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The Galle Medical Journal

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GALLE MEDICAL JOURNAL: INSTRUCTIONS TO AUTHORS

The *Galle Medical Journal* is published by the Galle Medical Association. The *Journal* is published quarterly in March, June, September and December each year. Submissions are accepted throughout the year. The aims of the journal are to foster co-operation among the medical fraternity and to be a forum to make literary contributions, share experiences encountered in medical practice, update their knowledge and have debates on topics related to all aspects of medicine. Also, we attempt to cater to the educational needs especially of the postgraduate trainees. The *Journal* publishes original articles, reviews, leading articles and case reports. When an article is submitted for publication, we expect that the work it reports has not been published, submitted simultaneously to another journal or accepted for publication elsewhere. All manuscripts will be reviewed anonymously before acceptance.

Manuscripts must be submitted with the text typed in 12-point Times New Roman font double spaced. Text and all illustrative material should be submitted in two hard copies and the electronic version in *Microsoft Word* document format. In order to avoid delay we require authors to comply with the following requirements. **All manuscripts should accompany a covering letter indicating the number of words in the manuscript, institution where ethical clearance was granted, conflict of interests and contact details of the corresponding author.**

Types of contributions:

Review articles and Leading articles: We encourage submission of review or leading articles which are less than 3000 words in length and address topics of current interest. They should be supported by no more than 20 references. Submissions may be subjected to external review before acceptance.

Original articles: Should normally be in the format of introduction, methods, results and discussion. Each manuscript must have a structured abstract of 200 words. The text should be limited to 3000 words and maximum of 5 tables/ figures taken together with no more than 15 references. Lengthy manuscripts are likely to be returned for shortening. The discussion in particular should be clear, concise and should be limited to matters arising directly from the results. Avoid discursive speculation.

Case Reports: These should not exceed 750 words and 5 references; no abstract is required. Case report should be informative and devoid of irrelevant details. Case report should have a clear message or learning point and this should be highlighted adequately. Rarity of the case does not mean it is suitable for publication. Written consent of the patient should be submitted together with the case report, especially when photographs are used.

References:
These should conform to the Vancouver style. The reference in the text should be numbered consecutively in Arabic numerals in parentheses in the same line of the text in the order in which they appear. The first five authors should be listed and if there are more than five, then the first three should be listed followed by *et al.* Examples are given below:

1. Kumar A, Patton DJ, Friedrich MG. The emerging clinical role of cardiovascular magnetic resonance imaging. *Canadian Journal of Cardiology,* 2010; **26**(6): 313-22.
2. Calenoff L, Rogers L. Esophageal complication of surgery and lifesaving procedures. In: Meyers M, Ghahremani G, eds. Iatrogenic Gastrointestinal Complications. New York: Springer, 1981: 23-63.

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Units / Abbreviations:

Authors should follow the SI system of units (except for blood pressure which is expressed in mmHg). Authors should use abbreviations sparingly and they should be used consistently throughout the text.
Manuscripts that do not conform to these requirements will be returned for necessary modifications.
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Editorial

Medical research; ethical propriety and conformity

The requirement to adhere to ethical norms **is** an essential universal prerequisite of medical research today. Ethical violations are of varying hues of severity. Gone are the days of cruel medical experiments done on live subjects by the Nazis and the inhuman Tuskegee study done in the United States during modern times. In the "Tuskegee study of untreated syphilis in the Negro male" the natural history of syphilis was studied without treating infected patients. The study commenced in 1932, and infected subjects were not given medication even when penicillin became the drug choice for syphilis in 1947 and they were left untreated until 1972. The patients were told that they were being treated for "bad blood", violating the fundamental tenet of *informed consent*. It is held that the Tuskegee experiment was ethically unjustified.

Going back farther in time, Edward Jenner, the English physician who is considered as the medical pioneer developed the smallpox vaccine in 1796, in the course of his 'research;' had injected an unsuspecting 8 year-old child with pus taken from a cowpox lesion and exposed her to an infected carrier of smallpox. Although Jenner is considered as a medical doyen, can his actions be held ethically acceptable from a current context? This shows that normative ethical standards have varied and progressed over time and space, and that they are in a state of flux.

Although ethical improprieties of such gruesome magnitude are not seen today, we note that there have been attempts at unethical research at different levels globally: paucity of information given to research subjects (violation of the concept of informed consent), poor study design, fabrication, plagiarism etc.

Fabrication and dishonesty have led to resignations of leaders in key professional and academic bodies; retraction of papers and orations. Ethics Review Committees have a wide societal view with a mixed composition of professionals and lay persons and they play a key role in assessing and reviewing study designs. Their role goes beyond the mere approval of studies as they have got to ensure that the research work conforms to and abides by the approved study design. Even if there is no dishonesty, bad research can be considered as being unethical.

It is equally important for the publication process to take the moral high ground and ensure that published papers have strictly followed ethical norms. The review process too should be of the highest moral, academic and professional level of integrity with a zero tolerance to ethical impropriety. The *Galle Medical Journal* too strives to maintain highest ethical standards at all times, with the trust reposed in the *Journal* by its readership and our mandatory moral obligation to the global medical community.

Satish K Goonesinghe
Eisha I Waidyarathne
Editors in Chief / GMJ

Constipation in children: The bird's eye view

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With a worldwide estimated prevalence of 9.5%, constipation is considered as a significant health problem in children (1). However, epidemiological research in Asian countries has shown a much higher prevalence of up to 32% according to standard Rome III criteria (2). Similar studies in Africa show a prevalence of 27% in Nigerian school children (3). The highest prevalence noted in Sri Lankan children is 15.5% (4). Therefore, it is evident that a disease previously thought to be highly prevalent in affluent societies is becoming common among more impoverished societies showing a clear epidemiological shift. This changing epidemiological pattern indicates that childhood constipation is glooming to become a significant public health problem, especially in developing countries across the world.

Risk factors for childhood constipation are also found to be common in all communities. Psychological stress has been identified as an essential risk factor for developing constipation (5). Stressors such as home-related events (divorce of parents, severe illness in a family member) and school-related events (bullying, failing an exam) are known to predispose children to develop constipation (6). Similarly, emotional, physical, and sexual abuse are also identified as precipitating factors (7). With the changing socio-economic landscape and pressure for education, these factors are becoming more common predisposing many children to develop constipation. The fast-food industry is proliferating across the world and in Sri Lanka during the recent decade. Recent studies have shown a higher prevalence of consumption of junk food and sugary drink in children (8, 9). Consumption of fast- food is a known predisposing factor for childhood constipation (10). Diet low in fibre is also associated with childhood constipation (11, 12). All these factors predispose current-day children to develop constipation, and therefore we are facing an uphill task in battling these worldwide trends shortly in view to prevent constipation.

Exact pathophysiological mechanisms of childhood constipation remain elusive and unclear. However, the majority believe it is a result of stool withholding after the painful passage of stools. When a child senses the necessity to pass stools, he / she tightens the gluteal muscles and resists the passage of stools to avoid the pain. This leads to an accumulation of faeces in the rectum. As the faecal mass gets larger, the rectal wall stretches to accommodate stools leading to dilatation of the rectum and loses the urge of defecation. When this mass finally passes through the anus, it leads to pain, which triggers more withholding behaviour. Once sets in, it is challenging to break the vicious cycle of pain-withholding behaviour.

The effects of constipation have significant personal and public health repercussions. Children with constipation have a poor health-related quality of life in all dimensions, namely physical, social, school, and emotional (13). Youssef, *et al.,* reported health-related quality of life of children with constipation was worse than children with severe organic gastrointestinal diseases such as inflammatory bowel disease (14). Furthermore, school absenteeism and poor school performances were also noted in children with constipation, indicating significant implications for their future as adults (15). Constipation is one of the leading

gastro-enterological conditions for healthcare consultation in children. It had been shown that children and young adults with constipation sought more medical consultation, higher emergency room visits, and higher outpatient costs (16).

The criteria for the diagnosis of constipation have changed. Rome III criteria were used to diagnose constipation from 2006 to 2016 (17) . In 2016, they were replaced by the new Rome IV criteria. The significant change in Rome IV criteria was bringing down the duration of symptoms from 2 months to 1 month (18). This trend will also contribute to an increase in the prevalence in future epidemiological studies.

Constipation is a clinical diagnosis, and can easily be made using the existing Rome IV criteria (Box 1). A thorough history of bowel habits is mandatory to evaluate a child with constipation. It is also essential to explore the other symptoms associated with constipation, family, and social history to elicit stressful events and other social determinants. A dietary history is a mandatory component as a diet low in fibre and junk food consumption is known factors that precipitate symptoms of constipation (10, 12). The clinician should also inquire about the impact of constipation, such as its effects on quality of life and school performances, to explicitly understand the clinical picture. The physical examination should begin with an assessment of growth and dysmorphic features. The faltering of the growth curve is an early indication of hidden organic disease in some children. An abdominal examination may reveal the presence of faecal masses, indicating significant faecal retention. The perianal examination is a mandatory component of examining a child with constipation, which reveals faecal matter staining underwear indicating the presence of faecal incontinence and fissures explaining the pain, which leads to retentive behaviour. Digital examination of the rectum is rarely needed and should only be performed by an experienced clinician to detect faecal masses in the rectum and the sphincter tone (19). Examination of the lumbosacral spine may reveal features of spinal bifida occulta (haemangioma, a tuft of hair, asymmetry of the gluteal cleft) indicating defective innervation of the rectum and the sphincter complex.

Clinicians tend to order several common investigations when they encounter a child with constipation. Testing for hypothyroidism is still practised even though most children with hypothyroidism tend to have normal bowel habits (20), and constipation being a rare occurrence in hypothyroidism (21). Abdominal X-ray is another investigation that is commonly used to assess the degree of faecal loading. Several studies have shown the poor inter- and intra-observer reliability of X-rays in assessing the severity of constipation in children (22, 23). Most other investigations such as colonic transit studies, high resolution anorectal and colonic manometry, and defaecography are only needed in children with severe constipation refractory to standard medical care at least for more than three months.

Box 1: Definition of functional constipation according to Rome IV criteria

Must include at least 2 of the following occurring at least once per week for a minimum of 1 month with insufficient criteria for a diagnosis of irritable bowel syndrome:

1. Two or fewer defecations in the toilet per week in a child of a developmental age of at least 4 years
2. At least 1 episode of faecal incontinence per week
3. History of retentive posturing or excessive volitional stool retention
4. History of painful or hard bowel movements
5. Presence of a large faecal mass in the rectum
6. History of large diameter stools that can obstruct the toilet

After appropriate evaluation, the symptoms cannot be fully explained by another medical condition.

Management of constipation in children is far beyond prescribing drugs. The main components include modifying lifestyle and diet, inculcating a toilet routine, judicious use of laxatives, use of biofeedback, and pelvic floor physiotherapy in children who do not respond to conventional medical interventions. When constipation is refractory to medical management, surgical interventions, and novel therapeutic strategies such as sacral nerve stimulation is indicated. Although commonly used in day to day clinical practice, some of these interventions has not been studied in randomized controlled trials. Therefore, most of the management strategies are not evidence-based and depend on the clinician's individual experiences.

As children with constipation are known to face stressful life events, careful consultation involving parents would help to alleviate problems at home. In addition, children need to be taught coping mechanisms. Avoidance of home and school-related punishments is another aspect that could minimize with adequate counseling of parents and teachers. Although diet low in fibre is a known precipitating factor, several studies have failed to show the benefit of a high fiber diet in treating constipation (24). The correct approach is not just to increase fibre in the diet but after the dietary assessment if the diet is low in fibre, to increase it to the recommended normal level (5 grams + the age of the child in years) (25). As most children have stool withholding behaviour, proper toilet training, and encouragement to use toilets with the urge of defaecation with a rewarding system is helpful in the management.

The first step in the pharmacological intervention is disimpaction of the rectum. Although many clinicians tend to use suppositories and enemas in Sri Lanka, most international guidelines recommend using high dose oral polyethylene glycol (1.5 g/kg/day) or lactulose (4-6 ml/kg/day) (25). Once disimpacted, it is imperative to prevent reimpaction by using maintenance therapy with osmotic laxatives (lactulose, polyethylene glycol), and stimulant laxatives (bisacodyl) in much lower dose compared to disimpaction. Other drugs such as magnesium sulfate, docusate sodium, and mineral oil have also been used during the maintenance phase. Novel drugs such as lubiprostone (a chloride channel activator specific to the gastrointestinal tract), linaclotide and plecanatide (guanylate cyclase C receptor activator), and prucalopride (5-HT receptor agonist) have not shown to be very useful in children during the maintenance phase. Pelvic floor physiotherapy consists of many facets, including training in the exercise of pelvic floor muscles, proper straining techniques, and increasing awareness of sensations. Novel data that are emerging show that this approach is more effective compared to standard medical management (26).

When the medical interventions fail, and symptoms of constipation persist, surgical interventions may be needed after proper evaluation of the colon with contrast studies, anorectal and colonic manometry. The interventions include botulinum toxin injection to anal sphincter complex, anal myectomy, antegrade continent enemas, colonic resection, and colostomies. However, currently, the determination of surgical interventions depends on the experience and the clinician's preference and therefore demands more evidence from novel research.

In summary, childhood constipation is a highly prevalent gastrointestinal disorder which amounts to a significant public health problem. The current evidence indicates the prevalence and risk factors are more commonly seen in developing countries and Asia and could contribute to draining the public health funds in the future unless the preventive measures are implemented soon. Constipation is a clinical diagnosis and can easily be made by using Rome IV criteria. Most of the currently available investigations are not helpful in the day-to-day management of children with constipation and only required in refractory constipation cases. Combination of both lifestyle modifications and medical management help to alleviate symptoms and improve the wellbeing of children. Surgical interventions are reserved for children with medically refractory constipation.

