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FACTORS ASSOCIATED WITH TUBERCULOSIS AMONG CHILDREN AND ADOLESCENTS IN KELANTAN: A CROSS-SECTIONAL STUDY

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Abstract

Objectives: This study aimed to estimate the proportion of tuberculosis patients among children and adolescents, to describe the socio-demography and clinical factors for tuberculosis infection among children and adolescents in Kelantan from 2012 until 2015. Methods: This study was a retrospective cross-sectional study between tuberculosis and non-tuberculosis cases among children and adolescents using Tuberculosis Information System as a source population. All notified cases that fulfilled the inclusion and exclusion criteria were included in the study. Descriptive statistics, simple and multiple logistic regressions were used for data analysis. Results: Out of 5412 tuberculosis cases, 8.4% were children and adolescents group with mean age of 15. Among 322 children and adolescents with tuberculosis, majority of them were Malay (91.2%), 7.5% illiterate and 79.6% resided in non-urban area. By clinical factors, 2.8% were Human Immunodeficiency Virus (HIV) positive and 14.6% were cigarettes smokers. Older age, cigarettes smoking, female gender, Malay ethnicity, good education level and non-urban residence were the significant associated factors for tuberculosis infection among children and adolescents with AOR 1.41 (95%CI: 1.29,1.54; p<0.001), 3.35 (95% CI: 1.86, 6.01; p<0.001), 1.88 (95% CI: 1.33, 2.65; p<0.001), 0.17 (95%CI: 0.07,0.44; p<0.001), 0.20 (95%CI: 0.12,0.33; p<0.001) and 1.92 (95% CI: 1.33, 2.79; p=0.001) respectively. Conclusion: The study provides important criteria of children and adolescents to be prioritized for tuberculosis screening, early diagnosis and prompt treatment, and might as well mitigate the dynamic transmission of tuberculosis in the community.

Keywords: Tuberculosis, Associated Factors, Children and Adolescents

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Introduction

Malaysia is a country located in the South-East Asia region and recognized as an upper middle-income country with 31 million people. The state of Kelantan is located in the northeast of Peninsular Malaysia and its people is made up of majorly Malay population (95.7%) [1]. The Western Pacific Region, of which Malaysia is part of it, accounted for nearly 60% of the world’s tuberculosis cases in 2012. Our adjacent neighbours Indonesia, the Philippines and Thailand were the three of the 22 countries with the world’s highest tuberculosis burden [2,3].

The World Health Organization (WHO) reported that in 2015, there were 1 million children and adolescents infected with tuberculosis around the world, and more than 136,000 die annually [2]. Recent report from Malaysian Ministry of Health (MOH) depicted that the proportion of tuberculosis cases among children and adolescents in Malaysia range between 17% until 20% out of total tuberculosis cases with increasing trend from year 2010 until 2015 [4]. Meanwhile, exclusively for Kelantan state, the proportion of tuberculosis cases among children and adolescents range from 1% to 3.01% out of total cases from year 2000 to 2015 also with increasing trend as well [5].

A retrospective cohort study of all patients registered in the 2012 Malaysian National Tuberculosis Surveillance Database showed that 1824 cases of tuberculosis were children and adolescents which comprised about 8.5% out of total tuberculosis cases [3]. Meanwhile, an analysis study of Malaysia tuberculosis surveillance data in 2000 found that the proportion of tuberculosis cases by age groups were 2.8% (<14 year old), 67.7% (14-54 year old) and 29.5% (>54 year old) [6]. A cohort study in Sabah in year 2001 found that 3908 patients were infected with tuberculosis. Out of these cases, 512 (13%) cases were children and adolescents and majority of the cases (59%) among children and adolescents were from the age strata of 15-19 year old [7].

Proportion of tuberculosis cases among children and adolescents globally varies from 6.6% to 39.2% [8-14]. According to the WHO regions, the proportion was higher in African region (16.0% to 39.2%), followed by Eastern Mediterranean region (35.0%), South East Asia region (20.0%), Region of the Americas (6.6% to 17.3%) and Western Pacific region (8.5%) [2].

A child or adolescent get infected with tuberculosis in the exact pattern as an adult, which is through inhalation of droplets of tuberculosis bacteria in the air deriving from person with active tuberculosis. The infection source for children and adolescents is usually a person living in the same house who has active tuberculosis and persistently cough. Besides that, children and adolescents can get infected in a communal setting such as nurseries, kindergartens, schools and colleges [15]. The risk of progression to tuberculosis disease is highest when the child age is less than four years old, and to a lesser extent when they are less than ten years old. There is also a higher risk of progression in children and adolescents who are immune-compromised, for instance Human Immunodeficiency Virus (HIV) positive individuals [15].

Children and adolescents comprises nearly 30% of total Malaysia population [1]. At the same time, tuberculosis cases among children and adolescents in Malaysia is increasing in number with almost 20% of tuberculosis cases in Malaysia are of
children and adolescents group [4]. And yet, there is no well-published local study in Malaysia to determine the associated factors for tuberculosis infection among children and adolescents. Therefore, this study aimed to estimate the proportion of tuberculosis patients among children and adolescents and tried to explore the associated factors for tuberculosis infection among children and adolescents particularly among Kelantan population. Among the known socio-demographic factors from existing literatures contributing to tuberculosis infection among children and adolescents are older children [12,16,17], Malay ethnicity [3,18,19], male gender [10,17], low education level [10,11] and resident of rural area [8]. Whereas the known clinical factors associated with tuberculosis infection included cigarette smoking [3,10] and positive HIV status [3,17,20]. We expect that the findings of our study could have a significant impact on the principles and practices of tuberculosis detection and control management in the local setting, and may help other National Tuberculosis Programs to review their criteria of detection with similar statistics.

**Methods**

**Study design and participants**

This study applied a retrospective cross-sectional study design and was conducted within three months period starting from January until March 2017 in Tuberculosis and Leprosy Control Unit, Kelantan State Health Department.

The reference populations were all children and adolescent tuberculosis patients in Kelantan and the study samples were children and adolescent with tuberculosis and non-tuberculosis in Kelantan registered in Tuberculosis Information System (TBIS) from 2012 to 2015 who fulfilled study inclusion and exclusion criteria. In this study, the inclusion criteria were confirmed cases of tuberculosis who were notified to respective District Health Offices in Kelantan and registered in TBIS from 1st January 2012 to 31st December 2015. Non-tuberculosis cases were tuberculosis contacts who have no symptom, negative Mantoux test, no chest radiograph abnormality and registered in TBIS from 1st January 2012 to 31st December 2015. Both cases and non-tuberculosis cases must be of 1 year old till 19 year old of age.

The sample size was calculated for each variable of associated factors for tuberculosis infection among children and adolescent using Power and Sample Size calculation software as well to compare two independent proportions. The largest estimated sample for each group was 322 using the proportion of non-tuberculosis children and adolescents by factor of urban residence 0.61 [21]. The estimated proportion of 0.49, 5% type 1 error, 80% power and additional 20% missing data. We used simple random sampling method to obtain 322 study samples from respective sampling frames for each comparison group between tuberculosis and non-tuberculosis.

Data were collected from Kelantan TBIS. TBIS is an online registry set up by the Ministry of Health for surveillance purpose of tuberculosis disease in Malaysia. The retrieved information includes data on socio-demography (age, ethnicity, gender, location of residence and education level) and clinical factors (HIV and cigarettes smoking status).

From Kelantan TBIS, we found a total of 15333 tuberculosis cases and tuberculosis
contacts among children and adolescents from 2012 till 2015. Then we subdivided them into tuberculosis cases and non-tuberculosis cases sampling frames. From each sampling frame, we used simple random sampling method to obtain 322 study samples for each group. The flowchart for this study is shown in Figure 1.

**Figure 1. Flowchart of the study for factors associated with tuberculosis infection among children and adolescents in Kelantan**

The study was approved by the Human Research and Ethics Committee, Universiti Sains Malaysia USM/JEPeM/16120592 and the Medical Review and Ethical Committee from National Institute of Health, Ministry of Health Malaysia NMRR-16-2348-33521 (IIR).

**Operational definitions**

In this study, good education level is defined as those above 10 years old who were attending or had attended school [22]. As for location of residence, urban areas are defined as gazetted areas which have a combined population of 10000 or more. Meanwhile, rural areas are defined as gazetted areas which have a combined population of less than 10000 [23].

**Statistical analysis**

Statistical Package for Social Science (SPSS) version 22.0 statistical software was used for data entry and analysis. Descriptive statistics with mean and standard deviation (SD), frequency and percentages were calculated. Simple and multiple logistic
regression analysis were used to determine factors associated with tuberculosis infection among children and adolescents. A *p*-value of less than 0.05 was considered statistically significant.

Results

There were 5412 tuberculosis cases and 36356 tuberculosis contacts notified and registered in Kelantan TBIS during the four year period (2012-2015). All tuberculosis cases were included to determine the proportion of tuberculosis cases among the studied population. The proportion of children and adolescents with tuberculosis out of total tuberculosis cases ranged between 8% to 9% annually between 2012 until 2015. Details regarding the proportion of tuberculosis patients among children and adolescents in Kelantan from 2012 till 2015 were shown in Table 1.

### Table 1. Proportion of tuberculosis patients among children and adolescents in Kelantan 2012-2015 (N=5412)

<table>
<thead>
<tr>
<th>Year</th>
<th>Total tuberculosis cases (N=5412)</th>
<th>Tuberculosis among children and adolescents (n=456)</th>
<th>Proportion (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>1411</td>
<td>116</td>
<td>0.08 (0.07,0.10)</td>
</tr>
<tr>
<td>2013</td>
<td>1402</td>
<td>123</td>
<td>0.09 (0.07,0.10)</td>
</tr>
<tr>
<td>2014</td>
<td>1366</td>
<td>118</td>
<td>0.09 (0.07,0.10)</td>
</tr>
<tr>
<td>2015</td>
<td>1233</td>
<td>99</td>
<td>0.08 (0.07,0.10)</td>
</tr>
<tr>
<td>Summative</td>
<td>5412</td>
<td>456</td>
<td>0.08 (0.08,0.09)</td>
</tr>
</tbody>
</table>

A total of 644 samples were included in this study with 322 samples for each group of tuberculosis and non-tuberculosis cases. The mean age of children and adolescents with tuberculosis was higher as compared to those with non-tuberculosis. For both groups, Malay was the predominant ethnicity and female gender slightly predominated the study. Tuberculosis cases showed higher percentage for residing in non-urban area and being educated as compared to non-tuberculosis cases. Higher percentage of cigarette smokers was observed among tuberculosis cases as nearly all non-tuberculosis cases were non-smoker. HIV status showed small discrepancy between these two groups with majority of them had negative HIV status. Details regarding socio-demographic and clinical characteristics of children and adolescents registered in Kelantan TBIS were shown in Table 2.
Table 2. Socio-demographic and clinical characteristics among children and adolescents registered in Kelantan TBIS 2012-2015 (n=644)

<table>
<thead>
<tr>
<th>Patients characteristic</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tuberculosis cases (n=322)</td>
</tr>
<tr>
<td>Age*</td>
<td>15.98 (3.74)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>207 (45.4)</td>
</tr>
<tr>
<td>Female</td>
<td>249 (54.6)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>416 (91.2)</td>
</tr>
<tr>
<td>Others</td>
<td>40 (8.8)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>422 (92.5)</td>
</tr>
<tr>
<td>Poor</td>
<td>34 (7.5)</td>
</tr>
<tr>
<td>Location</td>
<td></td>
</tr>
<tr>
<td>Non-urban</td>
<td>363 (79.6)</td>
</tr>
<tr>
<td>Urban</td>
<td>93 (6.4)</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>275 (85.4)</td>
</tr>
<tr>
<td>Yes</td>
<td>47 (14.6)</td>
</tr>
<tr>
<td>HIV status</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>313 (97.2)</td>
</tr>
<tr>
<td>Positive</td>
<td>9 (2.8)</td>
</tr>
</tbody>
</table>

*Mean (SD)

Simple and multiple logistic regression analysis were used to determine the significant associated factors. Age, gender, education level, location of residence and smoking status were the significant associated factors for tuberculosis infection among children and adolescents and the details were shown in Table 3.
Table 3. Factors associated with tuberculosis infection among children and adolescents in Kelantan 2012-2015 by multiple logistic regression (n=644)

<table>
<thead>
<tr>
<th>Factors</th>
<th>Crude OR&lt;sup&gt;a&lt;/sup&gt; (95% CI)</th>
<th>Adjusted OR&lt;sup&gt;b&lt;/sup&gt; (95% CI)</th>
<th>Wald statistics&lt;sup&gt;b&lt;/sup&gt; (df)</th>
<th>p-value&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.23 (1.17,1.29)</td>
<td>1.41 (1.29,1.54)</td>
<td>60.56 (1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1.29 (0.95,1.77)</td>
<td>1.88 (1.33,2.65)</td>
<td>12.90 (1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>0.22 (0.09,0.50)</td>
<td>0.17 (0.07,0.44)</td>
<td>13.35 (1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>0.24 (0.15,0.38)</td>
<td>0.20 (0.12,0.33)</td>
<td>39.32 (1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-urban</td>
<td>1.82 (1.28,2.61)</td>
<td>1.92 (1.33,2.79)</td>
<td>11.90 (1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2.58 (1.49,4.47)</td>
<td>3.35 (1.86,6.01)</td>
<td>16.33 (1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HIV infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>9.23 (1.16,73.28)</td>
<td>6.76 (0.83,54.77)</td>
<td>3.20 (1)</td>
<td>0.073</td>
</tr>
</tbody>
</table>

<sup>a</sup>Simple logistic regression, <sup>b</sup>Multiple logistic regression
Forward LR method applied
No multicollinearity and no interaction found
Classification table 74.5% correctly classified
Area under Receiver Operating Characteristics (ROC) curve was 79.5%

**Discussions**

Based on the findings of this study, the annual tuberculosis cases in children and adolescents in Kelantan was 8.0% (95% CI 0.08,0.09). Our finding is slightly lower than the national data study where children and adolescents comprised about 8.5% out of total tuberculosis cases nationwide [3]. The discrepancy in the findings could be attributed to the number of children and adolescents that get tuberculosis in Kelantan.
were possibly underestimated from the true incidence numbers which led to underreporting. The reasons for the underestimated numbers are poor accessibility to tuberculosis diagnosis and treatment, similarities in the clinical pictures with other typical childhood illnesses and inadequate routine recording and reporting of childhood and adolescents tuberculosis cases [24].

In Malaysia, high tuberculosis incidence of children and adolescents was seen among age strata of 10 to 19 year old [3]. The finding was consistent with the present study for Kelantan where the mean (SD) age for tuberculosis infection was 15.98 (3.74) years old. The finding was almost similar to a matched case-control study in Brazil to analyze the risk factor for tuberculosis infection among older children that identified the mean age of the enrolled patients was 14.4 years [10]. Another study on prevalence of tuberculosis among adolescents in Western Kenya also reported similar finding of mean (SD) age of infected adolescents with tuberculosis, reported as 14.4 (1.90) years [8].

In our study, age has been found to be a significant factor associated with tuberculosis infection. A person with an increase of one year of age has a 1.41 times the odds to get tuberculosis similar to the findings in a cohort study in South Africa among adolescents tuberculosis patients [16]. Possible explanation is that older age is associated with engaging in multiple health risk behaviors among adolescents hence exposing to various disease risks including tuberculosis [25].

