric populations with acute and chronic health conditions. This is a validated tool to assess the quality of life in children [16] was chosen considering both language and cultural adaptability.

The quality of life of the child was assessed separately by the child and the caregivers using both child-reported and caregiver-reported versions. A 5-point Likert response scale (0–4) was used for scoring responses from study participants. All items were reverse-scored and linearly transformed to a 0–100 scale (0=100, 1=75, 2=50, 3=25, 4=0) for better interpretation. The maximum possible score is 100 and the minimum possible score is zero. Higher scores indicate a better quality of life.

The quality of life of the caregivers was assessed using the Paediatric Asthma Caregivers Quality of Life Questionnaire (PACQLQ) Tamil version for India. This is a validated tool to assess the quality of life of the caregivers [13] it has 13 items. (activity limitation four items and emotional function nine items) A 7-point Likert response scale with 1 indicating severe impairment and 7 indicating no impairment was used to score the responses from study participants. Higher scores indicate a better quality of life.

Data collection

The investigators and data collectors collected data. Data collectors are pre-intern medical officers attached to the paediatric department, and the investigators trained them before commencing the data collection. Data was collected from June 2022 to April 2023 by consecutive sampling methods from all the eligible study populations after obtaining informed written consent. The repetition was prevented by placing the sticker on the clinic book.

Data analysis

The data obtained from the study was analysed using IBM SPSS statistics Version 22. Univariate analysis of the socio-demographic characteristics (age, sex), family history of asthma, and asthma control was carried out and basic summary statistics were produced for each variable.

Quantitative variables such as scores for asthma control and quality of life were described using means and standard deviation. The mean quality of life scores of each domain as well as the overall quality of life scores, were calculated and presented as mean scores and standard deviation. Analysis of variance (ANOVA) was used to identify the relationship between the different age groups and sex on asthma control.

An Independent t-test was used to determine the association between quality of life and sex, family history of asthma, and asthma control. Pearson's correlation coefficient was used to assess the correlations between child-reported and caregiver-reported quality of life, asthma score, and quality of life. A linear regression was done to identify whether the asthma score can predict the quality of life of the child.

The Ethical Clearance was obtained from the Ethical Review Committee Faculty of Medicine University of Jaffna, and the administrative approval was obtained from the Director of Teaching Hospital Jaffna. Permission was obtained to use the tools C-ACT, PedsQL Tamil version for India, and PACQLQ Tamil version for India.

Results:

A total of 99 children (6-16 years old) and their caregivers, fulfilled the eligibility criteria and completed the study. Table 1 demonstrates the socio-demographic characteristics of the study participants.

Table 1 : Socio-demographic characteristics of the study participants

Sociodemographic characteristics	Number	Percentage
Age group of the child		
72- 96 months	36	36..4
97 – 120 months	23	23.2
121- 168 months	34	34.3
>168months	6	6.1
Sex of the child		
Males	54	54.5
Females	45	45.5
Main respondent		
Mother	82	82.8
Father	9	9.1
Siblings	3	3
Other relatives	4	4
Guardian	1	1
Family history of asthma		
Presence of family history of asthma	73	73.7
Absence of family history of asthma	26	26.3

The mean age of asthmatic children was 115.5 (SD 31.6) months, with a male-to-female ratio of 1.2 :1. The main respondents are the parents (92%). About three-fourths (73.7%) of the asthmatic children had a family history of asthma.

The mean score for the childhood asthma control test was 19 with a standard deviation of 4.05. The minimum score recorded was 4 and the maximum was 27. Table 2 demonstrates the asthma control according to the childhood asthma control test.

Table 2: Asthma control depends on Childhood asthma control test

Asthma control	Males	Females	Total
Well controlled asthma (score >20)	26	25	51 (51.5%)
Partially controlled asthma (score between 19-12)	23	19	42 (42.4%)
Poorly controlled asthma (score <12)	5	1	6 (6.1%)

Asthma scores were higher for female children (M=19.53 SD3.23) when compared with male children (M18.56 SD4.59). There was a significant effect of sex on asthma score (t (97) F=4.509, p= 0.036.) There was no significant effect of family history (t (97) F=0.499 p=0.482) despite children with a positive family history (M=19.36, SD =4.13) attaining higher scores than those without a family history of asthma (M= 18 SD=3.69). A one-way ANOVA revealed that there was no statistically significant difference in the asthma scores and age groups (F (3,95) =0.219 p=0.883).

The mean child-reported total quality of life score was 74.47 ± 10.05 and the caregiver-reported total quality of life score was 70.87± 12.56. The child-reported and caregiver-reported total quality of life scores were strongly positively correlated (r = 724, p<0.001). There was a significant average difference between the child-reported and caregiver-reported total quality of life scores (t (196)=2.48, p=0.014). Figure 1 demonstrates different domains of the children's quality of life by child-reported and caregiver-reported scores

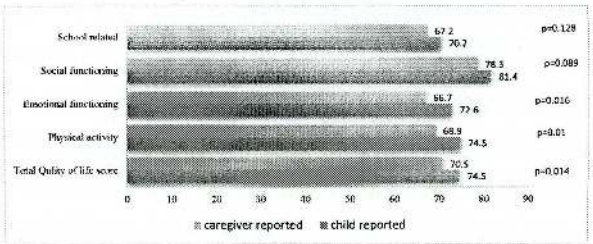

Figure 1: Child-reported and caregiver reported Quality of life scores for total and different domains

Table 3: Factors affecting the quality of life of asthmatic children

Variable	Quality of life domains				
	Physical function	Emo-tional function	Social function	School activity	Quality of life total score
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Controlled asthma	76.76 (13.06)	79.31 (13.86)	81.25 (12.73)	72.84 (11.32)	77.38 (9.83)
Uncontrolled asthma	72.07 (14.90)	65.52 (16.28)	81.46 (12.46)	67.29 (11.48)	71.37 (9.43)
Student t-test P value	0.09	0.000	0.936	0.017	0.003
Male	75.04 (14.09)	75.74 (16.06)	81 (12.72)	70.65 (12.48)	75.42 (9.9)
Female	73.82 (14.26)	68.89 (16.48)	81.78 (12.44)	69.56 (16.77)	73.33 (10.22)
Student t- test P value	0.67	0.039	0.76	0.65	0.30

Asthma control plays a significant role in the quality of life of children. Overall quality of life scores were low in children with uncontrolled asthma when compared with controlled asthma and the difference is statistically significant (p= 0.003) The scores were higher for children with controlled asthma on emotional components and school components when compared to uncontrolled asthma. Gender did not affect the total quality of life score but the emotional function is influenced by gender. The girls scored less for the emotional component when compared with boys and the difference is statistically significant (p= 0.039). (Table 3)

Table 4 demonstrates the quality of life of the caregivers. Physical activity component scores were slightly lower when compared with psychosocial scores. Pearson correlation analysis reveals a weak negative correlation between the quality of life of the caregivers and the duration of asthma (r -0.22, p=0.033) and income (r -0.24,p=0.021). Caregivers whose child with long duration of asthma and high income has a better quality of life.

Table 4: Quality of life of the caregivers with different components

Quality of life Domain	Minimum score	Maximum score	Mean score	Standard deviation
Physical acitivity	1.50	7.0	5.28	1.45
Psychosocial	2.22	7.0	5.58	1.07
Total quality of life of the care givers	2.0	7.0	5.50	1.14

A statistical analysis was conducted to examine the relationship between the quality-of-life score of the child and the asthma score among 99 participants. The mean score for the total quality of the child was 74.47 (SD = 10.05), while the mean for asthma score was 19.00 (SD =4.05). A Pearson correlation analysis revealed a weak, positive correlation between the child's total quality of life score and the asthma score, r=0.25, p=0.006, suggesting a slight association between higher asthma scores and higher child total scores. A simple linear regression was conducted with the child's total quality of life score as the dependent variable and the asthma score as the predictor. The model was statistically significant, F(1,97)=6.67, p=.011, explaining 6.4% of the variance in the total quality of life score of the child (R2=.06). The unstandardized coefficient for asthma score was B=0.63, SE=0.24, p=.011, indicating that each one-point increase in asthma score is associated with a 0.63-point increase in the total quality of life score of the child.

