CONTENTS

Editor-in-Chief, Editorial Board Members
and Advisor

Rosnah Bahar
Nurul Fathah Azman
Sarifah Hanafi
Muhammad Farid Johan
Rosline Hassan
B A Zifali

ii-iii

Review Article

Medical Professionals Support for Parents
to Improve Children’s Social Determinants
of Health: From Conception to Adulthood

Mungai Lucy N Wainaina

1-6

The Use of Malay Traditional Healers
in Childhood Cancer

Azizah Othman
Ariffin Nasir
Norsarwany Mohamad
Fahisham Taib

26-37

Original Article

Risk Factors for Iron Deficiency Anemia
Among School Going Children in Urban
South Bangalore, India

Rajashekar M GR H Ramachandrappa
Pradeep Rudramurthy
Dharmender V Gopalakrishna
Sahana Suryanarayana Rao
K R Bharath Kumar Reddy

7-11

Audit of Congenital Hypothyroidism
Newborn Screening in Sarawak
General Hospital

Wong Ann Cheng
Betty Ho Lee Sue
Chan Lee Gaik

38-46

The Comparison of Ciprofloxacin and
Cotrimoxazole in Shigellosis Therapy
in Children

Adhariana Haji Kaddas
Setia Budi Salekeda
Dasril Daud

12-20

Congenital Disseminated Herpes
Simplex Type 2 with Reactivations:
A Case Report

Ang Ee Lee
Mangalam Sinniah
Irene Cheah Guat Sim

47-52

TaqI Polymorphism of Vitamin D Receptor
Gene as a Potential Marker for Bone
Complications in Transfusion Dependent
Thalassemia Patients: Management
Implications

Diana Rashid
Wan-Zaidah Abdullah
Ariffin Nasir

21-25

Peutz-Jeghers Syndrome Anaemia as
Only Presentation

Pancham Kumar
Ashok Garg
Ambika Sood

53-58
EDITOR-IN-CHIEF

Zilfalil Bin Alwi
MBBS, MSc, MMed (Paeds), PhD
Professor, Consultant Paediatrician and Clinical Geneticist,
School of Medical Sciences,
Universiti Sains Malaysia

EDITORIAL BOARD

Hans Van Rostenberghe
MD (Ghent, Belgium)
Specialist in Pediatrics (Ghent, Belgium)
Professor, Neonatologist
Head of Department of Paediatrics,
Universiti Sains Malaysia

Cheah Fook Choe
MD, MMed(Paeds) (UKM), MRCPi
FRCPCH, FRACP, PhD (Otago, NZ), AM
Professor of Paediatrics (Neonatology)
Faculty of Medicine,
Universiti Kebangsaan Malaysia Medical Centre

Hany Ariffin
MRCP, PhD
Professor and Consultant Paediatric Haematologist-Oncologist
University of Malaya Medical Centre

Terrence Thomas
MD, MRCPCH
Consultant Paediatric Neurologist
Sabah Women & Children’s Hospital

Thiyagar Nadarajaw
MD (USM), M.Med Paediatrics (USM)
Fellowship Adolescent Medicine (Australia)
Consultant Paediatrician and Adolescent Medicine Specialist
Hospital Sultan Abdul Halim

Tang Swee Fong
MD (Hons) (UKM), MRCP (UK), MMMed (Paeds) (UKM)
Associate Professor and Consultant Paediatric Intensivist
Universiti Kebangsaan Malaysia Medical Centre

Ariffin Nasir
MD, MBChB.BAO (Ireland), MMed (USM)
Malaysia
Associate Professor, Consultant Paediatrician and Senior Lecturer
Department of Paediatric, School of Medical Sciences,
Universiti Sains Malaysia

Surini Binti Yusoff
BSc (Hons), PhD
Department of Paediatric,
School of Medical Sciences,
Universiti Sains Malaysia

ADVISOR

Zabidi Azhar Mohd Hussin
MBBS, MRCP, FRCPCH
Professor of Paediatrics
School of Medical Sciences,
Universiti Sains Malaysia
### ADMINISTRATIVE OFFICERS

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Abdul Halim Fikri Hashim</strong></td>
<td>School of Medical Sciences, Universiti Sains Malaysia</td>
</tr>
<tr>
<td>Bachelor of Applied Science</td>
<td></td>
</tr>
<tr>
<td><strong>Wan Khairunnisa Binti Wan Juhari</strong></td>
<td>School of Medical Sciences, Universiti Sains Malaysia</td>
</tr>
<tr>
<td>BSc</td>
<td></td>
</tr>
</tbody>
</table>
MEDICAL PROFESSIONALS SUPPORT FOR PARENTS TO IMPROVE CHILDREN’S SOCIAL DETERMINANTS OF HEALTH: FROM CONCEPTION TO ADULTHOOD

Mungai Lucy N Wainaina

Paediatric Endocrinologist, Department of Paediatrics and Child Health, University of Nairobi, Kenya

Abstract

The World Health Organization (WHO) defines social determinant of health as “the conditions or circumstances in which people are born, grow, live, work and age”. The family is one of the main institutions that shape these conditions. For children to grow from birth to adolescence and transform into healthy adults the social health determinants become important. The health outcome in adolescence is shaped by different institutions but the main one is the family. Adolescence period has one of the fastest growth velocities second only to infancy with rapid brain maturation leading to behavior change and more capacities that trigger the transition from childhood to adulthood. For adolescents to achieve full potential and the best health in the transition to adulthood it is crucial they have a safe and supportive family, safe and supportive schools and positive and supportive peers. It is therefore important for the government; guided by knowledgeable doctors especially pediatricians, to support future and current parents from prenatal period until their children become adults.

Keywords: Social Determinant Health, Environment and Child Development, Paediatrician and Child Development

Corresponding Author: Mungai Lucy N Wainaina, Paediatric Endocrinologist, Department of Paediatrics and Child Health, University of Nairobi, Kenya
Tel: +25472654135
Email: dr.lmungai@gmail.com

Introduction

Though the adolescents are influenced by a variety of social factors and institutions, the family is the most influential. Recent research confirms that the parents have the strongest influence in adolescents’ lives and this influence depends on the measures of involvement. For example, there has been shown to be an association between the level of parental involvement and delay of first sexual contact among teens. This depends on the positive parent-adolescent relationship, high quality of parental awareness and monitoring and family dinner routines. Specifically, adolescent girls who report higher quality relationships with their mothers and fathers and adolescent boys who eat dinner with their families every day are less likely to have precocious sexual
contact. The same holds true for both adolescent girls and boys whose parents keep close contacts on whom they are with when not at home. Thus, higher levels of parental involvement in their adolescents’ lives are linked with good health outcomes [1-3].

The timing of an adolescent’s first sexual contact is a key variable affecting these negative outcomes. Given the need to have upright citizens, prevention of early adolescent pregnancy and sexually transmitted diseases, the parents need to be empowered to handle their families. By 1997 when WHO study group checked on projects helping families to bring up healthy adolescents there were only 34 of which 15 had stopped and only 19 projects were going on in developing countries. The parents are usually unaware of the importance and consequences of their individual roles in interacting with their children [4].

Without help, the consequences of health risk behaviors in adolescence can be life threatening and life-long. Nearly two thirds of premature deaths and one third of the total disease burden in adults can be associated with conditions or behaviors that begin in youth. To protect and preserve our subsequent generations, no better investment can be made in the developing world than to foster promotion of adolescent development and prevention of health risk behaviors among adolescents through working with families.

Are there simple and affordable parenting practices that can help strengthen families and improve adolescent outcomes? Are there institutions or people who know the importance of the family? What are they doing to reduce the current and future health risk behavior the young people are indulging in? Is it ethical that people to just watch their neighbors struggle with delinquent teenagers while they can help alleviate the problem?

One fifth of the world’s population (a total of 1.2 billion people) is composed of adolescents, 85% of whom are in the developing world. During the second decade of life, young people are exposed to serious risks. Along with the growth and change in almost all aspects of physical appearance, adolescence marks the beginning of the child's journey into adulthood, which once started, cannot really be halted or reversed. In other words, once a child develops the physical changes of puberty, childhood, as we knew it, is gone. However, childhood experiences and teaching live with a person throughout life [4].

The Journey from Conception to Adolescence: What Can Go Wrong Before Birth

A lot of families think that parenting begins in labour ward, but the mother begins raising and nurturing a child long before birth. Research indicates that from the 21st week on, the unborn baby can hear sounds, is aware of movements and possibly demonstrate short-term memory. Several studies indicate that the unborn baby can become familiar with the voices of the parents. Other research shows that by the thirtieth week, external schedule cues influence the unborn baby's sleep habits. This is a stage in which the mother needs to accept her unborn baby even when her peers may think the contrary. Based on this evidence, parenting actually begins well before birth and future mothers need to be educated on this.
Research on animal models indicates that anxiety in pregnancy has negative effects on attention regulation, cognitive and motor development and fearful temperament in the first year of life. It has also been shown to have behavioural and emotional problems and decreased grey matter density in childhood and impulsivity, externalizing and processing speed in adolescents. This can be included in the pediatrics curriculum to empower the doctors to educate parents [5-9].

After Birth

The visible responsibilities of parenthood begin with the care of a newborn. The baby responds enthusiastically to all forms of gentle touch like, soft stroking, cuddling and caressing. Gentle rocking back and forth often calms a crying infant, as do massages and warm baths. At this stage attachment to the caregiver begins. The forming of attachments is considered to be the foundation of the infant/child's capacity to form and conduct relationships throughout life. Studies show that babies with secure attachment have the ability to form successful relationships, express themselves on an interpersonal basis and have higher self-esteem. In contrast, children who have caregivers who are neglectful or emotionally unavailable can exhibit behavioural problems such as a pattern of disobedient, hostile and defiant behaviour toward authority figures. The parents will need to be given these information during pregnancy, soon after birth and when they take the babies for vaccination.

From one to two years, the children recognize their own image in the mirror express negative emotions including anger and frustration, become more self-assertive and may try to manipulate the actions of others. Tantrums are often due to the child's frustration over the particular situation. Parents of toddlers are expected to help guide and teach the child basic routines. The frequent frustrations mark an essential step to their development. They learn through experience; trial and error. This means that they need to experience being frustrated when something does not work for them to learn when to let go [10].

Pre-Adolescent Years

The sense of confidence and independence becomes more pronounced in children of this age. They develop the sense of generosity and teamwork; share toys with others, make up games and ask other children to join in. They also know their gender and begin engaging in pretend play. By nine years of age the peers and the school play a big role in helping the virtues they have learned in early years. The parents need to be educated on how to intensify the interaction with their children at this age to help them preserve what they have taught them.

Family Matters

The WHO report notes that the family provides support and love promotes moral development and a sense of responsibility. In the family the parents provide role models and education about culture and sets expectations. The parents filter out or counteract harmful or inconsistent influences from the social environment and negotiate for services and opportunities from the government [3, 11-14].

On-going conflict at home has a great impact on the child. The family conflicts are linked to lower self-esteem among children especially adolescents. In a study of 6-18
year olds, parents' report of conflict at home was associated with children's self-reported aggression. Parents in an unhappy marriage may become withdrawn or hostile towards their children with lack of warmth, rejection and emotional withdrawal. They may attempt to gain the alliance of the child against the other parent. This may lead to spread of marital conflict to the parent-child relationship [15].

Lack of regular contact with a father may take particular emotional and developmental effects on sons. The loss of a male role model for the boys may seriously impact their well-being. A positive father figure is very important for young men and boys in helping them develop their gender identity and learn ways to regulate their emotions and enhance their mental health [16].

A positive, stable, emotional bond between parents and adolescents is an important protective factor for adolescent health and development. When parents divorce boys are likely to clam up and internalize their grief, whereas girls are more likely to talk it out. Boys in general are reluctant to reach out for help and sometimes this may lead to serious thoughts of suicide. They are also more prone to drug abuse which is linked with suicidal feelings [17].

In the absence of the father, the mother may encourage expressions of emotions and closeness, that contradict the message they are getting from society as a whole that boys should be able to handle their own emotion. Even when other stressors are factored in, men whose parents have divorced are 2.3 times more likely to say they had seriously considered suicide.

In spite of the effort put, the predictions for the future marital lives of these children are serious. These children are 50% as likely to divorce as are children from intact families. Divorce will always be stressful and especially to the children. Parents need support in form of counselling before divorce is granted.

The physical availability of both parent helps in behavior control which involves behavioral rules and consequences for disobedience and conveying respect for individuality. The availability of the parent also helps the children understand the consequences of their behavior to themselves, the family and the society [3].

The main resource for any country is its people and the family is the source from which spouts the citizens that form generations. As a nation, to improve and shape the future population, the most effective interventions are probably policies to improve access to medical attention and education by young people and knowledge to families as they bring up their children. This means working with families, peers and schools, addressing risk and protective factors in the social environment at a population level and focusing on factors that are protective across various health outcomes.