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The World Health Organization dengue case classifications

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Dengue, a viral haemorrhagic fever causes a significant burden to healthcare systems of countries in the tropics and subtropics (1,2). In recent years, considerable variations in disease presentations involving different organ systems have been documented (1, 3-7). The clinical importance of the different dengue case classifications has been a matter of debate (8,9). The 1997 World Health Organization (WHO) dengue classification, classified the disease as: dengue fever (DF), dengue haemorrhagic fever (DHF), and dengue shock syndrome (DSS). In 2009, a revised classification was released which classified the disease into "dengue" and "severe dengue", with or without "warning signs" (Table 1) (8,10).

Retrospective studies from Brazil and South-East Asia have compared the two WHO dengue case classification systems (Table 2 (11-16)). In 2011, Barniol, *et al.,* included patients from the Eastern Mediterranean, American and South-East Asian regions and concluded the 2009 classification had greater clinical usefulness in dengue case management and surveillance (16). A large retrospective Brazilian study found considerable agreement between the two classification systems, but the 2009 guidelines had a higher sensitivity in the diagnoses of severe cases (11). Similar studies from Southeast Asia also found the 2009 classification to be more useful clinically (14,15).

Studies from Sri Lanka have also compared the two dengue classification systems (Table 1). In 2017, Sri Lanka faced its largest dengue epidemic (17, 18). A large multicentre study (that included more than 1500 patients) from Sri Lanka during this epidemic compared the two WHO dengue classification systems (9). The 2009 dengue classification was found to be better at detecting disease severity. The number of warning signs correlated with the severity of dengue and the presence of four or more warnings signs was found to be significantly associated with severe dengue. A major drawback of the 1997 dengue classification is that it focuses mainly on plasma leakage and its associated haemodynamic instability, and fails to consider organ dysfunction as a manifestation of disease severity. For example, in the Jayarajah, *et al.,* study, three DF patients were reclassified as severe dengue (according to the 2009 classification) due to the presence of organ dysfunction and excessive bleeding (9). Wanigasuriya, *et al*., and Bodinayake, *et al.,* also found the 2009 dengue classification to be more useful (19, 20). Similarly, Jayaratne, *et al*., found the 2009 classification to be better and clinical findings such as abdominal pain, vomiting and bleeding manifestations were more prevalent in severe dengue (21).

Although the 2009 WHO dengue classification was more useful in diagnosing clinically severe disease, there are several practical concerns. According to the 2009 guidelines, only one warning sign is sufficient to alert physicians to the need for immediate assessment or intervention. Although, waiting for more than 3 warning signs to manifest would increase the predictive value, it may considerably delay diagnosis and intervention, and the patient may develop more severe disease with complications (9).

Table 1: WHO dengue case classifications

WHO 1997 dengue classification	WHO 2009 dengue classification	WHO classification of Dengue infections and grading of severity 2011			
		DF/DHF	**GRADE**	**SIGNS and symptoms**	**Laboratory**
Dengue Fever (DF) Acute febrile illness with two or more of the following: - Headache - Retro-orbital pain - Myalgia - Leukopenia - Arthralgia - Rash - Hemorrhagic manifestations - Supportive serology or occurrence at the same location as other confirmed cases of dengue fever **Dengue Hemorrhagic Fever (DHF)** All of the following must be present: Fever or history of acute fever, lasting 1-7 days, occasionally biphasic Hemorrhagic manifestations: - Positive torniquet test; - Petechia, equimosis, purpura or bleeding from mucosa, gastrointestinal tract, injection sites or other locations; or - Haematemesis/melena Thrombocytopenia (<100,000 platelets per mm^3) Evidence of plasma leakage due to increased vascular permeability **Dengue Shock Syndrome (DSS)** DHF with hypotension for age or narrow pulse pressure (<20 mmHg), plus one of the following: - Rapid and weak pulse - Cold, clammy skin, restlessness	**Dengue without warning signs** Fever and two of the following: - Nausea, vomiting - Rash - Aches and pains - Leukopenia - Positive tourniquet test **Dengue with warning signs** Dengue as defined above with any of the following: - Abdominal pain or tenderness - Persistent vomiting - Clinical fluid accumulation - Mucosal bleeding - Lethargy, restlessness - Liver enlargement > 2 cm - Laboratory: increase in HCT concurrent with rapid decrease in platelet count **Severe dengue** Dengue with at least one of the following criteria: Severe plasma leakage leading to: - shock (DSS) - fluid accumulation with respiratory distress Severe bleeding as evaluated by clinician Severe organ involvement - liver: AST or ALT > 1,000 -CNS: impaired consciousness - failure of heart and other organ	**DF**		Fever with two of the following: Headache. Retro-orbital pain. Myalgia. Arthtralgia / bone pain. Rash. Haemorrhagic manifestations. No evidence of plasma leakage.	Leucopenia (wbc 5,000 cells/mm^3) Thrombocytopenia (Platelet count <150,000 cells/mm^3) Rising haematocrit (5% - 10%) No evidence of plasma loss.
		DHF: non-shock	DHF-I	Fever and haemorrhagic manifestation (positive tourniquet test) and evidence of plasma leakage	Thrombocytopenia <100,000 cells/mm^3 HCT rise 20%
			DHF-II	As in Grade I plus spontaneous bleeding.	Thrombocytopenia <100,000 cells/mm^3 HCT rise 20%.
		DHF: shock	DHF-III	As in Grade I or II plus circulatory failure (weak pulse, narrow pulse pressure (20 mmHg), hypotension, restlessness).	Thrombocytopenia <100,000 cells/mm^3 HCT rise 20%.
			DHF-IV	As in Grade III plus profound shock with undetectable BP and pulse	Thrombocytopenia < 100,000 cells/mm^3 HCT rise 20%.
		Expanded dengue syndrome	Evidence of isolated organopathy (unusual manifestations)		

Table 2: Summary of studies comparing WHO 1997 and 2009 dengue case classifications

Author, Year and Country	Study design (N)	Results	Conclusion / Recommendations
Bodinayake, *et al.* 2018. Sri Lanka	Prospective (N=976)	The treating physician's clinical diagnosis of dengue at discharge was found to be more sensitive than the 2009 WHO classification. However, diagnosis on admission was less sensitive than the 2009 WHO classification.	The 2009 WHO dengue classification system had high sensitivity but low specificity vs. clinical diagnosis at presentation.
de Silva, *et al.* 2018, Brazil.	Retrospective (N=30,670)	The 2009 WHO classification was found to be more sensitive in identifying severe dengue cases than 1997 WHO classification. Most severe cases detected by 2009 WHO classification may be an overestimate, as of the 27.4% of patients who were classified as DWS, 90.4% did not develop hypotensive shock.	Patients with severe disease were detected more using the 2009 WHO classification. However, clinicians should chose the guideline by considering the applicability at ward setting.
Jayarajah, *et al.* 2017, Sri Lanka	Prospective (N=1878)	The correlation between the two dengue case classification systems was not satisfactory. Three patients with DF were reclassified as severe dengue using the 2009 WHO classification. Number of warning signs correlated with sever disease. The 2009 WHO classification was better for identifying patients who may develop severe disease.	The 2009 WHO classification was more useful than the 1997 WHO classification in predicting patients who were likely to develop severe disease.
Zakaria, *et al.* 2014, Malaysia	Retrospective (N=281)	Majority of patients who were categorized as DF using the 1997 WHO classification were categorized as DWS in the 2009 WHO classifications.	The revised WHO 2009 guidelines classified more patients into a category that needs a higher level of care.
Jayaratne, *et al,* 2012, Sri Lanka.	Prospective (N=184)	The presence of the warning signs were higher in patients with severe dengue. Presence of 5 or more warning signs as well as several laboratory investigations were associated with the development of severe dengue.	The 2009 WHO warning signs were useful in predicting patients who may develop severe dengue.

Author, Year and Country	Study design (N)	Results	Conclusion / Recommendations
Tsai, *et al.,* 2012, Taiwan	Retrospective (N=148)	2009 WHO classification was able to differentiate varying levels of clinical severity of DF better than the 1997 WHO classification.	The 2009 WHO classification was found to be more effective in identifying patients who may develop severe cases of dengue.
Barniol, *et al.,* 2011 18 Countries	Prospective (N=1156) and retrospective (N=2092)	The revised 2009 WHO classification system was shown to be more sensitive for early recognition of severe disease than the 1997 WHO classification.	The revised 2009 WHO dengue classification had better potential for case management and surveillance than the 1997 WHO classification.
Wanigasuriya, *et al.,* 2011, Sri Lanka	Prospective (N=106)	The revised 2009 WHO classification was more sensitive to cases that may progress to severe dengue than the 1997 WHO classification.	Revised 2009 WHO classification was more applicable and practical in the ward setting.
Basuki, *et al.,* 2010, Indonesia	Prospective (N=122)	Some cases with severe disease did not fit into the 1997 WHO classification	The revised 2009 WHO dengue classification system was better at detecting severe dengue infections than the 1997 WHO classification system
Lima, *et al.,* 2010, Brazil	Retrospective (N=187)	When the two classifications were compared, the majority of the DF patients (70%) were reclassified as DWS or severe dengue by 2009 WHO classification.	The 2009 WHO classification was more effective in identifying patients who developed severe cases of dengue.

DF: Dengue fever, DHF: Dengue haemorrhagic fever, WHO: World Health Organization, DWS: Dengue with warning signs

DSS can be difficult to diagnose by inexperienced health care professionals, as patients may remain remarkably well in the early stages of shock and then deteriorate rapidly. In the 2009 WHO dengue classification, some criteria are not well-defined and may lead to differences in clinical assessment among physicians. For example, criteria such as: presence of severe bleeding and severe organ dysfunction are expected to be clinically judged by the treating physician. Thus, the diagnosis of severe dengue may vary among clinicians. This limitation should be overcome by more specific criteria for assessment of bleeding and organ dysfunction (9). Furthermore, in the 2009 classification "clinical" accumulation of fluid" is recognised as a warning sign. Clinical fluid accumulation occurs late and when fluid leak becomes clinically detectable, progression to impending shock may have already occurred. Therefore, it is not a useful warning sign in the clinical setting (22).

Furthermore, the 2009 classification may be difficult to practically incorporate into clinical practice in resource limited settings of developing nations due to the lack of rapid diagnostic tests and as most warning signs are not specific to dengue and may be seen in other tropical infections in such settings (9). In dengue endemic countries like Sri Lanka, all patients who present with fever and warning signs will invariably be diagnosed as having dengue with warning signs and warrant hospital admission for observation. This may increase in-hospital case-loads and in-turn put pressure on limited health budgets (9). Therefore, the 2009 classification needs revision to overcome these limitations and to be more clinically relevant.

Plasma leakage leading to haemodynamic instability with organ failure is a central pathophysiological feature of dengue. This needs to be detected early and promptly managed with fluid therapy to prevent complications. Massive bleeding and shock is more common in adults than children due to intake of NSAIDs, underlying peptic ulcers or due to late presentation (9). Furthermore, comorbidities such as diabetes mellitus, hypertension, ischaemic heart disease, chronic liver or kidney disease are more prevalent among adults and may complicate the clinical picture. Thus, in the WHO SEARO 2011 massive bleeding, co-morbidity and co-infections were were added as Expanded Dengue Syndrome (EDS) (Table 1) (9).

In conclusion, from studies done so far, the 2009 WHO dengue classification appears to be clinically more useful in detecting severe disease. However, the 2009 WHO dengue classification is still not the ideal classification for clinical use especially in resource limited developing countries. We have highlighted several limitations that should be addressed to make it more clinically relevant. Furthermore, any future dengue case classifications should cater to developing countries with limited health resources.

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Clinical pattern, associated factors and impact of disease on quality of life among individuals with melasma visiting the dermatology clinic at Teaching Hospital Karapitiya

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ABSTRACT

Introduction: Melasma is an acquired form of hypermelanosis that results in symmetrical, brownish pigmentation commonly on the face. This study was aimed to assess its clinical pattern, associated factors and impact of melasma on quality of life.

Methods: A clinic-based descriptive cross-sectional study was conducted recruiting all individuals with melasma, attended to the dermatology clinic of Teaching Hospital Karapitiya for seven months. Both a self-reported questionnaire and an interviewer-administered data record sheet were used for data collection.

Results: There were 172 individuals with melasma. Dominated by females (n=168, 97.7%) and 52.3% (n=90) were with Fitzpatrick type V skin. The mean age of onset was 47.2 years and the predominant pattern was malar pattern (58.1%). Most common associated factor was sun exposure (n=76, 44.7%), followed by, menstrual irregularities (20.5%), hormonal treatment (19.4%), family history (19.8%) and pregnancy (10.4%). Though 65.1% reported exposure to sun more than two hours in the midday, only 31.4% (n=54) used a sun protection method and sunscreens were used by only 4.65%,

The mean MASI (Melasma Area and Severity Index) score was 12.7, with a range of 1.5 to 30.9. There were statistically significant correlations with family history, duration of sun exposure and the use of facial cosmetics ($p<0.05$). Mean Melasma Quality of Life Score (MELASQOL) was 28.86, but there was no significant correlation between MASI score and MELASQOL (Pearson correlation = 0.548, $p>0.05$).

Conclusions: Melasma starts at an older age in our study population. It causes a significant negative effect on psychosocial aspects of quality of life though not related to severity, suggesting that treatment decisions should not depend on severity. Appropriate usage of cosmetics and sunscreens must be advised.

Keywords: *Associated factors, Karapitiya, melasma, MASI score, MELASQOL, quality of life, Sri Lanka*

Introduction

Melasma is an acquired, form of hypermelanosis most prevalent in darker skin phenotypes. It is frequently seen in women and mostly starts between the ages of 20 to 40 years. It is characterised by irregular, light to dark brown macules and patches in sun-exposed areas, commonly the face (1, 2).

The precise cause of melasma is unknown, but several factors have been linked to its exacerbation. However, by considering the histopathological findings, recent studies revealed that melasma is not only a pigmentary disorder but a photo-aging disorder as well (1 - 3). Based on distribution over the face, three clinical patterns are recognised.

The centro-facial pattern involves the forehead, cheeks, upper lip, nose and chin, while malar pattern involves the cheeks and nose. The mandibular pattern involves the skin over the ramus of mandible (2, 4, 5).