In summary, although the asthma score was a statistically significant predictor of the child's total quality of life score, it explained only a small portion of the variance, suggesting additional factors likely contributed to the child's total quality of life score.

Discussion:

This study contributes to a growing body of literature on asthma in children, focusing on the associations between asthma control, socio-demographic characteristics, and quality of life (QoL) in children with asthma and their caregivers.

The results show that asthma control status and gender significantly influence children's QoL, although the asthma score is a relatively modest predictor, accounting for only 6.4% of the variance in QoL. These findings emphasise that while asthma severity impacts children's QoL, other factors may have considerable effects, warranting a holistic approach to managing children with asthma.

The findings indicate that asthma control plays a crucial role in the QoL of children with asthma. Children with well-controlled asthma report better QoL scores across most domains, especially in emotional and school functioning. These results align with prior research, consistently showing that improved asthma management is associated with enhanced QoL and reduced functional impairment in children [17]. Emotional and school functioning are likely to be compromised in children with poor asthma control due to limitations in physical activity, increased absenteeism, and psychosocial stress. Thus, achieving optimal asthma control through adherence to treatment regimens and lifestyle modifications remains essential to improving the QoL in children with asthma.

Our study found that gender differences significantly impacted the emotional domain of QoL, with females scoring lower than males. This finding is consistent with other studies that have documented that female children have a worse perception of asthma, feel it as more symptomatic, and suffer a greater impact on their QoL, even though having similar baseline severity and obtain similar levels of control. [18] The reasons for these differences may be multifaceted, including potential variations in coping mechanisms, social support systems, and societal expectations for emotional expression. Emotional support and tailored interventions for girls with asthma may, therefore, be essential to mitigate these disparities.

Notably, caregiver QoL in our study exhibited a weak but significant negative correlation with income and asthma duration, suggesting that caregivers with higher income and children with a longer duration of asthma might have adapted better or have greater resources to manage the condition effectively. This insight aligns with recent evidence indicating that Children with chronic diseases from lower socioeconomic backgrounds experience reduced QoL compared with their wealthier counterparts. [19]

The differences observed between child-reported and caregiver-reported QoL scores are notable, with caregivers typically rating the child's QoL slightly lower. This discrepancy is in contrast with a study done in America in children with sleep disorder where the child reported scores are low. [20] In our study, the caregivers may perceive the child's QoL more conservatively, potentially due to anxiety about the disease condition's impact or its long-term management implications. This difference highlights the importance of integrating child and caregiver perspectives in clinical assessments to comprehensively understand the child's QoL and its influencing factors. Future studies could examine the mechanisms underlying these differences, particularly the role of caregiver anxiety and its impact on reporting.

The weak, positive correlation between the child's asthma control score and total QoL score indicates that while asthma severity affects QoL, it is not the sole determinant. The asthma score explained only a small proportion (6.4%) of the variance in QoL scores, suggesting that other factors likely play more significant roles in determining QoL outcomes. For instance, psychosocial factors, environmental influences, and mental health status might contribute to the broader QoL landscape in asthmatic children [21]. This limited predictive value emphasises the need for a comprehensive approach that incorporates both clinical management of asthma symptoms and support for psychological and social well-being.

The findings emphasise the need for healthcare providers to consider asthma control alongside socio-demographic and psychosocial factors when addressing QoL in children with asthma. Interventions should focus on personalised asthma education, psychosocial support, and school-based interventions to address the emotional and academic challenges faced by children with poorly controlled asthma. Additionally, caregiver support programs may prove beneficial, particularly for those with lower income or limited resources, as these individuals may experience added stress related to the child's condition.

Further research is warranted to explore the broader determinants of QoL in children with asthma, particularly longitudinal studies that investigate the interplay between clinical, socio-environmental, and psychological factors. Such studies could help to identify modifiable risk factors and inform the development of multi-faceted interventions aimed at enhancing QoL among asthmatic children and their families.

In conclusion, this study highlights the significant impact of asthma control on QoL in children with asthma while also revealing important differences related to gender and caregiver perspectives. These insights point to a holistic model of care that integrates clinical management with family-centred and psychosocial support to address the complex needs of children with asthma and their caregivers.

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Brief Report

Feasibility of Engaging Community Healthcare Workers to Identify and Enhance Subfertility Care in The Northern Province, Sri Lanka.

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Abstract:

Subfertility is a significant global reproductive health challenge affecting approximately 1 in 6 individuals worldwide. Despite having a comprehensive healthcare system, Sri Lanka still faces challenges in providing timely and effective fertility care. We propose integrating Community Health Workers (CHWs) into the healthcare system to address these challenges. The present study aimed to assess the acceptability, appropriateness, and feasibility of the Community Health Worker Facilitated Fertility Care (CHWFFC) model in the Nallur MOH area, Jaffna, Sri Lanka. The intervention, conducted over six months, demonstrated promising outcomes, including positive stakeholder feedback, reduced PHMs' workload, and an effective identification and referral system for subfertile couples.

Introduction

Subfertility poses a significant global reproductive health challenge, impacting affected couples' mental, social, and economic well-being. Roughly 1 in 6 individuals worldwide experience subfertility, emphasising the need for accessible, high-quality fertility care services (2). In low- and middle-income countries, subfertility affects approximately 16.5% of the population. Sri Lanka, with a fertility rate of 2.128 births per woman (3), grapples with a considerable number of subfertile couples, estimated between 270,000 to 400,000, with about 1% requiring advanced treatments like Assisted Reproductive Technology (ART) (4). Studies in Sri Lanka, especially in Colombo and recently in Jaffna (22% - under review), indicate higher rates of primary and secondary subfertility, underlining the severity of the issue.

Despite free access to primary healthcare, delays in fertility care are found to be common in Sri Lanka. The healthcare system encompasses primary, secondary, and tertiary care, with primary diagnosis and referrals to tertiary centers (5). However, challenges, including social stigma, lack of knowledge among young couples, and inadequate primary healthcare resources, hinder effective subfertility care. The issue gets further exacerbated by the intense burden that Public Health Midwives (PHMs) endure when managing subfertility on top of their maternal care routine(6). Thus, we proposed a model that integrates Community Health Workers (CHWs) into the healthcare system to address these challenges. The CHWs model has been proven successful in providing primary health care globally and can be used to extend services, especially in underserved regions (7). Leveraging existing infrastructures such as mothers' clubs (8,9), we suggest training local women as CHWs to engage in subfertility care along with other women's health issues. Their community ties can assist in reducing stigma and improve engagement.

This study aims to assess the acceptability, appropriateness, and feasibility of the Community Health Worker Facilitated Fertility Care (CHWFFC) model in the Nallur MOH area in Jaffna, Sri Lanka.

Methodology

The intervention spanned from June 2023 to November 2023 and targeted six randomly selected PHM areas within the Nallur Medical Officer of Health (MOH) area

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in Jaffna, Sri Lanka. A multidisciplinary core team was formed in collaboration with the Faculty of Medicine, University of Jaffna, with support from the Centre for Digital Epidemiology (CoDE), to plan, implement, and evaluate the interventions.

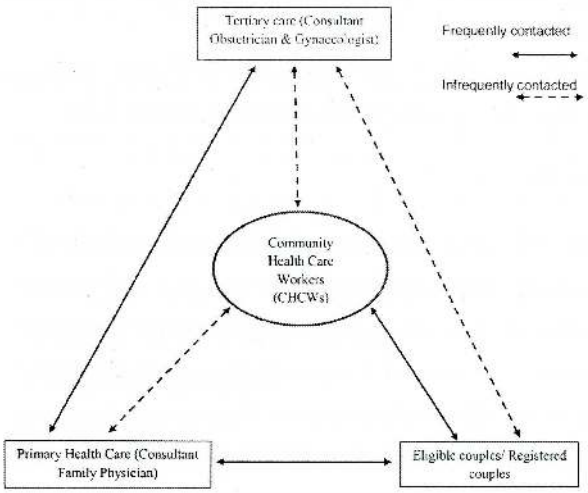
An exploratory sequential mixed-method design was employed, commencing with qualitative data collection and analysis and followed by quantitative data analysis. Qualitative data were gathered through focus group discussions, which the family physician then analysed using content and thematic analysis. Quantitative data were collected through a functioning triage system and analysed descriptively.