There are countries like Malaysia which has the ministry of Ministry of Women, Family and Community Development. One of the strategies of this ministry is to instill positives family values among the people by working with Government agencies, private sector and NGO's. Those parents who know the importance of the family need to come together to agitate for these kinds of structures in their country but guided by a Pediatricians who is in constant contact with the family.
References


[13] Blum RW, Halcon L, Beuhring T, Pate E, Campell-Forrester S, Venema A. Adolescent health in the Caribbean: risk and protective


ORIGINAL ARTICLE

RISK FACTORS FOR IRON DEFICIENCY ANEMIA AMONG SCHOOL GOING CHILDREN IN URBAN SOUTH BANGALORE, INDIA

Rajashekara Murthy GR Halli Ramachandrapa1, Pradeep Rudramurthy2, Dharmender V Gopalakrishna1, Sahana Suryanarayana Rao1, K R Bharath Kumar Reddy1

1. Department of Paediatrics, Indira Gandhi Institute of Child Health, Bangalore
2. Department of Pathology, Indira Gandhi Institute of Child Health, Bangalore

Abstract

Objective: Iron deficiency anemia (IDA) is a common problem in children of the school going age. In spite of government efforts, many reports suggest a high prevalence of anemia. Our study aims at identifying the prevalence of IDA and its associated risk factors. Methodology: We studied 372 children from an urban school in South Bangalore, India with age ranges between 5 to 15 years old. Complete Blood Count was done by using Mindray BC 5200 5 part Hematology cell counter and serum ferritin was estimated by using Chemiluminescence. Anemia was classified as per the WHO grading. Results: The prevalence of IDA was found to be 13.9% of which 9.1% was mild anemia. There was no significant correlation between age, gender, socioeconomic status and anemia. However, a significant correlation was found between lower body mass index (BMI), vegetarianism and anemia (p-value = 0.03 and 0.04 respectively). Conclusion: Anemia is still a public health problem in our country. Major risk factors for development of IDA were found to be low socioeconomic status, vegetarian diet and pubertal period. However, interestingly gender did not play any role in the development of IDA.

Keywords: Iron Deficiency Anemia, Serum Ferritin, School Children
Corresponding Author: Dr.Bharath Kumar Reddy K R, Department of Paediatrics, Indiragandhi Institute of Child Health, South Hospital Complex, DRC Post, Bangalore – 560029 India
Tel: +919845138419
Email: bharathreddykr@yahoo.co.in

Introduction

Anemia is a global public health problem affecting both developing and developed countries with major consequences for human health as well as social and economic development [1]. Anemia is a significant global health problem affecting nearly 305 million school aged children with an estimated prevalence of 70 to 80 percent as per the National Family Health Survey (NFHS-3) [2]. School aged children between
12 to 14 years are known to be at an increased risk of nutritional anemia due to incremental demands of iron due to rapid growth during this phase [3].

Anemia in children can result in impaired cognitive performance, delay in behavioral and motor development, abnormalities in coordination and language, decreased scholastic performance and increased morbidity from infectious diseases [4].

Our study aims at estimating the prevalence of iron deficiency anemia in school going children and to study its associated risk factors.

Study Methodology

Study type
Cross sectional study

Study subjects
372 school going children aged 5 to 15 years from an urban school of South Bangalore were enrolled in the study after taking consent. After enrolment, relevant history pertaining to anemia like easy fatigability, loss of appetite, decreased physical activity and their diet habits were taken. Subsequently, they were examined to look for signs of iron deficiency anemia. Socioeconomic status was analysed by Modified Kuppuswamy Classification of Socio Economic Status (SES).

Study methods
Relevant history was obtained and clinical examination performed. 2 ml each of blood samples were collected in EDTA and Gel vacutainers for complete blood count and serum ferritin analysis respectively. Hematological analysis was performed by Mindray BC 5200 hematology cell counter. Serum ferritin estimation was done by Chemilumiscence method. Children were classified as per WHO grades of anemia by hemoglobin estimation as mild (between 10 to 12 g/dl), moderate (between 7 to 10 g/dl) and severe (below 7 g/dl) [5]. Serum ferritin levels were considered to be low when below 15 ng/mL [6]. Children were classified as 'iron deficiency anemia' when both hemoglobin and serum ferritin were low and as 'iron deficient state' when serum ferritin was low and hemoglobin was normal. Children suffering from any acute or chronic illness or on any medications were excluded from the study. Any children with history of repeated blood transfusions or those having signs of hemolytic anemia clinically were also excluded from the study.

Results
There were 372 children involves in this study where 52.2% of them were males. There were 58.1% of children between the age of 10 to 15 years old and 41.9% were between 5 to 10 years old. The overall prevalence of anemia was found to be 13.9% of which 9.1% were mild anemia and 4.8% were moderate anemia as per WHO classification.

In children with mild anemia, average mean corpuscular volume (MCV) was found to be 71.4 fL. The average mean corpuscular haemoglobin (MCH) was found to be 24.8 pg and mean corpuscular haemoglobin concentration (MCHC) was found to be 29.7 g/dL. In those with moderate anemia, mean MCV was 60.8 fL, mean MCH was 20.6 pg and mean MCHC was 26.8 g/dL.

Serum ferritin was found to be low (<15 µg/L) in 114 (30.6%) of the 372 children.
Hence, 13.9% were found to be of iron deficiency anemia and 16.7% of iron deficient state. In the remaining 258 (69.4%) children, serum ferritin levels and hemoglobin were found to be normal.

Socioeconomic status

As per the Modified Kuppuswamy classification, 53.2% belonged to Class IV (Upper lower) and 41.4% to Class III (Lower middle). Of the children with anemia, the most common group was Class III and Class IV, with no significant difference (p=0.704) in the prevalence of anemia between the different socio economic groups studied.

Age and Gender

Of the children who had anemia, the most common age was between 10 to 15 years old. There was an equal distribution of both males and females with no significant difference in the prevalence of anemia between them.

Diet

There were 55.9% children practiced vegetarians in their dietary preference and had not consumed meat at any point in time. There was a significant difference in the prevalence of anemia between vegetarians and those who consumed meat (p=0.04), with 73.07% of anemic children being vegetarians.

We found that 77.4% children had regular breakfast consumption with 22.6% skipping breakfast in the morning and were irregular in their consumption. Of those who missed their breakfast, the most common reason (66.7%) cited was the lack of time early in the morning. There was however no significant difference (p=0.53) in the prevalence of anemia in those who consumed regular breakfast and those who did not.

Body Mass Index (BMI)

Our study revealed that 61.3% children had a BMI less than 15. There was a significant difference in the prevalence of anemia between those with low BMI and normal BMI (p=0.03). Of the children with anemia, 61.53 % (32) had a low BMI of less than 15.

Table 1. Prevalence of anemia in various studies

<table>
<thead>
<tr>
<th>Studies</th>
<th>WHO Worldwide study</th>
<th>Djokie D</th>
<th>N Saluja</th>
<th>Mutthayya S</th>
<th>Present Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence of anemia</td>
<td>25.4%</td>
<td>18%</td>
<td>37.7%</td>
<td>13.6%</td>
<td>13.7%</td>
</tr>
</tbody>
</table>
Table 2. Prevalence of anemia among vegetarians in various studies

<table>
<thead>
<tr>
<th>Studies</th>
<th>Djokic D</th>
<th>N Saluja</th>
<th>Present Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vegetarians</td>
<td>93.6%</td>
<td>59.7%</td>
<td>73.07%</td>
</tr>
<tr>
<td>Mixed</td>
<td>6.4%</td>
<td>40.3%</td>
<td>26.93%</td>
</tr>
</tbody>
</table>

Table 3. Prevalence of anemia with reference to BMI

<table>
<thead>
<tr>
<th>Studies</th>
<th>Djokic D</th>
<th>Present Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low BMI</td>
<td>72%</td>
<td>61.54%</td>
</tr>
<tr>
<td>Normal BMI</td>
<td>18%</td>
<td>38.46%</td>
</tr>
<tr>
<td>Overweight</td>
<td>10%</td>
<td>-</td>
</tr>
</tbody>
</table>

Discussion

This study was done to evaluate the prevalence and risk factors associated with iron deficiency anemia in school going children. We found a prevalence of 13.9% which was comparable to other studies (Table 1), such as those conducted by Djokic et al. [3] and S Mutthayya et al. [7] who reported a prevalence of 18% and 13.6% respectively. The WHO worldwide study reports a prevalence of 25.4% which is much higher than our study. This could be attributed to the smaller number of subjects in our study owing to our limitation with obtaining consent from parents for blood sampling. Also, the study was conducted in a Government aided school in urban South Bangalore, where children were given iron and folic acid supplementation as per the Ministry of Health and Family Welfare guidelines. Biannual deworming was done and all children were provided with a mid-day meal. This could also contribute to the lower prevalence noted in our study in comparison to the WHO study [7].

The higher incidence of anemia in vegetarians (Table 2) can be explained by the increased availability of heme iron in meat which was better absorbed than non-heme iron in a vegetarian diet. The missing of breakfast reflects on the general nutritional status of children in our country with a large number still missing breakfast. This however, did not directly contribute to the prevalence of anemia in the children. However, it was noted that low BMI and anemia were significantly related (Table 3). Thus, preventing malnutrition would definitely contribute to reducing the prevalence of anemia in the country.

Conclusion

This study inferred that the risk factors for
development of iron deficiency anemia in the school going children of urban south Bangalore were low socioeconomic status, vegetarian diet, pubertal period and those with low BMI. However, no significant association was found between development of anemia and gender. Our study thus adds value to show the prevalence of iron deficiency anemia in children in an urban school going population. Our study shows that in spite of different strategies to lower the prevalence in our country; it is still a significant problem in our country. Further, strengthening the government schemes to enhance nutrition in children would be a way toward decreasing the prevalence of iron deficiency anemia in children [8].

References


ORIGINAL ARTICLE

THE COMPARISON OF CIPROFLOXACIN AND COTRIMOXAZOLE IN SHIGELLOSIS THERAPY IN CHILDREN

Adhariana Haji Kaddas, Setia Budi Salekede, Dasril Daud

Department of Pediatrics, Medical Faculty, Hasanuddin University, Makassar, Indonesia

Abstract

Objective: In the last two decades, Shigella resistance towards antibiotics is getting more predominant in various parts of the world, including Indonesia. The resistance is especially observed in trimethoprim-sulfamethoxazole. This study was conducted to evaluate the efficacy of ciprofloxacin compared to cotrimoxazole in the management of shigellosis children with severe dehydration.

Methods: This is a controlled, randomized and double blind clinical trial. The study samples were obtained from Dr. Wahidin Sudirohusodo Hospital, Ibnu Sina Hospital, Faisal Islamic Hospital and Hasanuddin University Teaching Hospital from July 2013 until May 2014. Patients were the children who met the inclusion and exclusion criteria which were then divided into group of patient with cotrimoxazole (Group A) and ciprofloxacin (Group B) therapy. Subjects were followed-up for the frequency and duration of diarrhea by observing the decreased in fecal leukocyte count and the side effect of the therapy.

Results: The diarrhea duration, the decreased in fecal leukocyte and the side effect between Groups A and B were not statistically different, with p > 0.05. Only on the second day, the following treatment showed significant differences for diarrhea frequency between the two groups, with p < 0.05.

Conclusion: There was no significant difference in term of diarrhea frequency, the duration, the fecal leukocyte count and the side effect between the groups of shigellosis patients with severe dehydration who received the ciprofloxacin and cotrimoxazole therapies.

Keywords: Shigellosis, Ciprofloxacin, Cotrimoxazole, Severe Dehydration, Children

Corresponding Author: Adhariana Haji Kaddas, Department of Pediatrics, Medical Faculty, Hasanuddin University, Jalan Perintis Kemerdekaan Km. 11 Tamalanrea, Makassar, 90245, Indonesia
Tel: +085299649303
Email: rianaadha@gmail.com

Introduction

Diarrhea remains a global health problem with a high morbidity and mortality, especially in developing countries including Indonesia, particularly in Eastern Indonesia. In general, it is estimated more than 10 million children aged less than five die each year with about 20% of the cause is diarrhea. In 2007, the Riskesdas data
showed diarrhea as the most common cause of infant mortality (31.4%) followed by pneumonia (23.8%) and for the age group 1 - 4 years, the cause of death were diarrhea (25.2%) [1]. According to surveillance data report of sub directorate of Health Ministry of Indonesia in 2010, South Sulawesi ranks the third highest number of deaths due to diarrhea after the Central Sulawesi and East Java [2].

The determination of the effectiveness of antibiotic therapy is important in reducing the prevalence of *Shigella* and other organisms that causing dysentery in children. Provision of early and appropriate antibiotics is essential to shorten and ease the symptoms of the disease, minimize the possibility of complications, reduce the spread of the organism and reduce the mortality.