The precise cause of melasma is unknown and is thought to be multifactorial. Several predisposing/ aggravating factors are linked to melasma, namely, genetic predisposition, female hormonal activity, UV exposure, certain cosmetics and drugs such as photo-toxic drugs and anti-seizure drugs. Pregnancy and oral contraceptives play a major role as hormonal factors. This is evidenced by the fading of the pigmentation after parturition, discontinuation of oral contraceptives and avoidance of sun (1, 2, 4-6).

Its prevalence varies among different countries due to the variation of the Fitzpatric skin type in different ethnic groups and UV exposure within various geographic locations. Therefore, it is common in Caucasian women particularly in Latin America, Middle East and Asia (7).

The severity of melasma is assessed by the Melasma Area and Severity Index (MASI) which is based on the surface area involved, darkness, and homogenicity of pigmentation (4, 8).

For the reason of involvement of the face most commonly and the female gender being affected mostly, the disease has a significant emotional and psychological impact on the quality of life (1, 9). The quality of life of melasma is assessed by the MELASQOL scale with a standard structured questionnaire which includes ten questions assessing psycho-social aspect of quality of life (4, 10).

Treatment of melasma usually combines the elimination of possible causative factors, the use of sunscreens, hypo-pigmenting agents and cosmetic procedures. Combination of therapeutic modalities generally has better efficacy than monotherapy. The use of sunscreen is essential in the prevention of melasma and for the enhancement of the efficacy of other topical therapies (7).

There are wider differences in different ethnicities in prevalence, distribution, severity and pattern of this disease and there is no available literature on studies done in Sri Lanka. We planned to study the clinical pattern, associated factors and impact of melasma on quality of life of affected patients. Identification of common associated factors in our population will aid planning the treatment strategies and also would provide background information to educate people to avoid possible exacerbating factors, and to enhance the treatment outcome and the compliance.

Methods

A clinic-based descriptive cross-sectional study was conducted in the dermatology clinic at Teaching Hospital Karapitiya from October 2017 to May 2018. Patients, who were clinically diagnosed as melasma by characteristic clinical features of pigmented macules and patches with irregular geographic borders, were enrolled to the study. Only the patients who can read and understand the questionnaire were included. Patients with co-existent other pigmentary disorders such as lichen planus pigmentosus, erythema dyschromicum perstans, ochronosis, and people with pigmentary demarcated lines in addition to melasma were excluded from the study.

A pretested self-reported questionnaire with eighteen close ended questions and an interviewer-administered data record sheet were used for data collection. The questionnaire included demographic data, age at onset of the disease, known exacerbating factors and skincare habits. The average duration of exposure to the sun per day and the usage of sun protection methods were recorded.

Patients were examined to assess skin phenotype, distribution, intensity, homogeneity of pigmentation and recorded in the data record sheet. MASI score was calculated using these data with the clinical assessment of forehead, both malar regions and chin based on three variables: percentage of the total area involved (A), darkness (D), and homogeneity (H). The value assigned for the corresponding percentage area involved is, 0=no involvement; 1 = <10%; 2 = 10-29%; 3 = 30-49%; 4 = 50-69%; 5 = 70-89%; and 6 = 90-100% involvement. The darkness of the melasma (D) is graded on a scale of 0 to 4 : 0 = without evidence of hyperpigmentation; 1 = barely visible hyperpigmentation; 2 = mild hyperpigmentation; 3 = moderate hyperpigmentation; 4 = severe hyperpigmentation.

Homogeneity of the hyperpigmentation (H) is graded on a scale of 0 to 4: 0=without evidence of hyperpigmentation; 1=specks of involvement; 2=small patchy areas of involvement <1.5 cm diameter; 3=patches of involvement >2 cm diameter; 4=uniform skin involvement without any clear areas). Total MASI score was calculated with the formula of Forehead 0.3 (D+H) A + right malar 0.3 (D+H) A + left malar 0.3 (D+H) A + chin 0.1 (D+H) A (13). The distribution of MASI score was categorized using the quartile method, with MASI score of <7.2 defining as a mild disease, between 7.2 and 11.95 as moderate disease, between 11.96 and 18.07 as severe disease, and >18.07 as a very severe disease to analyse the significance of aggravating factors and MASI score (11).

A validated Sinhala translation of MELASQOL was used to assess the quality of life of the patients. The English version of MELASQOL was translated to Sinhala using a standard procedure after taking permission from the original author and copyright holder of the English version Professor Rajesh Balkrishnan (10). This was validated using the Sinhala adaptation of short version of the QoL assessment instrument of World Health Organization (WHOQOL-BREF). The Sinhala-MELASQOL showed negative correlation with psycho-social domains of the WHOQOL-BREF (Spearman correlation coefficient, -0.389; $p<0.05$ for social domains and -0.449; $p<0.05$ for psychological domains) demonstrating that the Sinhala-MELASQOL as an acceptable and reliable instrument to evaluate the quality of life in patients with melasma (12). MELASQOL scale measures the psychosocial aspect of disease. It is a 10 question scale, which requires the patients to rate how they feel about each issue rated on a Likert scale of 1 (not bothered at all) to 7 (bothered all the time). The score ranges from 10-70 with higher the score more the impairment of quality of life.

The ethical approval for the study was obtained from the Ethics Review Committee of the Faculty of Medicine, University of Ruhuna and conducted with the prior permission of the relevant administrative authorities. The participation was entirely voluntary and informed consent was obtained for the study as well as for the publication with photographs. Participants were ensured of the freedom to withdraw from the study at any stage. Confidentiality was met throughout the study and the individual identity of participants has not been disclosed. All data were analysed using a database created with SPSS and $p<0.05$ was considered as statistically significant.

Results

A total of 172 individuals with melasma were included in the study. The mean age (SD) of the participants was 54.97 (+/-8.34) years, with an age range between 28 - 76 years. The majority of them have been studied up to level of secondary education (36.6%, n=63) (Table 1).

Females dominated the study participants (n=168, 97.7%). All the participants were of Fitzpatrick skin type IV (n= 82, 47.7%) and V (n=90, 52.3%). The age of onset of melasma for most of them was between 40-49 years with a mean age (SD) of 47.2 (+/-9.78) years. The predominant pattern observed was malar pattern (58.1%) Mandibular only pattern was not observed in the study sample (Table 1). (Figures 1- 4).

When considering the associated factors, majority (n=76, 44.7%) of individuals have noted exacerbation due to exposure to sun and 34 (19.8%) individuals reported a positive family history of melasma. Among 138 women who reported of being pregnant, only 10.4% declared pregnancy as an aggravating factor (Table 2).

Majority (65.1%) of the patients studied were exposed to the sun >2 hours in midday where the intensity of sunlight is in its peak. Overall, only 54 (31.4%) use a sun protection method, namely, sunscreens, shades, and clothes. Among them, sunscreens were used by only 14.8% of individuals; which is 4.7% from the total number of study participants. Interestingly, majority has not responded to the question whether they use sun protection method or not. Concerning skincare habits, 50% declared regular application of cosmetics to face, with herbal and non-herbal products in almost equal amounts (45.7% and 48.6% respectively) (Table 3).

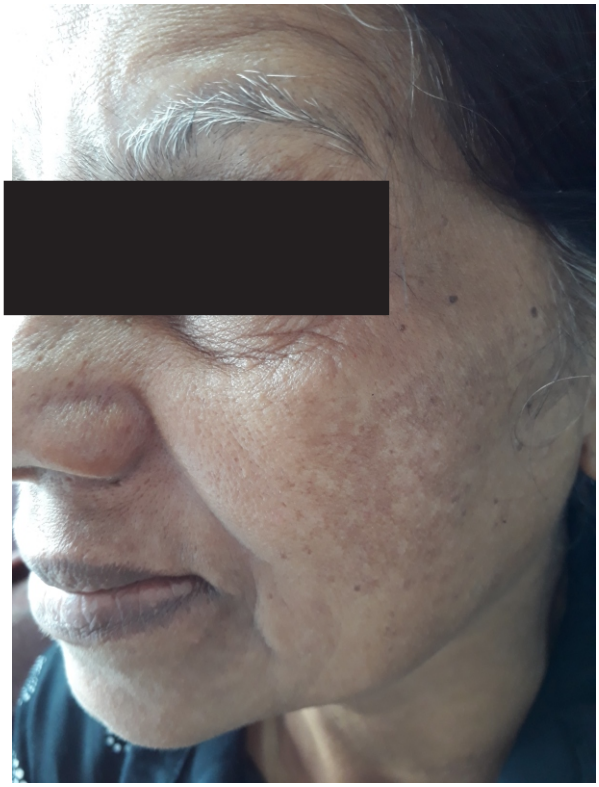

Figure 1: Malar pattern, Grade 2 pigmentation, Grade 2 homogeneity

Figure 2: Centro-facial pattern, Grade 3 pigmentation, Grade 2 homogeneity

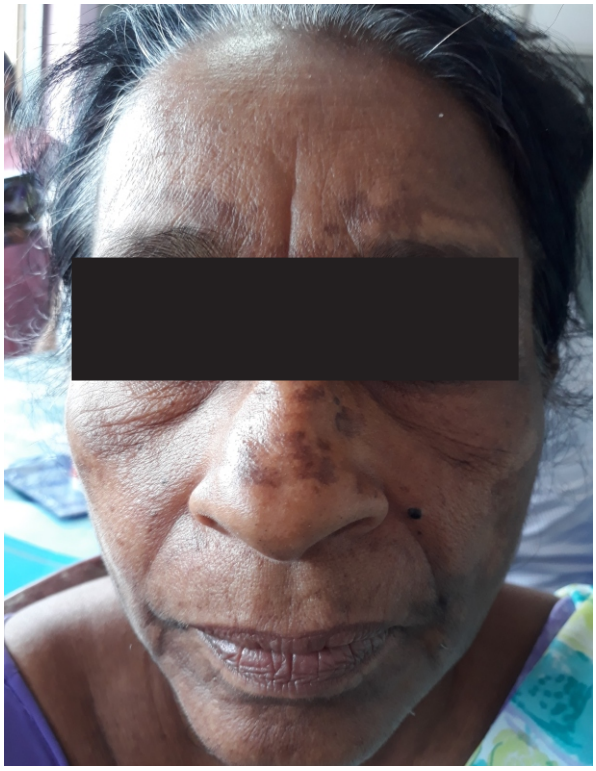

Figure 3: Centro-facial pattern, Grade 3 pigmentation, Grade 3 homogeneity

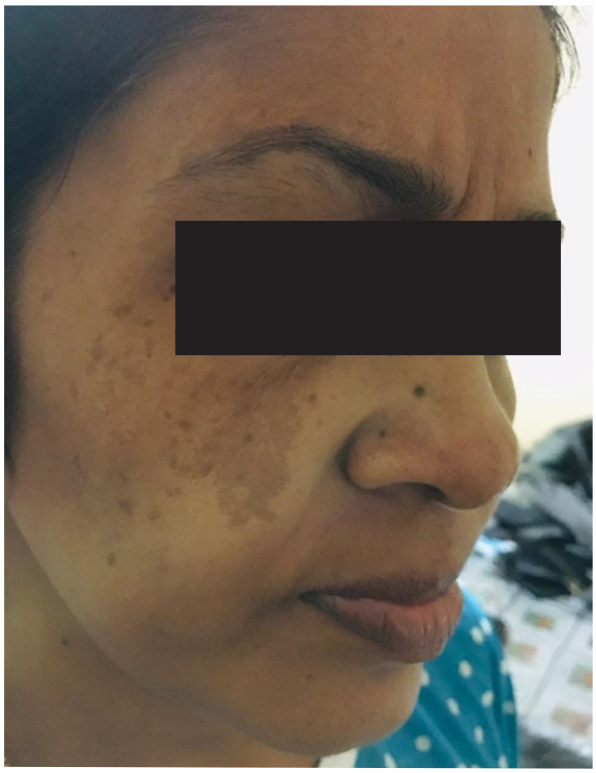

Figure 4: Malar pattern, Grade 2 pigmentation, Grade 3 homogeneity

Table 1: Demographic details and disease characteristics of melasma patients

	Category	Frequency	Percentage
Age in years	20-29	01	0.6%
	30-39	06	3.5%
	40-49	39	22.7%
	50-59	75	43.6%
	>60	51	29.7%
Sex	Female	168	97.7%
	Male	04	2.3%
Educational level	No	08	4.7%
	Gr 1-5	46	26.7%
	Gr 6-11	63	36.6%
	A/L	39	22.7%
	Higher education	14	8.1%
Fitzpatrick skin type	Type IV	82	47.7%
	Type V	90	52.3%
Age of Onset	<30	04	2.4%
	30-39	34	20.2%
	40-49	61	36.3%
	50-59	47	28.0%
	>60	22	13.1%
Pattern	Centro-facial	72	41.9%
	Malar	100	58.1%
	Mandibular only	00	00.0%

Table 2: Associated factors of melasma in the study sample

Factor	Positive		Negative	
	Frequency	Percentage	Frequency	Percentage
Family history	34	19.8%*	138	80.2%
Pregnancy	10	10.4%	96	89.6%
Hormone treatment	32	19.4%	133	80.6%
Menstrual irregularities	34	20.5%*	132	79.5%
Sun exposure	76	44.7%	94	55.3%

* There were 6 non-responders in the category of menstrual irregularities

Table 3: Sun exposure, protection behaviour and facial skin care habits among the patients

	Frequency	Percentage
Sun exposure in peak hours		
<2 hours	60	34.9%
>2 hours	112	65.1%
Type of protection used		
Sunscreens	04	7.4%
Dresses	08	14.8%
Sunshades	29	53.7%
Dresses and shades	09	16.7%
Sunscreens and shades	04	7.4%
No protection	26	15.1%
Type of cosmetics		
Herbal creams	32	45.7%
Non-Herbal creams	34	48.6%
Other	04	5.7%

The mean MASI score in the study population was 12.7+/- 7.07 which ranged from 1.5 to 30.9.