The recruitment and training of CHWs were executed in three steps. First, five community healthcare workers were purposively selected based on secondary education completion status and with a minimum of six months of experience in healthcare. Second, two training programs were conducted for CHWs and PHMs utilising the FIGO fertility toolbox, covering various topics related to subfertility, diagnostic methods, treatment modalities, community engagement, and communication skills. Third, CHWs were integrated into the primary healthcare team, assigned to selected PHM areas, and provided on-the-job training to effectively interact with sub-fertile couples, provide health education, and facilitate clinical work.

During field and clinic visits with PHMs, CHWs identified sub-fertile couples, provided health education, and facilitated referrals to family physicians at primary care centers. Specialist family physicians examined and tested identified couples to determine their treatment needs. Those with advanced fertility issues were referred to specialist obstetricians and gynecologists at tertiary care centres for further management.

The intervention's acceptability, appropriateness, and feasibility were evaluated through stakeholder engagement, focus group discussions with PHMs, and quantitative outcomes measured during monthly meetings. This comprehensive approach aimed to enhance fertility care delivery and improve outcomes for subfertile couples in the region.

Figure 1- Central Role of Community Health Workers in the Fertility Care



Results and Discussion

Acceptability:

Qualitative measures indicated positive stakeholder feedback during the Focus Group Discussion (FGD). Public Health Midwives (PHMs) expressed increasing acceptability of the CHCWFFC model as they became familiar with subfertility issues, although concerns about collaboration with CHWs were raised. During conversations, issues such as transportation, logistics, scheduling, and community acceptance of CHWs came up, highlighting potential implementation barriers despite overall positive attitudes.

Appropriateness:

Feedback from PHMs in FGD highlighted the model's appropriateness, emphasizing a significant reduction in their workload when supported by CHWs. They recognized CHWs' proactive nature in learning new tasks but suggested clarifying CHWs' roles and improving logistical support. Although further refinement was desired, the model demonstrated overall high appropriateness, contingent on adequate staff resources and clear intervention structures.

Feasibility:

Quantitative measures demonstrated the feasibility of the CHCWFFC model. Over six months, 47 awareness

programs and health education sessions were conducted, identifying and referring 61 subfertile couples to primary health care. Subsequent consultations with specialist family physicians and referrals to tertiary care centres further facilitated subfertility management. The involvement of CHWs proved instrumental in guiding couples through the healthcare system, ensuring timely access to quality fertility care. Helpline follow-ups improved continuity of care. These findings affirm the feasibility of the CHCWFFC model in effectively addressing subfertility burdens within the community.

Table 01- Findings showing the acceptability, appropriateness and feasibility.

Acceptability	- Positive feedback from stakeholders during the inauguration program.
	- Stakeholders promised administrative and financial backing.
	- Optimism regarding potential as a model for South Asian countries.
	- Public Health Midwives (PHMs) showed increasing acceptability over time.
	- Concerns about collaboration with Community Health Workers (CHWs) were noted.
Appropriateness	- Significant reduction in workload for PHMs when supported by CHWs.
	- CHWs showed proactive nature in learning new tasks.
	- Suggestions made to clarify CHWs' roles and increase frequency of clinic visits.
	- Desire for further refinement of the model.
	- Sufficient staff resources and clear intervention structure are necessary for high appropriateness.
Feasibility	- Specialist Family Physicians actively participated in community-based sessions.
	- 47 awareness programs and health education sessions conducted over six months.
	- 61 subfertile couples were identified and referred to primary healthcare.
	- 18 consultations with specialist family physicians and 5 referrals to tertiary care centers facilitated the management of subfertility.
	- CHCWs are instrumental in guiding couples through the healthcare system.
	- Helpline follow-up improved continuity of care for 59 couples.
	- Feasibility confirmed for effectively addressing subfertility burdens.

Conclusion and Recommendations

In conclusion, the Community Health Worker Facilitated Fertility Care Model (CHWFFC) has shown promising outcomes in addressing subfertility issues within the Nallur Medical Officer of Health (MOH) area, Jaffna, Sri Lanka. The study highlights this model's acceptability, appropriateness, and feasibility, emphasising the importance of positive collaboration among community health workers, Public Health Midwives (PHMs), and stakeholders. Challenges such as logistical issues and community acceptance of CHWs need to be addressed for successful implementation. Continued monitoring and refinement of the model are essential to optimise its effectiveness in improving fertility care accessibility and outcomes within the community.

The CHCWFFC model has proven effective for diagnosing new cases, operating at low costs, and alleviating the financial burden of subfertile couples. However, long-term effectiveness requires further investigation to ensure a sustained impact on fertility care accessibility and outcomes within the community. This model can be applied in similar settings in other parts of Sri Lanka to improve fertility care accessibility and outcomes with adaptations to local contexts.

Acknowledgement

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Case Report

The bilateral symmetrical neck of femur fracture in a child following trauma, successfully treated with surgical fixation

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Abstract

Neck of femur fracture in a child caused by trauma is rare and needs appropriate management to avoid complications. We present an 8-year-old child with a bilateral symmetrical delbet type III neck of femur fracture following a fall from height.

Clinical assessment revealed an isolated bilateral neck of femur injury. Radiographs reveal bilateral symmetrical intracapsular neck of femur fracture which is delbet type III. During initial medical management, adequate analgesics were given and traction was applied to the limbs. Surgical fixation of each hip was done in the next planned trauma list by the senior paediatric orthopaedic surgeon. A partially threatened cancellous cannulated screw and smooth K wires were used under the guidance of the image intensifier. The patient was followed in the clinic until the radiological evidence of healing and he regained the range of motion of the hip. He is still under follow-up for the late onset of complications.

A bilateral symmetrical intracapsular neck of femur fracture is rare. Awareness of this entity, early detection, and intervention in this condition may help preserve the native hip.

Keywords

The neck of femur fracture, paediatrics, Delbert classification, avascular necrosis of the femoral head.

Introduction

The neck of femur fracture is a rare injury in children, unlike adults. It comprises less than 1% of all fractures among children. A bilateral symmetrical-type neck femur fracture is even rarer (1). Many cadaveric models demonstrated that a neck of femur fracture in the paediatric population involves about 900 to 2000 pounds of weight-force transmission. In contrast, in older adults, it is an osteoporotic fracture. (2). Unlike in adults, the neck of the femur blood supply is severely compromised by the neck of the femur fracture. The difficult complications to manage following neck femur fracture in paediatric populations are avascular necrosis of the femoral head and non-union. So early and appropriate intervention is needed to produce a successful outcome (3). We present our experience in managing a bilateral symmetrical Delbet type 3 fracture neck of the femur with cancellous screw fixation.

Case History

An 8-year-old boy was admitted to the surgical casualty ward following a fall from eight feet height and landed on his feet. He was complaining of bilateral hip pain and was unable to move the limbs on both sides in the accident and emergency department. The primary and secondary surveys were normal, and he had no neurovascular deficit in both lower limbs. Radiographs of the pelvis with proximal hip anterior-posterior view showed symmetrical bilateral Delbet type III cervicotrochanteric fractures in both hips. Both lower limbs were splinted, and adequate analgesics were given to alleviate the pain.

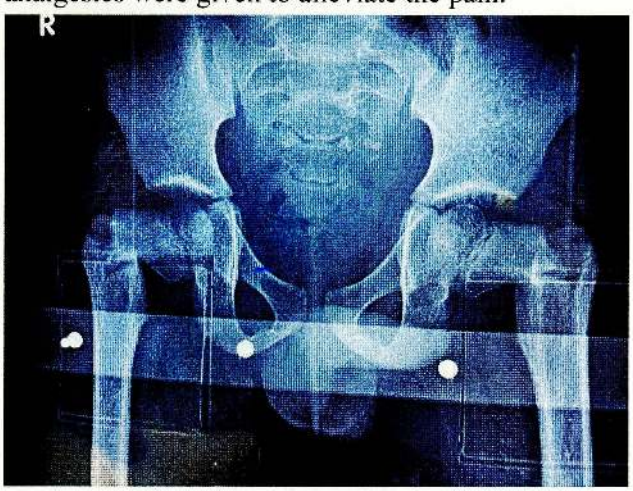

Figure 1: Anterior posterior view of pelvic radiograph including both hips shows bilateral symmetrical cervicotrochanteric (Delbet III) fracture.