In the past two decades, the resistance of *Shigella* to antibiotics is increasingly prominent. There are many reports of the trimethoprim-sulfamethoxazole resistance found in Asia, Africa, Central America and Europe. This resistance increases the risk of the epidemic shigellosis, no exception in Indonesia. A study conducted at several hospitals in Jakarta, Makassar, Medan, Denpasar, Pontianak and Batam indicating that there has been a *Shigella* sp. resistance to ampicillin, trimethoprim-sulfamethoxazole, chloramphenicol and tetracycline [3].

Finally in 2006, World Health Organization (WHO) issued a new recommendations, the use of ciprofloxacin (quinolone) as the first-line or one of the three second-line antibiotics, namely azithromycin and ceftriaxone (3rd generation of cephalosporin) [4]. The WHO concludes the diarrhea deaths that occur as a result of an inflammatory reaction in the dysentery (endotoxic and encephalopathy shock) almost all are caused by *Shigella* or the similar bacteria. Moreover, there has been a problem of resistance to the germs that cause the shigellosis. Thus, the research on shigellosis is necessary, especially in the matters relating to the appropriate antibiotic therapy in order to reduce the mortality and the complications caused by shigellosis.

Ciprofloxacin is a broad spectrum of fluoroquinolone antibiotic especially against the Gram-negative bacteria. This type of drug inhibits the action of the gyrase DNA (Topoisomerase II) enzyme in bacteria and it is bactericidal. The gyrase DNA functions as a negative super coiling before the double helix DNA reaching the point of separation during the replication and transcription occurrence.

The studies that prove the effectiveness of ciprofloxacin compared with other antibiotics particularly cotrimoxazole, which until now is the first-line antibiotic therapy in shigellosis is still lacking done. Thus, it is important to do a study to prove it. According to the author's, Adhariana HK, the studies comparing ciprofloxacin and cotrimoxazole provision to the patients with shigellosis has never been done in Indonesia. Therefore, this research is expected to enhance the knowledge and to provide a better clinical application in the future.

Until now, there is still concerns in the used of ciprofloxacin in children because of the toxic effects on cartilage obtained and arthropathy in animal experiments which occurs in mice with a certain doses [5]. However, there was no evidence of the permanent arthritis caused by the use of the quinolone antibiotics type in humans. The transient arthritis was found to be rare. Studies using a radiographic technique and
monitoring the growth and development of the joint over a long period of time frame is not enough to observe any adverse side effects. In addition, a recent study in neonates cartilage and joints are still vulnerable, showed no evidence of toxicity to the joint after monitoring for several years [6].

There were two case-control studies conducted by examining the use of intravenous ciprofloxacin. The first study conducted in 48 preterm infants and the average duration of therapy was 11 days. It is monitored for 2 years and no problem was found in its osteoarticular, joint deformity or impaired growth and development [7]. The second study was performed on 30 term infants which therapy was given for 14 days. They found no differences in biochemical, hematological or serial ultrasound knee joint at the first and the six months in the control group [8]. This study aims to evaluate the effectiveness of ciprofloxacin compared with cotrimoxazole in the treatment of shigellosis. Establishment of antibiotic efficacy is crucial in order to decrease the prevalence of dysentery caused by Shigella, to alleviate and shorten the course of disease, to minimize the possibility of complication and to decrease the mortality rate. It means that both of the ciprofloxacin and cotrimoxazole give a recover impacts on patients from the shigellosis.

Methods

This study is a randomized controlled clinical trial (RCT) to assess the effect of the use of ciprofloxacin and cotrimoxazole in the shigellosis children. The implementation of the study design was conducted by using a double blind manner. We conducted the study in the child’s care of Dr. Wahidin Sudirohusodo, Faisal Islamic, Ibnu Sina and Hasanuddin University Teaching hospitals starting from July 2013 until May 2014.

The population sample was the entire of the affordable male and female patients with age of 6 months - 18 years old who met the inclusion and exclusion criteria of the study. There were 100 patients met the criteria. The samples were undergone randomization by using a table of random sampling numbers into two, namely the group of receiving cotrimoxazole therapy (Group A) and the group who received ciprofloxacin therapy (Group B) which each group consisted of 50 patients with a standard medicine. Data for each sample such as the age, sex, weight, height, nutritional status, dehydration degree, diarrhea frequency, vital signs and the feces routine were collected. The data collection is the subject of consecutive sampling which is based on the order of entry into the hospital until later it been analysed. Further analysis of the data by using the appropriate statistical methods including univariate and bivariate analyses was performed.

Data of medical history and laboratory tests for each sample were recorded. Medical history including age, sex, weight and nutritional status as well as the laboratory test including examination of fecal leukocytes were recorded from the patients that met the inclusion and exclusion criteria. Then, the data were proceeded with identification and classification of variables. The identification of variables included the identification of cotrimoxazole, ciprofloxacin, the frequency of diarrhea per day, diarrhea duration, fecal leukocyte counts, antibiotic obtained, probiotics or symbiotic, age, acidosis, malnutrition, dehydration degree, diarrhea complication from other diseases, immunocompromised disease, sex and breast feeding. The classification variables was divided into
independent variable (cotrimoxazole and ciprofloxacin which are categorical variable), dependent variable (the frequency of diarrhea per day, diarrhea duration, fecal leukocyte counts which are numerical variables), between variable (pathological mechanism that occurs in shigellosis, ciprofloxacin, cotrimoxazole working mechanism and zinc supplements that affects shigellosis), the control variables (zinc, dehydration degree, malnutrition, acidosis, diarrhea complication from other diseases, age, antibiotic obtained, probiotics or symbiotic) and the random variables (sex and breast feeding).

**Results**

Table 1 shows the sample characteristics of 100 patients, which 50 children who obtained cotrimoxazole therapy (Group A) and the rest obtained ciprofloxacin therapy (Group B). There were 28 patients (45.9%) male and 22 (56.4%) female in Group A, while 33 (54.1%) male and 17 (43.6%) female in Group B. Nutritional status in the Group A consisted of 29 (52.8%) subjects with well nutrition and 21 (47.7%) subjects were malnutrition while Group B consisted of 27 (47.2%) subjects with well nutrition and 23 (52.3%) subjects were malnutrition. The patient’s age of the Group A ≤ 3 years was 41 (54.7%) and > 3 years was 9 (36%), whereas in Group B ≤ 3 years was 34 (45.3%) and > 3 years was 16 (64%). The breast feeding subjects in Group A were 17 (58.6%) and non breast feeding subjects were 33 (46.5%), whereas in Group B there were 12 (41.4%) of the subjects were breast feeding and 38 (53.5%) subjects were non breast feeding. The diarrhea frequency before therapy (times) in Group A had a mean value of 10.40, the median value of 10.00, a deviation standard of 2.31, with a range of 7-15. While Group B had a mean value of 9.88, the median value of 10.00, a standard deviation of 1.56, with a value ranges of 6 - 14. The diarrhea duration before therapy (days) in Group A had a mean value of 1.72, the median value of 2.0, a standard deviation of 0.45, with a value range of 1 - 2. The fecal leukocytes before therapy (large field of view) in Group A had a mean value of 15.04, the median value of 15.00 and a standard deviation of 2.64 with a value range of 10 - 20. Group B had a mean of 14.96, a median value of 15.0 and a standard deviation of 3.21 with a range of 10 - 20. Statistical analysis for sex, nutritional status, age, breast feeding/non breast feeding consumption, diarrhea frequency before therapy, duration of diarrhea before therapy and fecal leukocytes before therapy in both groups appears to have no significant differences with p > 0.05.

**Table 1. Sample characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group A n = 50</th>
<th>Group B n = 50</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>28 (45.9%)</td>
<td>33 (54.1%)</td>
<td>0.305*</td>
</tr>
<tr>
<td>Female</td>
<td>22 (56.4%)</td>
<td>17 (43.6%)</td>
<td></td>
</tr>
<tr>
<td>Nutritional status, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Well nutrition</td>
<td>29 (52.8%)</td>
<td>27 (47.2%)</td>
<td>0.687*</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>21 (47.7%)</td>
<td>23 (52.3%)</td>
<td></td>
</tr>
<tr>
<td>Age (years), n (%)</td>
<td></td>
<td></td>
<td>0.106*</td>
</tr>
</tbody>
</table>

© 2014 MJPCCH. All Rights Reserved.
The Comparison of Ciprofloxacin and Cotrimoxazole in Shigellosis Therapy in Children

≤ 3 years 41 (54.7%) 34 (45.3%)
> 3 years 9 (36%) 16 (64%)

Breast feeding/non breast feeding, n (%) 0.271*
Breast feeding 17 (58.6%) 12 (41.4%)
Non breast feeding 33 (46.5%) 38 (53.5%)

Diarrhea frequency before therapy 0.306**
(times)
Mean 10.40 9.88
Median 10.00 10.00
Standard Deviation 2.31 1.56
Minimum-maximum 7 - 15 6 - 14

Diarrhea duration before therapy (days) 0.064**
Mean
Median 1.72 1.54
Standard Deviation 2.00 2.00
Minimum-maximum 1 - 2 1 - 2

Fecal leukocytes before therapy (/LFV) 0.889**
Mean 15.04 14.96
Median 15.00 15.00
Standard Deviation 2.64 3.21
Minimum-maximum 10 - 20 10 - 20

*: X² test **: Mann-Whitney U test Group A: Cotrimoxazole Group B: Ciprofloxacin

Table 2 shows the statistical analysis for diarrhea duration before and after therapy. There was no significant difference found between both groups. This data shows that the diarrhea duration did not affect the study results.

Table 2. Diarrhea duration of Groups A and B

<table>
<thead>
<tr>
<th>Diarrhea duration (days)</th>
<th>Before therapy</th>
<th>After therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A (n = 50)</td>
<td>B (n = 50)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>1.72 (0.45)</td>
<td>1.54 (0.50)</td>
</tr>
<tr>
<td>Median</td>
<td>2.00</td>
<td>2.00</td>
</tr>
<tr>
<td>Minimum-maximum</td>
<td>1 – 2</td>
<td>1 – 2</td>
</tr>
</tbody>
</table>

**: Mann-Whitney U test  p = 0.064**  p = 0.108**

Table 3 shows the statistical analysis of the difference decrease in the number of fecal leukocytes at the third day after treatment in each group. There was no statistically significant difference found

© 2014 MJPCH. All Rights Reserved.
between the groups. Group A showed the mean value of 7.64/ (Large field of view) and 7.94/(large field of view) in the Group B. The result indicated a difference in the declining of the fecal leukocytes before treatment to the third day after treatment.

Table 3. The differences of leukocytes decrease in Groups A and B until 3rd day after treatment

<table>
<thead>
<tr>
<th>Leukocytes feces (/LFV)</th>
<th>Groups</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>B</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(n = 50)</td>
<td>(n = 50)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean(SD)</td>
<td>7.64 (2.01)</td>
<td>7.94 (2.05)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>7</td>
<td>8.50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum-maximum</td>
<td>5 - 10</td>
<td>5 - 10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

****: Mann-Whitney U test  \( p = 0.517**

Table 4 shows the side effects such as nausea and vomiting on patients to the group with ciprofloxacin (B), whereas in the group of cotrimoxazole (A) did not reveal any adverse effects. However, this side effect was not statistically significant.

Table 4. The side effects of therapy in Groups A and B

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Group A(n = 50)</th>
<th>Group B(n = 50)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>0(0%)</td>
<td>3(6%)</td>
<td>0.079*</td>
</tr>
<tr>
<td>Vomiting</td>
<td>0(0%)</td>
<td>2(4%)</td>
<td>0.153*</td>
</tr>
</tbody>
</table>

*: \( X^2 \) test

Figure 1 shows the diarrhea frequency per day from the first day until the fifth day after therapy in each group. There was a significant reduction (\( p < 0.05 \)) frequency of diarrhea per day from day to day, either in Groups A or B. Group A showed the median value of diarrhea frequency per day were 10; 6; 4; 1; 0; 0 times per day and Group B were 10; 6; 3; 1; 0; 0 times per day. There was a decrease with statistically significant difference of the diarrhea frequency between Group A and Group B in the second day (\( p = 0.023 \)). However, there were no significant differences on the day I, III, IV and V (\( p > 0.05 \)). The side effects of nausea and vomiting were found to be the most frequent effect related to ciprofloxacin. However these side effects were not observed in the group receiving cotrimoxazole, either initially, vomiting, dermatitis or Steven Johnson syndrome.
The Comparison of Ciprofloxacin and Cotrimoxazole in Shigellosis Therapy in Children

Figure 1. The diarrhea frequency per day from the 1st until the 5th days after therapy in Groups A and B

Table 5. The recovered results of Groups A and B on the 3rd days after therapy

<table>
<thead>
<tr>
<th>Groups</th>
<th>A</th>
<th>B</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recovered</td>
<td>38 (47.5%)</td>
<td>42 (52.5%)</td>
<td>80</td>
</tr>
<tr>
<td>Un-recovered</td>
<td>12 (60%)</td>
<td>8 (40%)</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 5 shows that Group B presented more recovered patients than in Group A. The recovered patients were 42 (52.5%) while the un-recovered patients were 8 (47.5%) in the Group B. Group A showed that the recovered patients were 38 (47.5%) and the un-recovered patients were 12 people (60%). The statistical analysis showed that there was no significant difference (p = 0.317) between the recovered patients in both groups.