According to the level of melasma severity, 85.3% of persons with a positive family history had a higher MASI score of more than 25th centile, with a statistically significant association. (p=0.033). Considering sun exposure, 75.9% of the study participants who were exposed to more than 2 hours of mid-day sunlight, had a higher severity score of more than 25th centile, while only 60.0% of participants who had less than 2 hours exposed to mid-day showed higher MASI scores, with a statistically significant correlation between duration of sun exposure and the severity of melasma. (p=0.03). The use of facial cosmetics also showed a significant correlation with higher melasma severity scores with 81.4% of participants who use cosmetics having a MASI score of higher than 25th centile, while 59.3% of those who do not use facial cosmetics show higher scores. (p=0.002) (Table 4). Other factors, namely, pregnancy, hormonal treatment and menstrual irregularity did not show a significant correlation with melasma severity.

Mean Melasma Quality of Life Score (MELASQOL) was 28.86 with most participants reported feeling depressed. There was no significant correlation between melasma severity (MASI) and quality of life (MELASQOL). (Pearson correlation = 0.548, p>0.05)

Both age and educational levels correlated with quality of life. 58.8% individuals who are less than 55 years had more than 50th centile of quality of life score, whereas only 38.4% participants who are more than 55 years had more than 50th centile of quality of life score, which shows a significant correlation of higher impairment of quality of life with lower age group. (p=0.012). In the sample, 57.6% of individuals with higher educational level than primary schooling shows higher impairment of quality of life score of more than 50th centile, while only 33.3% of those who had primary education or below showed higher impairment of quality of life, which is statistically significant. (p=0.004) (Table 5).

Table 4: The association between aggravating factors and melasma severity

Characteristics	MASI						*p*-value
	Mild		Moderate / Severe / Very severe		Total		
	n	%	n	%	n	%	
Family history							
Yes	5	14.7	29	85.3	34	100	
No	46	33.3	92	66.7	138	100	$p = 0.033$
Pregnancy							
Yes	5	50.0	5	50.0	10	100	
No	44	27.8	114	72.2	158	100	$p = 0.135$
Hormonal treatment							
Yes	11	34.4	21	65.6	32	100	
No	38	28.6	95	71.4	133	100	$p = 0.519$
Menstrual irregularity							
Yes	15	44.1	19	55.9	34	100	
No	34	25.8	98	74.2	132	100	$p = 0.036$
Sun exposure							
<2 hours	24	40.0	36	60.0	60	100	
>2 hours	27	24.1	85	75.9	112	100	$p = 0.030$
Use of facial cosmetics							
Yes	16	8.6	70	81.4	86	100	
No	35	0.7	51	59.3	86	100	$p = 0.002$

Table 5: The association between quality of life and age and educational level

	MELASQOL						*p*-value
	< 50th centile		> 50th centile		Total		
	n	%	n	%	n	%	
Age							
< 55 years	33	41.3	47	58.8	80	100	
> 55 years	45	61.6	28	38.4	73	100	$p = 0.012$
Educational level							
Non / Primary	36	66.7	18	33.3	54	100	
Secondary / Higher	42	42.4	57	57.6	99	100	$p = 0.004$

Discussion

Melasma shows a great variety of age distribution in different ethnicities, described in several studies. According to Yalamanchili, *et al.,* the common age group reported was between 31-40 years when they present at the clinic (1). Similarly, one British report shows, the mean age as 38 years (6). Guinot, *et al.,* reported that in Tunisian people, 58% of women had the onset of disease before thirty years of age and in 87% the onset was between 20 and 40 years (2, 13). In a Brazilian study, the mean age of onset in Brazilian people was 25 to 30 years (10). In India, Singapore and in a global study average age of onset was 30, 34 and 38 respectively (13). Compared to these, the age of onset in our study population lies between 40 and 49 years, which is higher.

A clear female predominance was identified in all published studies, generally estimated at around 90%. According to the Yalamanchili, *et al.,* a study conducted in India, 67.9% of females and 32% males were affected (1). Guinot, *et al.,* noted 188 women and 9 men affected in the Tunisian population (2). Sivayathorn, *et al.,* reported a female to male ratio of 6 : 1 in a Malaysian population and 24 : 1 in an Indonesian population (7). Brazil shows 39 : 1 and Singapore shows 21 : 1 preponderance (13). In our study, cases of melasma reported in men were amounting to 2.3% with Male female ratio of 1 : 42. The Indian studies only showed a lesser prevalence in females than males, whereas others show more or less similar results as our population.

Malar pattern was the predominantly involved pattern reported in our study. According to Yalamanchili, *et al.,* study in India, the malar pattern is the commonest (68%) which is much similar to our study results (1). This is in contrast to the Tunisian study where 76% of the sample reported centro-facial type (2). Brazil's population showed a predominance of centro-facial type (51.7%). The pattern exhibited regional variation in a study done in India showing mandibular pattern with 1.6% only among patients from the northern region in India (7).

Considering the associated factors, our study shows a positive family history of 19.8%. However, positive family history was reported with a very wide range in past studies published in other countries being 10% in Singapore, 18% to 33% in India, 48% worldwide and 61% in UK (1, 6, 13). In our study, positive family history was significantly associated with the severity of melasma.

Pregnancy is a well-known factor associated with melasma. Though in our study only 10.4% were declared it as an aggravating factor, prevalence of melasma during pregnancy shows wide variation according to population and ethnicities such as 51% in Tunisians, 16% in Iranians, 36.4% in Brazilians, 37% in Moroccan and 46% in Pakistanis (2, 13). Melasma has been reported to represent around two-thirds of cutaneous side effects of oral contraceptives and the incidence varies according to ethnic groups, showing 38% in Tunisia and 16.2% in Brazil (2, 13, 14). According to this study, 19.4% of participants declared to have taken OCP at one stage of their life.

Even though multiple causative factors have been implicated in the aetiology, UV radiation is the single most important factor mentioned in the literature. Pathak, *et al.,* reported that exposure to sunlight exacerbated melasma in 100% of patients (7). In Orientals, 72.4% of patients reported exacerbation due to sun exposure, whereas in India it shows 55.1% (7). Tunisian study showed it as an aggravating factor in 84% but Brazil showed only in 27.2% (13, 14). In our study population, 44.7% of individuals reported having an exacerbation following sun exposure and the hours of sun exposure amounted to a significant correlation with MASI score.

A review of the recent literature shows that sun exposure was reported as a triggering factor by 51% an aggravating factor by 84% (2). Similarly, sun exposure was the most frequently reported factor (44.7%) in our study population, as an aggravating factor than others and almost all declared having exposed their skin to the sun in the day time and majority of them (65.1%) declared that their average sun exposure per day is more than 2 hours.

Only 31.4% actively use a sun protection method and among them, 85.2% used sunshades and clothes, however, only 14.8% declared that they use sunscreens during the sunny period, which is well below than of a study in India which declared 57%

use of sun protection methods (2). This shows that awareness towards sun protection methods and sunscreen use is inadequate in our population.

Concerning skin care habits, 50% declared regular application of cosmetics to face, with herbal and non-herbal products in almost equal amounts (48.6% and 45.7% respectively). It is alarming that, despite the use of regular application of cosmetic products among the study participants, many were not aware of the importance of sunscreens in line with treatment and prevention of melasma which has pigmentary and photo-aging pathogenesis.

The mean MASI score in our study was 12.7±7.07. Guinot, *et al.,* also noted similar responses in his study with mean MASI score of 10.1±6.2 (2), but in contrast, the Indian population showed a much lower level at 5.7 (1). In our population, positive family history, use of cosmetics and the duration of sun exposure were significantly associated with severity scores of melasma.

Comparing the quality of life with other studies, we noted a similar response in the MELASQOL which was 28.86 with most patients reported feeling depressed causing psychosocial and emotional distress. Mean MELASQOL score was 28.28 with the majority reporting embarrassment and frustration in the study done in India and it showed a significant negative impact on the quality of life (1). A study conducted in Brazil using MELASQOL reported that facial lesions can cause low self-esteem, dissatisfaction, withdrawal from social life and lower productivity (13). Also, we noted, the lower age and higher educational level are correlated with higher impairment of quality of life. This implicates more educated people and younger people have more concerns about their appearance.

Although melasma affects the quality of life, according to the data from our population, the severity score of melasma does not correlate to the score of quality of life, suggesting that the subjective perception affects the quality of life than the clinical impression of the disease. This poor correlation was documented in the previous studies as well (13).

Limitations

The study was carried out among the clinic attendees at Teaching Hospital Karapitiya, therefore the findings may not be generalised to the whole population of the country.

Conclusion and recommendations

Comparing with other global studies, the age of onset of melasma is higher in our study population and it causes a significant negative effect on psychosocial aspects of quality of life, although, the effect is not related to the clinical severity. This warrants that the treatment decision should not be made by the severity scores of the disease.

Sun exposure was the major aggravating factor identified in this study population. Therefore, the key element in the prevention of melasma involves taking measures to minimize sun exposure, which need to be addressed in our population.

Although half of them use cosmetic products to face; sunscreens usage seems inadequate in the Sri Lankan population, showing the lack of awareness about sunscreens as a prevention method of photo aggravating dermatoses. Therefore, the gravity for protection from the sun should be a key factor to address from the young age.

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Community screening for undiagnosed dysglycaemia in a semi-urban locality in Sri Lanka

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ABSTRACT

Introduction: Previous studies on the prevalence of pre-diabetes and diabetes in Sri Lanka have shown conflicting results. We studied the prevalence of pre-diabetes and diabetes using fasting plasma glucose (FPG) and 75g oral glucose tolerance (OGTT) test among a representative sample of adults in a semi-urban locality in Southern Sri Lanka. Sensitivity and specificity of FPG over OGTT in diagnosing pre-diabetes and diabetes were calculated.

Methods: Healthy adults, aged 20-75 years, selected by multi-stage random sampling from one medical officer of health area in Southern Sri Lanka were screened with FPG and 75g OGTT. Subjects known to have diabetes were excluded.

Results: Mean (SD) age of men (n=234) and women (n=593) were 44 (10.1) and 43(10.8) years, respectively. With OGTT, 157 (19.0%) subjects had impaired glucose tolerance while another 60(7.3%) had diabetes. With FPG, 270 (32.6%) had impaired fasting glycaemia while another 51(6.2%) had diabetes. Prevalence of pre-diabetes or diabetes was not different among men and women by OGTT; 55 (23.5%) vs 162 (27.3%), p=0.293 while it was significantly different by FPG; 107 (45.7%) vs 214 (36.1%), p=0.011. Prevalence of pre-diabetes or diabetes was significantly higher in age group $\geqslant$ 45 yrs compared to age <45 yrs by both tests. FPG showed low sensitivity (44.7%) but higher (76.1%) specificity of detecting dysglycaemia. FPG showed sensitivity of 53.3% and specificity of 97.5% in detecting undetected diabetes.

Conclusions: Prevalence of pre-diabetes is higher than in previous studies in Sri Lanka. Significantly higher proportion of males compared to females, had pre-diabetes or diabetes by FPG test. Compared to subjects age <45 years, the prevalence of pre-diabetes or diabetes was significantly higher among those $\geqslant$ 45 years. FPG lacks adequate sensitivity and specificity to detect those with diabetes or dysglycaemia.

Keywords: *Fasting plasma glucose, OGTT-Oral glucose tolerance test, pre-diabetes*

Introduction

Abnormalities in glucose tolerance, also known as dysglycaemia, are broadly categorized into two groups; pre-diabetes and diabetes mellitus (1). Pre-diabetes is an intermediate stage which may progress to diabetes, remain same or revert back to normal glucose tolerance (2). Similar to diabetes, pre-diabetes also carries a higher risk of cardiovascular disease (CVD) compared to those with normal glucose tolerance (3,4).

Oral glucose tolerance test (OGTT) is considered the gold standard in detecting dysglycaemia (5). OGTT is more sensitive than fasting plasma glucose (FPG) to detect dysglycaemia (6). Compared to FPG, OGTT as a screening tool has shown more

accurate estimation of dysglycaemia and risk of cardiovascular disease (5).

Epidemiological surveys in Sri Lanka on the prevalence of dysglycaemia have mostly used FPG as the screening tool (7). We aimed to study the prevalence of dysglycaemia using both FPG and OGTT. We also studied the sensitivity and specificity of FPG over OGTT in diagnosing pre-diabetes and diabetes.

Methods

Participants in the age range of 20 - 75 years were selected from the Southern Province of Sri Lanka using a multi-stage random sampling method. Of the 44 Gramasewaka divisions in one Medical Officer of Health (MOH) area in the Southern Province 22 were selected randomly. Thirty-eight subjects were selected, randomly, from each Gramasewaka division using the latest Voters' register to make a total of 836 individuals in the study sample. Each selected participant was invited to attend a medical consultation during which a detailed medical history was obtained and a clinical examination was performed. Pregnant women and those who already had diabetes were excluded. People on long term medications such as glucocorticoids, statins or other lipid lowering drugs were also excluded from the study. Informed written consent was obtained from each participant after explaining the research protocol. Ethical approval was obtained from Ethics Review Committee, Faculty of Medicine, University of Ruhuna, Sri Lanka (Ref: 26.02.2015: 3.14 and 09.03.2016: 4.1).

A pre-tested, interviewer-administered question--naire was used to collect data. Data collection was done between January 2016 to January 2017. Height was measured to the nearest cm using a stadiometer and weight was measured to the nearest 100 gm without shoes and heavy cloths. A sample of venous blood (2.5 ml) was obtained after 10 hours of fasting for the FPG. Another 2.5 ml of blood was drawn after 2 hours of ingesting 75 g of glucose in 250 ml of clear water for OGTT. Criteria published by the American Diabetes Association for the diagnosis of diabetes and pre-diabetes were followed (1).

Analysis

Continuous variables of baseline characteristics between the two age groups (Age < 45years and ⩾ 45 years) and different glycaemic status were compared by t-test (unpaired) and categorical variables were compared with chi-squared test.

Results

Table 1 shows the baseline characteristics of the study sample. Based on FPG, 506 (61.2%) participants were normoglycaemic, while 270 (32.6%) had impaired fasting glycaemia (IFG) and 51 (6.2%) had diabetes. According to OGTT 2 hr plasma glucose test 610 (73.8%) were normoglycaemic while 157 (19%) had IGT and 60 (7.3%) had diabetes. Among the participants 20.8% had isolated IFG, 8.5% had isolated IGT, and 9.2% had both IGT + IFG.