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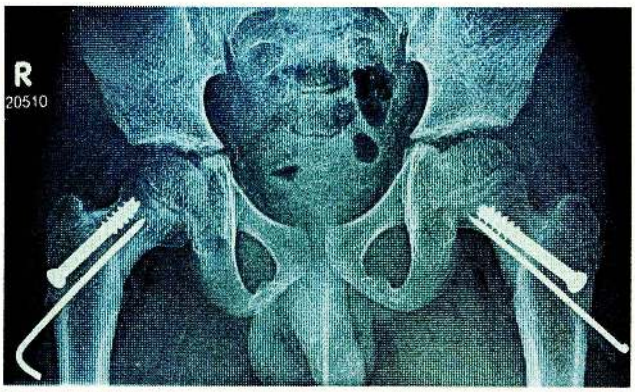

Figure 2 shows an anterior posterior view of Pelvis with both hips shows evidence of healing without complication.

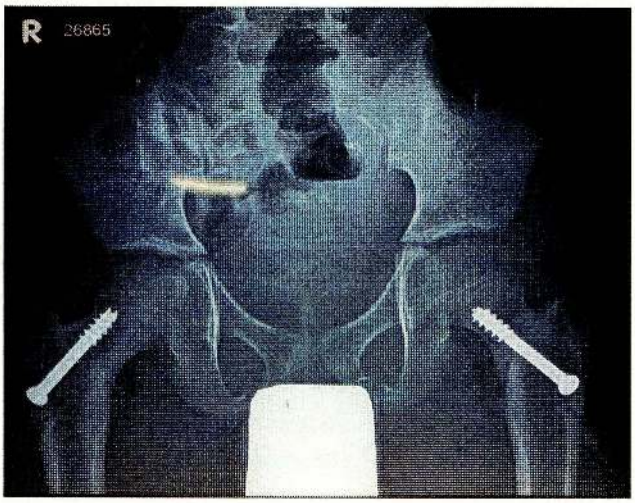

Figure 3 shows an anterior posterior view of Pelvis with both hips after removal of K Wires

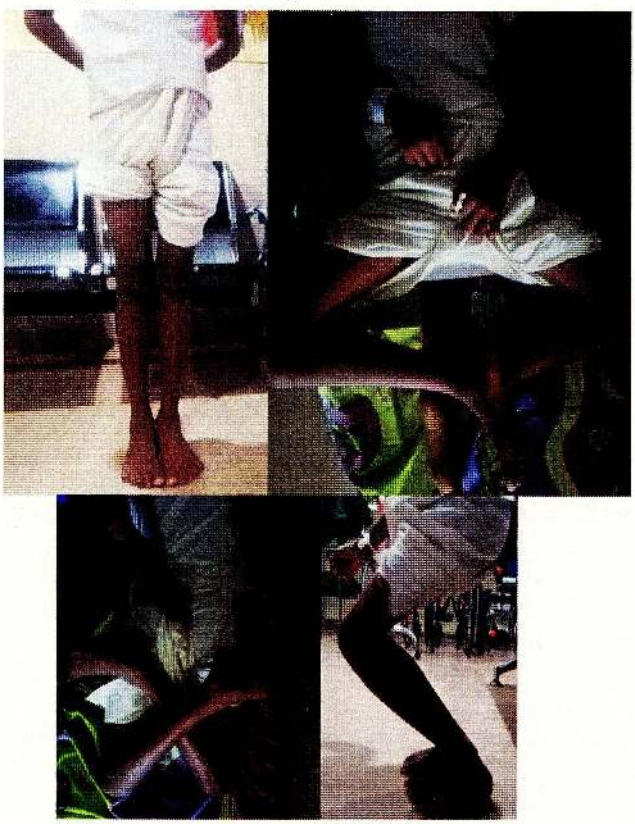

Figure 4 shows a range of motion of both hip

A closed reduction and percutaneous fixation of both neck of femur was planned on the next available list. Surgeries were performed by a senior consultant orthopaedic surgeon under general anaesthesia. Both fractures were reduced on the traction table with the fluoroscopic guidance and fixed with a cannulated cancellous screw and a smooth k wire.

Non-weight-bearing physiotherapy followed for the initial first six weeks of the postoperative period, and then protective weight-bearing gradually started. He was followed in the clinic regularly and fracture healing was assessed with radiographs. After one 1 year and 3 months, he was pain-free with a full range of movements achieved on both hips and his k wire was also removed.

Discussion.

The neck of femur fractures is an unusual injury among paediatric fractures, accounting for less than 1% of all paediatric fractures(1). The bilateral symmetrical neck of femur fracture in the paediatric population is reported rarely in the literature. Motor traffic accidents and falls from height are the main mechanisms of injury(3). Low-energy mechanisms are common in underlying bony pathology in children(3). The upper part of the femur consists of a strong medial calcar plate, which contains a complex mesh of traction and compression trabeculae. 85% of high-energy mechanism injuries are associated with other injuries e.g.: pelvic injury, and head injury.

The majority of the blood supply to the head of the femur in the paediatric population is derived from the posterior superior and posterior inferior branches of the medial circumflex artery, which travel along the retinacular fibres of the capsule (4). The lateral circumflex artery supplies the medial part of the physis, medial metaphysis, and greater trochanter(4). In addition to the medial circumflex and lateral circumflex artery, the head of the femur also acquires blood supply through the ligamentum teres which is a major blood supply in childhood(4). Blood supply from the Lateral circumflex artery and ligamentum teres begin to regress after the age of 4 until 10 years (3). The neck of femur fractures during this age are more vulnerable to avascular necrosis of the head of the femur due to this blood vessel arrangement(5).

The Delbet classification is widely used for paediatric neck of femur fractures, which was introduced in 1907 and modified in 1929 by Colonna(6).

Table 1 shows the Delbert classification for the paediatric neck of femur fractures, with the incidence and the risk of avascular necrosis.

Table 1: Delbert Classification

Type	Description	Incidence	Risk of AVN
I	Transphyseal fracture A: without dislocation, B: with dislocation	<10%	40% (7)
II	Transcervical fracture	40-50%	27% (7)
III	Cervicotrochanteric fracture	25-35%	20% (7)
IV	Intertrochanteric fracture	6-15%	5% (7)

Initial radiographic assessment should include an anterior-posterior view of the pelvis with the affected hip and a lateral view of the affected hip to study the fracture anatomy. The plain radiographic assessment of the femur full length needs to be performed to exclude concomitant femur shaft fractures. Plain radiographic assessment will be helpful in the study of the fracture pattern, determining the classification, degree of displacement, and status of the physis which are important points in the management of paediatric neck of femur fractures(3). When there is a high degree of clinical suspicion with negative X-ray findings, MRI is the gold standard investigation to rule out this entity. T1 weighted MRI study is 100% sensitive in diagnosing occult neck of femur fracture in coronal plan images(8)we retrospectively reviewed the MRI scans of the 35 patients who had no evidence of a fracture on their plain radiographs. In eight of these patients MR scanning excluded a fracture but the remaining 27 patients had an abnormal scan: one with a fracture of the pubic ramus, and in the other 26 a T(1.

Age and type of fracture according to the Delbet classification are considered during the decision-making. Anatomical reduction of the fracture segment and stable fixation will help in reducing the risk of the premature arrest of growth in the growth plate and avascular necrosis of the femoral head and allow the patient early weight-bearing(9). Cannulated screw fixation, K wire fixation, and dynamic hip screw are the available surgical optionsfor the stabilization of the fracture(4). A smooth K wire can be used to stabilize the fracture segment in Delbet type II and III fractures in less than 2 years. A cannulated screw can be used to treat this entity Delbet type I, II, and III fractures among 4–6 years of age. A dynamic hip screw can be used in Delbet type III and IV patients to stabilize the fracture segments(4).