Discussion

This study found that the diarrhea duration after therapy in Groups A and B showed a significant difference with p = 0.00. However, there was no significant difference in diarrhea duration before therapy between the two groups with p > 0.05. The diarrhea frequency after therapy on the 1st, 3rd, 4th and 5th days showed no significant difference in the reduction of diarrhea.
frequency between both groups. In general, our finding suggested that the two antibiotics equally have a good ability in reducing the diarrhea frequency in shigellosis patients. The reduction comparison in number of fecal leukocytes before therapy until the 3rd and 5th days after treatment between the groups was also have no difference. Therefore, a short treatment time of diarrhea shorten the duration of hospital admission, reduce the maintenance costs, reduce the risk of nosocomial infections, complications and reduce mortality.

A studies in Bangladesh by Salam et al showed the effectiveness of ciprofloxacin compared to other antibiotics in shigellosis. The study was conducted to compare the efficacy and toxic effects of ciprofloxacin with pivmecillinam in shigellosis and the result showed the same clinical efficacy (p = 0.10). However, the effectiveness of bacteriological was better (p = 0.03) and no correlation with the incidence of arthropathy (p > 0.2) [9]. In another study also conducted in Dhaka, Bangladesh to compare the clinical efficacy of ciprofloxacin with azithromycin in shigellosis showed no significant difference [-7% (95% CI, -23% to 10%)]. Similarly, a bacteriological efficacy also did not show any significant difference [-6% (CI, -14 to 2%)]. Therefore, the researchers concluded the azithromycin remains effectively used in moderate to severe shigellosis caused by multidrug-resistant of Shigella strains [10]. The decreasing number of diarrhea frequency per day is clinically important. Children who suffered from diarrhea needed less fluid requirement and dehydration can be prevented or making it less severe [11].

Lack of information and data on antibiotic sensitivity, especially trimethoprim-sulfamethoxazole and ciprofloxacin against Shigella is the limitation of this study. The data is important to observe the level of resistance and sensitivity for both antibiotics and as a comparison of different levels of resistance in various regions in Indonesia.

**Conclusion**

We conclude that the diarrhea duration, diarrhea frequency, fecal leukocytes and the adverse effects of dehydration after severe shigellosis in group who received the standard treatment using ciprofloxacin was not significantly different compared to those who received standard treatment using cotrimoxazole. Results showed that both antibiotics have the same effectiveness in the therapy of patients with shigellosis. We recommend the cotrimoxazole as the first choice antibiotics in shigellosis children due to the same effectiveness effect of ciprofloxacin. Besides, this antibiotic is cheaper, easier to obtain, available in a form that is more comfortable for the children to consume with minimal adverse effects. Further studies on the antibiotic sensitivity of Shigella especially against the cotrimoxazole and ciprofloxacin antibiotics are needed.

**References**


TAQI POLYMORPHISM OF VITAMIN D RECEPTOR GENE AS A POTENTIAL MARKER FOR BONE COMPLICATIONS IN TRANSFUSION DEPENDENT THALASSEMIA PATIENTS: MANAGEMENT IMPLICATIONS

Diana Rashid¹, Wan-Zaidah Abdullah², Ariffin Nasir¹, Rosnah Bahar², Nurul Fa’ithah Azman¹, Sarifah Hanafi¹, Muhammad Farid Johan², Rosline Hassan², B A Zilfalil¹

1. Department of Pediatrics, School of Medical Sciences, Universiti Sains Malaysia, Malaysia
2. Department of Hematology, School of Medical Sciences, Universiti Sains Malaysia, Malaysia

Abstract

Objective: Early detection of osteoporosis maybe possible by studying genetic factors which may include genetic differences in bone metabolism. These are imperative in the pathogenesis of thalassemia-induced osteoporosis which however the mechanism remains unclear. Till date this TaqI polymorphism of vitamin D receptor (VDR) gene is not widely studied in thalassemia that might have association with bone complications. This study was done to observe the frequency of TaqI SNPs in the VDR gene among transfusion dependent thalassemia patients. Method: Fifty transfusion dependent thalassemia patients were recruited in this study and DNA was extracted using QIAamp Blood Maxi Kit. Subsequently, genomic DNA was used for the genotyping using RFLP-PCR method. Polymorphism at rs731236 (c.1056T>C) was detected by the TaqI restriction enzyme where lack of digestion indicates the presence of wild type T allele representing TT genotype at the locus while the cleavage indicates the presence of mutant C allele with genotypes either CT or CC. Allele and genotype frequencies were estimated by gene counting and tested for Hardy-Weinberg equilibrium. Result: Out of 50 samples analyzed for TaqI polymorphism, the prevalence of TaqI VDR allele frequency ‘C’ found in our Malaysian transfusion dependent thalassemia patients was 16% (TT=68% and TC=32%). Conclusion: Further prospective studies on a wider scale are required to fully clarify the precise environmental and genetic mechanisms underlying bone metabolism derangement in thalassemia children. This preliminary report showed 16% TaqI polymorphism carrier, hence its contribution to the thalassemia-induced osteoporosis should be explored.

Keywords: Bone Complications, TaqI Polymorphism, Transfusion Dependent Thalassemia, Vitamin D Receptor Gene

© 2014 MJPCCH. All Rights Reserved.
Hematology (USM), Hematology and Blood Transfusion Department, School of Medical Sciences, Universiti Sains Malaysia Health Campus, 16150 Kubang Kerian Kelantan, Malaysia
Tel: +6097676194
Email: wzaidah@usm.my

Introduction

A spectrum of bone abnormalities including osteopenia/osteoporosis are frequent in thalassemia patients and occur as a consequence of the hematological disorder and its complications. It represents a major cause of morbidity in these patients [1]. Osteoporosis is characterized by low bone mineral density (BMD) and deteriorated skeletal micro-architecture, with consequently increased risk of fracture. The management of osteoporosis among thalassemia includes calcium supplement, adequate hormonal replacement, effective iron chelation, improvement of hemoglobin levels, vitamin D administration and enhancement of physical activity. Pathogenetic data revealed reduced osteoblastic activity and increased bone resorption are the basic mechanisms of bone loss in thalassemia. Consequently, bisphosphonates was availed as treatment due to the stint as potent inhibitor of osteoclastic activation [2].

Early detection of osteoporosis maybe possible by studying genetic factors which may include genetic differences in bone metabolism. These are imperative in the pathogenesis of thalassemia- induced osteoporosis. However the exact mechanism remains unclear [3].

Investigations of single nucleotide polymorphisms (SNPs) in the vitamin D receptor gene (VDR) may offer an insight into the etiologic relevance of vitamin D. Vitamin D regulates bone and calcium homeostasis which mediates calciotropic actions in the body and modulates the transcription of target genes for calcium uptake or bone formation like calcium binding proteins [4] and osteocalcin. Till date this TaqI polymorphism is not widely studied in thalassemia, which might be associated with bone complications.

VDR gene has been suggested as one of the candidate genes for genetic control of bone mass [5] and act as third modifiers in thalassemia disease. We studied the frequency of VDR gene polymorphism recognized by TaqI (allele T/C) restriction endonuclease, which had been reported to be associated with BMD [6]. Although not widely agreeable and no definite conclusions can be made regarding the association of VDR gene polymorphisms with BMD [7], its role in bone metabolism among thalassemia needs to be explored. Briefly, 50 cases of transfusion dependent thalassemia genotyping among Malaysians were successfully performed and the frequencies of alleles is show in Table 1.
Table 1. Probability of the $\chi^2$ test for Hardy-Weinberg equilibrium of genotype frequencies among transfusion dependent thalassemia patients

<table>
<thead>
<tr>
<th>Marker</th>
<th>Genotypes</th>
<th>TT</th>
<th>TC</th>
<th>CC</th>
<th>Chi$^2$ p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TaqI T/C</td>
<td>Observed</td>
<td>34</td>
<td>16</td>
<td>0</td>
<td>0.178</td>
</tr>
<tr>
<td>(rs731236)</td>
<td>Expected</td>
<td>H-W frequency</td>
<td>35.28(70.56%)</td>
<td>13.44(26.88%)</td>
<td>1.28(2.56%)</td>
</tr>
<tr>
<td>Allele frequency</td>
<td>T=84 (84%)</td>
<td>C= 16 (16%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The prevalence of TaqI polymorphism frequencies reported in the literature in other countries were 29% (TT=49%, TC=43% and CC=8%) in India [8] and 39.5% (TT=35%, TC=51% and CC=14%) in Lebanon [9]. The prevalence of TaqI VDR allele frequency ‘C’ found in this study among Malaysian transfusion dependent thalassemia patients was 16% (TT=68% and TC=32%). VDR gene allele’s frequencies and their association with low BMD is related to ethnicity and geographical distribution. The highest reported frequencies was among Caucasians followed by African and Japanese [10]. In considerations to our multi-ethnicity population including Malays, Chinese, Indians, indigenous people and others, we will need larger and more rigorous analytical studies with other intrinsic value parameters. Further investigation on the mechanisms by which VDR alleles influence not only BMD but also height, stature and other related bone complications in thalassemia patients are required.

Early recognition of genes that potentially cause osteoporosis and other bony complications will allow medical practitioners to deliver appropriate specific treatment of each complication which are the keys to successful management of thalassemia patients. A major prerequisite for reaching goals to excellent management of thalassemia patients include meticulous follow-up by multidisciplinary team as well as stringent compliance toward tailored treatment protocols should be practiced in an exhaustive thalassemia center.

The main challenges that still remain are the lack of awareness and underestimation of the thalassemia induced bony complications particularly osteoporosis and also the absence of affordable worldwide-established treatment protocols. Thus, we herein recommend to stick to early routine BMD screening before puberty started from 10 years old and to continue monitoring every year as stated in the Ministry of Health transfusion dependent thalassemia guidelines [11], which is proposed to be a sensitive predictor for early bone changes, in particularly at the lumbar spine. Further prospective studies on a wider scale are required to fully clarify the precise environmental and genetic mechanisms underlying bone metabolism derangement in thalassemia children. As this is a preliminary report with the finding of 16% TaqI polymorphism carrier, its contribution to the thalassemia-induced osteoporosis should be explored in Malaysian thalassemia populations.

Conflict of Interests

The authors declare no conflict of interests.
Acknowledgements

We would like to thank Universiti Sains Malaysia for funding this study with Research University Grant (1001/PPSP/853003) and Apex Delivering Excellent Grant (1002/PPSP/910343). We also like to thank lecturers, pediatricians, patients and the entire staff of Thalassemia Day Care, record unit and hematology department of Universiti Sains Malaysia for their help in carrying out this study. Special thanks also to Hospital Universiti Sains Malaysia, Hospital Raja Perempuan Zainab II, Hospital Kuala Krai, Hospital Tanah Merah, Hospital Gua Musang and Hospital Sultanah Nur Zahirah for the cooperation and support to this study.

References


ORIGINAL ARTICLE

THE USE OF MALAY TRADITIONAL HEALERS IN CHILDHOOD CANCER

Azizah Othman, Ariffin Nasir, Norsarwany Mohamad, Fahisham Taib

Department of Paediatrics, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, 16150  Kubang Kerian, Kelantan, Malaysia

Abstract

Seeking help from traditional healer is often reported as a treatment option especially in rural population. This study examines the use of Malay traditional healers or ‘bomoh’ for childhood cancer, in the east coast of Peninsular Malaysia. Using a semi-structured questionnaire, we interviewed parents whose children receiving cancer treatment, at paediatric oncology ward, clinic and through phone calls, to explore their knowledge and involvement in ‘bomoh’ for their children’s’ treatment. Of the 94 consented participants, all were Muslim and Malay by race, with a mean age of 37 year old. Majority of the respondents were females (63%), local residents (64%) and held jobs (53%) during the interview. Majority of the paediatric oncology patients were boys (64%), receiving an outpatient treatment (62%), with a range of age from 1 – 18 years. 53% of the children were diagnosed with haematological cancer and 47% were for solid tumour. Consulting ‘bomoh’ was cited as the second most popular alternative treatment option (as reported by 30 participants), after consulting spiritual healer or ‘ustaz’ (n = 43). Only 5.4% of the participants confessed of seeing ‘bomoh’ prior to seeking medical treatment. 40.6% of participants claimed the reason to consult ‘bomoh’ was mainly to avoid painful and extensive medical examination and procedures. Whilst only 7.4% respondents claimed that they believed ‘bomoh’ can treat childhood cancer, a higher number of respondents admitted to consult ‘bomoh’ for the same purpose (34.5%). The ‘bomoh’ consultation rate was found to be significantly higher among those diagnosed for solid tumour (60%) than for haematological cancer (40%). The lower than expected rate of responses in consulting ‘bomoh’ for treatment in this present study might be attributable to participants’ reluctance to disclose the practice to health care providers.