Table 1: Baseline characteristics of the study sample

Measurement	Mean (SD) (n= 827)
Age (years)	43 (10)
FPG (mg/dL)	98.1 (25.5)
2 hr plasma glucose value of OGTT (mg/dL)	128.7 (59.2)
BMI (kg/m^2)	24.7 (4.3)
Hip circumference (cm)	93.2 (8.5)
Waist circumference (cm)	85.9 (8.9)

FPG - Fasting Plasma Glucose, OGTT- Oral Glucose Tolerance Test, BMI- Body Mass Index.

With FPG, there were more males with IFG alone or combined IFG and DM. With OGTT, however, there was no significant gender difference in either IGT or combined IGT and DM. These results are shown in the Table 2.

As the American Diabetes Association recommends limiting community screening for those >45 years of age, we estimated the prevalence of dysglycaemia among subjects below and above the age of 45 years in this study sample. Results are shown in the Table 3.

Table 3 shows that age related rising prevalence of dysglycaemia with both methods of testing when the cut off age level is 45 years.

Table 2: Different glycaemic status among male and female participants

Glycaemic status (as %)	Male (n=234)	Female (n=593)	*p*-value*
FPG test			
Normoglycaemia	127 (54.3)	379 (63.9)	
Impaired fasting glycaemia	89 (38)	181 (30.5)	0.03
Newly diagnosed diabetes mellitus	18 (7.7)	33 (5.6)	
FPG test			
Normoglycaemia	127 (54.3)	379 (63.9)	
Impaired fasting glycaemia + Newly diagnosed diabetes mellitus	107 (45.7)	214 (36.1)	0.01
OGTT test			
Normoglycaemia	180 (76.9)	431 (72.7)	
Impaired glucose tolerance	37 (15.8)	120 (20.2)	0.3
Newly diagnosed diabetes mellitus	18 (7.7)	42 (7.1)	
OGTT test			
Normoglycaemia	179 (76.58)	431 (72.7)	
Impaired glucose tolerance + Newly diagnosed diabetes mellitus	55 (23.5)	162 (27.3)	0.3

*compares the gender difference of dysglycaemia. FPG- Fasting Plasma Glucose, OGTT- Oral Glucose Tolerance Test.

Table 3: Glycaemic status in different age groups

Glycaemic status	Age < 45 years (%)	Age ≥ 45 years (%)
FPG test		
Normoglycaemia	300 (66.1)	206 (55.2)
Impaired fasting glycaemia	134 (29.5)	136 (36.5)
Newly diagnosed diabetes mellitus	20 (4.4)	31 (8.3)
OGTT test		
Normoglycaemia	359 (79.1)	251 (67.3)
Impaired glucose tolerance	72 (15.9)	85 (22.8)
Newly diagnosed diabetes mellitus	23 (5.1)	37 (9.9)

FPG - Fasting Plasma Glucose, OGTT - Oral Glucose Tolerance Test

Table 4: BMI, waist to hip ratio and blood pressures (mean and SD) among individuals with dysglycaemia in two different age groups

	Age < 45 years	Age = 45 years	*p*-value
BMI (kg/m^2)	26.1 (3.8)	25.1 (4.3)	0.12
Waist to hip ratio for females	0.92 (0.05)	0.93 (0.05)	0.69
Systolic blood pressure (mmHg)	122 (13)	128 (14)	0.001
Diastolic blood pressure (mmHg)	77 (8)	80 (8)	0.01
Fasting blood sugar (mg/dL)	112 (34)	118 (39)	0.26

BMI - Body Mass Index

Subjects aged 45 years or above with dysglycaemia had higher systolic and diastolic blood pressures when compared with subjects below 45 years with similar condition (Table 4). Waist to hip ratio and BMI, however, were not significantly different between the two groups.

When OGTT was considered the gold standard to detect dysglycaemia, FPG had low sensitivity (44.7%) but higher specificity (76.1%) of detecting dysglycaemia. Furthermore, FPG showed a sensitivity of 53.3% and specificity of 97.5% in detecting undetected diabetes.

Discussion

This cross-sectional, community-based study conducted in a semi-urban area in Southern Sri Lanka reveals several important findings. We found 7.3% people to have undetected diabetes based on the OGTT. Prevalence of IFG was about 1.7 times higher than the prevalence of IGT. Further, males have a higher prevalence of dysglycaemia compared to females. Among our subjects, isolated IFG prevalence is 2.4 times higher than isolated IGT. Compared to subjects below 45 years, those aged 45 years or above had higher systolic and diastolic blood pressures and a higher prevalence of dysglycaemia.

Several community based studies have reported different prevalence rates of diabetes and pre-diabetes in Sri Lanka (8,9). Most of them have reported the overall prevalence (both previously known and newly diagnosed) of diabetes. Except one study which used both FPG and OGTT, all other studies have used only FPG as the screening test. The largest study conducted in Sri Lanka which included 6047 subjects from four provinces revealed diabetes prevalence of 14.2% in men and 13.5% in women (10). In the same study, IFG, was detected in 14.2% and 14.1% in men and women respectively. A national survey carried out in 2005 and 2006 representing all districts in the country including a sample of five thousand participants over the age of 18 years revealed 10.3% prevalence of diabetes with nearly one third (3.8%) of newly diagnosed patients (11). The prevalence of pre-diabetes (IGT) was 11.5% in this study. However, in this survey, OGTT was carried out only in participants who were not found to have diabetes with FPG test and this may have led to underestimation of prevalence of dysglycaemia. Pinidiyapathirage, *et al.,* in 2007 reported a prevalence of newly diagnosed diabetes as 9.4%. Prevalence of undiagnosed diabetes mellitus was high with increasing age and in female gender compared to males (7). In this study too, slightly more than one third (35%) of all patients with diabetes were newly detected subjects with diabetes. The prevalence of IFG in this study was 50.3%. The higher prevalence of dysglycaemia in this study could partly be due to the selection of study sample from an urban community. According to a recent study conducted in urban, rural and plantation sectors of Kalutara district, age and sex adjusted prevalence of IFG was 14.3% (8).

A national survey carried out in 2005 and 2006 showed non-significant difference of prevalence of pre-diabetes between males and females, even though the females found to have significantly higher prevalence of isolated IGT

and IGT+IFG (11). Pubudu De Silva, *et al.,* showed that females have significantly higher prevalence of IFG when compared to males (8). An Indian study done in 2011 showed almost similar results and prevalence of IFG was 2 to 2.4 times higher than IGT (12). A New Zealand study done in 2017 also showed 2.7 times higher prevalence of IFG than IGT (13).

According to the American Diabetes Association, screening for diabetes or pre-diabetes should be started at all asymptomatic adults at the age of 45 years (14). Sri Lankan studies conducted in 2005 - 2007 showed the rising prevalence of newly diagnosed diabetes with aging (11,15). Several studies in Asian countries and western countries also showed significant increase in prevalence of pre-diabetes or dysglycaemia with aging (16). A study conducted in Malaysia in 2011 showed almost half of the adults with pre-diabetes in aged group between 30 - 49 years and age as a risk factor for the development of pre-diabetes (17).

Current study, conducted in a semi-urban community in Southern Sri Lanka in 2017 revealed that the prevalence of newly diagnosed diabetes has doubled (from 3.8% in 2006 to 7.3% in 2017 with OGTT) in semi-urban setting. The prevalence of IGT has shown an upward trend from 11.5% in the nationwide study in 2006 to 19% in the current study. Exponential rise in the incidence of both forms of dysglycaemia; newly diagnosed diabetes and pre-diabetes, compared to last decade in the Sri Lankan community is the most striking finding of the current study.

With rising incidence of both forms of dysglycaemia in the Sri Lankan community, it would be useful to explore the sensitivity and specificity of the most commonly used screening tools, FPG estimation and OGTT in the diagnosis of diabetes mellitus and pre-diabetes. This would be relevant in the background of increasing evidence in the literature on the association of pre-diabetes with increased risk of CVD. Further, adherence to special lifestyle modifications and use of specific pharmacotherapy to delay the progression pre-diabetes to diabetes with favourable clinical outcomes is recommended by professional organizations (18). One study was conducted in 2019 to compare the sensitivity and specificity of FPG with OGTT in the diagnosis of pre-diabetes in the local setting and it showed low sensitivity to detect pre-diabetes similar to our finding. Even the nationwide survey conducted in 2006-2007, has not screened every participant with both FPG and OGTT (7). According to our findings in Sri Lankan setting, classification of IFG as pre-diabetes is not diagnostically accurate, when compared with the diagnosis of IGT with the gold standard OGTT. Studies conducted in Asian and Caucasian populations have revealed similar findings (6,19). One recent study was conducted to compare the sensitivity and specificity of FPG with OGTT in the diagnosis of pre-diabetes in the local setting and it showed FPG has low sensitivity to detect pre-diabetes similar to our findings (20). Use of OGTT or alternative screening tools such as glycosylated hemoglobin in addition to FPG to diagnose individuals with the pre-diabetes have been recommended to improve the diagnostic yield of pre-diabetes (5).

Although this study revealed the value of screening tests in the diagnosis of dysglycaemia in the community setting in Sri Lanka, it has few limitations. At the outset, this study sample excluded individuals with previous diagnosis of diabetes and it prevented us from the estimation of overall prevalence of diabetes in this community. As the study was conducted in a one semi-urban geographical area, findings on the prevalence rates of dysglycaemia may not extrapolated to the whole country. Comparison of prevalence of newly diagnosed diabetes and pre-diabetes in the rural and urban settings was also not possible with the finding of this study. The most significant strength of this study is that, it was done on a randomly selected large sample and all participants were tested with both FPG and OGTT. This enabled us to discover that FPG is not as good as OGTT to detect newly diagnosed diabetes in the community and its performance in the detection of dysglycaemia is also not satisfactory as a screening test. Diabetes needs to be excluded when patients present with vascular diseases like peripheral arterial disease, cerebrovascular disease and cardiovascular disease. As FPG has a limitation to diagnose dysglycaemia, we consider to use more specific investigations like HbA1c to screen individuals for dysglycaemia since OGTT is cumbersome. We hope these findings would be useful in planning out large-scale studies

in future and selecting appropriate screening tools to detect different categories of dysglycaemia.

In conclusion, we report that the prevalence rates of newly diagnosed diabetes and pre-diabetes have doubled during the last decade in Sri Lanka. As a screening tool in the community setting, FPG lacks adequate sensitivity and specificity to detect those with diabetes or dysglycaemia.

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Conflicts of interests

There is no conflict of interest.

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Comparison of maternal and foetal outcomes between adolescent and adult pregnancies; a descriptive cross sectional study

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ABSTRACT

Introduction: Adolescent pregnancy is a global issue and the trend is increasing specially in South East Asia. Pregnancies at a younger age have major maternal and fetal health consequences. The aim of this study was to compare selected maternal and fetal outcomes of adolescent pregnancies with its adult counterpart in a tertiary care center.

Methods: A hospital based descriptive study was conducted at Teaching Hospital Mahamodara (THM), Galle. One hundred adolescent mothers (10-19 years) were compared with 100 adult mothers (20 -35 years) who had singleton uncomplicated pregnancy. Pre-tested interviewer administered questionnaire was used as the tool to collect data on basic demography, perinatal, maternal outcomes and mode of delivery. Chi-squared test and t-test were used to compare data and presented as proportions, mean (SD), with 95% CI.

Results: Mean (SD) age at delivery of adolescent and adult mothers were 18 (0.2) and 27 (0.8) years respectively. Of the adolescent mothers 16% were unmarried. More adolescent mothers had anaemia compared to adults (38% vs. 32%), but the difference was not statistically significant (p=0.37). Adolescent mothers had higher pre term delivery rate compared to adult mothers (23% vs.15%) but the difference was not statistically significant (p=0.18). There were no significant differences in birth weight (2.77 vs. 2.82; p=0.5) rate of admissions to premature baby unit (6% vs. 7%; p=0.8) and mean APGAR scores (9.9 vs 9.8; p=0.3) between the two groups. A significantly greater proportion of vaginal deliveries were carried out in adolescents compared to adults (75% vs. 55%; p= 0.003).

Conclusions: Adolescent mothers underwent a significantly larger proportion of vaginal deliveries compared to adults. Though not significant, anaemia and preterm deliveries were higher than in their adult counter-parts. There was no significant difference between the two groups for the selected perinatal outcomes.

Keywords: *Adolescent pregnancy, obstetric outcomes, teenage mothers*

Introduction

Adolescent pregnancies are a global problem occurring in high, middle, and low-income countries. It is estimated that about 11% of births worldwide are due to adolescent mothers aged 15-19 years, and more than 90% of these births occur in low and middle income countries (1).

Adolescence is the period where structural, functional and psychological development occurs in a girl and prepares her for motherhood (2). According to UNICEF, adolescent period is a vulnerable phase in human development and it represents a transition from childhood to physical and psychological maturity. During this period, adolescents learn and develop their knowledge

and skills to deal with critical aspects of their health and development (3).

Adolescent pregnancy is a problem in both developed and developing countries. It raises various issues related to human rights. Adolescents are neither physically nor psychologically ready for pregnancy or childbirth. This reproductive event makes them more vulnerable to complications resulting in devastating health consequences. Obstetric risks are often divided in to categories of maternal complications, mode of delivery and its complications and neonatal outcomes. Complications during pregnancy and childbirth are the leading cause of death for 15-19 year-old girls globally (4). It is a health as well as economic burden to a low resource setting country with higher rates of adolescent pregnancies due to its added complications and social impact. During this period, WHO worked with partners to advocate for attention to adolescents, to build the evidence and epidemiologic base for action to develop and test programme support tools, to build capacity, and to pilot initiatives in the small but growing number of countries that recognised the need to address adolescent health.