The fracture should be tried to reduce closely with the guidance of fluoroscopy using traction, internal rotation, and abduction manoeuvres. If close reduction fails, the open reduction can be achieved by using a standard anterior (Smith Peterson) or anterior lateral (Watson Jones) approach(4). Early stabilization of the fracture with decompression of the capsule will reduce the incidence of complications. Although capsular decompression is a controversial topic, many surgeons prefer to do decompression.

The most common and difficult complication to manage following a neck of femur fracture in the paediatric population is avascular necrosis of the femoral head (10). It can be predicted using the Delbet classification. Patients should be followed up in the clinic for anterior thigh pain and reduced range of movement. They should be investigated with an anterior-posterior view of the pelvis with a frog lateral view radiologically to exclude the AVN of the femoral head during the follow-up (10). Early-stage AVN shows radiolucent patches within sclerotic epiphyseal margins known as patchwork appearance. An MRI study of the affected hip is the gold standard for diagnosing the condition. Early anatomical reduction of fracture with capsular decompression is considered a modifiable risk factor and older age, initial fracture displacement, and Delbert type are considered non-modifiable risk factors for AVN of the femoral head (10). Core decompression, free vascular fibular graft, proximal femoral osteotomy, total hip arthroplasty, and hip arthrodesis are the available treatment options for the avascular neck of the femoral head (10).

Informed consent

Informed written consent was obtained from the parent of the patient for the publication of the data and clinical images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Acknowledgements

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Case Report

Macrophage Activation Syndrome complicated with acute pancreatitis as the first presentation of Systemic lupus Erythematosus

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Abstract

Hemophagocytic Lymphohistiocytosis (HLH) is a severe hyperinflammatory syndrome induced by aberrantly acquired macrophages and cytotoxic T cells. The primary form is called the Genetic form where as the secondary acquired form is most common in adults. Secondary HLH induced by autoinflammatory or autoimmune disorders is called Macrophage activation syndrome (MAS or MAS-HLH). Here we present a case of Systemic lupus Erythematosus presenting for the first time with MAS-HLH associated with acute pancreatitis, emphasizing the challenges in early detection and the need for prompt treatment, given the high mortality associated with MAS-HLH.

Key Words

Macrophage activation Syndrome, SLE, Pancreatitis

Introduction

Macrophage Activation Syndrome (MAS) is a life-threatening disorder, first described by Hadchouel et al in 1985(1).It belongs to the hemophagocytic lymphohistiocytosis (HLH) group of diseases, which includes Primary HLH and secondary HLH. Primary is the genetic form caused by the mutations affecting lymphocyte toxicity and secondary HLH is caused by infections/malignancies/ autoinflammatory or autoimmune disorders.

Secondary hemophagocytic lymphohistiocytosis associated with autoimmune diseases or autoinflammatory disorders is said to be Macrophage activation syndrome. As there will be overwhelming immune activation leading to cytokine storm, patients with MAS-HLH present with fever, cytopenia, liver dysfunction and a sepsis like syndrome that can rapidly progress into multiple organ failure(2)..

The incidence of MAS associated with Systemic Lupus erythematosus is re about 0.9% to 4.6%(3). Acute pancreatitis, can occur as an uncommon initial manifestation of SLE, can complicate MAS. Acute pancreatitis can be an associated or triggering factor for MAS in patients with SLE. Acute pancreatitis in SLE may arise from various causes like autoimmune inflammation, drug induced reactions or secondary to infections. We present here a case of MAS-HLH complicated with acute pancreatitis as the first presentation of SLE.

Case presentation

A 16-year-old female patient presented with a history of high-grade fever for 10 days duration, associated with nausea and abdominal pain. There were no respiratory symptoms, and she denied joint pain or hair loss. She complained of abdominal pain in the epigastric area. Her past medical and family history was non-significant.

On presentation to the ward, she was conscious and oriented with the GCS 15/15. She was febrile, with a temperature of 39.8°C, a Pulse rate of 102 bpm regular sinus rhythm, BP 90/60mmHg, and SPO_2 on room air 99%. She was also pale, and oral ulcers were noted. There was epigastric region tenderness, but no organomegaly or lymphadenopathy. The rest of her examination was unremarkable. Her abdominal ultrasound was normal, without evidence of organomegaly. Her chest X-ray was normal. A blood picture revealed pancytopenia. She was given barrier nursing care and has been started on empirical broad-spectrum antibiotic meropenem based on her clinical presentation and initial investigations after taking blood and urine cultures. Despite treatment with broad-spectrum antibiotics, she continued to have a fever. Her further investigations revealed that LDH-281u/l, serum ferritin-3390ng/ml, fasting triglycerides

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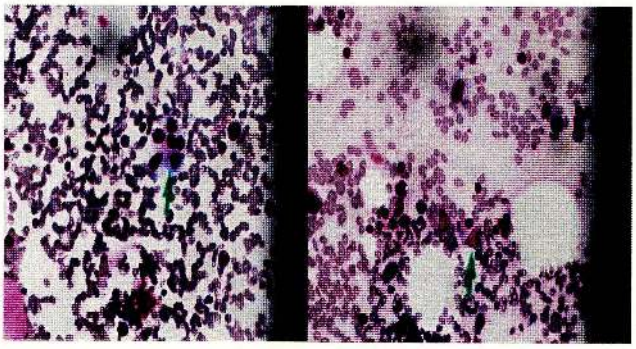
3.55U/L, and elevated liver transaminases. Viral serology for HIV and Ebstein bar virus was negative. Blood culture and urine culture showed no growth.

Table 1: Investigation

Investigation	On admission
WBC	$0.74 * 10^9$
Neutrophil	$0.21 * 10^9$
Lymphocyte	$0.48* 10^9$
Hemoglobin	9.2g/dl
MCV	84fL
MCH	29pg
Platelet	$119 * 10^9$
LDH	2815u/l
Ferritin	3000 ng/ml
Fasting Triglyceride	309 mg/dl
ESR	14 mm in first hour
CRP	4.6mg/l
Serum amylase	1940u/l
Sodium	128 mmol/l
Potassium	4.2mmol/l
Serum Creatinine	48 micromol/l
AST	296u/l
ALT	172u/l

On the 3rd day of admission, she complained of worsening abdominal pain mainly epigastric pain radiating to the back which was unrelated to meals. There was severe tenderness noted in the epigastric region. Blood was taken for serum amylase, and it was elevated at 1940u/l. A clinical diagnosis of acute pancreatitis was made. She was given intravenous fluid, and continued antibiotics, and analgesics. After 2 days her abdominal pain improved, and her general condition got better.



Figures 1 and 2- Bone marrow biopsy showing evidence of prominent histiocytes with hemophagocytic activity

In the meantime, her bone marrow biopsy showed evidence of prominent histiocytes with hemophagocytic activity as shown in Figures 1 and 2. Together with other clinical and biochemical parameters, she met the diagnostic criteria of HLH.

Her ANA was 1:2560 with a homogenous pattern, Ds DNA was negative and complement levels were low. With these results, she met the diagnostic criteria of SLE and the diagnosis of MAS-HLH was established she was treated with methylprednisolone pulse therapy for five days followed by oral prednisolone. Her counts started to rise, her fever subsided and her general condition improved and subsequently discharged home.

Discussion

MAS, which is currently grouped under secondary or acquired hemophagocytic lymphohistiocytosis (MAS_HLH), is a rare and fatal disorder that results from excess activation of T-cells and macrophages (4).

Clinically, MAS is characterized by symptoms such as persistent fever, cytopenia, liver dysfunction, and elevated levels of ferritin, LDH, and triglycerides. The hallmark of MAS is hemophagocytosis observed in bone marrow, liver, or lymph nodes, where activated macrophages engulf red blood cells, white blood cells, and platelets. Diagnosing MAS is challenging due to its overlap with other inflammatory conditions and infections, especially in patients with underlying autoimmune diseases like SLE. The criteria for diagnosing MAS include clinical features, laboratory abnormalities, and histopathological evidence of hemophagocytosis. The H-score, a diagnostic tool that incorporates clinical and laboratory parameters, is often used to assess the likelihood of HLH/MAS. However, differentiating MAS from other causes of systemic inflammation can be difficult, necessitating a high index of suspicion and prompt investigation. Our patient had a fever, a history of oral ulcers, cytopenia and low C3 and C4 levels, fulfilling the SLE diagnostic criteria. The association between SLE and MAS is well-documented, with studies indicating that up to 15% of SLE patients may develop MAS during their disease course.