Keywords: Cancer, Children, Malay Traditional Healer, ‘Bomoh’

Corresponding author: Fahisham Taib, Department of Paediatrics, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia
Tel: +609 767 6536
Email: fahisham@usm.my

Introduction

Diagnosis of childhood cancer can be devastating to the respective parents. The condition imposes them to look for all possible ways to help and protect the
children. Whilst the conventional medical treatment for childhood cancer is promising, many of the parents would seek for non-conventional, alternative treatment, in preference to or complimenting the medical intervention. The willingness of patients and their families to try all possibilities for an eventual cure has been the reason for the availability of complementary and alternative medical therapies. It is thought the use of complementary and alternative medicine (CAM) can bring psychological benefits in a sense of optimism, control and hope during the uncertainty period.

A study conducted in Singapore estimates the prevalence use of CAM in paediatric oncology setting reaches 67% - 84.5% [1]. In Malaysia - a country with a population of approximately 26 million, the utilization rate of CAM among adult patients with chronic illnesses is reported to be 63.9% [2]. Interestingly, the use of CAM in Malaysian paediatric oncology patients is much higher whereby the prevalence is reported up to 84.5% [3]. Being a multicultural society which is rich of natural forestry resources, a wide availability and usage of CAM is expected in this country. One of the most commonly seek non-conventional treatment in the Malay community is to visit Malay traditional healers or ‘bomoh’. They are considered as famous and highly regarded indigenous medicine man in the society.

Based on their mode of practice, Malay traditional healers are classified into four categories which are spiritual healer, religious healer, herbalists and bone setters [4]. Religious healers are often referred as ‘Ustaz’ whose practices are based on Islamic principles; for example, their rituals are drawn from Quranic verses. Herbalists mainly use traditional herbs in healing and bone setters mainly focus on body massaging and relocating bones. ‘Bomoh’ in this study refers to Malay traditional healer, who uses spiritual medium to treat illnesses.

‘Bomoh’ often sees illnesses as being caused by physical or supernatural factors. These include food, heat, wind, evil spirit, witchcraft, black magic, loss of inner strength and severe mental stress. The healing processes are done through incantation, holy water, herb prescription and sometimes using supernatural being [5]. Some people believe that ‘bomoh’ are equipped with the task of healing since they know about disease causation and has mystical power to ascertain the cause of ill health. They provide medication by therapeutic usages of herbs, metals, animals’ parts, spiritual support and physical massage depends on specific ailment and needs of the patients. As they were consulted for variety of physical, spiritual and psychological ailments, the basis of treatment are related to whole body-mind-spirit complex approach [6-7].

The traditional and alternative therapy has been commonly used by the locals following diagnosis of spiritual, psychological and even medical problems. ‘Bomoh’ or sometimes locally known as ‘dukun’ or ‘pawang’, is an important individual in Malay society. They are regarded highly in the Malay hierarchical and societal status due to their involvement in treating of many illnesses especially in the rural setting. Mutual recognition of individual such as ‘bomoh’, in a rural socio-demographic structure, has allowed a greater privilege among the locals [8]. Easily accessible, personalized and convincing communication, as well as simple, non-invasive treatment modalities conducted at familiar setting surrounded with family members, could be the reasons people opt for ‘bomoh’ treatment.
Whilst ‘bomoh’ can always be regarded as a complementary treatment option for the patients, problems occur when ‘bomoh’ becomes the only consultant and patients delay their appointment for medical treatment. For example, Ariffin et al [9] found one third of the patients attended oncology treatment sought medicine man or traditional healers help and there were delayed in seeking medical treatment in 13% of the cases. Delayed presentation for early treatment is influenced by complex interaction of demographic, clinical, cognitive, behavioural and social factors [10]. Our clinical experiences in Kelantan - a state in the north east of Peninsular Malaysia where Malays form the majority, suggest that a significant number of paediatric oncology patients spending a lot of time seeing ‘bomoh’ for cure, thus presented at a later stage and jeopardizing the optimal treatment and health outcomes. Therefore, there is a need to study the utilization of this special type of CAM on children with cancer.

Existing local studies have examined the use of various types of CAM on adult with chronic illnesses [2] and cancer [11], and focused solely on reasons these adult patients seeking for traditional healers [12]. This study highlights the utilization of ‘bomoh’, in particular, in the treatment of childhood cancer among the local population. It aims to examine parents’ knowledge and practice in visiting ‘bomoh’ for the treatment of cancer in their children.

Methods

Study tool

Based on extensive review and discussion amongst experts including paediatric oncologists, public health expert and clinical psychologist, a semi-structured, open and close ended questionnaire was developed by the researchers (Appendix 1), as a guide for the trained research assistant to collect data. Socio-demographic and children’s basic medical information was acquired. The questionnaires covers parents’ efforts in seeking treatment for the child, use of alternative treatment, beliefs in ‘bomoh’ in treating cancer, reasons for seeking and/or stopping the treatment from ‘bomoh’ and knowledge on details of the treatment including ways to assess and treat the condition. The items were designed qualitatively with a purpose to obtain descriptive nature of practice and perceived ideas of ‘bomoh’ treatment among Malaysian society. A pilot study was initially performed on 10 participants to assess the understanding and clarity of questions.

Study participants

One hundred parents or family members of children with cancer who received treatment from the only tertiary hospital in the east coast of Peninsular Malaysia were approached to participate in the study, either face-to-face at paediatric oncology ward and clinic or via telephone calls. The list of participants was obtained from the admission record to oncology ward and from those who attended the weekly Haematology-Oncology clinic using convenience sampling. Consented parents of children with cancer were included in the study. Those who refused or whose children have passed away as a result of the disease or treatment were excluded. Two potential participants refused to be interviewed and four did not complete the interview.

Procedure

The proposed study was presented at the department and approval to conduct the study was obtained from the department...
research committee prior to the study commencement. Participants were recruited using convenience sampling in a 4-month study period. The interview was conducted soon as the consent was given, based on researcher-developed semi-structured questionnaires. Each interview took around 30 to 45 minutes. The interview was done by a trained research assistant in order to probe into the depth of the issues. The interview transcripts were reviewed, analyzed and manually coded by the researchers. Given very consistent themes emerged, the data was categorized accordingly and analyzed using SPSS version 18.0 software package (SPSS Inc., Chicago, USA). The data were analyzed using Chi square test and Independent t-test as appropriate.

**Results**

A total of 94 participants consented and completed the interview. Seventy three were approached individually by the interviewer (face-to-face interview) and the other 21 were interviewed by telephone. All participants were Muslim and Malays by race. The mean age was 37 years; the youngest was 20 years old and the oldest was 55 years old. The majority of the participants were females (n = 59, 63%) and the mothers of the children (60%). About 53% of the participants held jobs during the interview either with government service (21%), private sector (16%) or self-employed (16%). Participants from Kelantan formed 64% of the participants whereas the rest were from outside Kelantan that included those from Terengganu, Kedah, Pahang and Pulau Pinang.

With regard to the children, majority of them were boys (64%). The mean age during the interview was 7.5, the youngest was 1 year old and the oldest was 18 years old. Fifty children (53%) were diagnosed for haematological malignancy, such as leukemia and 44 (47%) children were diagnosed for solid tumour. The mean age when they were diagnosed to have cancer ranged from less than 1 year old to 13 years old. During the interview, 58 children were the outpatients and 35 were treated in the ward. One participant contacted via telephone reported that their child had passed away.

**Table 1. Baseline demographic of participants and children with cancer**

<table>
<thead>
<tr>
<th></th>
<th>(n)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Participants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mode of interview</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Face to face</td>
<td>73</td>
<td>77.7</td>
</tr>
<tr>
<td>Telephone calls</td>
<td>21</td>
<td>22.3</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>35</td>
<td>37.2</td>
</tr>
<tr>
<td>Female</td>
<td>59</td>
<td>62.8</td>
</tr>
<tr>
<td><strong>Relationships with the children</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>56</td>
<td>59.6</td>
</tr>
<tr>
<td>Father</td>
<td>31</td>
<td>33.0</td>
</tr>
<tr>
<td>Close relatives</td>
<td>7</td>
<td>7.4</td>
</tr>
</tbody>
</table>
The Use of Malay Traditional Healers in Childhood Cancer


Occupation
- Government service: 20 (21.3)
- Private sector: 15 (16.0)
- Self-employed: 15 (16.0)
- Housewives: 41 (43.6)
- Unemployed: 3 (3.1)

Children

<table>
<thead>
<tr>
<th>Age (Range 1 – 18)</th>
<th>Mean 1</th>
<th>SD 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7.48</td>
<td>4.27</td>
</tr>
</tbody>
</table>

Gender

<table>
<thead>
<tr>
<th>Gender</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boy</td>
<td>60</td>
<td>63.8</td>
</tr>
<tr>
<td>Girl</td>
<td>34</td>
<td>36.2</td>
</tr>
</tbody>
</table>

Diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haematological malignancy</td>
<td>50</td>
<td>53.0</td>
</tr>
<tr>
<td>Solid tumor</td>
<td>44</td>
<td>47.0</td>
</tr>
</tbody>
</table>

Current treatment/management

<table>
<thead>
<tr>
<th>Current treatment/management</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-patient</td>
<td>35</td>
<td>37.2</td>
</tr>
<tr>
<td>Out-patient</td>
<td>58</td>
<td>61.7</td>
</tr>
</tbody>
</table>

1 Mean   2 SD

First treatment-seeking action

When asked about the first action taken when the children started to complain about the illness, majority of the participants (n= 88) reported to consulting doctors whether at private clinics (n= 50) or government hospitals (n= 38). Five participants claimed had first consulted traditional healers. Of these, four children suffered from solid tumour and one child suffered from haematological malignancy.

Use of alternative/complimentary treatment

In addition, we inquired about the use of alternative treatment on the children for example homeopathy, acupuncture, spiritual healer or ‘Ustaz’, herbal medicine, goat milk, special drink, vitamin and ointment. Except for consulting religious person or ‘Ustaz’ (n= 43) and Malay traditional healer or ‘bomoh’ (n = 30), other types of treatments were not reported as commonly given to the children (Refer Table 2).

Table 2. The use of complementary alternative treatment reported by participants

<table>
<thead>
<tr>
<th>Alternative Treatment</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consulting spiritual healer or ‘Ustaz’</td>
<td>43</td>
</tr>
<tr>
<td>Consulting Malay traditional healer or ‘bomoh’</td>
<td>36</td>
</tr>
<tr>
<td>Ointment</td>
<td>13</td>
</tr>
<tr>
<td>Vitamin</td>
<td>10</td>
</tr>
<tr>
<td>Goat milk</td>
<td>8</td>
</tr>
<tr>
<td>Homeopathy</td>
<td>6</td>
</tr>
<tr>
<td>Herbal medicine</td>
<td>2</td>
</tr>
<tr>
<td>Special drinks</td>
<td>2</td>
</tr>
</tbody>
</table>

* multiple responses are acceptable

© 2014 MJPCH. All Rights Reserved.
Source of information on alternative treatment

Seventy-two participants answered the question on how they received information about alternative treatment for childhood cancer. Source of information were mostly came from other family members, relatives, neighbours and friends (n = 35), people with similar illnesses (n = 21) and mass media (n = 15). One participant claimed the ‘bomoh’ volunteered to treat the child.

Reasons people consult ‘bomoh’ for childhood cancer

Of 64 who responded to this question, majority of them (n = 26) claimed the reason people seek for ‘bomoh’ treatment was because they wanted to avoid painful, scary and discomfort procedures being conducted on their small children in the hospital such as needle injection, surgical operation, amputation, lumbar puncture, lengthy hospitalization and multiple invasive examinations. Other respondents stated it was due to their confidence and belief that ‘bomoh’ could cure cancer (n = 7) or the illness was within ‘bomoh’ expertise (n = 22). A small number of respondents (n = 7) claimed the reason to visit ‘bomoh’ was because of the influence from others such as relatives, friends or neighbours.