In Sri Lanka, only a few studies have been conducted to study the obstetric-outcomes in adolescent pregnancies (5-7). In obstetrics unit in Galle 62% of teenage pregnancies were unplanned mainly due to ignorance of contraception (7). Teenage pregnancies particularly in those below in 17 years of age have increased risk of adverse pregnancy outcomes mainly psychological morbidity (8).

Adolescent pregnancy plays a significant role in maternal and perinatal health. Identification of the problems associated with adolescent pregnancy help to make decisions to improve reproductive health. Being the only obstetric tertiary care centre in the Southern Province of the country Teaching Hospital Mahamodara (THM) cater to a large number of mothers that include adolescent mothers as well. The aim of this study was to identify maternal and fetal outcomes of adolescent and adult pregnancies comparatively by studying the deliveries that took place at THM during a specified time period. The findings of this study could be useful to the national and regional policy makers to take steps to improve the outcome of adolescent pregnancies.

Methods

A descriptive cross sectional study was carried out in THM, Galle during the period of 13th June 2019 to 28th December 2019 to compare the maternal and fetal outcomes between a selected group of adolescent and adult mothers. Adolescent mothers were selected according to the WHO definition of age ranging from 10 to 19 years (9). Adults were selected from the age group of 20 to 35 years. Participants were recruited from postnatal wards following childbirth. In both groups, postnatal mothers with pre-pregnancy medical co-morbidities, multiple gestations and psychiatric illnesses were excluded. Sample size calculation was done allowing 95% CI with the precision of the estimate of 0.05 and adding 20% for dropouts (10). According to the final calculation, 200 mothers were needed for the study.

Convenient sampling method was used with the recruitment of consecutive mothers who were admitted to postnatal ward to achieve a total number of 200 mothers with 100 for each group. Data collection was done using pre tested interviewer administered questionnaire by the principal investigator. Bed head tickets and hand held notes were used to retrieve necessary data. The questionnaire consists of four main sections. Part A of the questionnaire consisted of the details regarding basic demographic data of both groups of mothers (age, Body Mass Index (BMI), parity, ethnicity and educational status) Part B was included adverse maternal outcomes; anaemia, Pregnancy Induced Hypertension (PIH) and Gestational Diabetes Mellitus (GDM). Part C included selected perinatal outcomes; Pre Term Delivery (PTD), Birth Weight (BW), admission to premature baby unit (PBU) and APGAR score and part D included the mode of delivery (VD) and Caesarean section.

Data were analysed using the Statistical Package of Social Science version 25 (SPSS). Numerical variables were analysed using independent t-test and categorical data were analysed using chi-squared test. Results of the study were compared and presented as proportions and means with 95% CI.

The ethical approval was obtained from the Ethics Review Committee, Faculty of Allied Health Sciences, University of Ruhuna before the

commencement of the study. Informed written consent was obtained from all participants prior to data collection. Inclusion of the eligible participants was done entirely on voluntary basis.

Results

A total of 200 postnatal mothers were included in the study; 100 adolescents and 100 adults. The response rate was 100 %.

The mean (SD) age of adolescents and adults were 18.4 (0.2) and 27.6 (0.8) years respectively. There was no significant difference in the mean Period of Gestation (POG) at delivery between adolescent and adult mothers (37.8 vs. 38.0 weeks p=0.7). Adult mothers had significantly higher BMI than adolescents (23.1 vs. 20.3kg/m^2, p=<0.001) at booking visit. Adolescent group was significantly less educated than adult group (p<0.001). All adult women were married while 16% in adolescent group were unmarried (p<0.001). Majority were Sinhalese in both adolescent and adult mothers (78% vs. 89%).and there was a higher proportion of Muslim mothers in adolescent group than in the adult group (16% vs. 8%) (Table 1).

Table 2 demonstrates presence of the selected maternal outcomes in the participants. No statistically significant difference was observed between the two groups with regards to aneamia, while numbers with PIH and GDM were low.

Table 03 summarizes perinatal outcomes of study participants. Rate of PTD was higher among adolescents when compared to adult mothers (23% vs. 15%). But this was not statistically significant (p=0.2). There were no statistically significant differences in other perinatal outcome variables such as: BW, admission to PBU and APGAR score at 10 min.

Table 04 shows mode of deliveries among participants. The number of women delivered by vaginally was significantly higher in adolescent group compared to adults.

Table: Socio-demographic characteristics of study participants

Maternal Characteristics	Adolescents n=100		Adults n=100		χ^{2*} / t**	95% CI	p-value
POG at delivery (days) Mean±SD	37.8	(±7.6)	38.0	(±8.6)	0.3 (t)	(-0.9) - (-0.6)	0.7
Age at delivery (years) Mean±SD	18.4	(±0.2)	27.57	(±0.8)	-21.8 (t)	(-10.0) - (-8.4)	<0.001
BMI at booking visit (kg/m^2) Mean ± SD	20.3	(±0.6)	23.14	(±1.0)	-4.5 (t)	(-4.1) - (-1.6)	<0.001
Parity							
1	94	(94%)	42	(42%)	62.1 (χ^2)	8.7 - 54.0	<0.001
>2	6	(6%)	58	(58%)	-	-	-
Marital status							
Married	84	(84%)	100	(100%)	17.4 (χ^2)	0.4 - 0.4	<0.001
Unmarried	16	(16%)	0	(0%)	-	-	-
Educational level							
≤ O/L	95	(95%)	52	(52%)	47.7 (χ^2)	6.6 - 46.8	<0.001
≤ A/L	5	(5%)	48	(48%)	-	-	-
Ethnicity							
Sinhala	78	(78%)	89	(89%)	5.4 (χ^2)	(0.2) - (0.9)	0.02
Others	22	(22%)	11	(11%)	5.4 (χ^2)	(0.2) - (0.9)	0.02

POG - Period of gestation
* Chi-squared test ** Independent sample t-test

Table 2: Maternal obstetric outcomes of study participants

Maternal Outcomes	Adolescents (n = 100)	Adults (n = 100)	χ^2	95% CI	*p*-value
Anaemia	38 (38%)	32 (32%)	-0.9	-0.2 - (0.1)	0.4
PIH	3 (3%)	6 (6%)	-	-	-
GDM	3 (3%)	9 (9%)	-	-	-

Table 3: Perinatal outcomes of study participants

Perinatal outcomes	Adolescents (n=100)	Adults (n=100)	χ^2 * / t**	95% CI	*p*-value
PTD (<37 weeks)	23 (23%)	15 (15%)	2.9 (χ^2)	1.7 - 1.8	0.2
Birth weight (kg) Mean±SD	2.8 (0.5)	2.8 (0.7)	0.5 (t)	(-208.8) - (117.98)	0.5
Admission to PBU	6 (6%)	7 (7%)	0.1 (χ^2)	(0.3) - (2.6)	0.8
APGAR score at 10 min Mean±SD	9.9 (0.3)	9.8 (1.4)	1.1 (t)	(-0.1) - (0.4)	0.3

* Chi-squared test ** Independent sample t-test

Table 4: Mode of deliveries among participants

Mode of deliveries	Adolescents n =100	Adults n = 100	χ^2 * value	95% CI	*p*-value
Vaginal delivery	75 (75%)	55 (55%)	8.791	1.3 - 4.5	0.003
LSCS**	25 (25%)	45 (45%)	8.8	0.2 - 0.7	0.003

* Chi-squared test ** LSCS – Lower segment caesarian section

Discussion

Adolescent pregnancy and motherhood have remained a major health and social issue as it is associated with adverse consequences to the health of the mother and the child in short and long term basis to a country. Teenage mothers are also likely to suffer from severe complications during pregnancy, child birth and postnatal life, which can be detrimental to both mother and child.

Sri Lanka has achieved substantial improvements in maternal and child health compared to regional countries. WHO recognized that despite low resources, Sri Lanka has highest achievement in teenage pregnancy care in their "Adolescent Pregnancy in South East Asia" report (11). Yet, Sri Lanka has much room to optimize outcomes of adolescent pregnancy with different strategies.

The study found that adolescent mothers were more likely to have vaginal delivery and had more of them affected with PTD and anaemia than in their adult counter-parts even though the differences were not significant. But there was not much difference between them and adults when we looked into selected perinatal outcomes such as APGAR score and number of PBU admissions of their newborns.

Current study reported higher rate of anaemia among adolescent group compared to adults (38% vs. 32%) even although this is not statistically significant. A study done by Goonewardene, *et al*., in 2005 in the same setting found that those below 17 years of age had a significantly higher risk of having anaemia compared to controls (6). Nutritional anaemia predominantly due to iron deficiency is the commonest prenatal complication observed in teenagers even in the UK (12). Neuro-developmental delay in younger generation is the most alarming long term consequence due to iron deficiency during pregnancy. This could be prevented with recognition of high risk group such as teenage mothers and implementation of effective strategies such as early booking visit, screening for anaemia and supervised iron supplementation.

In this study, development of PIH was not significantly different between adolescent mothers and adult group, and this finding is consistent with the study done by Kayastha, *et al*., in 2012 (13). In their study they have found that incidence of hypertensive disorders was not statically significant between adolescent and adult groups. However, some studies reported controversial findings to current study (14, 15). In those, a significantly higher risk of PIH in adolescents was reported compared to adults. This difference could be explained with diversity of occurrence of PIH in different geographic locations and methodological differences in above studies. This clearly shows that need of large multicenter study to find out whether there are differences for the incidence of PIH between the two groups of mothers.

We also examined the presence of GDM during pregnancy in adolescents and older mothers. The study failed to show any statistically significant difference in presence of GDM in two groups. But, the incidence of GDM were three times higher in pregnant adults than pregnant adolescents. A study done by Kositworakitkun, *et al.*, 2016 found that teenage pregnancies had lower rate of GDM than adult pregnancies (16). This could be explained by the risk of occurrence of diabetes in advance maternal age in general population compared to young women.

Management of preterm birth is a challenge in low resource setting such as in Sri Lanka. Current study found that a higher percentage of adolescents had PTD than their adult counterparts even though the difference is not statistically significant. Similar findings were found in a study conducted in Pakistan (14). Another study done in the same setting in 2005 showed that younger teenagers had higher risk of preterm delivery than older teenagers (6). The current study also found that there were no significant differences in other perinatal outcomes such as PBU admissions and APGAR score at 10 min in both groups. Similar finding was reported by Al-Haddabi, *et al.,* in 2014 (17). On the other hand, Aung, *et al.,* in 2017 found that adolescent mothers had significantly higher percentage of babies with poor APGAR score (10% vs. 3%) than adult mothers. These differences may be due to heterogeneity of studies.

This study found that vaginal delivery rate is higher in adolescent mothers than in adult mothers (75% vs. 55%) and on the other hand, cesarean section rate was higher in adult mothers than adolescent mothers (45% vs. 25%). Reviewing previous studies, there were conflicting results regarding mode of delivery. Naz U in 2014 found similar result in line with our study (18). However, different results were described by Sarwar & Iftikhar in 2016 (14).

There were some limitations of this study. Sample size was too small to find out real difference between groups with regards to some important maternal and perinatal outcomes due to lack of power of study. This study did not examine the other significant parameters of interest such as occurrence of perineal tears, postpartum haemorrhage and maternal psychological morbidity. Choosing adult women would have led to selection bias as they are having higher likelihood of developing medical co-morbidities such as diabetes and hypertension due to advanced maternal age. This could have overestimated the proportion with these diseases

of the adult group. The recruitment of a sample from a tertiary care referral center could have led to over-representation of adult mothers with medical comorbidities assessed in this study.

Conclusions

The study found that adolescent mothers were more likely to have vaginal delivery compared to their adult counter-parts. When considering the selected perinatal outcomes; PTD was higher among the adolescent mothers, but there were no comparable differences in the numbers with APGAR score and PBU admissions in both groups and the numbers were low. A higher percentage of adolescent mothers had anaemia compared to adult mothers though the difference is not statistically significant.

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Association between bone mineral density and vertebral fractures among patients with diabetes attending Teaching Hospital Karapitiya

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ABSTRACT

Introduction: Diabetes mellitus (DM) impairs bone strength resulting in an increased risk of fractures. This study was designed to determine the association between bone mineral density (BMD) and vertebral fractures among a selected group of patients with Type 2 diabetes mellitus.

Methods: This cross-sectional study included patients with diabetes, selected from clinic attendees at Teaching Hospital Karapitiya. Serum creatinine, urine microalbumin to creatinine ratio and a lateral radiograph of the thoraco-lumbar spine were done in all patients. Those who were detected to have vertebral fracture/s underwent bone densitometry. BMD was also measured in a group of patients selected from the rest of the group who did not have vertebral fractures and another group of healthy individuals selected from the same community. They were matched for the age and gender.

Results: In patients with diabetes (n=160, females 110), the mean (SD) age and the duration of the disease were 62 (10) years and 10 (3) years, respectively. Of patients with diabetes screened, 20 had vertebral fractures (12.5% prevalence). Compared to healthy controls, patients with diabetes without vertebral fractures had significantly low BMDs in the proximal femur but comparatively higher BMD in the total spine. BMDs measured in the total spine and proximal femur were not different between patients with DM vertebral fractures and without vertebral fractures.

Conclusions: Our data indicate a 12.5% prevalence of vertebral fracture among patients with DM. Although patients with diabetes in general had lower BMDs in most of the regions examined, there was no significant difference in regional BMDs between those with fractures and without fractures.

Keywords: *Bone mineral density, cross-sectional study, diabetes, vertebral fracture*

Introduction

Diabetes mellitus (DM) and fragility fractures are associated with increased morbidity, mortality and health-care cost, hence they have become major public health issues, globally. According to predictions, diabetes and fragility fractures will be more prevalent in the future but an exponential rise is expected in certain regions such as Asia.

Although diabetes is not counted in fracture risk assessment tools such as FRAX algorithm, many studies have demonstrated that patients with type 2 DM are at increased risk of fractures at hip, proximal humerus and foot (1). Studies related to vertebral fractures among patients with DM, however, are limited and inconsistent. While Vestergaard, *et al.,* and Yammamoto, *et al.,* found an

increased prevalence of vertebral fracture (VF) among adult patients with DM, Gerdhem, *et al.,* and Schwartz, *et al.,* found no such association (1).