We found significant association between gender and tuberculosis infection through this study. More than half of patients were female (54.6%) as compared to male (45.4%), and being female children and adolescents were almost two times more likely to get tuberculosis infection, compared with male group. Findings of this study are in line with three other different studies conducted among children and adolescents with tuberculosis in Uganda, Pakistan and South Africa. All of these studies showed that female children and adolescents had higher odds of getting tuberculosis infection [11,12,16]. Some worldwide studies have shown that male has higher risk factors like smoking, alcoholism, drug addiction and HIV infection to acquire tuberculosis compared to female, thus the sex difference in tuberculosis prevalence was attributable by all these factors [26,27]. However, there is possible explanation for the shift of notification rate towards female group. It is possible that female adolescents are simply more likely to use health services during their reproductive years. A study in United States reported that different health seeking behaviour by female group would increase their chance of being diagnosed should they have symptoms of tuberculosis [28].

The result of our study also showed significant association between other socio-demographic determinants such as ethnicity and education level with tuberculosis infection among children and adolescents. From this study, it is reported that Malay population in Kelantan is less likely to get infected with tuberculosis (AOR 0.17; 95%CI: 0.07,0.44). However, Malay people comprised the majority of the studied patients compared to other races such as Chinese, Indian and Siamese, most probably due to enormous Malay population (95.7%) in Kelantan [1]. Conclusion of tuberculosis was prevalent among Malay children and adolescents cannot be made because there
Factors Associated With Tuberculosis Among Children And Adolescents In Kelantan: A Cross-Sectional Study

were few non-Malay samples in this study. Therefore the variable cannot be used to test the causal hypothesis. Nevertheless, other studies in Malaysia pointed out that tuberculosis is prevalent among Malay population. A retrospective cohort study of all patients registered in the 2012 Malaysian National TB Surveillance Database reported that 50.8% of patients were of Malay ethnicity [3]. Another study by Hooi (1994) on tuberculosis patients visiting Chest Clinic, Penang Hospital reported that 59.3% of patients were Malay people [18] whereas Nissapatorn et al. (2004) reported that 49.2% of total patients with extrapulmonary tuberculosis diagnosed at the National Tuberculosis Center, Kuala Lumpur were of Malay ethnicity [19].

Study by Liew et al. (2015) showed that patients without any formal education were 1.94 fold more likely to develop tuberculosis infection compared to educated group, contradicting with this current study [3]. Our study revealed that educated children and adolescents were more prone to get infected with tuberculosis. This finding is supported by previous study in Brazil which reported that there is evidence indicating the lack of knowledge and misinformation about tuberculosis among educated group could expose them to the same risk of getting tuberculosis as the uneducated ones [29]. Possible reasons could be due to lack of tuberculosis awareness or education programmes that focused among educated group. There are many issues that contributed to the lack of tuberculosis awareness or education programmes in Malaysia. Among the issues was the community’s reluctance to take ownership of health issues as educated people are more reluctant to participate in health activities [30].

Moreover, tuberculosis awareness among public in Malaysia is still low due to lack of health education or promotion focusing on tuberculosis issue. Currently, tuberculosis awareness programmes are not being promoted aggressively since tuberculosis is no longer the number one killer disease in Malaysia and also due to the emergence of new outbreaks such as rabies, leptospirosis and others. Thus, the concentration on addressing tuberculosis in Malaysia has become less. Additionally, dengue fever cases keep burgeoning every year and this indirectly changes the priority of Ministry of Health to overcome the disease accordingly [31].

We also found that there was significant association between area of residence and tuberculosis infection among children and adolescents. Children and adolescents residing in rural area had 1.92 times higher odds of getting tuberculosis, compared to those in urban area. The result was in line with a study in Western Kenya which reported that rural children were more likely to get tuberculosis, which accounted for 87% of total case load [8]. The prevalent of tuberculosis among rural residents are majorly due to lack of knowledge regarding the disease itself. It is reported through a study in a northern rural area of Vietnam that knowledge of causes, transmission routes, symptoms and curability of tuberculosis was low among rural people. They reported that, 82% of the women and 74% of the men resided in rural area did not know that tuberculosis is caused by bacteria. A large proportion reported that tuberculosis is caused by hard work or it is a hereditary disease [32]. In contrast to the finding of our study, a nationwide study in Malaysia reported that patients residing in urban area were more likely to get tuberculosis as
Factors Associated With Tuberculosis Among Children And Adolescents In Kelantan: A Cross-Sectional Study


compared to those residing in rural area (OR 1.22; 95%CI 1.14,1.30; p<0.001) [3].

The result of this study showed that children and adolescents who smoke cigarette were three times more likely to develop tuberculosis infection, compared to non-smoking group. Findings of this study are in line with another study conducted among older children in Brazil which showed that tobacco smoking has a significant impact on tuberculosis infection [10]. Similarly, a local study conducted in Penang and Kuala Lumpur reported that cigarette smoking was a substantial determinant in 817 of 943 new cases of tuberculosis [33]. A case-control study on association between tobacco smoke and tuberculosis among children in Thailand revealed that children who were also exposed to tobacco smoke were almost four times more likely to get tuberculosis infection compared to unexposed group [34]. Smokers were more likely to develop tuberculosis due to pathophysiological changes in their respiratory pathway. Smoking not only induces local anatomical disruption, it also elicits a complex immunological response among smokers [35]. Eventually, the natural lung defense mechanisms against mycobacterium or its elimination among smokers will be impaired, hence explain how smoking could increase the probability to contract tuberculosis [36].

Multivariable analysis showed no significant association between HIV status and tuberculosis infection among children and adolescents, after controlling potential confounding factors. This finding was in agreement with study in rural Eastern Uganda which also projected there was no significant association between HIV status and tuberculosis infection among children and adolescents [17]. However, it is well-known that tuberculosis is among the commonest opportunistic infection in HIV infected patients [37]. HIV positive people are about 20-30 times more likely than HIV negative people to develop tuberculosis in countries with a generalized HIV epidemic. Liew et al (2015) reported that HIV positive patients in Malaysia were 5 times more likely to get tuberculosis infection as compared to HIV negative patients (AOR 5.01; 95%CI 4.27,5.88; p<0.001) [3]. Tuberculosis is also a major cause of morbidity in HIV infected children, with HIV infected children having a 20–25-fold higher incidence of tuberculosis than HIV uninfected children, with an overall tuberculosis incidence in South African HIV infected children of 9.2% (95%CI:0.14–0.97) [38].

Small sample size for HIV positive patients was one of the limitations of this study because small sample size would limit the findings on its association with tuberculosis infection. There was also a limitation to identify ethnicity as one of possible associated factors for tuberculosis infection owing to Kelantan population are made up mainly of Malay ethnicity. Conclusion of Malay ethnicity being the highly prevalent group for tuberculosis infection certainly inappropriate as there were few non Malays recruited in this study.

This study had demonstrated that the significant associated factors for tuberculosis infection among children and adolescents in Kelantan were older age, female gender, good education level, rural residence and cigarettes smoking. By delineating these possible significant risk factors for tuberculosis infection, it will assist and guide health authorities to design a better and comprehensive plan for the national tuberculosis control programme,
focusing more attention towards children and adolescents group without marginalizing them. Consequently, dynamic transmission of tuberculosis in our community would be mitigated.

Acknowledgements

The authors would like to thank the Director General of Health Malaysia for allowing us to do data collection from TBIS database in which ethical approval was obtained from Ministry of Health. Our gratitude also goes to the Kelantan Tuberculosis and Leprosy Control Unit for their assistance during data collection.

Conflict of interest

The authors have no conflicts of interest associated with the material presented in this paper.

References


Factors Associated With Tuberculosis Among Children And Adolescents In Kelantan: A Cross-Sectional Study


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Factors Associated With Tuberculosis Among Children And Adolescents In Kelantan: A Cross-Sectional Study


THE RELATIONSHIP BETWEEN SOCIO-DEMOGRAPHIC AND ILLNESS-RELATED VARIABLES WITH THE QUALITY OF LIFE AMONG MALAYSIAN ADOLESCENT WITH THALASSAEMIA: A MULTI-CENTRE STUDY

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Abstract

Thalassaemia is a life-long illness that exists globally. The quality of life of adolescents with thalassaemia could differ based on the health policies of a specific region, existing level of socio-economic development and the illness related variables. This study examines the relationship between socio-demographic and disease-related variables with the quality of life among adolescents with thalassaemia involving multiple treatment centers spread throughout various locations in Malaysia. Participants included 218 adolescents (male=108; female 112) with mean age of 13.86 (SD=2.40). They completed the questionnaire consisting of demographic information, illness-related variables, and Pediatric Quality of Life Inventory 4.0 (PedsQL). The participants in this study was found to have higher total summary score (Mean = 69.64, SD = 14.03), psychosocial health (Mean = 70.23, SD = 14.91), emotional (Mean = 72.12, SD = 20.66), social (Mean = 79.82, SD = 17.37), and school (Mean = 58.69, SD = 16.77) functioning but with lower physical health (Mean = 68.50, SD = 17.22) as compared to previous study that was done in Kuala Lumpur. Findings also shows a significant positive correlation between level of education and frequency of hospitalization (r = .156, p < 0.05), frequency of transfusion (r = .152, p < 0.05), and physical health (r = .186, p < 0.01). An increase in the frequency of transfusion was found to significantly increase social functioning (r = .137, p < 0.05). Other significant correlations are discussed in addition to the quality of life experienced by patients with thalassaemia in different region of the world.

Keywords: Thalassaemia, Adolescent, Illness-Related Variables, Transfusion, Quality of Life
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Introduction

Thalassaemia is a life-long illness due to hereditary anemia from defects in hemoglobin production [1]. Malaysia Thalassaemia Registry reported that as of 2009, a total of 3,310 patients are registered as having beta-thalassaemia (β-thalassaemia) while an estimated of 600,000 to 1,000,000 individuals are carriers of thalassaemia in Malaysia. The numbers of individuals with thalassaemia are increasing throughout the years [2] and as such greater emphases are being placed on the identification of genetic markers of thalassaemia for treatment and preventative purposes [3]. Additionally, various medications with high efficacy have been produced to reduce the mortality and morbidity related to thalassaemia [4]. The current focus on optimal clinical management is not only towards the management of the symptoms but has also been shifted to the physical health, psychosocial health, and the overall quality of life (QoL) of patients with thalassaemia. Ismail et al. [5] found that the QoL for children with thalassaemia in Malaysia is significantly lower than their healthier counterparts. This is due to how the illness impacts their school performance, self-image, financial problems, and their ability to integrate with the society [6]. Previous studies also found that individuals with β-thalassaemia had a significantly lower QoL as compared to their healthier counterparts [6, 5].

The poor QoL experienced by patients with thalassaemia can be explained by disease-related variables and demographic factors such as frequency of hospitalization, onset of illness, and social economic status [7, 8]. However, the predictors of the QoL for patients with thalassaemia may differ based on the cultural differences and the health policies of the respective region [9]. In Thailand, age of patients and household income were found to be significant predictors of QoL [8] which differs from Malaysia in which age and household income are not significant predictors for the QoL [5]. Although a study in India found that age is a significant predictor of QoL, no other socio-demographic variables were found to be a significant predictor [10]. Elalfy and colleagues [11] on the other hand found that the predictors of QoL for patients with thalassaemia in Egypt are pretransfusion hemoglobin (Hb) and serum ferritin (SF). Similarly, a study that examined the QoL of multiple countries in Middle East (Kurdistan, Libya, Palestine, Syria, and Iraq) found that the start of iron chelation is associated with the QoL of patients with thalassaemia [12]. Early start of treatment and the adherence to the treatment itself was found to be significantly associated with individual’s QoL [13 – 15]. These suggest the experience of patients with thalassaemia differs in different country with various factors affecting the QoL.

Therefore, it is important to consider the health policies of a specific region, existing level of socio-economic development and the illness related variable in examining the relationship between patients QoL [9]. The aim of this research is to examine the relationship between socio-demographic and disease-related variable with the QoL among adolescents with thalassaemia particularly in Malaysia. This research involves multiple treatment centers spread throughout various locations in Malaysia as compared to a...
single-location study. It is hypothesized that: (i) adolescents with thalassaemia experiences lower QoL; (ii) there is a positive relationship between frequency of transfusion and QoL; (iii) there is a positive relationship between duration of hospitalization and QoL.

### Methods

#### Participants

This was a cross-sectional design study on adolescent with β-thalassaemia in the state of Kelantan, Terengganu, Pahang, Kedah and Sabah located in Malaysia. Convenient sampling was used to gather the participants from government hospitals when they attend the Day Care Clinic for medical check-up in the period of May 2013 to May 2016. Patients diagnosed with thalassaemia whose age range from 9 to 19 years old and are able to read, understand, and write in Bahasa Malaysia was approached. For participants 18 years old and above, consent was obtained from the patients themselves while consent from patients 17 years old and below was obtained from their caregiver. A total of 218 patients agreed to participate in the research. Once the patients or caregivers have consented to be part of the research, the patients were given a set of self-report questionnaire to be completed. A small token of appreciation was given to all the participants once the self-report questionnaire was completed and returned. Ethical approval for this study was granted by the Human Research Ethics Committee, Universiti Sains Malaysia (FWA Reg. No: 00007718; IRB Reg. No: 00004494) and ethics committee of the Ministry of Health, Malaysia.

#### Measurements

Socio-demographic and illness related variables were obtained through self-report where participants were asked to fill in their background information in the demographic section of the questionnaire. Some items are open ended such as age, age of diagnosis, and level of education while others are given specific answers to select from such as items related to gender, treatment center, level of education, frequency of hospitalization, and frequency of transfusion.

The Pediatric Quality of Life Inventory 4.0 (PedsQL) was then administered to mainly assess health-related QoL among children and adolescents. Participants were presented with 23 items related to physical, emotional, social, and school functioning for example: “I feel afraid and scared” and “I have trouble getting along with other kids”. Each item has a Likert scale of 0 (never) to 4 (almost always) to be responded by the participants. Scores were transformed into percentage in which high percentage either represents higher functioning, health, or QoL. The validated and reliable Malay translated version of the PedsQL [16] was used in this study. The reliability of the tool in this research was found to be within the acceptable range (Cronbach alpha = .87)

### Results

#### Socio-demographic and illness-related information

The socio-demographic and illness related information are summarized in Table 1. A total of 218 patients with the age ranging from 9 to 19 years old (Mean = 13.86, SD = 2.40) participated in the research in which
107 (48.64%) are males and 113 (51.36%) are females. The age of diagnosis ranges from a few month after birth to 16 years old with the mean of 3.00 and a standard deviation of 3.18. A total of 47 (21.4%) participants were from Kelantan, 32 (14.5%) from Terengganu, and 40 (18.2%) from Pahang; representing the East Coast of Peninsular Malaysia while 36 (16.4%) patients were from Kedah representing the Northern of Peninsular Malaysia, and 65 (29.5%) from Sabah in East Malaysia. The patients’ level of education ranges from not schooling to college or equivalent to college in which 74 (33.6%) participants are currently attending primary school while 113 (60.5%) are attending secondary school. The majority of the participants are hospitalized at least once a month (45.5%) with only two participants hospitalized once to three time a year (0.9%). The most common frequency of transfusion is once every month which applies to 134 (60.9%) participants.