Reasons people stop consult ‘bomoh’ for childhood cancer

Seventy-three respondents had given various reasons why people stopped from consulting ‘bomoh’ for childhood cancer. For instance, they stopped consulting ‘bomoh’ when the diagnosis was confirmed and believed the treatment should be given by doctor in the hospital and not by ‘bomoh’ (n = 9). Others heard (n = 44) or experienced themselves (n = 4) that particular ‘bomoh’ was not capable to cure cancer and some admitted that the method used was not convincing (n = 5) or the cancer had spread (n = 3). Other reasons included refusal to have both hospital and ‘bomoh’ treatment simultaneously (n = 3), being informed by doctor that ‘bomoh’ cannot cure cancer (n = 3) and believed that hospitals have more sophisticated treatment and equipment (n = 3).

Believe in and consultation with ‘bomoh’ for childhood cancer

Majority of participants (n = 87) claimed that they did not believe that ‘bomoh’ could treat childhood cancer. However, this belief alone did not guarantee that they would not consult ‘bomoh’ for treatment of cancer in children. Whilst only 7 respondents believed ‘bomoh’ could treat childhood cancer, thus went for the treatment, interestingly those who claimed otherwise did the same. We found more than half of the number consulted ‘bomoh’ for the same purpose (n = 30).

Table 3. Participants believe in ‘bomoh’ by consultation with ‘bomoh’ for childhood cancer

<table>
<thead>
<tr>
<th>Consult ‘Bomoh’</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Believe in ‘bomoh’</td>
<td>7 (100)</td>
</tr>
<tr>
<td>Do not believe in ‘bomoh’</td>
<td>87 (100)</td>
</tr>
</tbody>
</table>

*Fisher’s Exact Test
Of those 36 participants who reported to have consulted ‘bomoh’ for treatment of their children, almost half of them (n = 17) claimed to visit ‘bomoh’ before they started treatment in the hospital. Another 16 visited ‘bomoh’ while receiving hospital treatment. Two claimed to consult ‘bomoh’ both before and during hospital treatment and one participant admitted to consult ‘bomoh’ at almost all the times during the child’s illness. The frequency of visits varies from 1 to 2 times (n = 24) to more than 10 times (n= 4).

**Consultation with ‘bomoh’ and type of childhood cancer**

With regard to type of cancer and question whether or not ‘bomoh’ was consulted, the consultation rate was found to be significantly higher among those diagnosed for solid tumour (n = 21) than haematological malignancy (n= 14) (21 vs 14: $X^2 = 3.9$ (34): $p = 0.04$). There were no significant differences of other demographic factors related to respondent’ or patients’ such as origin, age, gender, mode of getting information, in-patients and out-patients, that influence the tendency of consulting ‘bomoh’ or otherwise.

**Parental self-reporting on bomoh’s assessment and treatment**

Parents’ knowledge about techniques used by ‘bomoh’ to detect and treat childhood cancer was enquired. The interviewer used an analogy that doctors may use radiological investigations (X-ray or MRI) to diagnose cancer and chemotherapy for treatment and asked what the respondents know about the methods used by ‘bomoh’ to achieve the same goals.

The ‘bomoh’ claimed to identify what the medical problems were by touching parts of the child’s body (n = 17) including pulse and head. The other methods included simply looking at the child (n = 9), use of their experience, gut feeling and prediction (n= 14), looking for something in a bowl of water (n= 8) or reading specific verses (n= 17).

With regard to the treatment method, almost all respondents claimed that ‘bomoh’ used holy water or ‘air tawar’ (n= 48). Other methods involved were the use of holy flour or ‘tepung tawar’ (n= 4), consumption of medicated leaves (n= 4), body massaging (n= 2) and reciting special prayers or ‘jampi’ (n= 12).

**Discussion**

The present study explores the use of Malay traditional healers or ‘bomoh’ for treatment of childhood cancer, in the east coast of Peninsular Malaysia, which is largely comprised of Malay ethnicity.

Whilst majority of the respondents claimed that healthcare professional was the first person they approached to seek treatment, this study revealed that consulting ‘bomoh’ is very common practice in paediatric oncology. The usage of the alternative therapies is very much recognized in local population and based on our clinical experience they were consulted throughout the disease trajectory. High utilization of traditional and alternative medications might be due to local medical tradition between ethnics, cultures and availability of rich tropical biodiversity which is a reliable source to produce traditional medicine. Alternative and traditional medicine is reported to be practiced by adult patients with other chronic medical conditions [2]. This finding adds to the existing knowledge which identified the use of other types of CAM such as water therapy, vitamins and
supplements, is very prevalent in patients with chronic and threatening illnesses [2 – 3]. The current Malaysian healthcare system offers free treatment for many medical conditions in our conventional system. Effort has been introduced by the government to establish and integrate medical and traditional therapy but this is long way ahead.

It is interesting to point out that whilst only a very small number of respondents admitted to believe that paediatric cancer can possibly be cured by ‘bomoh’, there is a large number of respondents consulted ‘bomoh’ for treatment. The incongruence of parents’ perception and action could be as a result from many factors especially when their focus is on putting effort to cure their children from cancer. In addition to seeking conventional medical treatment, the parents also consulted ‘bomoh’ as an extra effort for cure. This is termed as “double insurance” [12]. In addition, parents’ efforts and motivation to avoid conventional medical treatment that often associated with long treatment schedule, invasive and traumatized procedures is another reason for seeking ‘bomoh’ treatment. Apparently, this was cited as a primary reason for people seeing ‘bomoh’ in this study. ‘Bomoh’ is also perceived as an expert in their field, thus treatment is acquired. This finding is consistent with previous study which indicated that traditional healers were approached due to their high credibility and ability to heal cancer, sometimes within a short time frame [12].

One third of the respondents claimed to have consulted ‘bomoh’ sometimes during the children’s illness for treatment. The findings indicated that significantly higher number of patients with solid tumour visited ‘bomoh’ compared to haematology malignancy. We noted that about 60% of caregivers went for ‘bomoh’ consultation was from solid tumour group as compared to 40% in haematological malignancy. The decision of using traditional healer for solid tumour could be related to the nature of the diseases. Patients with solid tumour often mistakenly diagnosed with curable medical condition until the condition affecting functionality of the patients, thus presenting late to the hospital. This late presentation mainly due to misdiagnosis of the disease related to slow growing nature of the solid tumour and the repeated attempt and use of alternative therapy at home. In haematological malignancy, patients often presents with chronic state such as anaemia and infection which warrants acute hospital admission.

**Limitations**

We presume many participants opted to offer negative responses when we inquire about their visits to ‘bomoh’ to treat childhood cancer. This might be attributable to participants’ reluctance to disclose their practice as many patients whom parents we recruited are still receiving continuous hospital treatment. The number of positive responses that we reported may be underestimated. The answers given during the interview were brief and some inferred to their view on other people rather than their actions on visiting the ‘bomoh’. Disclosure of the information about visiting ‘bomoh’ is often considered a sensitive issue, due to reasons such as perceived fear of termination of treatment by doctors, cross reactions between CAM and conventional medicine and physicians’ lack of interest and knowledge of CAM [13], such as seeking ‘bomoh’ treatment. Most of the information related to alternative treatment is considered as not relevant by the patients and therefore concealed [2]. The interviewer spent relatively brief interview session and the queries included close-ended
items might have limit the possible responses. There is also limitation on sampling of the participants as the convenience sampling was applied in view of accessibility and close proximity of the subjects. The richness of information related to differences in practice, cultural, ethnical and religious background may be failed to be recognized. Financial limitation restricted the study to only one hospital in the east coast of Malaysia. However, noteworthy effort was attempted to include significantly high number of possible respondents to achieve descriptive data about population practice especially at Hospital USM.

**Conclusion and Recommendations**

The study demonstrated population practice in the east coast of Peninsular Malaysia by seeking Malay traditional healers in children with childhood cancer. The finding suggested that ‘bomoh’ service has been used despite lack of belief regarding the effectiveness of bomoh’s treatment. Beliefs among the local population could be related to customary way of life, social structural and individual hierarchy in the society. Paradigm shift in a population can be a monumental task. The public discourse about traditional medicine and modern medicine may influence the decision taken by the caregivers. Children with solid tumour are more likely to spend some times seeking ‘bomoh’ treatment, thus are at more risk for delayed presentation in the hospital. Resolution does not stop by continuous education, but to embark on win-win situation for the benefit of our patients. The complimentary or even traditional medicine might have some roles especially for patients who are terminally ill and requiring palliative service. A number of patients are still using traditional medicine while having an ongoing chemotherapy for their cancer. Discourse and decision on opting for modern or traditional medicine depends on multiple psychosocial influences. Healthcare professionals should be non-judgmental when receiving disclosed information about the use of ‘bomoh’ to prevent defaulting of treatment in these contexts [13]. Cooperation between modern and the traditional health practitioners must be commenced to allow successful early oncological intervention. The education has to be two ways – educating the community as well as the traditional healers. Collaboration between both teams will allow for earlier referral to paediatric oncology centre. This task requires the society to understand the importance of parallel approach of conventional and traditional medical systems, in order to maximize survival in the management of childhood cancer.

**Conflict of interest statement**

We have no conflict of interest.

**References**


Appendix 1. Interview Guide

1. Apakah langkah pertama bila anda dapati anak tidak sihat?
   
   *What is the first step taken when you noted that your child is sick?*

2. Pernahkah anda mencuba rawatan lain/alternatif seperti di bawah untuk merawat kanser?
   
   *Have you ever tried other treatment/alternative as below in the cancer treatment?*

<table>
<thead>
<tr>
<th>Jenis rawatan (Type of treatment)</th>
<th>Ya (Yes) atau tidak (No)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homeopathy</td>
<td></td>
</tr>
<tr>
<td>Akupantur (Acupuncture)</td>
<td></td>
</tr>
<tr>
<td>Ustaz/ Perawat Islam (Islamic healer)</td>
<td></td>
</tr>
<tr>
<td>Bomoh (Traditional healer or shaman)</td>
<td></td>
</tr>
<tr>
<td>Herba (Herbalist)</td>
<td></td>
</tr>
<tr>
<td>Susu kambing (Goat milk)</td>
<td></td>
</tr>
<tr>
<td>Air khas i.e ECPI (Special water)</td>
<td></td>
</tr>
<tr>
<td>Vitamin (Vitamin)</td>
<td></td>
</tr>
<tr>
<td>Ubat/ Minyak sapu (Ointment)</td>
<td></td>
</tr>
<tr>
<td>Lain-lain (others): ..................</td>
<td></td>
</tr>
</tbody>
</table>

3. Di manakah anda mendapat maklumat tentang kewujudan rawatan alternatif untuk kanser?
   
   *Where did you get the information regarding the existence of alternative therapy for cancer?*

4. Adakah anda percaya bomoh boleh mengubati kanser?
   
   *Do you believe that Malay traditional healer (bomoh) can treat cancer?*

<table>
<thead>
<tr>
<th>Ya/ Yes</th>
<th>Tidak/ No</th>
</tr>
</thead>
</table>

5. Pernahkah anda berjumpa bomoh untuk mendapatkan rawatan kanser?
   
   *Have you seen 'bomoh' for cancer therapy?*

<table>
<thead>
<tr>
<th>Waktu (Time)</th>
<th>Kekerapan (Frequency)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sebelum ke hospital (before attending the hospital)</td>
<td></td>
</tr>
<tr>
<td>Semasa mendapat rawatan hospital (during the treatment)</td>
<td></td>
</tr>
<tr>
<td>Selepas selesai rawatan hospital (after treatment completion)</td>
<td></td>
</tr>
</tbody>
</table>

6. Siapakah yang mempengaruhi keputusan anda untuk mendapatkan rawatan bomoh?
   
   *Who does influence your decision making to obtain 'bomoh' treatment?*

7. Setahu anda, bagaimana bomoh 'mengesan' sesuatu penyakit atau puncanya?
   
   *In your opinion, how do you think that 'bomoh' screen for the disease or causes?*

8. Apa kaedah biasa digunakan bomoh untuk merawat kanser?
   
   *What do you think of the techniques used by 'bomoh' for cancer treatment?*
9. Pada pendapat anda, apakah sebab orang pergi mendapatkan rawatan kepada bomoh untuk penyakit kanser?
   *In your opinion, what are the reasons for getting cancer treatment with the 'bomoh'?*

10. Pada pendapat anda, apakah sebab orang berhenti/tidak menyambung rawatan dengan bomoh?
    *In your opinion, what are the reasons for not stopping or defaulting treatment with the 'bomoh'?
ORIGINAL ARTICLE

AUDIT OF CONGENITAL HYPOTHYROIDISM NEWBORN SCREENING IN SARAWAK GENERAL HOSPITAL

Wong Ann Cheng, Betty Ho Lee Sue, Chan Lee Gaik

Paediatric Department, Sarawak General Hospital, Jalan Hospital, 93586 Kuching, Sarawak, Malaysia

Abstract

A cross-sectional study using secondary data was conducted in Sarawak General Hospital with a review of congenital hypothyroidism screening daily return census from 2008-2010 to determine the effectiveness of the screening programme based on the ministry of health set performance indicators and the birth prevalence of congenital hypothyroidism in Kuching, Sarawak. From this 3 years audit, 34715 newborn babies were screened out of a total of 35019 live births. There were 14 cases of congenital hypothyroidism detected of which 2 cases were later found to be transient hypothyroxinaemia. The average duration from birth to starting treatment was 23 days and only 3 cases were treated within 14 days. The shortest time to treatment was 8 days while the longest was 44 days. A total of 12 confirmed cases of congenital hypothyroidism were detected which gives a birth prevalence of 1 in 3502 live births. There has been an underperformance in terms of the duration from birth to treatment in confirmed cases. The causes of delay were multifactorial ranging from interruption of service from automated machine breakdown, delay in the review of results during festive seasons and difficulty in locating patients for retesting.