Acute pancreatitis, although an uncommon initial manifestation of SLE, can complicate MAS, as

highlighted in this case. However, the relationship between acute pancreatitis and HLH was first considered in 1998 by Kanaji et al, who found that HLH can be associated with fulminant ulcerative colitis and acute pancreatitis (5).

Several studies have indicated that 53% to 85% of SLE patients with pancreatitis also have MAS (6). Acute pancreatitis in SLE patients with MAS is particularly concerning due to the additional inflammatory burden it imposes. Hence, The pancreas can be the target organ in MAS in patients with SLE warranting evaluation of pancreatic enzymes (7).

It is important to be aware that pancreatitis and MAS can occur concurrently, with an underlying autoimmune disease, such as SLE. As patients with MAS associated with pancreatitis have a high mortality rate, early recognition and prompt treatment help prevent complications(8).

Conclusion

Hemophagocytic Lymphohistiocytosis syndrome can present with a wide range of symptoms making the diagnostic approach challenging. A high degree of suspicion is required for the possibility of HLH and the early diagnosis should be done through the diagnostic criteria in addition to looking for causative factors of secondary HLH. MAS with acute pancreatitis in SLE needs early identification and prompt treatment to avoid complications and to improve the outcome

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Case Report

Late Onset Systemic Lupus Erythematosus Manifests As Lupus Nephritis, A Rare Presentation

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Abstract

Systemic lupus erythematosus(SLE) is a chronic, multisystemic autoimmune disorder typically affecting middle-aged individuals predominantly in women. Late-onset SLE occurs in individuals over 50, differs from classic SLE in terms of age, symptoms, organ involvement and severity. This case describes an elderly South-Asian woman who was under evaluation for skin rashes with impaired renal function, diagnosed to have discoid lupus with lupus nephritis(LN). She was treated with glucocorticoids and mycophenolate mofetil effectively, with improved renal function, thus delaying the need for dialysis. This case emphasizes timely diagnosis and treatment can significantly improve the outcome in late onset SLE with lupus nephritis(LN).

Keywords

South Asian woman, discoid lupus, lupus nephritis, late-onset SLE.

Introduction

Systemic lupus erythematosus(SLE) is a chronic, autoimmune disease with multisystem involvement that presents with a wide range of symptoms(1). It is more prevalent in women between the ages of 20 and 40, with a 10:1 female-to-male ratio(4). The aetiopathogenesis results from a combination of genetic, environmental, and hormonal factors that disrupt immune tolerance and trigger autoimmunity. Due to multi-system involvement, diagnosis and treatment of SLE requires a multidisciplinary approach. Late-onset SLE begins after the age of 50 yrs and differs from the classic form as they are less likely to develop skin manifestations, photosensitivity, arthritis, and nephritis but more prone to get serositis, lung involvement, and Sjögren's syndrome (2, 3). Additionally, there is a higher prevalence of positive rheumatoid factors, anti-Ro and anti-La antibodies, while anti-RNP antibodies and hypocomplementemia are less common(2). The case underscores the importance of detailed assessment, continuous monitoring, and collaboration between specialties to effectively diagnose and manage SLE in the elderly, particularly with atypical presentation, and highlights the need for a methodical diagnostic and individualized management strategies for late-onset SLE.

Case presentation

A 69-year-old female recently diagnosed with hypertension and dyslipidemia, presented with non-pruritic, hyperpigmented skin rashes over sun-exposed areas (Figure 1) which started as small patches and have been progressively worsening for four months duration. In addition, she reported hair loss, loss of weight, loss of appetite and early morning headache over the same period. She also complained of productive cough with yellowish sputum for 1 month duration. She didn't have chest pain, palpitation, orthopnea, paroxysmal nocturnal dyspnea. No dysuria, hematuria, or frothy urine. No history of fever, abdominal pain, nausea, vomiting, altered bowel habits, or gastrointestinal bleeding. No visual disturbances or seizures. She didn't have joint pain, back pain, oral or genital ulcers. No features of hypothyroidism. No bleeding manifestation. Medications before admission were Losartan, Prazosin, and Atorvastatin. No pet exposure recent travel history or high-risk behavior. Family, allergic, and past surgical histories were unremarkable.

On examination, she was pale and her body temperature was 38.3°C. Hyperpigmented skin rashes were noted over the face, neck, bilateral forearms, and hands (Figure 1) with bilateral pitting ankle edema. Her blood

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pressure was 180/90mmhg and her heart rate was 110 beats per minute and no murmur. The respiratory system examination revealed vesicular breathing with coarse crepitations and increased vocal resonance over bilateral lower zones with a respiratory rate of 15 per minute and saturation was 96% on room air. Abdominal and neurological examinations were unremarkable except for grade 2 hypertensive retinopathy changes in fundus examination.

Figure 1: Photosensitivity rash

Table 1: Baseline Investigations

Investigations	Results
WBC	6.88x10^9/l (4-10)
Neutrophil	60.8% (50-70)
Lymphocyte	28.2% (20-40)
Hemoglobin	8.4g/dl (11-15)
MCV	85.1fl (80-100)
MCH	26.3 pg (27-34)
RDW	16.2% (11-16)
Platelets	281x10^9/l (150-450)
ESR	83mm/hr (<20)
CRP	12.6mg/l (0-3)

Her Potassium was slightly elevated(5.2 mmol/l), Serum creatinine increased(233mmol/l) with eGFR of 18ml/min/1.73m^2. Urine full report showed Protein – 3+, dysmorphic RBC with ring form 95%, pus cells – 6-8 /hpf, RBC–20-25/hpf, epithelial cells–few. UPCR was elevated (882.4mg/mmol). C-ANCA was positive, but P-ANCA was negative. Her DS-DNA was equivocal. ANA was Positive(1/640). Sputum culture isolated Coliform and Pseudomonas species. Serum Corrected Calcium was normal and Tuberculosis was excluded.

ECG was unremarkable except sinus tachycardia and 2D Echocardiography was normal. Blood Picture showed anemia of chronic disease. An ultrasound scan of the abdomen showed bilateral renal parenchymal changes. Serum protein electrophoresis showed decreased albumin with increased alpha-1 globulin but no Monoclonal peak. HRCT Chest showed Bronchiectasis of the lingula lobe and middle lobe and no evidence of pulmonary hemorrhage.

Renal Biopsy -Features are compatible with lupus nephritis. Class IIIC, Activity index–2/24, Chronicity index–6/12. Skin biopsy was not performed as the diagnosis was made with renal biopsy.

The activity index was 2/24 and the chronicity index was 6/12. She was commenced on oral Hydroxychloroquine 200mg/daily and mycophenolate mofetil 600mg/m^2.

Discussion

This case features a 69-year-old woman diagnosed to have late-onset SLE supported with discoid lupus and biopsy-proven lupus nephritis(LN) but lacked common features seen in early-onset SLE. In atypical presentations like this, the American College of Rheumatology(ACR) and Systemic Lupus International Collaborating Clinics(SLICC) criteria are helpful in confirming diagnosis. The SLICC allows diagnosis with fewer markers if lupus nephritis is confirmed on biopsy alongside positive ANA and/or anti-dsDNA antibodies. Lupus nephritis, a serious complication involving the kidneys, is less common in late-onset SLE but can still occur(4), as seen in this case. Usually, kidney biopsy reveals the characteristic "full-house" immunofluorescence pattern. There is immunostaining for IgG in more than 90%; IgA and IgM in 60-70%; and C3 and C1Q in around 80% of cases(5), indicating a widespread polyclonal autoimmune response due to autoreactive B-cells. This is a hallmark finding in lupus nephritis(4).

Managing lupus nephritis is crucial due to its potential to progress to end-stage renal disease in around 10% of cases. Treatment usually starts with high-dose glucocorticoid pulse therapy, followed by daily glucocorticoids combined with immunosuppressive agents like cyclophosphamide, azathioprine, or mycophenolate mofetil. Induction therapy focuses on reducing inflammation, while maintenance therapy with

mycophenolate mofetil helps prevent further immune-related kidney damage. Although lupus nephritis is a serious condition, late-onset SLE generally has a milder course with less systemic involvement compared to early-onset cases(4).In this case, she responded well to the treatment with steroids, Hydroxychloroquine and immunosuppression, led to a reduction in creatinine levels and significant clinical improvement. This case highlights the importance of timely diagnosis and appropriate management, even in older patients with atypical SLE presentations, to achieve better clinical outcomes.