Table 1. Socio-demographic and illness-related characteristics of participants

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Adolescents with β-Thalassaemia (n = 218)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean (SD) 13.86 (2.40) Range 9 – 19 years old</td>
</tr>
<tr>
<td>Age diagnosed</td>
<td>3.00 (3.18) &lt;1 – 16 years old</td>
</tr>
<tr>
<td>Gender</td>
<td>n (%)</td>
</tr>
<tr>
<td></td>
<td>Male 108 (48.6)</td>
</tr>
<tr>
<td></td>
<td>Female 112 (51.4)</td>
</tr>
<tr>
<td>Centre of treatment</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kelantan 47 (21.6)</td>
</tr>
<tr>
<td></td>
<td>Terengganu 32 (14.7)</td>
</tr>
<tr>
<td></td>
<td>Pahang 39 (17.9)</td>
</tr>
<tr>
<td></td>
<td>Kedah 35 (16.1)</td>
</tr>
<tr>
<td></td>
<td>Sabah 65 (29.8)</td>
</tr>
<tr>
<td>Recent educational level</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not schooling 1 (0.5)</td>
</tr>
<tr>
<td></td>
<td>Primary 1 8 (3.7)</td>
</tr>
<tr>
<td></td>
<td>Primary 2 64 (29.4)</td>
</tr>
<tr>
<td></td>
<td>Secondary 1 93 (42.7)</td>
</tr>
<tr>
<td></td>
<td>Secondary 2 40 (18.3)</td>
</tr>
<tr>
<td></td>
<td>College or equivalent 12 (5.5)</td>
</tr>
<tr>
<td>Frequency of hospitalization</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1-3 times a year 2 (0.9)</td>
</tr>
<tr>
<td></td>
<td>Once every 4 months 4 (1.8)</td>
</tr>
<tr>
<td></td>
<td>Once every 3 months 21 (9.6)</td>
</tr>
<tr>
<td></td>
<td>Once every 2 months 48 (22.0)</td>
</tr>
<tr>
<td></td>
<td>Once every month 99 (45.4)</td>
</tr>
<tr>
<td></td>
<td>Once every 2-3 weeks 9 (4.1)</td>
</tr>
</tbody>
</table>

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The mean scores of the four PedsQL subscales and the Psychosocial Health Summary can be seen in Table 2. In addition to the findings from the current study, findings from previous studies using similar outcome measure from different regions are presented to provide a purposeful comparison. The participants in this study was found to have higher total summary score (Mean = 69.64, SD = 14.03), psychosocial health (Mean = 70.23, SD = 14.91), emotional (Mean = 72.12, SD = 20.66), social (Mean = 79.82, SD = 17.37), and school (Mean = 58.69, SD = 16.77) functioning as compared to previous study done in Kuala Lumpur, Malaysia [5]. However, the physical health (Mean = 68.50, SD = 17.22) was found to be lower than the previous study [5]. A detailed comparison can be seen in Table 2.
Table 2. QoL scores based on PedsQL of adolescents with thalassaemia of current and previous studies

<table>
<thead>
<tr>
<th>Authors (Year)</th>
<th>Location</th>
<th>Patients with thalassaemia (N)</th>
<th>Age range (years)</th>
<th>Total Summary Score</th>
<th>Physical Health</th>
<th>Psychosocial Health</th>
<th>Emotional Functioning</th>
<th>Social Functioning</th>
<th>School Functioning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current findings (2017)</td>
<td>Multi-centre (Kelantan, Pahang, Terengganu, Kedah, Sabah), Malaysia</td>
<td>218</td>
<td>9 – 19</td>
<td>69.64 (14.03)</td>
<td>68.50 (17.22)</td>
<td>70.23 (14.91)</td>
<td>72.12 (20.66)</td>
<td>79.86 (17.37)</td>
<td>58.69 (16.77)</td>
</tr>
<tr>
<td>Ismail et al. (2013)</td>
<td>Kuala Lumpur, Malaysia</td>
<td>75</td>
<td>5 – 18 (12.1; 3.5)</td>
<td>65.35 (10.57)</td>
<td>69.67 (12.51)</td>
<td>63.91 (14.65)</td>
<td>59.92 (16.83)</td>
<td>78.01 (13.92)</td>
<td>50.59 (15.31)</td>
</tr>
<tr>
<td>Boonchooduang et al. (2015)</td>
<td>Chiang Mai, Thailand</td>
<td>64</td>
<td>13 – 18 (15.18; 1.72)</td>
<td>76.10 (12.69)</td>
<td>77.27 (14.96)</td>
<td>75.80 (12.86)</td>
<td>74.02 (17.26)</td>
<td>85.81 (14.08)</td>
<td>67.58 (17.30)</td>
</tr>
<tr>
<td>Elalfy et al. (2016)</td>
<td>Ain Shams, Egypt</td>
<td>127</td>
<td>5 – 18 (11.80; 4.78)</td>
<td>63.74 (13.2)</td>
<td>58.46 (18.09)</td>
<td>Not reported</td>
<td>68.22 (13.88)</td>
<td>67.48 (19.31)</td>
<td>63.15 (19.31)</td>
</tr>
<tr>
<td>Gupta &amp; Jindal (2016)</td>
<td>Northern India</td>
<td>50</td>
<td>2 – 18 (Not reported)</td>
<td>Not reported</td>
<td>71.40 (33.5)</td>
<td>67.80 (32.9)</td>
<td>66.50 (33.9)</td>
<td>75.50 (36.9)</td>
<td>60.40 (35.4)</td>
</tr>
<tr>
<td>Shakib et al. (2016)</td>
<td>Northern Iran</td>
<td>45</td>
<td>8 – 12 (Not reported)</td>
<td>75.90 (20.1)</td>
<td>70.60 (24)</td>
<td>77.70 (19.7)</td>
<td>73.30 (22.9)</td>
<td>85.90 (21)</td>
<td>74.10 (20.1)</td>
</tr>
</tbody>
</table>
Relationship between socio-demographic and illness related variables, and QoL

The associations between the variables of interest were obtained through Pearson product-moment correlation (see Table 3). There is a significant positive correlation between age and age of being diagnosed ($r = .223, p < 0.01$), level of education ($r = .824, p < 0.01$), frequency of transfusion ($r = .161, p < 0.05$), physical health ($r = .210, P < 0.01$), and QoL ($r = .155, p < 0.05$). In addition, age the patient was diagnosed was found to be significantly correlated with level of education ($r = .238, p < 0.01$). Findings also shows a significant positive correlation between level of education and frequency of hospitalization ($r = .156, p < 0.05$), frequency of transfusion ($r = .152, p < 0.05$), and physical health ($r = .186, p < 0.01$). An increase in frequency of transfusion was found to significantly increase social functioning ($r = .137, p < 0.05$).
Table 3. Pearson product-moment correlations between socio-demographic and illness related variables with the QoL of adolescents with thalassaemia

<table>
<thead>
<tr>
<th>VARIABLES</th>
<th>MEAN (SD)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Age</td>
<td>13.86 (2.40)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2. Age diagnosed</td>
<td>3.00 (3.18)</td>
<td>.223**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Education</td>
<td>2.91 (.94)</td>
<td>.824**</td>
<td>.238**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>4. Frequency of hospitalization</td>
<td>3.45 (.92)</td>
<td>.055</td>
<td>.140</td>
<td>.156*</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>5. Frequency of transfusion</td>
<td>2.95 (.75)</td>
<td>.161*</td>
<td>.043</td>
<td>.152*</td>
<td>.036</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Pediatric Quality of Life (PedsQL)</td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>6. Physical</td>
<td>68.50 (17.22)</td>
<td>.210**</td>
<td>.082</td>
<td>.186**</td>
<td>-.016</td>
<td>.047</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>7. Emotional</td>
<td>72.12 (20.66)</td>
<td>.076</td>
<td>.094</td>
<td>.086</td>
<td>.052</td>
<td>.020</td>
<td>.424**</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Social</td>
<td>79.86 (17.37)</td>
<td>.116</td>
<td>.071</td>
<td>.081</td>
<td>.029</td>
<td>.137*</td>
<td>.508**</td>
<td>.586**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. School</td>
<td>58.69 (16.77)</td>
<td>.033</td>
<td>.135</td>
<td>.002</td>
<td>-.043</td>
<td>.089</td>
<td>.473**</td>
<td>.471**</td>
<td>.426**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Psychosocial health</td>
<td>70.23 (14.91)</td>
<td>.093</td>
<td>.124</td>
<td>.072</td>
<td>.018</td>
<td>.094</td>
<td>.570**</td>
<td>.865**</td>
<td>.818**</td>
<td>.757**</td>
<td></td>
</tr>
<tr>
<td>11. Total Summary Score</td>
<td>69.64 (14.03)</td>
<td>.155*</td>
<td>.123</td>
<td>.130</td>
<td>.005</td>
<td>.087</td>
<td>.822**</td>
<td>.781**</td>
<td>.783**</td>
<td>.727**</td>
<td>.937**</td>
</tr>
</tbody>
</table>

*p<.05  
**p<.01
Discussion

The objective of this study was to examine the relationship between socio-demographic and disease-related variables with the QoL among adolescents with β-thalassaemia in multiple treatment centers in Malaysia. As a group, adolescents with β-thalassaemia in this multi-center study were found to have a slightly higher emotional and social functioning as compared to their counterparts in Kuala Lumpur – the capital city of Malaysia [5]. However, the school functioning and physical health was found to be slightly lower while their psychosocial health and total summary score of the participants in this research was found to be slightly higher than the participants in the previous study done in Kuala Lumpur [5]. When compared to studies carried out in Thailand [6] and Northern Iran [17], participants in the current study were found to have slightly lower scores in all domains of PedsQL including the total summary score and psychosocial health. However, only the psychosocial health, emotional functioning and social functioning of adolescents with thalassaemia in Malaysia is slightly higher when compared to individuals with thalassaemia in Northern India [10]. The physical health and school functioning of individuals with thalassaemia in Northern India was found to be higher than that of Malaysian [10]. Although these differences may not be statistically significant, it provides an understanding of the QoL among adolescents with thalassaemia with respect to the different socio-economic development and the illness related variable of each region.

The positive association between age and education level is expected for their chronological age, the scores for their school functioning is the lowest compared to their emotional and social functioning. This is similar to numerous studies in the past, in which adolescents with thalassaemia is able to obtain equivalent academic exposure but is not present in school as frequent as their peers due to treatment [5, 6, 10]. However, in some regions, the school functioning is not the most effected functioning since treatment related to transfusion is done on weekends [11, 17]. This suggests that adolescents with thalassaemia has the capability to function well in school but is hindered due to the treatment that requires them to be absent from school. This is where the understanding of health policies in different countries and its implication to the QoL of adolescents with thalassaemia is helpful in providing optimal care for them.

Additionally, the frequency of performing transfusion was found to increase significantly as the age of the patient increases, which is consistent with findings from previous studies [18, 19]. This could be due to the increase in blood volumes [18] and the increase in severity of the symptoms as they grow older [19]. The increased in the frequency of transfusion could also be reflected from the treatment adherence which could be explained from the developmental perspective. Taddeo et al. [20] considered developmental stages as one of the critical factors when discussing treatment adherence. As an individual age increases and their cognitive development transitions from a concrete thinking to a more abstract thinking, they are able to think more hypothetically and analyze many different evidences that help them appreciate the treatment process. Treatment adherence can be improved by taking into consideration the child’s cognitive
development and providing appropriate information clearly and concisely using short and simple sentences [20]. This explains how adolescents with thalassaemia who may have transitioned from concrete thinking to a more abstract thinking are able to critically assess the importance of the transfusion with information provided by the medical providers, leading to an increased in transfusion for older participants. The finding that an increase in education level significantly increased frequency of transfusion could also support this view.

The physical health and QoL of adolescent with thalassaemia increases as they grow older contradicts previous studies that found significant growth retardation as compared to healthy group [21, 22]. However, patients with thalassaemia are physically stable and fit so much so that they are capable of performing near-normal physical activity similar to the healthy population [23, 24]. This means that even though the physical growth of adolescent with thalassaemia is delayed as compared to healthy population; they are able to perform physical activity that is appropriate to their growth, with them experiencing a slight difficulty in performing activities of daily living independently. This also applies to their QoL that gets better as their age increases [23]. Additionally, the advancement of medication ensures that the growth retardation does not influence the functioning of adolescents with thalassaemia [25]. This is reflected in the findings in this study that showed an increase in frequency of transfusion significantly increased their social functioning.

**Conclusion**

The QoL of adolescents with thalassaemia for states in the East, North and East Coast of Malaysia was found to be slightly higher than the patients with thalassaemia in Kuala Lumpur. However, there are still rooms for improvements as the QoL of adolescents with thalassaemia in Malaysia is found to be lower than that of other regions such as Thailand and Northern Iran. There is a need to study the cross cultural differences that exist in the health policies or socio-demographic and illness related variables to ensure a universal optimal care for adolescents with thalassaemia regardless of the region they are in.

**Acknowledgement**

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**References**


HOW CAN WE IMPROVE CODE BLUE TRAINING FOR NON-PAEDIATRICIANS: AN EXPERIENCE FROM STUDENTS-CONDUCTED ASSESSMENT IN NATIONAL CLINICAL SKILLS CONFERENCE

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Abstract

Introduction: Training of all health personnel involved in paediatric care is a key determinant of successful outcome during paediatric emergencies. We aimed to identify the need for paediatric Mock Code Blue skills training among non-paediatricians in a pre-hospital setting through checklist assessment of their performance. Methods: A paediatric septic shock and cardiac arrest Mock Code Blue pre-hospital scenarios were presented for non-paediatricians during a National Clinical Skills Conference. Eight medical student assessors and four clinical facilitators were involved in this training. Participants were expected to be able to demonstrate the skills and teamwork necessary to manage paediatric emergencies according to the learning outcomes. Results: A total of 97 delegates participated in a facilitated paediatric Mock Code Blue for multidisciplinary groups of health personnel. Outcome measures showed a significant lack of communication and teamwork skills, and weakness in “closing the loop” as barriers to successful resuscitation. Conclusion: We recommend Mock Code Blue simulation training to be offered regularly to all groups of healthcare providers involved in paediatric and neonatal care while not overlooking the emphasis on non-technical skills.

Keywords: Assessment, Emergency Paediatric, Simulation Training, Student Assessors

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Introduction

Paediatric emergency training is crucial for all health professionals involving in paediatric care. Children, adolescents and adult’s physiological, anatomical, cognitive, social and emotional attributes differs and can effect the way a child presents acutely. This necessitates non-paediatric health professionals to receive specific training on paediatric emergencies. The Malaysian pediatric health system (Ministry of Health,
Health Education Division organises training in health promotion and education for health personnel and non-health staff, non-governmental organisations and in the private sector. However, there are no uniform training or education policies that integrate non-paediatricians for prehospital care. Because most Emergency Medical Service providers infrequently encounter ill paediatric patients, it is important to regularly refresh their psychomotor resuscitation skills for a safe transfer to a higher level of care. Moreover, studies have shown that many healthcare providers do not have sufficient training and skills to perform resuscitation effectively in an emergency situation, particularly in low- and middle-income countries [1,2,3,4].

Code Blue is an emergency announced intended for a team of healthcare providers to initiate immediate and skilled resuscitation. A Mock Code Blue simulation can provide an ideal structured and standardised learning approach for multidisciplinary health personnel in different settings. It also offers a safe context where confidence and competence can be assessed [5] through training of both technical and non-technical skills. Similarly to the Neonatal Resuscitation Programme that had significantly reduced mortality rates [6], Mock Code Blue simulation training is known to promote safety and improve outcomes [7,8,9].