Keywords: Newborn Screening, Congenital Hypothyroidism, Sarawak

Introduction

Early detection of congenital hypothyroidism and institution of thyroxine replacement result in improved cognitive outcome [1]. Since 2003, congenital hypothyroidism screening has been introduced in the hospitals in the state of Sarawak. The prevalence of congenital hypothyroidism differs between regions. In Malaysia, the estimated birth prevalence of congenital hypothyroidism range from 1:2500 to 1:3500 live births[2]. No data on congenital hypothyroidism has been published for Sarawak as far as we know. Newborn screening is a complex process that can be divided into 3 stages; pre-analytical (education and specimen collection), analytical (laboratory testing) and post-analytical (follow-up, diagnosis, education, management and evaluation) [3]. Programme evaluation is important.
organizational practice in a public health sector which may not be practiced consistently or sufficiently integrated into a daily management of the programme [4]. It is important to undertake periodic audits of the system to identify any deficiency and improve on the overall quality of the newborn screening programme. The objective of the study was to estimate the birth prevalence of congenital hypothyroidism in Kuching and determine the effectiveness of the screening programme based on Ministry of Health set performance indicators.

**Methods**

A cross-sectional study using secondary data was conducted in Sarawak General Hospital with a review of congenital hypothyroidism screening daily return census from 2008-2010. The period of the study was chosen as the source data was readily available for verification.

Daily return census were obtained from the labour room for all babies delivered on the day which includes babies that were born before arrival (BBA) to ensure that all live births are accounted for. All newborns delivered in Sarawak General Hospital have their cord blood taken for testing of thyroid stimulating hormone (TSH) and supplementary total thyroxine T4 testing done in borderline cases as per national screening programme for congenital hypothyroidism guideline. Newborn born before arrival and those babies who have missed or rejected cord blood samples will be recalled after 72 hours to have a repeat sample using venous blood sample as per flow chart standard operating procedure (Figure 1).

All blood samples (cord blood and venous) were processed daily on weekdays while weekend samples were only processed the following Monday. On a long stretch of weekends with public holidays, the blood samples were processed no later than 72 hours after collection to ensure timely results. Cord blood TSH and total T4 were measured by automated chemiluminescence immunoassay system using Modular E170 (TSH analytical sensitivity 0.005 mU/L) and backup machine Advia Centaur (TSH analytical sensitivity 0.008 mU/L). All tests were subjected to the internal quality procedure.

All the abnormal results with the TSH more than 25 mU/L were reviewed twice a week during the general clinic session by a designated paediatrician in charge once the results were available while TSH of more than 60 mU/L were informed directly through phone to the paediatrician by the paediatric clinic staff nurse in charge of the screening programme on the same working day. The recall and tracing of repeat samples were done by the assigned paediatric clinic staff nurse every working day. The patients that failed to be recalled were informed to the paediatrician and referred to the booking maternal child health clinic for tracing of the patient’s whereabouts. The confirmed cases were seen by the paediatrician on the earliest clinic or working day. Treatment was initiated then and the patient’s particulars (perinatal history and physical examination) were captured on a congenital hypothyroidism registry form. The goal of the treatment was to keep the T4 at the upper half of normal range and TSH at the lower end of normal. The infants were monitored every 2 weekly until normalization of thyroid function, then 1-2 monthly until 6 months old and subsequently 3 monthly until 3 years old. The infants were reassessed at 3 years old for permanence of hypothyroidism.
All the screening results were compiled and entered into a monthly census. The data were then tabulated into an Excel spreadsheet and analyzed using the Microsoft Excel software to determine the total number of babies screened, coverage rate, the sample rejection rate, the rate of recall and retesting. The cases of confirmed congenital hypothyroidism were further reviewed to determine the duration from birth to treatment. Any cases found to have delayed treatment defined as initiation of treatment after 14 days of life were further looked into to ascertain causes for the delay.

**Figure 1. The flow chart standard operating procedure**
Out of a total 35019 live births, 34715 newborn babies were screened from 2008-2010 with the mean coverage of screening of 99.1% (Table 1). Out of these, 136 babies required retesting due to abnormal results; of which 11 had TSH more than 60 mU/L and remaining 125 had borderline TSH between 25-60 mU/L with low total T4 of less than 100 µmol/L. Among the group with borderline TSH, a new level was adopted since the last 2 months of 2010 (November and December) in line with the national directive with the borderline TSH level taken between 21-60 mU/L and low free T4 of less than 15 pmol/L in place of total T4. This resulted in a much higher recall rate for the last 2 months of 2010. The recall rate for abnormal results was 0.38, 0.31 and 0.49 for the year 2008, 2009 and 2010 respectively (Table 2).

However, the actual recall rate for venous testing was much higher as it includes all the newborns with abnormal cord sample results as well as those that were born before arrival and those that had missed or rejected cord samples. The actual recall rate for venous sampling at 72 hours was 0.73, 0.57 and 1.51 for 2008, 2009 and 2010 respectively (Table 2). Not all those that needed repeat venous sampling were able to be recalled. A total of 5 cases, 7 cases and 9 cases were unable to be recalled back for the year 2008, 2009 and 2010 respectively. This put the percentage of recalled patients seen for retesting at 94.1%, 89.6% and 94.8% respectively for the year 2008, 2009 and 2010.

The mean sample rejection rate was 0.11% with 39 samples rejected out of 34715 samples that were screened. This was well within the Malaysian Ministry of Health (MOH) performance indicator of less than 1% rejection rate. The majority of the samples rejection was due to insufficient sample followed by mucoid samples and haemolyzed samples. Haemolyzed sample was rarely rejected except if it was badly haemolyzed.

There were 14 cases of congenital hypothyroidism detected; 3 cases in 2008, 8 cases in 2009 and 3 cases in 2010. Out of the 14 cases, 2 were later found to be transient hypothyroxinaemia. The average duration from birth to starting treatment was 23 days. Out of the 14 cases, only 3 cases managed to have the treatment started within 14 days. The shortest time to treatment was 8 days while the longest was 44 days (Table 3). This fell well below the MOH performance indicators with 33.3%, 12.5%, and 33.3% compliance respectively for the year 2008, 2009 and 2010 (Table 4).

Table 1. Status of screening programme

<table>
<thead>
<tr>
<th>Year</th>
<th>Total live births (including BBA)</th>
<th>Number of Newborns screened</th>
<th>Percentage of births screened</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>11686</td>
<td>11588</td>
<td>99.2%</td>
</tr>
<tr>
<td>2009</td>
<td>11760</td>
<td>11657</td>
<td>99.1%</td>
</tr>
<tr>
<td>2010</td>
<td>11573</td>
<td>11470</td>
<td>99.1%</td>
</tr>
<tr>
<td>Total</td>
<td>35019</td>
<td>34715</td>
<td>99.1%</td>
</tr>
</tbody>
</table>

BBA = Born before arrival

© 2014 MJPCH. All Rights Reserved.
### Table 2. Outcome of screening results

<table>
<thead>
<tr>
<th>Year</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live births</td>
<td>11686</td>
<td>11760</td>
<td>11573</td>
<td>35019</td>
</tr>
<tr>
<td>BBA</td>
<td>70</td>
<td>80</td>
<td>82</td>
<td>232</td>
</tr>
<tr>
<td>Samples screened</td>
<td>11588</td>
<td>11657</td>
<td>11470</td>
<td>34715</td>
</tr>
<tr>
<td>Missed samples</td>
<td>28</td>
<td>23</td>
<td>21</td>
<td>72</td>
</tr>
<tr>
<td>Rejected samples</td>
<td>15</td>
<td>10</td>
<td>14</td>
<td>39</td>
</tr>
<tr>
<td>Samples rejection rate (%)</td>
<td>0.13</td>
<td>0.09</td>
<td>0.12</td>
<td>0.11</td>
</tr>
<tr>
<td>Normal TSH</td>
<td>11420</td>
<td>11486</td>
<td>11237</td>
<td>34143</td>
</tr>
<tr>
<td>Samples with high TSH (&gt;60mU/L)</td>
<td>3</td>
<td>5</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>Samples with borderline TSH (25-60mU/L)</td>
<td>109</td>
<td>125</td>
<td>163</td>
<td>397</td>
</tr>
<tr>
<td>Samples with borderline TSH (25-60mU/L) and low T4 (&lt;100 µmol/L)</td>
<td>41</td>
<td>31</td>
<td>53</td>
<td>125</td>
</tr>
<tr>
<td>Number needing retesting</td>
<td>44</td>
<td>36</td>
<td>56</td>
<td>136</td>
</tr>
<tr>
<td>Number recall for venous sample after 72 hours</td>
<td>85</td>
<td>67</td>
<td>173</td>
<td>325</td>
</tr>
<tr>
<td>Recall rate for abnormal results (%)</td>
<td>0.38</td>
<td>0.31</td>
<td>0.49</td>
<td>0.39</td>
</tr>
<tr>
<td>Actual recall rate for venous sample (%)</td>
<td>0.73</td>
<td>0.57</td>
<td>1.51</td>
<td>0.94</td>
</tr>
</tbody>
</table>

### Table 3. Data collection of confirmed cases

<table>
<thead>
<tr>
<th>Year</th>
<th>No</th>
<th>Date screening</th>
<th>cTSH (mU/L)</th>
<th>cT4 (µmol/L)</th>
<th>Date retesting</th>
<th>vTSH (mU/L)</th>
<th>V total T4 (µmol/L)</th>
<th>Duration from birth to treatment</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>1</td>
<td>16.4.08</td>
<td>38.62</td>
<td>173</td>
<td>26.4.08</td>
<td>67.54</td>
<td>185</td>
<td>21 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>2.7.08</td>
<td>28.89</td>
<td>82</td>
<td>10.7.08</td>
<td>55.82</td>
<td>93</td>
<td>14 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>26.12.08</td>
<td>&gt;100</td>
<td>72</td>
<td>21.1.09</td>
<td>&gt;100</td>
<td>18</td>
<td>35 days</td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td>1</td>
<td>27.1.09</td>
<td>97.61</td>
<td>71.48</td>
<td>2.2.09</td>
<td>64</td>
<td>79</td>
<td>15 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>25.3.09</td>
<td>26.85</td>
<td>84</td>
<td>24.4.09</td>
<td>18.93</td>
<td>83</td>
<td>44 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>26.3.09</td>
<td>25</td>
<td>68</td>
<td>30.3.09</td>
<td>34.85</td>
<td>133</td>
<td>27 days</td>
<td>Premature 33 weeks</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>27.7.09</td>
<td>91.42</td>
<td>27</td>
<td>31.8.09</td>
<td>21.36</td>
<td>38</td>
<td>10 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>8.9.09</td>
<td>36.35</td>
<td>93</td>
<td>18.9.09</td>
<td>26.1</td>
<td>103</td>
<td>22 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>7.11.09</td>
<td>26.45</td>
<td>56</td>
<td>25.11.09</td>
<td>10.65</td>
<td>78</td>
<td>25 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>9.12.09</td>
<td>50.59</td>
<td>85</td>
<td>7.1.10</td>
<td>80.88</td>
<td>75</td>
<td>35 days</td>
<td></td>
</tr>
</tbody>
</table>
Audit of Congenital Hypothyroidism Newborn Screening in Sarawak General Hospital

Table 4. Performance indicators for screening programme

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Coverage at hospital level</td>
<td>&gt;99% of births in hospital</td>
<td>99.2%</td>
<td>99.1%</td>
<td>99.1%</td>
</tr>
<tr>
<td>Screening sample rejection rate</td>
<td>&lt;1%</td>
<td>0.13%</td>
<td>0.09%</td>
<td>0.12%</td>
</tr>
<tr>
<td>Percentage of recalled patients seen for re-testing</td>
<td>100%</td>
<td>94.1%</td>
<td>89.6%</td>
<td>94.8%</td>
</tr>
<tr>
<td>Duration from birth to treatment for confirmed cases &lt;14 days</td>
<td>100%</td>
<td>33.3%</td>
<td>12.5%</td>
<td>33.3%</td>
</tr>
</tbody>
</table>

QA = Quality assurance

Discussion

Congenital hypothyroidism is the most common preventable cause of mental retardation. Early treatment with thyroxine replacement ensures maximal benefit with normal growth and development of the affected child [5]. However, signs and symptoms of congenital hypothyroidism are usually not apparent at birth and by the time the typical features have developed and become obvious irreversible brain damage has occurred [6]. Therefore, the only way to detect congenital hypothyroidism early and enable timely thyroxine replacement is through routine screening for biochemical abnormalities.