DM could influence bone strength in many ways. Factors such as hyperglycaemia, hypercalciuria, elevated levels of cytokines and impaired renal function seen in DM could reduce bone strength (2). Hyperglycemia could affect bone strength by increasing formation of advanced glycated end products in collagen which is a determinant of load bearing of bone tissue. Furthermore, microvascular complications of DM could reduce the bone strength resulting in fractures.

Although Bone Mineral Density (BMD) is a strong predictor of fractures among postmenopausal women (3) and in patients on long-term glucocorticoids (4), previous studies have not shown BMD to be a significant predictor of fractures among patient with DM. Normal or even higher BMD values have been seen in patients with type 2 DM with vertebral and non-vertebral fractures suggesting that BMD is not a major determinant of microarchitectural deterioration in them (5, 6). Hence, the aetiology and mechanism of the mechanical failure of bone tissue among patients with DM remain poorly understood.

Owing to the scarcity of studies, there is no uniform opinion whether patients with DM should be routinely screened for fracture risk. Further, if a patients with DM is found to have a fracture, the value of BMD assessment is not certain. Similarly, the contribution of other risk factors; skeletal and extra-skeletal, to the occurrence of fractures in diabetics is not known.

Osteoporosis and DM are prevalent diseases in Sri Lanka and the co-existence of DM and either vertebral or non-vertebral fracture is not an uncommon clinical observation (7). Furthermore, the number of patients with this disease combination can be expected to increase in the future. Physical activity, socio-economic and nutritional factors that are related to both DM and bone health are different among Asians compared to other populations and this disparity may play an important role in determining fractures among patients with DM in Asia. This research was designed to study the association between BMD and fractures among a selected group of diabetics.

Methods

Patients with Type 2 DM attending adult medical clinics at Teaching Hospital Karapitiya were invited to participate in a cross-sectional study of vertebral fractures. Written informed consent was obtained from all participants and the study protocol was approved by the Ethics Review Committee of Faculty of Medicine, University of Ruhuna.

Demographic and disease-related data were collected using a pre-tested interviewer-based questionnaire and by perusing medical records. Serum creatinine and urine microalbumin to creatinine ratio were measured adhering to standard protocols. Body weight was measured to the nearest 0.1kg without footwear and height was recorded using a portable stadiometer (Weight Master International, Model BW-110H) to the nearest 0.5cm while on barefeet. Estimated Glomerular Filtration Rate (eGFR) was calculated with the Cockcroft-Gault formula (8).

Lateral radiographs of the thoraco-lumbar spine were taken in all patients recruited for the study. Radiographs were taken under standard conditions by one technician using the same x-ray machine. X-ray beam was focused on to T10 vertebra with the tube-patient distance of 6 cms. Radiographs were assessed by two investigators, in blinded manner, using a semi-quantitative method described by Genant, *et al.,* in 1993 (9). VFs were classified as follows: mild, a reduction in height of 20 - 25%; moderate, 25 - 40%; severe, more than 40%. An agreement of both assessors was required to define a VF and when in disagreement, they came to consensus after a discussion.

All patients who were detected to have VFs underwent bone densitometry and BMD values of the lumbar spine (L1-L4; total spine) and proximal femur were measured by dual-energy X-ray absorptiometry (Hologic Discovery, Bedford, USA). Using a random number generating table, an equal number of age and sex matched patients were selected from the rest of the group who had diabetes but not VFs and they too underwent DXA evaluation similar to patients with VFs. Lateral radiographs of the thoraco-lumbar spine and BMD measurement were done in a group of age and sex matched healthy individuals who had no DM, selected from the community. These healthy

controls were selected in a random manner using the latest voters' registers from the community catchment area of the same hospital. All BMD measurements were done by the same technician adhering to the manufacture's guidelines. In-vitro precision of the DXA machine was checked on each scanning day by calibrating the phantoms provided by the manufacturer and in-vivo precision of the BMD estimations of the same machine has been published earlier (10).

Statistical analysis

Data are given as mean (SD) unless stated otherwise. ANOVA with Bonferroni correlation for multiple comparisons was used to compare continuous numerical data of the three groups. Comparisons of categorical variables were done using chi-squared test and $p<0.05$ was used to define statistical significance.

Results

There were 160 (110 females) patients included in the study and the mean (SD) age and the duration of the disease were 62 (10) years and 10 (3) years, respectively. Of 160 clinic attendees screened, 20 had vertebral fractures (12.5% prevalence) and 19 of them were females. Among the patients who had fractures 13 (65%) had mild fractures, 5 (25%) had moderate and 2 (10%) of them had severe fractures. Two patients had multiple fractures and each one of the rest had a fracture of a single vertebra. The distribution of fracture sites was as follows: 8 in T12, 4 in T11, 2 in T8, T10, T4, T7 each, 00 in L1 and 00 in L2. When demographic and biochemical data were compared, there was no significant difference in BMI, duration of DM, smoking habits, alcohol consumption, post-menopausal status (among women) and glomerular filtration rate between patients with DM with and without VFs (Table 1).

There were no VFs among the age and sex matched non-diabetic controls. Analysis of variance showed a significant difference between three groups of patients with regards to their BMDs at the neck of the femur, hip, and trochanteric region (Table 2). Post-hoc comparisons showed significantly lower BMD values in all regions of proximal femur among diabetics, regardless of the presence of VFs, compared to healthy controls. Total spine BMD among all patients with diabetes was significantly higher compared to healthy controls but the total body BMD was not different. There was no significant difference in BMDs at any skeletal site examined between patients with DM with VFs and without vertebral fractures (Table 2).

Table 1: Demographic and disease related data about the patients

Variable	Diabetics with vertebral fractures (n-19)	Diabetics without vertebral fractures (n=16)	Non diabetic controls (n=18)	*p*-value
Age (years)	64.5 (11)	59 (7.5)	62 (11)	0.13
BMI (kg/m^2)	25 (3.8)	23.2 (2.9)	24.2 (3.1)	0.17
Duration of DM (years)	9.5 (3.1)	8.9 (3.3)	-	0.25
eGFR (Estimated Glomerular Filtration Rate)	61.8 (26)	66.7 (15.7)	-	0.16
% currently on atorvastatin	73.7	87.5	-	0.31
% currently on metformin	68.4	62.5	-	0.71
% currently on insulin	5.3	2.5	-	0.10
% currently smoking	10.5	12.5	13	0.66
% current alcohol users	10.5	12.5	14	0.56
% menopausal women	88	79	81	0.17

None were on pioglitazone

Table 2: Comparison of bone mineral densities (BMDs) between patients with DM with and without VFs and healthy controls

Site	Patients with diabetes, with vertebral fractures (n=19)	Patients with diabetes, without vertebral fractures (n=16)	Healthy controls (n=18)	*p*-value
Total Body BMD	0.984 (0.160)	0.955 (0.120)	1.096 (0.120)	0.15
Femoral Neck BMD	0.706 (0.12)*	0.693 (0.09)*	0.780 (0.06)	0.02
Trochanter BMD	0.586 (0.10)*	0.593 (0.07)*	0.680 (0.05)	<0.01
Total hip BMD	0.832 (0.15)*	0.819 (0.09)*	0.940 (0.076)	<0.01
Total spine BMD	0.780 (0.17)*	0.751 (0.13)*	0.680 (0.05)	0.57

* indicate significant differences ($p<0.05$) when compared with corresponding values of the healthy controls

Discussion

Our data indicates the differences in BMD among patients with diabetes with VFs compared to those with DM without fractures and healthy controls. There was 12.5% prevalence of VFs among patients with diabetes and they were mostly seen in women. Patients with diabetes have lower BMDs in all sites in the proximal femur regardless of the presence of VFs. Total spine BMD was higher among patients with diabetes and this probably a result of aortic calcification and degenerative changes commonly seen among patients with diabetes. Soft tissue such as major vessel and ligament calcification is common in diabetes and this may have erroneously increased spinal and total body BMDs (11, 12). BMDs in the proximal femur are relatively less affected due to above changes and more likely to reflect real BMD changes in diabetes.

In a previous study by Yammato, *et al.,* where 90% of study subjects were postmenopausal women with type 2 DM with a mean age of 63 years, 17.3 % were detected to have VFs (5). In another study which comprised of 76 postmenopausal diabetic women, 26.3% were detected to have VFs (13). A cross-sectional study with 137 postmenopausal women and 161 men reported prevalence figures 31.4% among women and 37.9% among men (14). Compared to all other studies this reported a very high prevalence of vertebral fractures among the diabetics. This could partly be due to the sample they recruited. Compared to patients in other studies, these patients had advanced diabetes with worse HbA1C profiles (14). A study conducted in Brazil, reported a fracture prevalence of 23% (2). Volha, *et al.,* reported a prevalence vertebral fracture among patients with type 1 diabetes as 25% (Volha, Christina, *et al.,* 2013). Among the 82 patients they studied 20 patients had vertebral fractures. We found 12.5% prevalence of vertebral fractures among patients with Type 2 DM in our sample and this is relatively a low prevalence compared to other studies.

We found no difference in the duration of diabetes, diabetes complications, alcohol consumption, smoking status and postmenopausal status between those with and without vertebral fractures. Our findings are in keeping with observations made by Touminun*, et al.,* in 1999. (15). Furthermore, regional BMD values were not different between patients with VFs and without VFs among patients with DM. Hence we could assume that mechanism of VFs among patients with DM must be a result of reduced material quality independent of BMD. Accumulation of Advanced Glycation end-products (AGE) which lead to diabetic complications such as nephropathy and neuropathy have been found in bone tissue as well. These products may affect the mechanical properties of the bone and deteriorate the strength of the bones. Researchers have found

that pentosidine which is an AGE, present in the trabecullar and cortical bones is associated with VFs , (16). They also proved that these changes in the bone quality occur independent of BMD values.

Previous studies examining BMD differences between Type 2 diabetics and non-diabetic controls have reported conflicting results. They reported higher (17), similar (15) and lower BMD values (18, 19) among diabetic patients compared to healthy controls. Our analysis showed lower BMD values among patients with DM with or without VFs compared to healthy controls at all sites except the spine. This difference could be explained by the methodological differences among the studies. For example Rotterdam study, which showed a higher BMD values for patients with type 2 DM than controls contained many patients who had mild disease and previously undiagnosed diabetes (17). In contrast, our study included patients with long standing disease. Different BMD values between the patients with DM and healthy controls could be explained by changing insulin levels over time in patients with type 2 DM. Insulin levels are usually high at the onset of disease and become low in long standing diabetes mellitus. Insulin by a direct act on bone probably via IGF 1 receptor and by an inverse effect on sex hormone binding globulin (SHBG) increases BMD. BMD can be expected to be higher among early diabetics with relatively higher insulin level compared to long standing diabetics who have depleted insulin level.

This was a cross-sectional study and we only considered vertebral fractures in this analysis. Longitudinal studies are needed to prove the importance of BMD in assessing vertebral fractures among diabetics.

The present study shows reduced BMDs in the proximal femur among diabetics regardless of the presence of VF. BMDs, however, were not different among patients with diabetes with and without fracture indicating that BMD is not a reliable measure of VF and BMD cannot be included in the fracture risk assessment in diabetes. Further studies should be done to assess bone quality such as microarchitecture to detect the determinants of mechanical failure of bone tissue among diabetics. Until such studies are done, clinicians will have to consider routine radiography as the reliable and easy way to detect those with VFs.

Conflict of interest

All authors have no conflict of interest.

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A case of fatal haemorrhage due to ruptured varicose veins

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Introduction

Presence of varicose veins in lower limbs is a common condition in the community affecting 14 to 59% of the population (1). It has been estimated that >20 million people in the United States have some form of symptomatic chronic varicose vein- related conditions (2). Varicose veins appear as tortuous dilated veins with associated oedema and induration of the skin (1). The most frequently affected veins are the superficial veins of the lower extremities (3). While complications such as leg oedema, varicose eczema and ulceration are not unusual, fatal haemorrhage from rupture is a rare event in most forensic practices. This rupture can happen spontaneously or as a result of minor trauma and in general is not fatal (2). However, if unattended, a fatal outcome can occur in a small percentage of cases (3). The investigation of such cases is usually straightforward, although the amount of blood at the scene, and the elderly and frail nature of many of the victims may raise the possibility of an assault.

Case presentation

A 60-year-old woman was found dead in bed at her home by a neighbour. As there was blood pooling all over the place, the neighbor had immediately contacted the police. According to the neighbour, the deceased was living alone at this place for the last six months after the demise of her husband. She was suffering from diabetes mellitus and hypertension, however was not on regular treatment. She also had varicose veins over her lower limbs, for which she occasionally took treatment from a general practitioner. She was not on any anticoagulants at the moment.

A scene visit was arranged by the police with the participation of the magistrate, scene of crime officers and the judicial medical officer. There were no signs of breaking and entering at the scene. The deceased was found lying on the bed with blood staining over her left shin and foot. Pooling of blood was seen at the foot end of the bed (Figure 1), the bed room floor and the bathroom floor. A pattern of fine elliptical bloodstains around blood pools were present on the floor (Figure 2).

Autopsy was performed after the body was transported to the mortuary. The body was that of an elderly female with features in keeping with the mentioned age. No fresh or old injuries were found over the body suggestive of assault. Evidence of chronic varicose veins was present over both lower limbs. Marked discolouration was seen over the medial aspect of the left lower leg and ankle. An acute varicose ulcer measuring 2 x 3 millimeters in size was present anterior to the medial malleolus of the left lower leg (Figure 3). Associated haemorrhage was seen in and around the wound. The ulcer was shallow in depth with irregular shaped edges. There was oedema and varicose eczema surrounding the ulcer. The systematic dissection of the ulcer revealed communication with a superficial varicosity that drained into the great saphenous vein. The only other significant finding was the marked coronary artery atherosclerosis. The left main, left circumflex and right coronary artery showed significant atherosclerotic narrowing. Toxicological evaluation was negative for common poisons and illicit drugs.