However using simulation training requires active trainer involvement and low learner-to-trainer ratios to ensure sufficient training. This comes with hidden costs and faculty time. To avoid burnout and successfully sustain investment in Mock Code Blue simulation, programmes need to be creative in building, sustaining, and managing the trainer workforce [10]. In this manner, using students or peers as assessors are not only reliable [11] for psychomotor skills training but feasible and cost effective that can be transferable across multidisciplinary healthcare professionals.

To provide health professionals and students opportunity to gain such experience, a National Clinical Skills Conference (NSC) was held from Sep 25-27, 2014 in Seremban, Malaysia [12]. The event was organised collaboratively by Hospital Tuanku Ja’afar and the International Medical University (IMU) where general practitioners, medical officers, house officers, paramedics and medical students from different regions in Malaysia received a run-through knowledge and paediatric skills training over two days. The goal was to offer an opportunity for delegates to gain or refresh their psychomotor skills in the management of paediatric emergencies through paediatric Mock Code Blue simulation. This study aims to identify the most appropriate training needs for paediatric resuscitative care among non-paediatricians in a prehospital setting through checklist assessment carried out by final year medical students.

**Methods**

**Setting**

Participants of the NSC attended four concurrent workshops held at IMU Clinical School campus in Seremban, Malaysia. They were offered a theoretical update through a 30-minutes key lecture on paediatric Mock Code Blue presented by the chief facilitator. The lecture and training covered the American Heart Association (AHA) Guidelines for Cardiopulmonary Resuscitation (CPR) and Emergency Cardiovascular Care (Paediatric Advanced

**Preparation**

The setup of two different scenarios were prepared and conducted by a group of four facilitators: septic shock in an infant (Appendix 1) and cardiac arrest in a child (Appendix 2). The paediatric Mock Code Blue addresses skills training in the areas of clinical assessment, airway and breathing, cardiovascular and drugs involved in resuscitation. Non-technical components focus on leadership, roles of team members, communication, mutual performance monitoring with peer feedback as well as task management [14]. The overarching criteria for achieving learning outcomes were situational awareness, decision making, task management and team work [15].

A total of 16 final year medical students volunteered to test the feasibility, logistics and quality of the two scenarios to achieve the expected learning outcomes. Four PALS certified clinical facilitators - two senior clinical lecturers, one senior paediatrician with educational experience and one associate professor- from the Department of Paediatrics developed the construction of standardised checklists (Appendix 3) and feedback rubrics. The validated checklist items were sourced from the AHA PALS guidelines [13]. These checklists were piloted and their accuracy was tested through quality assurance and revised where necessary (Figure 1). Students confirmed the appropriateness and usefulness of the final setup of the scenarios. They assured that all scenarios were delivered in a uniform fashion through instruction and this was confirmed by the chief facilitator.

Measurements were assumed to be valid because they related to clearly defined activities monitored by assessors and data were disaggregated according to resuscitation items. Standardisation of scenarios, checklist items and student assessment are expected to increase the probability of collecting reliable data.
How Can We Improve Code Blue Training For Non-Paediatricians: An Experience From Students-Conducted Assessment In National Clinical Skills Conference

Figure 1. Flow of the national paediatric Mock Code Blue simulation for non-paediatricians in Malaysia involving medical students as assessors

Then 8 out of the 16 student volunteers were selected to be assessors during the NSC event based on their level of confidence and knowledge in their (1) technical skills in septic shock and cardiac arrest emergency scenarios, (2) capability to appreciate technical oversight and inaccuracies of resuscitation algorithm; and (3) understanding of variation in team approach to paediatric resuscitation emergencies. These students were thereafter individually trained two weeks before the event through one-to-one supervision until they had demonstrated their ability to use the checklist tool prior to its actual implementation before the mock (Appendix 4).

During the Mock Code Blue in NSC, equipment and supplies (Appendix 1 and 2) were available in the same approach each time a new group started the Mock Code Blue simulation. Group members were encouraged to participate actively and they were expected to take roles as team leader or otherwise defined by placement determined by priority of proximity to manikin.
Participants

Participants were randomly divided by the organisers into groups of four to five each and moved from station to station to have hands-on experience in various areas of clinical skills, among them the two scenarios that required the initiation of a paediatric Code Blue (Figure 1).

Intervention

Groups were assigned to one of two identical septic shock and to one of two cardiac arrest scenarios (Appendix 1 and 2). Each scenario training lasted for 20 minutes plus 10 minutes for feedback and debriefing. Facilitators started by informing participants of the learning outcomes during a briefing session. The learning outcomes were defined as participants being able to assess the patients’ medical condition and to respond immediately through team approach action. This includes early recognition of patients with respiratory and circulatory problems as well as managing them accordingly, demonstrating basic resuscitation skills, knowing and applying equipment and tools, awareness of working environment and efficient teamwork and communication. The skills training focused on assessment, airway management, resuscitation skills, managing cardiac arrhythmia using automated external defibrillator, intravenous access and insertion of intra-osseous cannula. Both scenarios demanded an efficient emergency response communication. The four facilitators briefed the participants on the set up of the two stations and the equipment as well as on the learning outcomes. Two student assessors marked each group performance according to the checklist collaboratively (Appendix 3). A debriefing session and feedback on clinical assessment, management and collaborative skills was given after the Mock Code Blue by the PALS certified facilitators (Figure 1).

Ethical considerations

This study is part of event evaluation and feedback from participants from NSC 2014. It involves testing within normal educational requirements with no research question involved.

Analysis of data

Data samples from the checklists representing group performance were proceeded to descriptive statistical analysis.

Results

A total of 125 physicians, paramedics and medical students (49 male and 76 female) had applied for the 2014 NSC. Of them, 97 (medical officers 52.8% - from emergency department; medical students 20.8%, others 20% – including nurses and medical attendants; house officers 4.8%; and, general practitioners 1.6%) attended the hands-on training session and agreed in participating in the evaluation of the Mock Code Blue simulation training. None of them were paediatricians.

Groups performed well in technical skills for both scenarios and aced in fluid resuscitation (septic shock scenario) and cardioversion (cardiac arrest scenario). The majority of teams also performed well in the basic ABCs – airway, breathing and circulation - of resuscitation and intravenous (IV) and intraosseous (IO) access (Figure 2).
Figure 2. The achievement of the 20 groups in the Septic Shock and Cardiac Arrest stations (N = number of participants)

<table>
<thead>
<tr>
<th>Resuscitation items</th>
<th>Successful achievement</th>
<th>%</th>
<th>Resuscitation items</th>
<th>Successful achievement</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluids</td>
<td>20 / 20</td>
<td>100</td>
<td>Cardioversion</td>
<td>20 / 20</td>
<td>100</td>
</tr>
<tr>
<td>resuscitation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV / IO</td>
<td>19 / 20</td>
<td>95</td>
<td>Breathing</td>
<td>17 / 20</td>
<td>85</td>
</tr>
<tr>
<td>Circulation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Airway</td>
<td>18 / 20</td>
<td>90</td>
<td>IV access /</td>
<td>17 / 20</td>
<td>85</td>
</tr>
<tr>
<td>Breathing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inotropic</td>
<td>15 / 20</td>
<td>75</td>
<td>Algorithm CPR</td>
<td>16 / 20</td>
<td>80</td>
</tr>
<tr>
<td>support</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Team</td>
<td>15 / 20</td>
<td>75</td>
<td>Circulation</td>
<td>14 / 20</td>
<td>70</td>
</tr>
<tr>
<td>leadership</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reassessment</td>
<td>10 / 20</td>
<td>50</td>
<td>Airway</td>
<td>13 / 20</td>
<td>65</td>
</tr>
</tbody>
</table>
How Can We Improve Code Blue Training For Non-Paediatricians: An Experience From Students-Conducted Assessment In National Clinical Skills Conference


<table>
<thead>
<tr>
<th>Communication</th>
<th>7 / 20</th>
<th>35</th>
<th>Reassessment</th>
<th>12 / 20</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loop</td>
<td>6 / 20</td>
<td>30</td>
<td>Team</td>
<td>11 / 20</td>
<td>55</td>
</tr>
<tr>
<td>communication</td>
<td></td>
<td></td>
<td>leadership</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics</td>
<td>4 / 20</td>
<td>20</td>
<td>Loop</td>
<td>9 / 20</td>
<td>45</td>
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<tr>
<td>communication</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose Check</td>
<td>3 / 20</td>
<td>15</td>
<td>Communication</td>
<td>7 / 20</td>
<td>35</td>
</tr>
</tbody>
</table>

While 65% of the groups (mean percentage of teams achievement in both scenarios) showed team leadership skills, only 38% demonstrated awareness on closing the loop. 35% demonstrated commendable team interaction skills. Appropriate considerations of clinical reassessment were only seen in about half of the participants. Less than one fifth of the participants checked blood glucose and provided antibiotics when needed (Figure 2).

Outcome measures revealed variations in teamwork. Not all participants were familiar with each other and some team leaders were not familiar with Code Blue and paediatric resuscitation. Lack of ‘close the loop’ communications was associated with reduced readiness and proactivity.

**Discussion**

While there is evidence of specific potential avoidable human factors in child deaths [16,17], outcomes for out-of-hospital paediatric resuscitation remains low. This is particularly when educational messages about bystander paediatric resuscitation are not tailored to the audience receiving them [18,19]. Although training may provide learners with required skills, we cannot define with certainty factors that mostly influence motivation to perform resuscitation. Both situational and procedural context may affect motivation and coordination.

In this study we observed that the participants’ performance were hampered in either individual or collaborative tasks in an *a priori* unknown simulated learning environment. Participants were unable to clearly define their team roles and responsibilities in the Mock Code Blue simulated sessions. Perhaps being too cautious or getting lost in their ‘bustle’ prevented them from creating a satisfactory critical action plan. Likewise, randomisation of participants to groups that consisted of mix physicians and medical students may have affected application of non-technical skills involved in resuscitation. There is increasing evidence that team-oriented behaviour during resuscitation is as important as task-oriented approaches [20,21]. We found that the most significant barriers to successful skills performance and efficient resuscitation in the two paediatric Mock Code Blue scenarios were lack of communication, team work and leadership.
skills. There were also a significant lack of clinical reassessment after treatment initiation and poor communication that contributed to poor outcomes. These findings are comparable to studies that revealed that non-technical skills were suboptimal in medical emergency teams [22].

There is a need for paediatric resuscitation training of non-paediatricians in pre-hospital settings, particularly focusing on non-technical skills. Tindale et al. identified team processes as a factor in explaining negative performance in ‘low’ performance versus ‘high’ performance groups. They argued that shared preferences and task presentations must be appropriate to a given situation to lead groups to make the right decisions [23]. In our experience, poorly operated group communication and incorrect influencing processes among group members could explain the varying degree to which they preferred a particular decision alternative, that in turn could explain the different outcomes in performance quality. Poor task presentation such as overlooking the need of glucose-check and urgent antibiotics administration is one aspect of poor shared preferences due to the stressful character of the scenario training. Fostering trans-active group training in simulated scenarios on a regular basis is expected to solve these problems and improve results [24,25]. Hagemmann et al. highlights the effectiveness of even a single brief seminar on non-technical skills to strengthen the learning from the skill training exercise. Such combination of theory and practice may improve the quality of treating acutely ill patients and their outcomes [26]. Over the years, tool such as the Team Emergency Assessment Measure (TEAM) has been validated and shown potential to improve team training in non-technical performance [27].

There are a number of limitations in this study that needs to be highlighted. In reality, ad-hoc groups are frequently formed on a need-to-do basis to perform specific task. In such situation, Emergency Medical Service providers exercise a certain degree of influence as each one react to their own abilities and limitations. Such realisation affect decisions and outcomes. In the present study, the composition of groups and logistics were entrusted to the NSC organisers. It was evident that ‘low’ performing teams assumed less responsibility for their actions. In some groups where medical officers, house officers and students were working together, the juniors expected the seniors to make decisions. In cases where the senior lacked leadership skills the group performed poorly. Participants who do not know each other in an unfamiliar simulated environment may account for ‘low’ performance. Furthermore, although international studies have shown that students as assessors are realiable, feasible and cost-effective [11], our results should be taken with caution as local students-assessors could be influenced by what they felt rather than the true value of what had happened [28].

We address these limitations by ensuring consistency in the evaluation of participants’ groups. As a standard criterion, students-assessors were only deemed eligible for assessing participants using the checklists after approval by the senior paediatricians. The scoring sheet may be sophisticated for a medical student to use, especially the subjective components. However, a review of the students' assessments by four experienced PALS
providers revealed that the score sheets were used accurately and in a standard format during training of assessors. Random observations of the students-assessors showed a nearby total agreement among the four paediatricians. However, it is acknowledged that this is subjected to subjectivity and bias.

To conclude, the implementation of a Mock Code Blue simulation in acute paediatric care is recommended in the training for all health personnel. There is a universal acceptance that proper emergency care can make an important contribution to reducing avoidable death and disability in low- and middle-income countries [29]. The findings of the present study are relevant to Malaysia and low- and middle-income countries to develop uniform training opportunities. There are several applications for improving Mock Code Blue simulation; the first step should integrate collaborative and operational values that establish ground rules for a team-directed approach including general practitioners, nurses, medical assistants, medical students and paramedics. Personnel should participate in a minimum of one Mock Code per calendar year that include a brief seminar on non-technical skills. Measurable outcomes using assessment tool such as TEAM and standardised checklist can be used to improve training of healthcare professionals. This study further adds that students or peers can take a role in evaluation of Mock Code Blue performance. We therefore urge the public boards of health and education, with respective national medical societies to initiate annual Mock Code Blue drills in hospitals and communities, and assess the team approach in meeting performance expectations. While paramedics, non-paediatric trainees and house officers are responsible for their own training and development, programme directors should advocate such educational activities. A wider availability of Mock Code Blue simulation opportunities would enhance the competence and confidence of healthcare professionals for safer management of critically ill children in a pre-hospital setting and help identify appropriate training needs and development opportunities.

Competing Interests

At the time of submission, authors were employees of Internatinal Medical University, Malaysia. There were no funding for the study.

Acknowledgment

We would like to thank Associate Professor Lim Kean Ghee for his work on proofreading and grammatical structure correction of the manuscript.

References:


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### Learning outcome:
Participants should be able to demonstrate the initial treatment priorities, monitoring and ongoing management of septic shock through team approach and effective communication.

### Clinical scenario (for participants):

**Information:** Felix, a 5 month old boy was brought to the emergency department for a history of being less active with high grade fever for the past 2 days. There is no history of vomiting or diarrhea. His intake has been poor over the past 18 hours.

**On assessment:** You note that the infant was lying supine and appear lethargic with mottled skin.

### Equipment and setup:

- Infant mannequin wrapped lying on the bed.
- Oxygen tubings; face mask; nasal prongs; intubation and endotracheal tube set; pulse oximeter with saturation and heart rate simulation cards; cardiac monitor; glucometer reading; bladder catheter; intravenous and intra-osseous set; set of syringes
- One pint of normal saline, ½ Saline, dextrose 5%, and water
- One ampule of Ceftriaxone, Ampicillin, Dopamine, Noradrenaline, Adrenaline

### Events occurring during scenario:

- Infant’s heart rate: 165/min; respiratory rate: 60/min; temperature: 40.1°C; blood pressure: 68/20 mm Hg; oxygen saturation: 94% on high flow oxygen; glucose concentration: 2.6mmol/l. Auscultation reveals clear lungs with good and equal air entry with a short systolic ejection murmur. After obtaining intravascular / intraosseous access, fluid resuscitation fails despite of three 20ml/kg bolus. Felix becomes unresponsive to voice and barely respond to painful stimulation. His distal pulses are no longer palpable. Participants should recognise compromise airway and consider intubation. Hypoglycemia should be corrected and broad spectrum antibiotics administered with inotropic support for fluid refractory shock.