Conclusions

Photosensitive skin rashes with nephritic syndrome can be a first presentation of SLE even in elderly. Clinicians should strongly consider SLE, when a renal biopsy shows a full-house immunofluorescence pattern, which strongly indicates lupus nephritis(LN) a life-threatening complication. Early detection and prompt treatment are crucial, because it may lead to organ failure if not addressed on time. Personalized approach enhances patient outcomes and reduces the risk of treatment-related complications.

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Case Report

Markedly high peripheral blood eosinophilia: A rare manifestation of Eosinophilic granulomatosis with polyangiitis

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Abstract

Eosinophilic granulomatosis with polyangiitis (EGPA) is a systemic necrotizing multi-system vasculitis. EGPA presents with severe eosinophilia is rare. Here we report a case of EGPA, presenting with markedly high eosinophilia with tissue infiltrates. It was successfully treated with immunosuppressive medications.

Keywords

EGPA, Late-onset asthma, Peripheral neuropathy, Markedly high eosinophilia

Introduction

EGPA is a multi-system disorder, predominantly affecting small to medium vessels and is associated with allergic rhinosinusitis, late onset poorly controlled asthma, blood and tissue eosinophilia, peripheral neuropathy, migratory lung opacities, vascular and extravascular granuloma (1). This could be fatal if left untreated. Treatment is primarily with corticosteroids and, severe disease is managed with the addition of other immunosuppressants (2).

Case presentation

A 57-year-old previously healthy female has presented with chronic cough with non-purulent sputum and wheeze for more than six months. She also had exertional breathlessness of mMRC Grade 3, and chest tightness. She also reported anorexia and unintentional weight loss of 5kg over the same duration. She didn't recall a history of fever or night sweats. There was no history of atopy. She was a non-smoker. There were no focal symptoms of malignancy such as altered bowel habits, hemoptysis, hematuria, or abdominal pain. Her BMI was 18kg/m^2. There was a polyphonic wheeze in both phases of respiration. She developed progressive, asymmetrical sensory-motor neuropathy involving both upper and lower extremities manifested as right-sided foot drop and left-sided ulnar claw hand. Cranial nerves were normal. The rest of the examination was normal.

Her laboratory data revealed leukocytosis (50,780/microL) with markedly high eosinophilia (74%-37,580/microL) with high ESR (88mm/1st hour) and CRP of 24 mg/L. Her renal and liver function tests, urinalysis, Chest X-ray, Ultrasonography of the abdomen and pelvis, and transthoracic echocardiogram were all normal. Further, her contrast-enhanced computed tomography of Chest-Abdomen-Pelvis, upper and lower gastrointestinal endoscopic examinations did not reveal any significant pathology. Her blood picture revealed marked eosinophilia and bone marrow biopsy showed active marrow with granulocytic hyperplasia with predominant eosinophil lineage. Histology of combined sural nerve and muscle biopsy showed tissue eosinophilia. Her pANCA was positive with negative cANCA. Diagnosis of EGPA was made as she was having unexplained eosinophilia, late onset of asthma, mononeuritis multiplex and extravascular eosinophil accumulation on biopsy with positive pANCA.

She was initiated on treatment with oral Prednisolone 1mg/kg/day for 6 weeks and pulse therapy of IV Cyclophosphamide 15mg/kg monthly for 3 months with MESNA. After the induction of remission, a maintenance dose of azathioprine was commenced with low-dose prednisolone. Her respiratory and neurological symptoms improved with therapy and follow-up at the clinic.

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Discussion

EGPA, previously known as Churg-Strauss syndrome is a rare, progressive small to medium vessel vasculitis that can lead to death due to multi-organ failure. It manifests into a unique sequence of prodromal, eosinophilic, and vasculitic phases. The prodromal phase is usually adult onset and is characterized by atopy, allergic rhinitis, and bronchial asthma. The eosinophilic phase is distinguished by peripheral blood eosinophilia with organ infiltration, especially lung and gastrointestinal tract. Subsequently patient develops life life-threatening systemic vasculitic phase, often associated with vascular and extra-vascular granulomatosis and constitutional symptoms, especially fever, fatigue and weight loss. Asthma is the cardinal feature of EGPA. Patients can have life-threatening cardiac, skin, nervous and gastrointestinal manifestations (3).

Most commonly used criteria for diagnosis is the American College of Rheumatology (ACR). It includes the following six criteria: asthma, eosinophilia of more than 10% (more than 1500/microL), mono or polyneuropathy, transient or migratory pulmonary opacities, paranasal sinus abnormality and extravascular eosinophils accumulation on biopsy. The presence of at least four criteria confirms EGPA firmly. Our patient fulfilled 4 criteria. Patients with EGPA often have eosinophilia of 5000-9000/microL. However, our patient had eosinophilia of 37,580/microL. Markedly high eosinophilia is described in eosinophilic leukemia and idiopathic as well as a malignancy-related hypereosinophilic syndrome (4). 30 to 60 % of patients have positive ANCA with a majority (70 to 75 %) of pANCA.

Commonly using a scoring system to assess the disease activity is the "Five-Factor Score" (FFS), used to guide initial therapy and prognosis. Age >65, cardiac insufficiency, gastrointestinal involvement, renal insufficiency, absence of ear, nose and throat manifestations are considered in FFS. This score ranges from 0 to 2. A score of 0 when all factors are absent, a score of 1 for one factor, and a score of 2 for two or more factors. (5) (6). Our patient's FFS score is 1.

Early initiation of immunosuppressive therapy is mandatory for good clinical outcomes. EGPA is treated with Prednisolone doses of 0.5 to 1 mg/kg/daily for 6 to 12 weeks, or until remission. Glucocorticoid is combined with Cyclophosphamide for induction of severe disease (FFS >2), FFS of 1 (especially with cardiac or central nervous system manifestations) or FFS of 0 with positive ANCA as these patients tend to develop multi-organ failure. After induction of remission, Prednisolone was gradually tapered, and maintenance therapy with Azathioprine was commenced as a steroid-sparing agent and continued for 12 to 18 months. The disease has a risk of relapse hence close follow-up is necessary (6).

Conclusion

This case illustrates the fact that treating clinicians to always consider atypical presentations of rare diseases to avoid diagnostic delays of fatal disorders.

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Case Report

Small vessel vasculitis

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Abstract

Vasculitis is inflammation of vessel walls. Different types of vasculitis preferentially affect different sizes of blood vessels. Small vessel vasculitis is a rare immunological disease that affects arterioles, capillaries and venules. The inflammation can restrict blood flow and damage vital organs and tissues.

Keywords

Small vessel vasculitis, ANCA negative

Introduction

The SVV are divided into those conditions associated with circulating ANCA, and those not associated with ANCA. Those conditions that are not associated with ANCA, are associated with immune-complex deposition.

Case report

A 15-year-old girl, presented with 25 days of high-grade fever associated with chills and bilateral knee joint pain which is preceded by sore throat. After 10 days she developed a reddish rash on the bilateral lower limb (feet) later it progressed to the bilateral upper limb. She complained of numbness of bilateral hands and feet, then it progressed to gangrene formation. In due course, she also complained of abdominal pain but no history of malena, hematuria, oliguria, and breathlessness. Also, she had a history of hair fall, dry eyes, and dry mouth but no history of rashes, oral ulcers and Raynauds. She started with intravenous methylprednisolone pulse and continued with high-dose steroids. However, while on treatment she defaulted.

She had no significant past medical and surgical history, but she had an unknown drug allergy. On examination she was febrile, ill-looking, and pale, her pulse rate was 80 beats/min, blood pressure in her right arm was 133/90 mmHg, her left arm was 130/89 mmHg, there was no lymphadenopathy and no peripheral edema. The right-side radial artery pulse was weak whereas the left was normal. Posterior tibial and dorsalis pedis artery pulses were unable to feel bilaterally. Wet gangrene was noted in bilateral toes and dry gangrene was noted in the 2nd finger of the right hand. The ulcer was noted on the anterior aspect of the medial malleolus of the right lower limb. Other systemic examinations were normal.