Figure 1: Pooling of blood on the foot end of the bed

Figure 2: Fine elliptical bloodstain pattern around blood pools on the floor

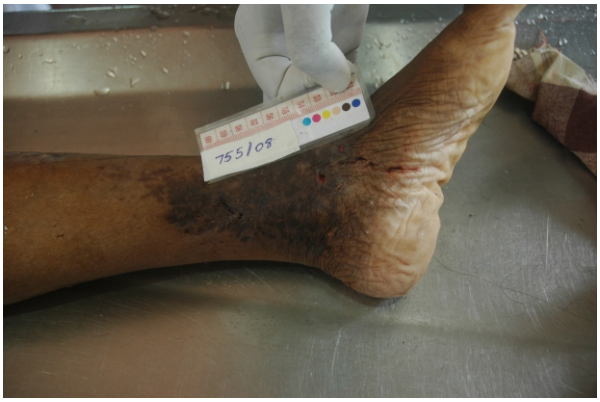

Figure 3: Acute varicose ulcer with discolouration of the skin over the medial malleolus

Discussion

Varicose veins are dilated and tortuous veins that are usually found in the legs, associated with valvular incompetence. The aetiology is multifactorial, with suggestions that congenitally defective valves may be responsible for chronic venous distension, being superseded by the theory that valve incompetence follows dilatation of inherently weak vein walls (4).

Varicose veins are extremely common in the adult population, occurring in 10% to 40% of western men and 25% to 33% of western women, with the most commonly affected vein being the great saphenous (5).

The reported cases illustrate a number of characteristic features of deaths due to haemorrhage from varicose veins. Victims are characteristically elderly, and haemorrhage may occur from rupture of an intact varix, sometimes associated with minor trauma, from chronic venous ulceration into a superficial varix, or from more substantial trauma, causing laceration of skin and soft tissues overlying a varicosity. The fragility of skin and soft tissues in the elderly means that more significant injuries may result from relatively less severe trauma than in younger individuals (6).

Failure to adopt swift measures to control bleeding is a characteristic feature in these cases. This failure to control the bleeding by way of using simple measures, such as applying direct pressure or by elevating the affected limb, could be due to many reasons. Lack of awareness and failure to recognise the seriousness of bleeding and absence of training in simple first aid measures are commonly known causes. Underlying psychiatric conditions such as dementia, which can alter the level of mental state and memory and use of some of the medications and substance of abuse also could play a vital role in this scenario.

Co-morbidities such as ischaemic heart disease may predispose to death following significant exsanguination, or may result in death from less severe blood loss than in an individual with unimpaired coronary artery circulation. Alcohol may enhance the speed of bleeding due to peripheral vasodilation, and anticoagulant medications, may also predispose to significant haemorrhage from apparently trivial defects (7).

Bloodstain pattern analysis and interpretation are a standard part of many crime scene investigations. Examination of the characteristics of bloodstains may provide important information about the events leading up to their deposition.

Classically, arterial bleeding is associated with a projected bloodstain pattern with significant volume and spines (the pointed edges that radiate out from the center of stains due to the volume and force of the haemorrhage) (8). Clusters of large elliptical stains and drip patterns occur with significant lacerations or incisions of large arteries causing an arterial spurt or gush that differs from impact spatters or low-velocity, free-falling droplets of blood (5). Lesser injuries to smaller arteries may produce a much finer pattern from smaller droplets. As blood that escapes from veins is under much lower pressure it tends to pool until gravitational forces acting on it exceed the surface tension of the blood. This result in the formation of spherical droplets in free-fall that produce approximately circular stains upon impact with a horizontal surface such as a floor. These stains are characterized by their large size (13 -21.5 mm) and their lack of directional indicators (5).

The unique situation of lower limb varicose veins, with incompetent valves and pooled venous blood under higher than normal pressure, may result in fine 'arterial-type' blood spatter, as in this case, if a small defect occurs in the wall of a varicosity. An awareness of this possibility may assist in the evaluation of death scenes where there is extensive haemorrhage with apparent arterial blood spray. The identification of an acutely ulcerated lower leg varicosity beneath adherent blood clot, with blood spatter either on the floor, or at a level that corresponds to the height above the floor of the vascular defect, are all features that support higher than normal pressure venous, and not arterial, haemorrhage.

Conclusions

This case has demonstrated the uncommon occurrence of death due to haemorrhage from varicose veins. Despite the rarity of these events, the entirely preventable nature of the deaths by the application of simple first aid procedures suggests that the possibility of this outcome should be discussed with all individuals who are afflicted with varicose veins. The speed at which death may occur under these circumstances, underlines the vulnerability of socially isolated individuals to a lethal outcome once a varicosity has been breached.

Autopsy examinations should include careful layer dissection of the area of haemorrhage to demonstrate ruptured varices and to enable directed histologic examination of ulcers. Toxicological evaluation and drug histories may provide useful information on drugs or medications that may enhance bleeding. Full autopsy evaluation is also required to determine whether there are underlying organic diseases, such as ischaemic heart disease, that may have contributed to or hastened death or whether there is evidence of any sequelae to collapse from blood loss, such as hypothermia, that may also have played a role in the terminal mechanism.

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Vertical transmission of dengue haemorrhagic fever; anticipation and early detection leading to success in management

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Introduction

Dengue is a vector borne disease responsible for nearly 4 billion infections annually, prevalent in the tropics with seasonal outbreaks (1). *Aedes* spp. act as the vector (1). There were 105,049 cases of dengue reported in Sri Lanka in 2019 (2). Neonatal dengue infection can result from vertical transmission through placenta (3). We report a case of a newborn with dengue haemorrhagic fever due to vertical transmission. Anticipation and early detection was the key to successful management.

Case presentation

A baby girl was born by vaginal delivery to a primigravida mother with dengue fever at 38 weeks of gestation. She weighed 2300g at birth. Antenatal period was uncomplicated except maternal fever which developed 2 days prior to the delivery. Mother's febrile illness was initially managed as dengue fever (DF) and it was subsequently progressed to dengue haemorrhagic fever (DHF). She was managed in an intensive care unit where she gave birth. The baby was immediately admitted to the Special Care Baby Unit (SCBU) following birth for observation with the suspicion of vertical transmission of dengue. In baby's blood, NS1 antigen was negative on day 2 but become positive on day 4. Ultrasound scan (USS) of abdomen and thorax did not show evidence of leaking on day 4. Results of serial haematological investigations are shown below (Table 1). Baby was fed with expressed breast milk from day 2 of life and started on prophylactic antibiotics; intravenous crystalline penicillin and cefotaxime on day 4.

She developed a significant drop in platelet count down to 58,000/mm^3 with a rise of total white cell count on 5th day. Repeat USS of abdomen and thorax on day 5 showed pericholecystic fluid and pericardial effusion confirming the diagnosis of DHF (Figures 1 and 2). She was managed as leaking phase of DHF from day 5 with fluid management and monitoring of haemodynamic parameters (pulse rate, blood pressure, capillary refilling time, urine output). She was given maintenance fluid intravenously according to the day of life starting with 60 ml/kg in day 1. Maintenance fluid was increased 15ml/kg per day till day 7. Urine output was measured and targeted to keep above 1 ml/kg/ hour. Urine output and haemodynamic parameters were used to guide the fluid management. A cocktail mixture of fluids with sodium 2-3 mmol/kg, potassium 1-2 mmol/kg and 5% dextrose was used as intravenous fluids from day 2. Our patient did not need any fluid boluses. Microhaemaocrit centrifugers to measure packed cell volume (PCV) were not available in the hospital. Hence the measurement of PCV frequently was not possible. Oozing from puncture sites was noted on day 7 which settled subsequently. No other bleeding manifestations were noted. Platelet count started to rise on day 7 indicating the beginning of the recovery phase of DHF. Baby's haemodynamic parameters were stable throughout the leaking phase. DEN 3 virus was isolated in a blood sample obtained on day 5 of life by Reverse Transcriptase - Polymerase Chain Reaction (RT - PCR). Mother also had DEN 3 virus isolated in her blood in day 7 of her illness. Baby did not have

Table 1: Serial haematological investigations of the newborn

Age in days	Day 0	Day 1	Day 2	Day 4	Day 5	Day 5.5	Day 6	Day 6.5	Day 7	Day 7.5	Day 8	Day 8.5
WBC (/mm^{-3})	11840	22580	17980	12740	9000	6250	8500	11520	11600	10710	15560	18010
Neutrophils (/mm^{-3})	7340	17160	9277	7886	5640	4000	3910	4147	3132	3160	5240	5170
Lymphocytes (/mm^{-3})	2960	3297	6724	3491	999	1375	3145	5299	6612	6051	8520	9220
Hb (g/dL)	14.2	15.7	14.8	12.5	12.4	12.9	13.4	13.3	14.0	12.8	12.3	13.0
Haematocrit (%)	45	50.4	48.9	39.2	39.2	40.2	42.3	40.6	43.1	40.4	38.6	39.7
Plt count (x10^3 /mm^3)	253	309	231	372	204	184	114	58	48	39	54	64
ALT (U/L)	11								34			
AST (U/L)	97								204			

Hb - Haemoglobin, Plt. - Platelet, ALT - Alanine Aminotransferace, AST - Aspartate Aminotransferace

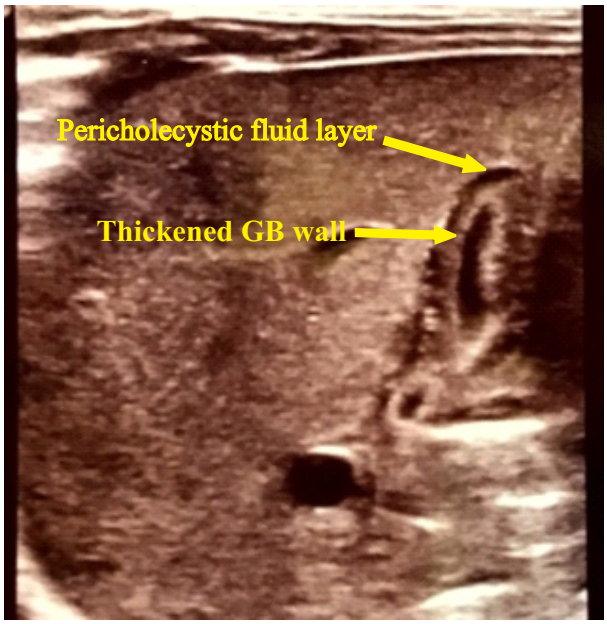

Figure 1: USS Abdomen showing pericheolestatic fluid

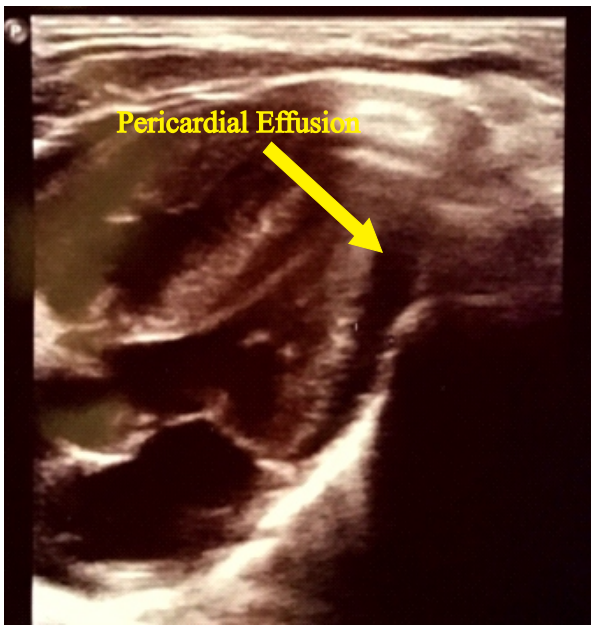

Figure 2: USS Thorax with evidence of pericardial effusion

Dengue antibodies were done on day 7 of life and showed dengue IgM positive with IgG negative. Mother's dengue IgG and IgM both were positive on day 9 of her illness.

Baby recovered fully from the illness without any complications.

Discussion

Vertical transmission of dengue could occur transplacentally or via breast milk. Transplacental transmission of dengue virus can occur in late pregnancy (3). A study in New Caledonia showed a vertical transmission rate of 90% in the perinatal period in mothers who had dengue fever close to delivery and dengue virus was detected in breast milk in 75% of breast feeding mothers with DF (4). As this baby was taken into SCBU following birth, it was highly unlikely to have a mosquito bite. Hence, vertical transmission was the only possible mode of transmission. It was not possible to conclude whether mother had primary or secondary dengue infection.

SD BIOLINE Dengue NS1 antigen rapid test which was used to detect NS1 antigen has a specificity of 98.3% and sensitivity of 76.7% (5). Dengue RT-PCR was used to detect dengue virus in blood of mother and baby. It revealed the same serotype. NS 1 antigen was not detected in day 2 but was positive on day 4. Breastfeeding was started on day 2. It was possible to have vertical transmission either transplacentally or via breast milk. We could not perform dengue RT-PCR on cord blood which might have been helped to confirm transplacental transmission.

A marked drop in the platelet count and an increase in the dropping of the WBC count were noted during the onset of leaking which occurred on day 6 of life. Subsequent USS confirmed leaking. Lack of guidelines to manage neonates with DHF and unavailability of microhaematocrit measurements were challenges in the management. Monitoring the vital parameters and trends of WBC and platelets were important to monitor the clinical course of DHF.

A review of 17 neonates with vertical transmission of DF showed fever occurring from day 1 - 11 of life with a median on day 4 (6). There are neonatal dengue cases reported in South Asian region including Sri Lanka and rest of the world (7-9). Most neonates recover without complications. Awareness of the possibility of vertical transmission of DF was very important as our patient never had fever during the course of the illness.

DENV- 1 and DENV- 3 serotypes of dengue virus are known to cause DHF on primary dengue infection (9). DENV -3 was isolated in our patient.

Management of neonate with DHF is challenging. Early suspicion of vertical transmission, SCBU care with continuous monitoring and fluid management leads to the successful outcome in our patient. Further studies on the possibility of transmission of dengue via breast milk are needed. A guideline on management of DHF in neonates will be helpful.

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