### Scenario end point

Felix continues to receive assisted ventilation while waiting to be transported to paediatric ICU, where his blood pressure and perfusion continue to improve.
APPENDIX 2

Scenario: A child with cardiac arrest

Learning outcome:
Participants should be able to demonstrate the treatment steps (including electrical and pharmacologic therapy) while recognizing the common arrest rhythms through team approach and effective communication

Clinical scenario (for participants):

Information: Harry, a 3 year old boy was brought to the emergency department after being found submerged in a monsoon drain near his house. His parents last saw him cycling his tricycle on the street 30 minutes prior to being found.

On assessment: You see a lifeless child who is flaccid with mottled skin colour. You confirm that Harry is in cardiac arrest.

Equipment and setup:
Child mannequin (wet clothes) lying on the bed.
Defibrillator; oxygen tubings; face mask; nasal prongs; intubation and endotracheal tube set; pulse oximeter with saturation and heart rate simulation cards; cardiac monitor (showing asystole then VT); glucometer reading; intravenous and intra-osseous set; set of syringes
One pint of normal saline, ½ Saline, dextrose 5%, and water
One ampule of Dobutamine, Dopamine, Noradrenaline, Adrenaline

Events occurring during scenario:
Participants secure the airway and assist ventilation while continuing quality CPR. Venous access, cardiac monitor and preparation of adrenaline are done with good team work. After about 3 minutes of CPR following one dose of intravenous adrenaline (0.01mg/kg), a shockable rhythm (VT) is seen on the monitor. Participants give a shock 2J/kg and restart CPR. After about 2 minutes of CPR and following the first shock, the rhythm is unchanged from before. Participants should now be delivering 4J/kg shock whilesearching for treatable possible contributing factors (e.g. tension pneumothorax). After about 2 minutes of CPR following the second shock, Harry now has a perfusing rhythm.

Scenario end point
Harry continues to receive assisted ventilation while waiting to be transported to the paediatric ICU, where his blood pressure and perfusion continue to improve.
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APPENDIX 3

RESUSCITATION CHECKLIST FOR SCENARIO: A CHILD WITH SEPTIC SHOCK

<table>
<thead>
<tr>
<th>Group:</th>
<th>Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time start:</td>
<td>Time end:</td>
</tr>
<tr>
<td>Facilitator:</td>
<td>Assessor:</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Resuscitation item</th>
<th>Checklist (Ticked if achieved)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Airway</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Give oxygen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recognise compromise airway</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consider intubation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 Breathing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recognise impending respiratory failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assist ventilation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitor pulse oximetry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 Circulation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recognition of shock</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attach monitoring / defibrillator</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 • Establishing IV / IO access</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 • Fluid resuscitation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20ml/kg bolus of isotonic saline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Up to 60ml/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 Correct hypoglycaemia</td>
<td></td>
<td></td>
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<tr>
<td>7 Antibiotics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Broad-spectrum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 Inotropic support</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Fluid refractory shock)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Able to differentiate a cold and warm shock</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reverse cold shock by titrating dopamine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reverse warm shock by titrating norepinephrine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 Reassessment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Mention target endpoints)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure (5th percentile minimum)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quality of pulses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin perfusion (warm, cap refill &lt;2seconds)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine output</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 Team leadership</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decision making</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 Communication</td>
<td></td>
<td></td>
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<tr>
<td>Team introduction</td>
<td></td>
<td></td>
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<tr>
<td>Distraction avoidance</td>
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<tr>
<td>Situational awareness</td>
<td></td>
<td></td>
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<tr>
<td>Team work</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 Loop communication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reveal roles verbally or non-verbally</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Task management</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Critical items numbered and highlighted

Comments: ____________________________________________________________
How Can We Improve Code Blue Training For Non-Paediatricians: An Experience From Students-Conducted Assessment In National Clinical Skills Conference

APPENDIX 3

RESUSCITATION CHECKLIST FOR SCENARIO: A CHILD WITH CARDIAC ARREST

<table>
<thead>
<tr>
<th>Group:</th>
<th>Date:</th>
</tr>
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<td>Time end:</td>
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<td>Facilitator:</td>
<td>Assessor:</td>
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<table>
<thead>
<tr>
<th>Resuscitation item</th>
<th>Checklist (Ticked if achieved)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Airway</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Give oxygen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manually open airway</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clear airway</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perform intubation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 Breathing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assist ventilation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitor oxygenation by pulse oximetry</td>
<td></td>
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<tr>
<td>3 Circulation</td>
<td></td>
<td></td>
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<tr>
<td>Attach monitoring / defibrillator</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 • Establishing vascular access</td>
<td></td>
<td></td>
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<tr>
<td>5 Paediatric Cardiac Arrest Algorithm</td>
<td></td>
<td></td>
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<tr>
<td>Quality CPR</td>
<td></td>
<td></td>
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<tr>
<td>Correct sequence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 • Adrenaline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 • Cardioversion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 • Reassessment</td>
<td></td>
<td></td>
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<tr>
<td>Rhythm shockable?</td>
<td></td>
<td></td>
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<tr>
<td>Return of spontaneous circulation</td>
<td></td>
<td></td>
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<tr>
<td>Identify reversible causes</td>
<td></td>
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<tr>
<td>9 Team leadership</td>
<td></td>
<td></td>
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<tr>
<td>Decision making</td>
<td></td>
<td></td>
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<tr>
<td>10 Communication</td>
<td></td>
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<tr>
<td>Team introduction</td>
<td></td>
<td></td>
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<tr>
<td>Distraction avoidance</td>
<td></td>
<td></td>
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<tr>
<td>Situational awareness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Team work</td>
<td></td>
<td></td>
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<tr>
<td>11 Loop communication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reveal roles verbally or non-verbally</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Task management</td>
<td></td>
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</tr>
</tbody>
</table>

Critical items numbered and highlighted

Comments:

___________________________________________________________________
___________________________________________________________________
___________________________________________________________________
___________________________________________________________________
___________________________________________________________________
How Can We Improve Code Blue Training For Non-Paediatricians: An Experience From Students-Conducted Assessment In National Clinical Skills Conference

APPENDIX 4

ASSESSOR’S TRAINING RECORDING SHEET

Name: _______________  Credentials: Final Year Medical Student
Date: _______________  Training session: 1 / 2 / 3 / 4 / 5

At the end of this training, assessor should be able to demonstrate:

- Technical skills at both Septic Shock and Cardiac Arrest stations
- Capability to appreciate technical oversight and inaccuracies of resuscitation algorithm
- Understanding of variation in team approach to paediatric resuscitation emergencies

✓ Set up skills stations
✓ Equipment check
✓ Perform advanced airway management
  - Effective bag-mask ventilation
  - Endotracheal tube placement
✓ Algorithm and scenario awareness
✓ Use of oxygen with pulse oximeter and cardiac monitor
✓ Obtain vascular access quickly (IV/IO) for fluid resuscitation and correct hypoglycaemia
✓ Cardioversion
✓ Medication and reassessment
✓ Appreciate non-technical skills
  - Environmental awareness
  - Anticipation and planning
  - Assignment and articulation of leadership roles
  - Effective communication
  - Workload delegation
  - Use of all available information
  - Use of all available resources and calling for help when needed
  - Maintain professional behaviour
✓ Demonstrate administration of resuscitation checklist

Comments:
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________

Educator: _______________  Additional training required: Yes / No

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ORIGINAL ARTICLE

PREVALENCE AND FAMILY HISTORY CHARACTERISTICS OF TYPE 1 DIABETES MELLITUS IN CHILDREN AND ADOLESCENTS: A NIGERIAN TERTIARY-HEALTHCARE BASED STUDY

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2. Endocrinology and Metabolism Unit, Department of Child Health, University of Benin Teaching Hospital, Benin City, Nigeria.
3. Endocrinology and Metabolism Unit, Department of Paediatrics, Federal Teaching Hospital Gombe, Nigeria.

Abstract

Background: Family history of diabetes mellitus is a useful tool for detecting children and adolescents at risk of the disease. The aim of this study is to determine the prevalence and describe the characteristics of family history of diabetes mellitus in Nigerian children and adolescents with type 1 diabetes.

Methods: A retrospective chart review of children and adolescents newly diagnosed with type 1 diabetes was conducted in three tertiary-healthcare institutions in Nigeria. In addition to the review of charts of old patients, other children and adolescents who presented with new-onset diabetes during the review process were also included. An interviewer-administered questionnaire was used in obtaining information from the patients and their parents. Using the criteria suggested by Scheuner et al, the family history risk category was stratified into average, moderate and high. Results: Out of a total of 65 children and adolescents with type 1 diabetes, 29(44.6%, 95% CI= 32.6-56.7) had a positive family history of diabetes mellitus. Of the affected family members, 42.9% were first-degree relatives. The frequencies of family history risk category were average 65.5%, moderate 27.6% and high 6.9%. Among the affected family members in whom information on their diabetes status was available, 19(86.4%) had type 2 diabetes and only 3(13.6%) had type 1 diabetes. Conclusion: Four out of every ten patients with type 1 diabetes in the paediatric age group, have a first-degree relative with a positive family history of diabetes.

Keywords: Family History, Family Health History, Family Medical History, Medical Family Tree, Paediatric Type 1 Diabetes

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Introduction

Family history (also referred to as family medical history or family health history or medical family tree) is a record of relevant information about medical conditions affecting a patient and his or her close family members [1,2]. It represents an essential component of a patient’s medical history, typically obtained at admission to a healthcare facility as one of the components of a comprehensive patient assessment [3]. The scope of family members typically embraces three generations of relatives by birth [4] which includes the child, his/her siblings, parents, maternal and paternal grandparents and maternal and paternal aunts and uncles and first cousins [3]. Although there is no standard operational definition of a positive family history, having one or more first- or second-degree relatives who are affected with a condition is often considered a positive family history for an individual person [5]. A family history represents a valuable genomic information because it reflects the consequences of inherited genetic susceptibility, shared environmental factors and common lifestyle behaviours [6,7]. In recognition of the importance of family history, the American Society of Human Genetics states that family health history is the most important genetic test for all [8]. Although family history is easily available, inexpensive to obtain and conveniently conveys information on genes and environment shared by close relatives, it may be underutilized in health-care practice [7,9]. At the level of the individual, family history of diabetes (FHD) can serve as part of a comprehensive risk assessment required for prevention, early diagnosis and therapy of diabetes mellitus whereas at the population level, it may help tailor health-promotion messages for specific-population groups [9].

The association between FHD and risk for the disease has been well documented with the risk varying according to which family member is affected [10,11]. Epidemiological studies have shown that the risk of developing type 1 diabetes is 8- to 15-fold higher when a first-degree relative is affected [12-15] and two-fold higher when a second-degree relative is affected [12,16]. The reports of other studies indicate that the proportion of children with affected first-degree relatives at the time of diagnosis was 10-12% [16-19]. The report of a study from the Finnish Paediatric Diabetes Register revealed that a total of 12.2% of the subjects had first-degree relatives with type 1 diabetes (father 6.2%, mother 3.2% and sibling 4.8%) and 11.9% had affected second-degree relatives [20]. Other studies have shown that 5% to 16% of children with type 1 diabetes have affected second-degree relatives with diabetes [12,13,21]. The results of a study in Oman revealed that 58.3% of children and adolescents had a positive FHD [22]. FHD has been shown to have a significant independent and graded association with the prevalence of diabetes [5,10,11]. In addition, the risk is higher when multiple family members or the father is affected, particularly if the father was below the age of 45 years at the point of diagnosis [14,23]. A family history of co-existence of both types 1 and 2 diabetes has been shown to influence the phenotype of patients with type 2 diabetes, suggesting a genetic interaction between types 1 and 2 diabetes [24]. Some studies have shown that patients with T1D have an increased prevalence of positive family history of T2D [17,18]. In Nigeria, epidemiological data on the prevalence and characteristics of FHD in children and adolescents with type 1 diabetes is scarce.
Subjects And Methods

During the six-year period (January 2012 to December, 2017) covered by this review, the hospital records of all cases with paediatric diabetes mellitus admitted in the three participating Nigerian tertiary-healthcare hospitals were retrieved and audited. In addition, an interviewer-administered questionnaire was used in obtaining information from the patients and their parents. Patients with type 1 diabetes along with their parents/guardian were asked whether any biological member (i.e., blood relatives) of their family, living or deceased, had ever been told by a healthcare worker that he/she had diabetes? If the answer was yes, then the subject was asked to specify his/her relationship with the affected family member. According to the criteria suggested by Scheuner et al [25], the family history was stratified into three risk categories as follows: (i) Average: At most, one second-degree relative with diabetes; (ii) Moderate: One first-degree plus one second-degree relative with diabetes or only one first-degree relative with diabetes or at least, two second-degree relative with diabetes from the same maternal or paternal lineage; and (iii) High: At least two first-degree relatives or one first-degree plus at least, two second-degree relatives with diabetes from the same lineage [25]. In addition to the interview, the medical records of the patients were retrieved and reviewed. Ethical approval was obtained from LUTH Ethics and Research Committee. In addition, consent was obtained from the parents/guardian and when appropriate, assent from the child, respectively. Similar standards of anthropometric measurements were used in the study centres [26]. The height was measured to the nearest 0.1cm, using a stable fixed stadiometer and weight was measured to the nearest 0.1kg with the subject in light clothing and bare foot. To minimize errors, if a duplicate measurement differed by > 0.5cm or > 0.5kg respectively, a third measurement was performed and the average of the two closest measurements was recorded as the final value. The body mass index of each of the subjects was computed, using the standard formula [26]. Using appropriate cuff, the blood pressure was measured in a sitting position after 5 minutes of rest, using a mercury sphygmomanometer. Steps were taken to ensure accuracy of all the measurements.

The data were collated and entered in Excel spread sheet. Accuracy of the data entered was double checked. Data were analysed, using Microsoft Excel and SPSS (Statistical Package for Social Sciences) version 20.0. Descriptive statistics such as frequencies, means, standard deviations were used in describing all the variables. Confidence intervals, percentages and ratios were calculated. Z-test and Student t-test were used in ascertaining the significance of difference between two proportions and means, respectively. The p-values were set at < 0.05.

Results

A total of 65 children and adolescents with type 1 diabetes from three Nigerian tertiary-healthcare institutions participated in this study. The distribution of the participants according to healthcare institution was as follows: 30, 21 and 14 from University of Benin Teaching Hospital (UBTH), Benin City, Lagos University Teaching Hospital (LUTH), Lagos, and Federal Medical Centre (FMC), Gombe, respectively. There was a female preponderance with a ratio of 1:1.75. Overall mean age at diagnosis was 13.0±2.7 years (95% Confidence Interval, CI = 12.3-13.7). The health-institution-
specific mean age at diagnosis were 14.3±2.4 years (95% CI =13.0- 15.6), 12.1±3.2 years (95% CI=10.7-13.5) and 11.2±3.7 years (95% CI= 10.0-12.4) in FMC, Gombe, LUTH, Lagos and UBTH, Benin City, respectively. The mean ages of patients with positive and negative family history of diabetes were 11.9±3.8 years (95% CI=10.5-13.3) versus 12.4±4.0 years (95% CI= 11.1-13.7); p < 0.05. The mean HbA1c level of all participants at admission was 10.6±2.6% (95% CI= 10.0 - 11.2). As shown in Table 1, the peak age at diagnosis was 10 to 14 years in both boys and girls. Of the 65 children and adolescents with type 1 diabetes, 29(44.6%, 95% CI= 32.6-56.7) had a positive family history of diabetes mellitus. Healthcare institution-specific frequencies of positive family history of diabetes mellitus were as follows: FMC, Gombe 71.4% (10/14); LUTH, Lagos 42.9% (9/21); and UBTH, Benin City 33.3% (10/30). The proportion of subjects with a positive family history of diabetes mellitus was higher in Gombe (71.4%) in Northern Nigeria compared to Lagos plus Benin City (37.3%), both in Southern Nigeria, Z-statistic = 2.463, p < 0.01.