Figure 1. Bilateral foot wet gangrene

Figure 2. Wet gangrene in hands

Figure 3. Right medial malleolus ulcer

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Table 1: Laboratory and special investigations

WBC	21.40	ASOT	400	Total protein	69	Serum creatine	54
NEUTROPHIL	16.87	RF	<20	Albumin	21	ESR	116
LYMPHOCYTE	3.4	ANA	NEGATIVE	Globulin	48	UPCR	1.02
Hemoglobin	8.58	DsDNA	NEGATIVE	Total bilirubin	10.1	Serum ferritin	234
Platelet	570	TSH	0.88	Direct bilirubin	7	HepB surfaceAg	NEGATIVE
AST	68	Ft4	1.74	Na^+	130	Hep C Ab	NEGATIVE
ALT	88	PT	13.4	K^+	4	P ANCA	NEGATIVE
ALP	209	APTT	22	CRP	154	C ANCA	NEGATIVE
Mantoux	NEGATIVE	Cryoglobulin	POSITIVE	VDRL	NEGATIVE	HIV	NEGATIVE

Cryoglobulin may be false positive as the test done on while on enoxaparin, UFR protein +, pus cells 8-10, red cells- nil, Bilateral distal arterial duplex- monophasic flow in distal arteries could be due to arterial spasm/ vasculitis. Arterial duplex of right upper limb normal, 2D Echo- normal, Blood culture- negative, sputum AFB- not seen, Urine culture- coliform isolated, sensitive to amikacin, co-amoxiclav, cotrimoxazole, nitrofurantoin, piperacillin, Wound swab- 2 types of coliforms, coagulase-negative staphylococcus isolated.

Skin biopsy- appearance is in keeping with early features of SVV, Blood picture- reactive neutrophil leukocytosis and thrombocytosis, anemia with marked roulcaux compatible with anemia of chronic disease, red cell microcytosis,

She had undergone amputation of 4 toes in her right foot. She developed wet gangrene on the left 2^{nd},5^{th} and right 2^{nd} fingers. She was managed with intravenous antibiotics. She was started with an intravenous methylprednisolone pulse of 1g daily for 3 days and changed to oral prednisolone 45mg/day also she started with an intravenous cyclophosphamide pulse of 75mg fortnightly for 6 weeks and planned to continue 3 weekly intervals. With these treatments progression of the disease was controlled. She was discharged with a tail-off regimen of steroids.

Discussion

SVV can be categorized as ANCA associated or non-ANCA associated vasculitis. SVV caused by the deposition of immune complexes leads to hemorrhaging from the involved vessels.

A purple or reddish rash on the legs, buttocks, torso or upper body is the telltale symptom of SVV. Other symptoms of SVV include fever, weight loss, myalgia and arthralgia, kidney and gastrointestinal involvement. A physical examination can help confirm if the disease is limited to skin or systemic.

Skin biopsies can provide valuable diagnostic information. Relevant antibody and blood testing can be done during the diagnosis. SVV can co-occur with other autoimmune diseases such as rheumatoid arthritis, Crohn's disease, SLE, etc.

The first step of management is to address the causative agent. Some will also require corticosteroids in combination with other immunosuppressive medications such as azathioprine and methotrexate. Other potential medications may include colchicine, antihistamines, hydroxychloroquine and dapsone alone or in combination. Symptoms of SVV will often resolve within a few weeks to months if there is no organ involvement.

Local ulceration from cutaneous small vessel vasculitis can lead to wound infection or cellulitis, chronic leg ulceration and scar formation.

Referneces

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3. https://pmc.ncbi.nlm.nih.gov/articles/PMC10236953/
4. https://journals.lww.com/mjdy/fulltext/2014/07020/a_case_of_small_vessel_vasculitis.21.aspx
5. https://www.merckmanuals.com/professional/musculoskeletal-and-connective-tissue-disorders/vasculitis/overview-of-vasculitis
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7. https://dermnetnz.org/topics/cutaneous-small-vessel-vasculitis#:~:text=The%20most%20severe%20complications%20of,Chronic%20leg%20ulceration.

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1. Author. Eisen HN. *Immunology: An Introduction to Molecular and Cellular Principles of the Immune Response*. 5th ed. New York: Harper and Row, 1974.

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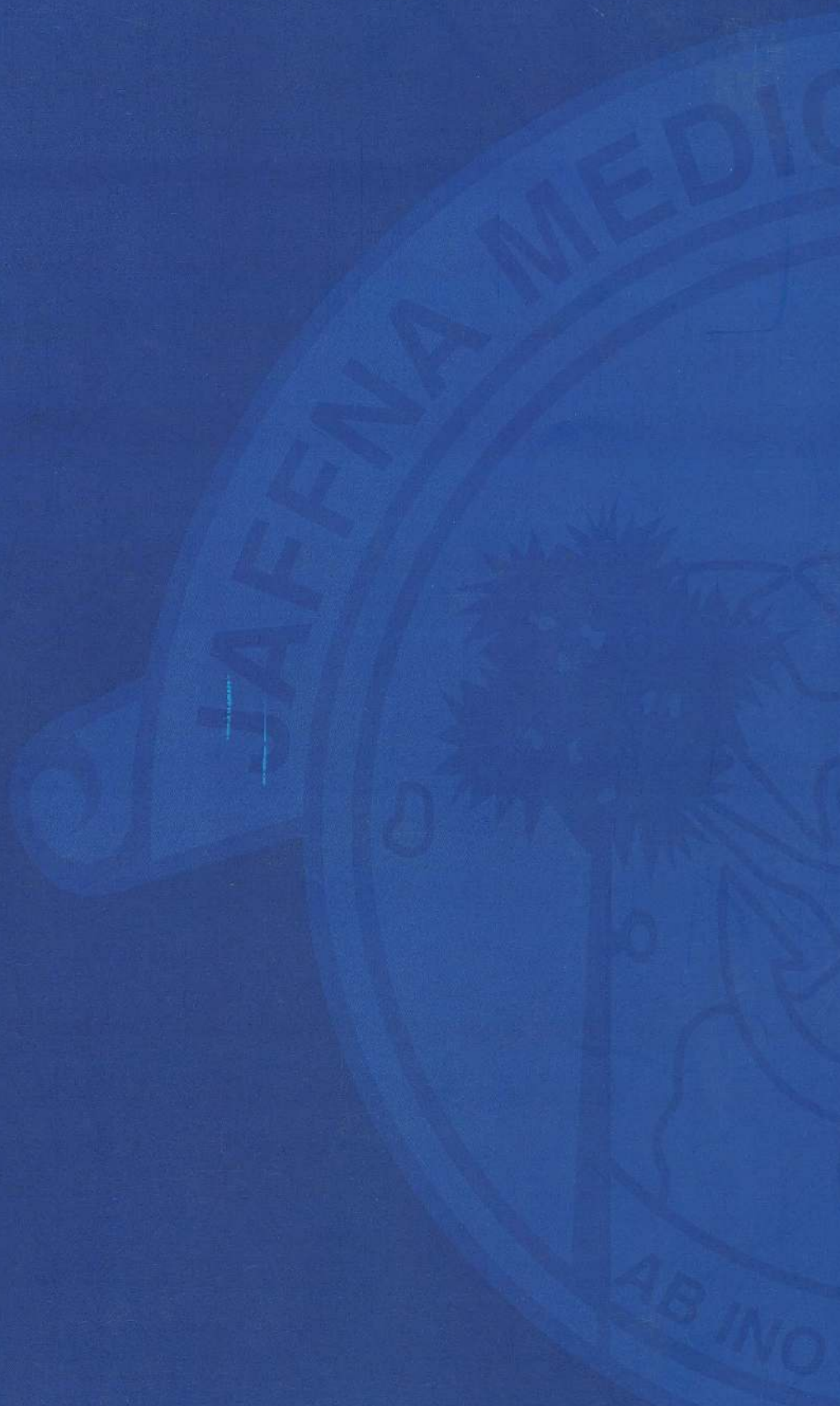

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