Table 1. Age groups and gender distribution of children and adolescents with type 1 diabetes mellitus in three Nigerian tertiary-healthcare institutions

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Males</th>
<th>Females</th>
<th>Both sexes</th>
</tr>
</thead>
<tbody>
<tr>
<td>at diagnosis</td>
<td>No (%)</td>
<td>No (%)</td>
<td>Combined</td>
</tr>
<tr>
<td>Below 5 years</td>
<td>4(16.7)</td>
<td>1(2.4)</td>
<td>5(7.7)</td>
</tr>
<tr>
<td>5-9 years</td>
<td>6(25.0)</td>
<td>2(4.9)</td>
<td>8(12.3)</td>
</tr>
<tr>
<td>10-14 years</td>
<td>10(41.6)</td>
<td>21(51.2)</td>
<td>31(47.7)</td>
</tr>
<tr>
<td>15 years and above</td>
<td>4(16.7)</td>
<td>17(41.5)</td>
<td>21(32.3)</td>
</tr>
<tr>
<td>Total</td>
<td>24(100.0)</td>
<td>41(100.0)</td>
<td>65(100.0)</td>
</tr>
</tbody>
</table>

Table 2 shows that the frequency of impaired consciousness and ketoacidosis were significantly lower in subjects with positive family history of diabetes mellitus. In addition, subjects with positive family history of diabetes mellitus had a significantly shorter mean duration of symptoms before presentation (Table 2).

Table 2. Characteristics of subjects according to presence or absence of family history of diabetes (FHD)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>FHD present&lt;sup&gt;a&lt;/sup&gt; (n=29 subjects)</th>
<th>FHD absent&lt;sup&gt;b&lt;/sup&gt; (n=36 subjects)</th>
<th>p-value</th>
<th>FHT1D present (n=3 subjects)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FHD present&lt;sup&gt;a&lt;/sup&gt; (n=29 subjects)</td>
<td>FHD absent&lt;sup&gt;b&lt;/sup&gt; (n=36 subjects)</td>
<td>p-value</td>
<td>FHT1D present (n=3 subjects)</td>
</tr>
</tbody>
</table>
As shown in Table 3, majority of the affected family members were second-degree relatives. Multiple number of family members were affected in 41.4% of cases (Figure 1). In two (6.9%) of the 29 subjects, both mother and father were affected. Both first- and second-degree relatives were affected in 8 (27.6%) of the 29 subjects with positive family history of diabetes. All three degrees (i.e., first-, second- and third-degree) of relatives were affected in 2 (6.9%) of the 29 subjects. Regarding affected siblings of parents (uncles and aunts), 7 (24.1%) were paternal uncles, 3 (10.3%) paternal aunts, one (3.4%) maternal uncle and 4 (13.8%) maternal aunts. The proportion of subjects with affected grandparents was 27.6% (8/29). Among them, 4 (13.8%) were maternal grandmother, 3 (10.3%) were maternal grandfathers and 1 (3.4%) was paternal grandmother. None of the affected relatives was a paternal grandfather. As shown in Figure 2, majority of the subjects with positive family history were in average family history risk category. The age of the subjects did not differ with family history risk categories. One of the subjects aged 9 years had a father with type 2 diabetes (who required switching to insulin therapy) and
three elder sisters with prediabetes. Information on type of diabetes in the affected family members was available in 22 (75.9%) of the 29 subjects with positive family history of diabetes mellitus. Among the affected family members in whom information on their diabetes status was available, 19 (86.4%) had type 2 diabetes and only 3 (13.6%) had type 1 diabetes.

Table 3. Distribution of study subjects according to which family member is affected

<table>
<thead>
<tr>
<th>First-degree relatives</th>
<th>Number (n=42*)</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Father</td>
<td>7</td>
<td>16.7</td>
</tr>
<tr>
<td>Mother</td>
<td>10</td>
<td>23.8</td>
</tr>
<tr>
<td>Sibling- brother</td>
<td>1</td>
<td>2.4</td>
</tr>
<tr>
<td>Sibling- sister</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Siblings- brothers plus sisters</td>
<td>1</td>
<td>2.4</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>42.9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second-degree relatives</th>
<th>Number (n=42*)</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grandparents</td>
<td>7</td>
<td>16.7</td>
</tr>
<tr>
<td>Siblings of parents (uncles/aunts)</td>
<td>15</td>
<td>35.7</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>52.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Third-degree relatives</th>
<th>Number (n=42*)</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Great grandparents</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>First cousins</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Other relatives of parents</td>
<td>2</td>
<td>4.8</td>
</tr>
<tr>
<td>Total</td>
<td>2</td>
<td>4.8</td>
</tr>
</tbody>
</table>

*Some of the subjects have more than one family member affected.
Figure 1: Distribution of number of family members affected.

- One family member affected (58.6%)
- Two family members affected (24.1%)
- Three family members affected (10.3%)
- Four family members affected (7.0%)

Figure 2: Distribution of family history risk category among subjects with positive family history of diabetes mellitus

- Average family history risk category (65.5%)
- Moderate family history risk category (27.6%)
- High family history risk category (6.9%)
Prevalence And Family History Characteristics Of Type 1 Diabetes Mellitus In Children And Adolescents: A Nigerian Tertiary-Healthcare Based Study

Discussion

Data from the present study indicate that at least four out of every ten (44.6%) children and adolescent with type 1 diabetes have a positive family history of diabetes mellitus. This frequency is higher than the 24.1% reported from Finnish Paediatric Diabetes Register [21] but lower than 58.3% and 74.0% reported from Oman [21] and Saudi Arabia [27], respectively. The observed variation in frequency may be explained by the fact that a family history of a disease is reflection of the consequences of inherited genetic susceptibility, shared environmental factors and common lifestyle behaviours [6,7]. The magnitude of the contribution of each of these predisposing factors vary from country to country, accounting for the observed differences in frequencies of positive family history. The public health implication of the prevalence of positive family history of diabetes mellitus found in the present study is that true sporadic cases of newly diagnosed type 1 diabetes is less than 60% in our environment. In addition, the frequency of positive family history of diabetes was significantly higher in Gombe (Northern Nigeria) than Lagos plus Benin City (Southern Nigeria). The common practice of consanguinity in marriages in the northern part of Nigeria in contrast to the southern Nigeria may account for the higher frequency of positive family history of diabetes in the north [28]. This view is supported by literature which has documented that a consanguineous couple is at increased risk for disorders inherited either as autosomal recessive or multifactorial traits [29]. Diabetes mellitus is inherited as a multifactorial trait. We encourage other researchers who have the necessary data to follow up on our hypothesis by using a larger sample size involving more healthcare institutions in Nigeria.

We found that in over one half (53.7%) of the subjects, second-degree relatives were affected. This is in keeping with 54.6% reported from Finland [10]. In contrast, a study in Saudi Arabia reported that 52.5% of affected family members were first-degree relatives [27]. The higher frequency among first-degree relatives found in Saudi Arabia compared to our study may be due high frequency of consanguinity in Saudi Arabian families. In the same study [27], the authors reported consanguineous union in 40.0% of all admitted children’s parents. In consonance with some studies [6,10], we found that a larger proportion of maternal relatives than paternal relatives were affected. Although we do not have any readily available explanation for this finding, differential expression of inherited susceptibility genes in the paternal and maternal generations (i.e., genomic imprinting) has been proposed [30]. In the present study, multiple number of family members were affected in at least, four out of every ten cases (41.4%). This is in keeping with the results of other studies [10,11,23]. The high proportion of multiple family members found in our study is worrisome because for any given individual, both prevalence and odd ratio estimates are known to be significantly increased with number of relatives affected by diabetes [5,6,11]. Our data indicate that majority (86.4%) of the affected family members had type 2 diabetes. Therefore, the high proportion of family history of type 2 diabetes along with multiple family members affected in our study is of public health importance.

Concerning stratification into family history risk categories, we found that one in 16...
cases (6.9%) were in the high family history risk category. This finding agrees with 7.5% found in USA (using the same criteria for definition as in the present study) [5]. In the same study, the authors reported a moderate risk category of 22.7% and an average risk category of 69.8% [5], both of which are comparable with 27.6% and 65.5%, respectively found in our study. In contrast, the results of a study in China revealed frequencies in a reversed order. In that study, the reported frequency of the family history risk categories was high 32.7%, moderate 20.1% and average 8.4%, respectively [11]. The reason for the differences in proportion of family history risk category in our study compared with the Chinese study [11] is not clear. However, it may be related to differences in the criteria used in defining the family history risk category. The USA study [5] as well as the present study used the criteria suggested by Scheuner et al [25] which considered both first- and second-degree relatives while the Chinese study [11] used only the first-degree relatives. Indeed, the authors mentioned limiting family history to only first-degree relatives as a drawback of their study [11].

The public health importance of family history risk category is that it is significantly related not only to level of islet β-cell dysfunction but also a significant and independent rank correlation with prevalence of diabetes in individuals [5,11].

Presence of family history of diabetes was associated with a relatively less severe metabolic decompensation at first diagnosis. The evidence is reflected in the significantly lower proportion of subjects with impaired consciousness and ketoacidosis in the group with positive compared to negative family history. Similarly, subjects with positive family history of diabetes had shorter duration of symptoms before diagnosis. This trend is in consonance with the reports of previous studies [10,31]. This finding may be due to better awareness of the parents with regard to early symptoms of type 1 diabetes, resulting in a relatively early diagnosis and initiation of treatment. This view is reinforced by the shorter duration of symptoms in patients with positive compared to negative family history of diabetes found in our study. The present study did not investigate for the association between high blood pressure and family history of diabetes. It is possible that the tendency for high blood pressure in patients with positive family history of diabetes is due the fact that both hypertension and diabetes mellitus are inherited as a multifactorial trait.

Some limitations of the present study need to be considered. First, our inability to encourage the subjects/parents to contact relatives to confirm family history of at least three generations of relatives. This probably would have increased the number of affected third-degree relatives found in this study. This view is supported by the finding in a study in USA where 2.7% and 2.0% of men and women, respectively lacked knowledge of family history of diabetes [6]. Secondly, we did not assess the prevalence of diabetes in various family history risk categories. Our study did not have a control group because the study was largely retrospective. The small number of patients did not allow for adequate comparison of patients with positive family history of type 1 diabetes and type 2 diabetes. Despite these limitations, our study is the first to provide an insight into the prevalence and characteristics of family history of diabetes mellitus in the paediatric age group in Nigeria. Therefore, it can serve as part of the public health tool for screening and
preventive programmes in paediatric diabetes mellitus.

References


Prevalence And Family History Characteristics Of Type 1 Diabetes Mellitus In Children And Adolescents: A Nigerian Tertiary-Healthcare Based Study


PREDICTION OF HEMOPHILIA JOINT HEALTH SCORE BASED ON AGE AND DISEASE SEVERITY OF HEMOPHILIA A AND B WITH ON DEMAND THERAPY IN WEST JAVA

Iin K Rambe, Ellyana S, Marina A Moeliono, Astini S

Department of Physical Medicine and Rehabilitation, Padjadjaran University/ Hasan Sadikin Hospital, Bandung, Indonesia.

Abstract

Objectives: This study aimed to compose a formula to predict the Hemophilic Joint Health Score (HJHS) for hemophilia patients in West Java, find out the validity of the prediction formula and identify the difference between observational HJHS and predicted HJHS. Methods: This observational, cross-sectional study involved hemophilia patients that were registered with the Indonesian Society of Hemophilia Patient in West Java aged 4-18 years old with all stages of severity. All participants were assessed with the observational HJHS using HJHS version 2.1. Regression analysis between age and disease severity was done to compose a prediction formula. Residual analysis was performed to determine the validity of HJHS prediction formula. The HJHS of all participants was calculated with the prediction formula and mean of observational HJHS and predicted score was compared. Results: Regression analysis yielded HJHS prediction formula based on age and severity of disease, is: Total HJHS = - 7.57 + 0.952 x AGE + 2.369 x DISEASE SEVERITY (age in years, disease severity, mild =1, moderate = 2 and severe = 3). This HJHS prediction formula is valid because mean of residual analysis is 0, with normal data distribution. Comparison of the mean of observational HJHS and prediction HJHS did not show any significant difference (p=0.51). Conclusion: The prediction formula obtained in this study is valid and can be applied to hemophilic patients in West Java. The HJHS calculated with prediction formula does not have significant difference compared to the observational HJHS.

Keywords: Hemophilia, Hemophilia Joint Health Score, Joint Damage, Hemophilic Arthropathy

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Introduction

Hemophilia is an X-linked recessive disorder caused by deficiency of coagulation factor VIII (hemophilia A) or deficiency of coagulation factor IX (hemophilia B). Hemophilia is traditionally classified as mild, moderate or severe, depending on the degree of clotting factor deficit compared with that found in the general population. Hemophilia is classified as severe if clotting factor (activity level) is <1 IU/dl or <1%, moderate if clotting factor is 1–5%) or mild (clotting factor activity level: >5–40%) [1,2].

The prevalence of hemophilia in Indonesia is approximately 4.1/100000 population. Based on data from Indonesian Society of Hemophilia Patient (Himpunan Masyarakat Hemofilia Indonesia/HMHI), the number of registered hemophilic patients in West Java chapter of HMHI is 106 people [3].

The most common bleeding manifestation in hemophilia is joint bleeding or hemarthrosis that account for 80% cases of bleeding [4,5]. Repeated bleeds into joints in persons with hemophilia result in lasting changes in the joint capsule, joint cartilage, synovium and bone leading to classical hemophilic arthropathy. Hemophilic arthropathy is a progressive and irreversible disease occurring after a number of joint hemorrhages in childhood, usually as early as the second decade of life [4,5].

The only treatment of hemophilia available in Indonesia is on demand therapy, as the first line treatment for acute bleeding events, but does not prevent the repetitive bleeding in the joint [5]. Patients with on demand therapy still acquire arthropathies that cause permanent joint damage and disability, problems in mobilization and activities of daily living decrease quality of life [6,7].

Assessment of joint health in hemophilia is important for early detection of joint damage and prevent further damage of the joint [8]. One of the standardized tools is HJHS (Hemophilia Joint Health Score), developed by The Physiotherapy Expert Working Group of International Prophylaxis Study Group (IPSG) [9]. HJHS is used to assess joint damage and associated functional impairment in children aged 4-18 years. The assessed joints are the knee, elbow and ankle joints, since they are the most commonly affected by hemarthrosis. HJHS is objective, can detect minimal to severe joint damage as well as associated functional impairment, has good reliability and validity, and may be compared from time to time to evaluate treatment or exercise [9,10].

Ideally HJHS should be done by direct measurement to get HJHS and detailed assessment of joints. Assessment of HJHS requires a standardized room, trained and experienced assessors in musculoskeletal field, such as skill to measure the range of motion using goniometer, determine muscle strength, and observe posture and gait. The room should have sufficient source of lighting, large enough to accommodate walking, running, stair climbing and the floor should be a smooth firm surface. HJHS requires long time to be assessed, approximately 45-60 minutes in one patient [9]. Not all health facilities in West Java have the necessary facilities and personnel to perform HJHS measurement, therefore a formula is needed to predict HJHS score based on available data, which are age and disease severity.

This formula will help to score HJHS without objective measurement. There is no
previous study that produced a formula to obtain HJHS score. This formula takes short time and can be used by general physician, nurse and other health workers without experience in assessment of joint range of motion, muscle strength, posture and gait to assess joint health in hemophilia.

This study aimed to compose a prediction formula of HJHS in hemophilia patients in West Java and determine its validity of the prediction formula and to identify the difference between observational HJHS score and predicted HJHS score.

Methods

The study involved hemophilia patients that are registered in the Indonesian Association of Hemophilia Patient (Himpunan Masyarakat Hemofilia Indonesia/HMHI) in West Java Region. This was an observational, cross-sectional study, conducted at the Department of Physical Medicine and Rehabilitation of Padjadjaran University, and has been ethically approved by the Health Research Ethics Committee of Faculty of Medicine Padjadjaran University. Signed informed consent for the evaluation was obtained from patients or their parents following written and verbal information.

The study was conducted starting from March to April 2017. The inclusion criteria were: subjects diagnosed as hemophilia A or B with known severity of disease (mild, moderate, severe), aged 4–18 years, on demand therapy and able to stand with or without walking aid. The exclusion criteria were bleeding, occurred <2 weeks before collecting data, subject refused to participate or subjects were absent during the data collection. Subjects were stratified into two groups, according to age: group I consisted of patients 4–9 years of age and group II consisted of patients 10–18 years of age. In each group the subjects were further stratified according to severity: mild, moderate and severe.

Each subject was assessed for joint health using HJHS version 2.1 by one examiner. HJHS measures elbow, knee and ankle joints using eight impairment items (swelling, duration of swelling, muscle atrophy, crepitus of motion, flexion loss, extension loss, joint pain and strength). Each of the six joints were assessed individually and numerically scored in categories of severity, with a total score for each single joint ranging from 0 to 20. A global gait score was assessed separately with 0 indicating that all skills (walking, stairs, running, hopping on one leg) are within normal limits, and 4 indicating that no skills are within normal limits. All joint scores are added to the global gait score adding up the total HJHS, range from 0 (healthy score) to 124 (worst score). The HJHS obtained from this measurement is termed “observational HJHS”.

Statistical analysis

Mann-Whitney U test was applied to compare the median of total HJHS score between age groups and disease severity groups. Spearman correlation analysis was conducted to evaluate the relationship between total HJHS score, patient age and disease severity. Regression analysis between age and disease severity was done to compose a prediction formula using multi regression forwards stepwise method. Residual analysis using t-test was performed to determine the validity of HJHS prediction formula. The HJHS of all participants was calculated with the prediction formula and mean of observational HJHS and predicted
HJHS was compared using Wilcoxon Match pair test.

**Result**

A total of 87 diagnosed cases of hemophilia aged less than 18 years participated in this study. The mean age of subjects was 11.4 years. Thirty-five subjects (40.23%) were between 4-9 years of age and 52 (59.77%) were between 10-18 years. Sixty (68.97%) cases were diagnosed as hemophilia A, while 27 cases (31.03 %) were diagnosed as hemophilia B. According to their severity, 56 (64.37 %) cases had severe disease, 17 (19.54%) had moderate disease and 14 (16.09 %) had mild disease. The baseline characteristics of the patients are presented in Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Percentage n (%)</th>
<th>Mean</th>
<th>Median (minimum – maximum)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td>11.144</td>
<td></td>
</tr>
<tr>
<td>4-9 years</td>
<td>35 (40.23)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-18 years</td>
<td>52 (59.77)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Disease Severity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>14 (16.09)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>17 (19.54)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>56 (64.37)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Type of Hemophilia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>60 (68.97)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>27 (31.03)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Observational HJHS</strong></td>
<td></td>
<td>9.724</td>
<td>7 (0 - 35)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>2.954</td>
<td>2 (0 - 13)</td>
</tr>
<tr>
<td>Elbow</td>
<td></td>
<td>3.966</td>
<td>3 (0 - 17)</td>
</tr>
<tr>
<td>Knee</td>
<td></td>
<td>2.552</td>
<td>2 (0 - 15)</td>
</tr>
<tr>
<td>Ankle</td>
<td></td>
<td>35.243</td>
<td>32 (15 - 80)</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td></td>
<td>141.644</td>
<td>135 (103 - 175)</td>
</tr>
<tr>
<td>Body height (cm)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 2 shows the HJHS was highest in severe hemophilia (median 8.5), followed by moderate hemophilia (median 7) and mild (median 6). It showed statistical significant differences in HJHS between age group (p = 0.002), and between mild disease and severe disease (p=0.046). However there were no statistical significant differences in HJHS between mild disease and moderate disease (p= 0.184) and moderate disease and severe disease (p = 0.189).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Observational HJHS</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>Minimum-maximum</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-9 years</td>
<td>6</td>
<td>0-35</td>
</tr>
<tr>
<td>10-18 years</td>
<td>8.5</td>
<td>1-35</td>
</tr>
<tr>
<td>Disease Severity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>6</td>
<td>0-21</td>
</tr>
<tr>
<td>Moderate</td>
<td>7</td>
<td>2-10</td>
</tr>
<tr>
<td>Mild</td>
<td>6</td>
<td>0-21</td>
</tr>
<tr>
<td>Severe</td>
<td>8.5</td>
<td>0-35</td>
</tr>
<tr>
<td>Moderate</td>
<td>7</td>
<td>2-10</td>
</tr>
<tr>
<td>Severe</td>
<td>8.5</td>
<td>0-35</td>
</tr>
</tbody>
</table>

Table 3 showed significant positive correlations with a p-value of less than 0.05 between HJHS with each age group (p 0.000001) and disease severity (p 0.0239).
Table 3. Correlation between Observational HJHS of Age and Severity

<table>
<thead>
<tr>
<th></th>
<th>Valid</th>
<th>Spearman</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>R</td>
</tr>
<tr>
<td>Observational HJHS &amp; Age</td>
<td>87</td>
<td>0.505799</td>
</tr>
<tr>
<td>Observational HJHS &amp; Disease Severity</td>
<td>87</td>
<td>0.242033</td>
</tr>
</tbody>
</table>

Variables that were used in the regression analysis were age and disease severity. During the analysis, 3 outliers were found. After excluding the outliers from the regression analysis, the regression coefficient for predicted HJHS was calculated. This data is presented in Table 4.

Table 4. Regression Analysis of HJHS with Age and Disease Severity

<table>
<thead>
<tr>
<th></th>
<th>St. Err. of</th>
<th>St. Err.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BETA</td>
<td>BETA</td>
</tr>
<tr>
<td>Intercept</td>
<td>-7.5699</td>
<td>2.5559</td>
</tr>
<tr>
<td>Age</td>
<td>0.5621</td>
<td>0.0870</td>
</tr>
<tr>
<td>Disease Severity</td>
<td>0.2726</td>
<td>0.0870</td>
</tr>
</tbody>
</table>

Residual test showed that \( t-test \) for mean =0, and Saphiro Wilk presented a normal distribution. Based on this result, the prediction was valid to predict HJHS based on age and disease severity. The formula to predict HJHS is 
\[
-7.57 + (0.952 \times \text{age}) + (2.369 \times \text{disease severity})
\]
(constant : age in years, for disease severity, 1 =mild, 2 = moderate and 3 = severe).

Table 5 showed there were no statistically significant differences between observational HJHS and predicted HJHS (p = 0.51).
**Table 5. Comparison of predicted HJHS with observational HJHS**

<table>
<thead>
<tr>
<th></th>
<th>Predicted HJHS</th>
<th>Observational</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HJHS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>8.833</td>
<td>8.833</td>
<td>0.51</td>
</tr>
<tr>
<td>Median</td>
<td>8.123</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Minimum-maximum</td>
<td>(-1.393 – 16.668)</td>
<td>(0-28)</td>
<td></td>
</tr>
</tbody>
</table>

**Discussion**

In this study, there were 60 cases with hemophilia A and 27 cases with hemophilia B. Subjects with severe disease were 56 cases, more than those with moderate and mild disease. This finding matches with prevalence of type and disease severity of hemophilia worldwide, where hemophilia A accounts for 80% and hemophilia B for 20% of cases. Severe hemophilia accounts for 50-60% of cases, moderate for 25-30% and mild for 15-20% of cases. Knee score is worse than elbow score and ankle score. Similar result was shown in the study of Moshin, and Zeze. Both studies found that the joint with the most frequent recurrent bleeding is the knee joint, followed by the elbow and ankle joint [11,12].

Table 2 shows statistically significant difference in median between age groups in this study. Study of Trakymiene of 21 severe hemophilic A and B also found that there was statistically significant difference HJHS (p=0.0002) with 19.9 point higher in age group of 10-18 years [13]. Chen et al also found that the mean of HJHS in children aged 5-17 years old was higher in teenagers than children [14].

Table 3 shows strong correlation between HJHS and age. This study found that HJHS increases as the patient ages. The correlation of HJHS to age in this study is similar to that of Payal et al, Zeze et al, Trakymiene et al, and Bladen et al. They found that HJHS showed a significant positive correlation with patient’s age [12,13,15,16]. The tendency of joint bleedings and joint damage tend to increase as increasing age. Numbers of bleeding that cause joint damage remains unanswered in all of those studies [12,13,15,16].

The median in HJHS between severity of the disease showed statistically significant only between mild and severe hemophilia (p = 0.046) in Table 2, whereas between mild and moderate hemophilia there was no significant difference, as well as between moderate and severe hemophilia. The difference in observational HJHS was not significant between moderate and severe hemophilia. The results of this study were similar to the results of the study of Christoforodis of 26 patients with moderate and severe hemophilia A [17]. There was no significant difference between HJHS for the moderate and severe hemophilia (p = 0.24). Christoforodis research was also different from this study, since it did not involve mild
hemophilia, with the result that the difference of HJHS between mild and severe hemophilia was not known [17].

Table 4 shows a weak correlation between disease severity and HJHS (p = 0.0239), which is different from the study of Payal et al., who found that there was no correlation between HJHS and disease severity in hemophilia A and B. This difference may be due to other factors that can affect HJHS, such as age, frequency of joint bleedings, onset of bleeding, hemophilia treatment and level of daily physical activity [15]. Zeze et al. found that body mass index was not correlated with HJHS. Factors other than age and severity of the disease were not analyzed in this study [12].

Age was strongly correlated with observational HJHS, while the disease severity correlated weakly with observational HJHS. To ensure the validity of the prediction, it requires that regression equation of residuals must be 0 and data spread normally. In this study the residual is 0 and the data spread normally. The result of this study shows a valid regression equation that can be used to predict HJHS based on age and severity of disease, as follows:

\[-7.57 + (0.952 \times \text{age}) + (2.369 \times \text{disease severity})\]

(constant : age in years, disease severity, 1 =mild, 2 = moderate, and 3 = severe).

Table 5 shows there was no significant difference between mean of predicted HJHS compared with observational HJHS (p = 0.51). About 60% of the subjects had higher prediction HJHS than observational HJHS. In this study, analysis was done to the mean of differences, but not done for each individual subject. The diversity of HJHS of each subject suggests that there are other factors may also affect HJHS.

The range of observational HJHS (0-28) was higher than the range of predicted HJHS (-1,393 -16,668), which is caused by the manner of assessment to obtain observational HJHS, by which each joint was assessed very detailed. Every detail will affect the observational HJHS. Older subjects will have greater prediction HJHS than younger subject because the prediction HJHS predicts that hemophilia arthropathy becomes worse with increasing age.

The use of prediction HJHS formula can be used by health workers with no training in assessment of joint health in hemophilia patients. Observational HJHS is not categorized, but the higher score indicates a higher degree of joint damage. According to Sluiter’s study, observational HJHS between 0-3 is considered normal without any joint damage and is also used for the predicted HJHS. A predicted HJHS more than 3 indicates joint damage and the hemophilia patient should be referred to health centers with more adequate facilities [18].

HJHS formula can be used for early detection and can be used during joint bleeding because the assessment does not have to wait for the bleeding to stop, while the observational HJHS can be measured two weeks after bleeding [9,16]. Predicted formula can be applied without fear of complication like acute bleeding while examining a joint.

The use of HJHS prediction formula is not appropriate to evaluate joint health periodically, because the prediction HJHS will automatically increase with age. This increasing should be confirmed with the observational HJHS because the increasing
cannot confirm further damage or new
damage of the joint.

HJHS prediction formula does not include
treatment or exercise variables, so it is also
not appropriate to evaluate treatment and
exercise. For evaluation of treatment and
rehabilitation programs, observational HJHS
should be used, where changes in each item
will be assessed to adjust treatment and
rehabilitation program.

Limitations of this study is other factors that
affect HJHS like the frequency of joint
bleeding, age of onset of bleeding, the
recurrent treatment, body mass index and
the level of everyday physical activity were
not assessed. The study compared only
average between HJHS prediction and HJHS
observation, regardless of individual.

This study has produced a formula to predict
HJHS using age and disease severity as
variables. Statistical analysis found that this
formula is valid to be used in hemophilia
patients with on demand therapy. HJHS
prediction formula cannot be used for
periodic evaluation or monitoring of
treatment and rehabilitation programs.

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Dyslipidaemia Associated With Daily Consumption Of Fried-Chicken Eggs In A 22-Month-Old Boy With Type 1 Diabetes Mellitus


CASE REPORT

DYSLIPIDAEMIA ASSOCIATED WITH DAILY CONSUMPTION OF FRIED-CHICKEN EGGS IN A 22-MONTH-OLD BOY WITH TYPE 1 DIABETES MELLITUS

Alphonsus Ndidi Onyiriuka, Aisha Oiza Suleiman

Endocrinology and Metabolism Unit, Department of Child Health, University of Benin Teaching Hospital, PMB 1111, Benin City, Nigeria.

Abstract

Background/Aim: Management of toddlers with type 1 diabetes poses a challenge not only to their families but also to the healthcare professionals involved in their care. The aim of this report is to highlight the potential adverse effect of daily consumption of excess amount of fried- chicken eggs on the serum lipid profile of a toddler with type 1 diabetes and the usefulness of computing the serum non-HDL-C in the detection of dyslipidaemia. Case report: We report a case of a 22-month-old boy on follow up in our Endocrinology and Metabolism Clinic for type 1 diabetes. Maternal grandmother was feeding him daily with two fried chicken eggs with the aim of providing adequate nutrition as well as satisfying the perceived child’s likeness for eggs. Four months after commencement of daily consumption of two fried-chicken eggs, the child’s serum cholesterol (223mg/dl) and HDL-C (103mg/dl) increased by 2-folds. The patient’s serum triglyceride, low-density lipoprotein cholesterol, non-high-density lipoprotein cholesterol, and very-low-density lipoprotein cholesterol levels were all found to be borderline high, using the National Heart, Lung and Blood Institute 2011 criteria. The serum lipid profile normalized after adjusting the child’s dietary practice. Conclusion: Daily consumption of excess amount of fried chicken eggs can potentially lead to dyslipidaemia in a toddler with type 1 diabetes and this is easily detectable by computing the serum non-HDL-C concentration.

Keywords: Dyslipidaemia, Egg Consumption, Type 1 Diabetes, Non-HDL-C

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Email: alpndiony@yahoo.com

Introduction

Eggs are an inexpensive and highly nutritious functional food, providing both macro- and micronutrients essential for health, particularly in growing children. According to nutritional experts and health agencies, eggs are considered a controversial food because of its saturated fat and cholesterol content [1]. One boiled- or fried-chicken egg contains approximately 200mg and 240mg of cholesterol,
Dyslipidaemia Associated With Daily Consumption Of Fried-Chicken Eggs In A 22-Month-Old Boy With Type 1 Diabetes Mellitus

respectively [2]. With regard to fatty acid content of egg, the approximate concentrations per egg of saturated-, polyunsaturated- and monosaturated-fatty acids are 1.5g, 0.7g and 1.9g, respectively [2]. Chakrabarty et al [3], demonstrated that there was a large variability in individual response to dietary cholesterol. In this regard, dietary cholesterol has been shown to increase plasma cholesterol in hyperresponders [4,5] but no effect was documented among hyporesponders [3,6]. The pattern of individual serum cholesterol changes in relation to dietary cholesterol consumption is influenced by several factors such as ethnicity, genetic makeup, hormonal factors and the nutritional status (body mass index) of the consumer [7,8]. Adamopoulos et al [9] demonstrated that diet enriched with egg yolk was associated with elevated plasma glucose compared with control diet in rats. In the same study, it was noted that all-cause mortality was affected by egg consumption. The American Heart Association recommendation for primary prevention of cardiovascular disease (CVD) in children and adolescents is an intake of ≤ 10% of total calories from saturated fat with ≤ 30% of the calories from total fat and intake of 300mg per day dietary cholesterol with adequate energy to support growth and development [10].

Disorders of lipoprotein metabolism are one of the key risk factors involved in atherogenesis, accounting for approximately 50% of the population-attributable risk of developing CVD [11]. Therefore, estimation of cardiovascular disease risk has become the cornerstone for prevention of CVDs. Viewed from this perspective, several lipoprotein ratios (also called atherogenic ratios) have been defined with the aim of optimizing the predictive capacity of the conventional lipid levels, such as serum levels of triglyceride (TG), low density lipoprotein cholesterol (LDL-C), total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C). Some of the atherogenic ratios suggested for predicting CVD risk include Castelli’s Risk Index (CRI) I and II and Atherogenic Coefficient (AC) [12,13]. These ratios can provide information on risk factors which are difficult to quantify by routine analyses of serum lipid levels and could be a better reflection of metabolic and clinical interactions between lipid fractions [14]. In 2011, the American Academy of Pediatrics redefined dyslipidaemia by adopting the non-HDL-C level (instead of LDL-C level), triglyceride (TG) level and HDL-C level as the three major criterions [15]. It has been stated that at no additional cost, non-HDL-C measures all atherogenic apolipoprotein B-containing lipoproteins, including LDL-C, very low-density lipoprotein cholesterol (VLDL-C), and to lesser extent intermediate density lipoprotein cholesterol (IDL-C), lipoprotein(a), chylomicrons and chylomycron remnants [16]. Thus, making estimation of non-HDL-C in any individual a useful screening tool. According to National Heart, Lung and Blood Institute (NHLBI) guideline in 2011, serum non-HDL-C levels 120-144mg/dl and ≥ 145mg/dl represent borderline- and abnormally-high levels, respectively [15].

Diabetes mellitus diagnosed during the first 2 years of life differs from the disease in older children regarding its causes, clinical characteristics, treatment options and needs in terms of education and psychosocial support [17]. Although hypoglycaemia is a major acute complication of diabetes mellitus in children less than 5 years old, hyperglycaemia and blood glucose variability is a cause for concern because of its association with microvascular
complications, even in prepubertal children and those who have diabetes for only 1 to 2 years [18]. Therefore, the presence of dyslipidaemia in a toddler with diabetes mellitus could worsen the blood glucose variability, thereby potentially increasing the risk of microvascular complications (retinopathy and nephropathy). In addition, the presence of severe hypertriglyceridaemia can complicate diabetic ketoacidosis by its association with development of pancreatitis, leading to increased morbidity and mortality [19,20]. Djoussé et al [21], found that daily consumption of eggs was associated with increased risk of type 2 diabetes. In that report, the authors postulated that excessive egg consumption may potentiate the risk of cardiovascular disease by inducing impaired glucose metabolism and insulin resistance [21]. In literature, there are no reports on the health effects of daily egg consumption in children with either types 1 or 2 diabetes. To the best of our knowledge, this is the first report on the subject. The aim of this report is to highlight the potential adverse effect of excessive daily consumption of fried-chicken eggs on the serum lipid profile of a toddler with type 1 diabetes and the usefulness of computing the serum non-HDL-C in detection of dyslipidaemia.

Case report

We report a case of a 22-month-old Nigerian boy who was successfully managed for new-onset type 1 diabetes complicated by diabetic ketoacidosis (DKA). He was diagnosed at the age of 18 months based on polyuria, polydipsia, and weight loss, all of one week duration. In addition, he had increased tendency to fall asleep. He also had four episodes of vomiting associated with weakness and tendency to fall asleep. His biochemical parameters showed hyperglycaemia (blood glucose 497mg/dl), ketonuria (2 pluses), acidosis (10mmol/L), and HbA1C 8.5%. Glutamic acid decarboxylase antibody profile was positive. He is currently being followed up in the endocrinology and metabolism clinic of the University of Benin Teaching Hospital (UBTH). After his treatment for DKA, he was discharged home on basal-bolus regimen with long-acting insulin (glargine) and rapidly-acting insulin (aspart). His glycaemic control was satisfactory. At home, grandmother was worried about the adequacy of the child’s nutritional intake and decided to feed him with two fried chicken eggs daily. This daily consumption of fried eggs was for a period of 4 months. This was revealed during an interaction with the grandmother when the child presented with a febrile illness (malaria). Subsequent evaluation of his serum lipid profile revealed dyslipidaemia despite being normal at the time of initial presentation with DKA. His serum lipid profiles are summarized in Table 1. When the total as well as high density lipoprotein cholesterol levels at presentation and after 4 months on daily fried chicken eggs were compared, there was a 2-fold increase.

<table>
<thead>
<tr>
<th>Table 1. Serum lipid profiles at presentation and follow-up visits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum lipids</td>
</tr>
<tr>
<td>TCh(mg/dl)</td>
</tr>
</tbody>
</table>
Using the appropriate formulae [13], the atherogenic lipid ratios were computed and the cut-off points suggested by Bonito et al [22] and Lloyd-Jones et al [23], respectively were applied to define normal values. The results of the computed atherogenic lipid ratios are summarized in Table 2.

### Table 2. Summary of serum atherogenic lipid ratios of our patient

<table>
<thead>
<tr>
<th>Serum atherogenic lipid ratios</th>
<th>Normal values</th>
<th>Patient’s results</th>
</tr>
</thead>
<tbody>
<tr>
<td>TG/HDL-C [22]</td>
<td>&lt;2.0</td>
<td>0.99</td>
</tr>
<tr>
<td>Castelli’s Risk Index I (CRI-I) [23]</td>
<td>&lt;4.4</td>
<td>2.17</td>
</tr>
<tr>
<td>Castelli’s Risk Index II (CRI-II) [23]</td>
<td>&lt;2.9</td>
<td>0.97</td>
</tr>
<tr>
<td>Atherogenic Coefficient (AC) [23]</td>
<td>3.01±0.16</td>
<td>1.17</td>
</tr>
</tbody>
</table>

TG = Triglyceride; HDL-C = high density lipoprotein cholesterol

As shown in Table 2, based on adult values, his TG/HDL-C ratio, CRI-I, CRI-II and AC were apparently normal. Normative values are not available for children. In the index case, we computed the non-HDL-C (total cholesterol minus HDL-C) and it was 120mg/dl (3.1mmol/L), representing borderline high serum level based on the most recent American Academy of Pediatrics definition of dyslipidaemia [15]. In sum, our patient’s serum non-HDL-C level was clearly elevated. The patient’s serum very-low-density lipoprotein cholesterol (VLDL-C) level was borderline high (20.4mg/dl) [15].

The grandmother was advised against this practice. She now gives boiled egg to the child three times a week. His first presentation at UBTH followed referral from a private hospital. At the onset of the symptoms, he was taken to the first private hospital where some blood tests were performed and he was said to be “fine” and so, was taken home. The next day, with persistence of the vomiting, he was taken to another private hospital where his random blood glucose was found to be 497mg/dl. He was then commenced intravenous fluid (4.3% Dextrose in 0.18% saline) and referred to UBTH, Benin City. There is no family history of diabetes mellitus or previous illness requiring a hospital admission. Birth weight is unknown to the grandmother. He was fed with breast milk for the first four months of life. Thereafter, artificial formula was added. Guinea-corn pap with milk as well as other family diet were added at the age of eight months. He is on cereals and family diet at the time of presentation. The child has been living with his grandparents since the age of four months when his mother left the country (Nigeria). On examination at presentation, the child was found to be acutely ill-looking, afebrile, not pale or icteric or cyanosed. He
was dehydrated (sunken eyes, loss of skin turgor and slow capillary refill). Anthropometric measurement showed weight 11kg (50th percentile), length 86cm (50th percentile) and occipitofrontal circumference 49cm (75th percentile). He had tachycardia with pulse rate 146 beats per minute. His blood pressure was normal for age, sex and height. Respiratory rate was 40 cycles per minute. Other examinations were unremarkable. At first presentation in UBTH, the biochemical findings were blood glucose 533mg/dl, serum bicarbonate 14mmol/L, ketonuria (3+), glycosuria (2+), urea 44mg/dl, HbA1C 8.5%. The results of his full blood count and differentials were: WBC 24.8 x 10^3/µL with lymphocyte 28.7%; granulocyte 63.2%; and monocyte 8.1%. His platelet count was 468x10^3/µL and haematocrit was 40.1%. The concentrations of serum sodium, potassium, chloride and creatinine were within normal limits. A diagnosis of new-onset type 1 diabetes with ketoacidosis was made. Using ISPAD 2014 Guidelines [24], he was successfully treated for diabetic ketoacidosis (DKA). Intravenous cefuroxime (100mg/kg/day) was added to the therapy for suspected bacterial infection. The patient responded well to treatment and was discharged to the clinic for follow up.

Over a 4-year period (2014-2017), only five children below the age of five years with type 1 diabetes were seen in our hospital (UBTH), representing an incidence of approximately one case per annum. Of the five patients, one was below 2 years old.

Discussion

In the index case, the diagnosis of dyslipidaemia was based on the presence of hypercholesterolaemia (≥ 200mg/dl) and high HDL-C, hyperalphalipoprotein (≥ 65mg/dl), indicating atherogenic dyslipidaemia. In addition, the LDL-C and triglycerides were slightly elevated in our patient. All pointing to dyslipidaemia in our patient. Both the serum total cholesterol and HDL-C demonstrated a two-fold increase from the levels before commencement of daily consumption of excess amount of fried-chicken eggs. The serum levels of total cholesterol (TC) of 223mg/dl represents hypercholesterolaemia in children, based on NHLBI criteria [15]. The high serum HDL-C level (103mg/dl) represents hyperalphalipoproteinemia [15]. Studies in adults indicate that very high HDL-C is associated with adverse cardiovascular health consequences [25,26]. The observed rapid and dramatic rise in serum total and HDL-C levels over a short period of 4 months is also a cause for concern. The dyslipidaemia in the index case is most probably due to the daily consumption of excess amount of fried-chicken eggs. According to the American Heart Association, consumption of two fried-chicken eggs daily for 4 months was well above the recommended intake for both cholesterol and saturated fat in children and adolescents for primary prevention of cardiovascular disease [10]. This view is supported by the fact that the abnormal serum lipid levels normalized following reduction in frequency of egg consumption and change from fried to boiled eggs. Secondly, dyslipidaemia associated with diabetes most commonly manifests as elevated triglycerides and low levels of HDL-C [27]. In our patient, the HDL-C was markedly elevated while the triglyceride showed only slight increase above normal for age and gender, further supporting the view that the dyslipidaemia observed in the index case was associated with the excessive fried-egg consumption. Dietary macronutrient intakes are strongly linked to
Dyslipidaemia Associated With Daily Consumption Of Fried-Chicken Eggs In A 22-Month-Old Boy With Type 1 Diabetes Mellitus


blood lipid levels. Mensick et al [28] in a meta-analysis of 60 controlled trials, revealed that diets high in saturated fat increase total cholesterol as well as LDL-C whereas diets high in mono- and polyunsaturated fats increase HDL-C. Diets high in carbohydrate intake increase serum triglyceride level [28]. Fried chicken eggs contain cholesterol, saturated fat, mono- and polyunsaturated fat, all of which are known to influence serum lipid levels [1,2].

The serum non-HDL-C level in our patient was remarkably high. In this regard, his serum level of non-HDL-C (which measures all atherogenic apolipoprotein B-containing lipoproteins) was nearly twice the cutoff point (≥ 65mg/dl) that defines high HDL-C [15]. Serum level of non-HDL-C varies inversely with age. Such an unfavourable lipid profile in childhood has been linked to future hypertension and atherosclerotic disease in adulthood [29]. Goff et al [30], reported that mean serum total cholesterol levels tended to be steady during prepubertal period, dropped during puberty in both sexes, with the drop being more profound in boys, and then rise again in late adolescence.

Madsen et al [31] reported that HDL-C level greater than 77mg/dl in adults was associated with adverse cardiovascular health. Our patient had HDL-C level of 103mg/dl, suggesting a potential risk for cardiovascular disease. The adverse health effects of very high serum HDL-C levels has also been noted by Ko et al [26]. In the index case, the reason for the markedly elevated serum HDL-C level may be multifactorial (dietary and genetic). The results of a meta-analysis of cholesterol feeding studies using a variety of sources of dietary cholesterol (including eggs) showed that for every 100mg per day increase in dietary cholesterol intake, circulating high-density lipoprotein increased by 0.01mmol/L (0.4mg/dl) [32]. Alternatively, the markedly elevated serum HDL-C level in our patient may be due to the presence of genetic variants of HDL-C. Such variants are found in mutations due to cholesterol ester transfer protein(CETP), ATP-binding cassette transporter A1 (ABCA1), hepatic lipase (LIPC) and scavenger receptor B1 (SCARB1) [33,34]. We could not investigate for these HDL-C variants because of inadequate laboratory facility in our centre. This is an important finding because it implies that non-HDL-C is sensitive screening tool for detecting abnormal serum lipid levels, in the face apparently normal lipid ratios. Based on the lipid ratios, the index case was not at risk of cardiovascular disease but surveillance is indicated.

In our patient, some clinical data negate the diagnosis of monogenic diabetes mellitus. Such negative findings include age 18 months at first diagnosis, and presence of ketoacidosis as well as glutamic acid antibodies at first presentation. More importantly, absence of family history of diabetes mellitus makes monogenic form of diabetes less likely [35]. Typically, maturity onset diabetes of youth (MODY) (excluding neonatal diabetes) is characterized by early onset between the ages of 9 and 30 years [35].

In conclusion, daily consumption of excess amount of fried-chicken eggs can potentially lead to dyslipidaemia in a toddler with type 1 diabetes and this is easily detectable by computing the serum non-HDL-C concentration. We advocate intensification of education regarding medical nutrition therapy in parents/caregivers.
References


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