The screening strategy adopted is primary TSH measurement supplemented by total T4 in borderline samples. Infants with elevated TSH levels or borderline high TSH levels and low total T4 are recalled for retesting. This approach is the least expensive option with the lowest recall rates. However, this approach runs the risk of missing out on secondary and tertiary hypothyroidism [2]. Therefore the current screening strategy which has been adopted since November 2010, uses a new cut-off level for TSH at 21 mU/L (reduced from 25 mU/L previously), with supplementary free T4. This is expected to improve the pickup rate of congenital hypothyroidism but also the recall rate of borderline cases.

The purpose of this audit was to review the effectiveness of congenital hypothyroidism screening in a busy government hospital with an average of 11500 births per year. The coverage rate of 99.1% of births and sample rejection rate of 0.11% are in keeping with the MOH performance criteria. The sample rejection rate in our centre is

© 2014 MJPCH. All Rights Reserved.
much lower than the ministry’s reported rate which is between 0.87% to 2.92% (Mean 1.47%) [7]. The low sample rejection rate in our centre may be a reflection of familiarity and excellent sampling technique by the labour room nurses and midwives who have been doing this since the introduction of the screening programme since 2003.

The recall rate for abnormal results of 0.39% in our centre is similar to the MOH reported rate which was between 0.03-0.8% [7]. However, the recall rate is expected to increase following adjustment of the TSH cut-off level and use of supplementary free T4 instead of total T4 [8]. A total of 21 cases failed to be recalled. The most common reason for failure of recall was that the mothers were no longer staying at the addresses that were used for registration during first booking for antenatal care. This could be due to a cultural reason and the practice of confinement especially among the natives who would return to their villages in the interior weeks following birth, and could therefore not be contacted [8,9,10]. The second most common cause for failure of recall was the baby died and this accounted for 7 of the cases. Causes of death include prematurity and congenital abnormalities. For the remaining 6 cases, the mothers were non-attenders of antenatal care and did not provide valid addresses and phone numbers.

A total of 14 cases of congenital hypothyroidism were detected out of 35019 live births. However out of the 14 cases, 2 of the cases were later found to be transient hypothyroxinaemia. The biochemical results for the 2 cases normalized rapidly after starting treatment and subsequently resulted in suppression of TSH with elevated total T4. The thyroxine replacement was stopped after only a few months and further follow-up revealed normalization of thyroid function. Therefore by omitting the 2 cases, the birth prevalence of congenital hypothyroidism in the region of Kuching served by Sarawak General Hospital would be 1 in 3502 live births. The birth prevalence of congenital hypothyroidism in Sarawak and Sabah is thought to be much higher than the national birth prevalence due to iodine deficiency in the interior districts [11, 12]. This was not shown in this audit possibly because the cohort of newborns was mainly from the urban areas within or surrounding the city of Kuching.

According to MOH guidelines, thyroxine replacement should commence within 2 weeks of life in confirmed cases of congenital hypothyroidism. This has been a major underperformance for our centre. Only 3 of the 14 cases detected, started treatment within 14 days of life. A review of the cases noted that reasons for the delay can be explained by turnaround time (TAT) at 3 different points – laboratory service level, clinical service level and subject level [9]. Firstly, TAT at the laboratory service level is from the time the samples were taken to the time the results were available. We do not have data of the laboratory TAT. However during the period of the audit the automated instruments broke down a number of times with the longest duration being 2 weeks. This resulted in a delay in receiving the results and subsequent delay in retesting and a further backlog of samples. Secondly, TAT at the clinical service level is the time when the samples were taken to the time the results were available. We do not have data of the laboratory TAT. However during the period of the audit the automated instruments broke down a number of times with the longest duration being 2 weeks. This resulted in a delay in receiving the results and subsequent delay in retesting and a further backlog of samples. Secondly, TAT at the clinical service level is the time when the results were available to the paediatric team. Three out of the 11 cases of the delay occurred during the festive season and therefore the results were not reviewed until after the public holidays. In addition to that, the previous practice was to have only one designated paediatrician in charge of reviewing abnormal results. Therefore, in his or her absence, there could be a delay in
reviewing the results. Thirdly, TAT at the subject level is the time it took for a recalled case to return for retesting. For a number of cases, there were difficulty contacting and getting the patient to come back for retesting. The reasons identified were indifference due to lack of awareness, mothers not contactable during the confinement period and logistics such as transport problem for those staying far in the interior.

To ensure timely treatment of confirmed cases of congenital hypothyroidism, a few measures were implemented. First, a functional backup machine is made available in the laboratory in case the main machine breaks down. Second, more than one paediatricians are assigned to review abnormal results. Third, the help of the state public health department was enlisted to trace cases not contactable by the hospital or maternal child health (MCH) clinics. For cases that were highly suggestive with TSH of more than 60 mU/L, the parents were counseled when they come back for retesting and thyroxine was prescribed with the instruction to take if the repeated result, which would be informed to them by phone, turned out to be confirmatory. This avoids another visit to the clinic before the medication can be started.

This study has several strengths. As far as we know, this is the first study conducted on congenital hypothyroidism newborn screening in Sarawak. It involves a large cohort of more than 35000 babies over a course of three years. This analysis has several limitations. It is a single centre study which involves only babies born in a public tertiary hospital in Kuching which may therefore not be representative of the overall prevalence in the state and cannot be generalized to other geographic or healthcare settings. The descriptive nature of the study presents possibility of subjectivity or bias that may affect the result analyzed.

**Conclusion**

The estimated birth prevalence of congenital hypothyroidism in Kuching, Sarawak is 1 in 3502 live births which is similar to the national quoted prevalence. This audit has shown a good uptake of the congenital hypothyroidism newborn screening with coverage of 99.1% and a low sample rejection rate of 0.11% which is within the MOH performance indicators. However the mean percentage of patients seen for retesting is 92.8% and the mean percentage of confirmed cases receiving treatment less than 14 days old is only 26.4% which fell short of the set performance indicators. There is a need to improve on the laboratory and clinical services to ensure that cord blood results are available and reviewed within the stipulated time frame especially during long festival period. Liaison with the state public health department is important to promote community awareness and trace cases that required retesting. Further audit will be needed to assess for improvement following the measures adopted.

**Acknowledgements**

The authors thank Anna Chin and the other nurses of paediatric clinic Sarawak General Hospital for their help with the data collection and census compilation. We also acknowledged the assistance and support of the laboratory staff who provided information on the laboratory services. Portion of this study have been presented in abstract and poster form at the 19th Annual Congress of Perinatal Society of Malaysia.
References


CASE REPORT

CONGENITAL DISSEMINATED HERPES SIMPLEX TYPE 2 WITH REACTIVATIONS: A CASE REPORT

Ang Ee Lee¹, Mangalam Sinniah², Irene Cheah Guat Sim³

1. Neonatal Unit, HTAR, Jalan Langat, Taman Chi Lung, 41200 Klang, Selangor, Malaysia
2. Pathology Unit, HKL, Jalan Pahang, 50586 Kuala Lumpur, Malaysia
3. Neonatal Unit, HKL, Jalan Pahang, 50586 Kuala Lumpur, Malaysia

Abstract

Congenital disseminated herpes simplex type 2 (HSV-2) infections is rare. The incidence varies from countries to countries but it is in the rise especially in the developing countries like Malaysia. Although this condition is rare in neonate but it causes high mortality and morbidity in these neonates despite of prompt treatment. According to the World Health Organization (WHO) report, it was estimated that 536 million people aged 15-49 years were living with HSV-2 worldwide in 2003 this will indirectly lead to the increase congenital herpes simplex infections incidence if not treated promptly. We would like to share an interesting and uncommon case of congenital disseminated herpes simplex type 2 infections with recurrent reactivations. Patient presented with cutaneous skin lesions at birth associated with retinal scarring and multicystic periventricular lesions and liver calcifications. Congenital herpes simplex type 2 infections though is rare but is a disease of high morbidity and mortality despite prompt treatment. Therefore awareness among health workers and pregnant mothers of this increasingly common disease are more cost effective. Early screening and treatment of these pregnant mothers will definitely improve the babies’ outcomes.

Keywords: Herpes Simplex, Congenital, Neonates, Infectious diseases

Corresponding Author: Dr Ang Ee Lee, Paediatric Department, Hospital Tengku Ampuan Rahimah, Klang, Jalan Langat, 41200 Klang, Selangor, Malaysia
Tel: +60162981743
Email: ee_lee_ang@yahoo.com

Introduction

Congenital disseminated herpes simplex type 2 infections are rare; it occurs at approximately 1 in 300,000 deliveries [1]. The incidence varies from country to country but it is in the rise especially in the developing countries like Malaysia. Though this condition is rare in neonate, the outcome has remained poor despite of availability and prompt antiviral therapy. According to the World Health Organization (WHO) report [2], it was estimated that 536 million people aged 15-49 year were living with HSV-2 worldwide in 2003; this will indirectly lead to the increased in congenital herpes simplex infections incidence if not treated promptly. The mortality of disseminated HSV-2 is as
high as 30% and 20% of those who survived develop neurological impairment [1, 3]. Cutaneous reactivation/recurrence after HSV-2 is generally high in the first 2 years of life and about 25% have at least once in the first 5 years [5, 6].

**Case Presentation**

UF is a baby boy born via vaginal delivery at 30 weeks of gestations in our institution with the birth weight of 1.2 kg. His mother an 18 year old Gravida 1 Para 0, housewife was first referred to our institution at about 29 weeks of gestations for foetal anomaly, detailed antenatal scan showed bilateral ventriculomegaly in the foetus. His mother subsequently presented at 30 weeks gestation with history of leaking liquor for more than 72 hours, in labour. Baby UF was born not vigorous via spontaneous vaginal delivery, intubated at birth and was given surfactant. He was treated for presumed sepsis with intravenous antibiotics. At birth vesicles were noted (Figure 1) over dorsal and hypothenar surface of left hand and left foot which resolved at third day of intravenous acyclovir. Baby had completed a total of 12 days of intravenous acyclovir. He was then extubated at day 2 of life.

Retrospectively mother gave a history which was suggestive of HSV infection at forth month of gestation. Mother gave history of low grade fever for 3 days associated with painful vesicular rashes over chest, abdomen and back which resolved after 1 week without scarring. These lesions was suggestive of herpes infections but was not brought to medical attention. There was no history of vaginal discharge. Screening for HIV and syphilis were negative. Father, a 35 year old Cambodian businessman had a history of penile pus discharge which was treated.

Figure 1. Vesicles over the palm and forearm

Chest X-ray (CXR) on admission was suggestive of hyaline membrane disease (Figure 2). Ultrasound brain showed multiple cystic areas in the cerebral hemisphere bilaterally and cerebellum without distinct parenchymal calcification. Corpus callosum was thinned out with enlarge ventricles from ex-vacuo effect from parenchymal volume loss (Figure 3).
Patient deteriorated at day 4 of life and desaturated which required reintubation. On auscultation crepitations and a grade 3 systolic murmur were present. There was worsening chest X-ray with pneumonic changes (Figure 4) and echocardiography showed patent ductus arteriosus.

Apart from the cutaneous, brain and lung involvement, UF also had evidence of eye and liver involvement. There were vitreous haziness and pigmented lesions in macula area. Ultrasound abdomen showed scattered calcification in segments IV, VII, V of the liver (Figure 6) with a normal spleen. The liver enzymes remained normal throughout the stay.
At day 18 of life, UF developed cutaneous reactivations. There were crops of vesicles on the left forearm, palm, axilla, foot and ear lobe (Figure 5). He had completed second course of intravenous acyclovir. Patient developed second cutaneous reactivations at day 44 of life, 5 days after completing 3 weeks of intravenous acyclovir. During second cutaneous reactivation oral acyclovir was started for 6 months to reduce further cutaneous reactivations in infancy.

Viral DNA PCR samples taken from vesicles for both episodes of reactivations were positive for herpes and negative for varicella zoster virus. Serum viral immunology (ELISA) assay for VZV IgG was positive but IgM was negative, these probably indicate maternal in origin. Serum antibody for HSV-2 IgM and IgG were confirmed to be positive. Other viral screening like toxoplasmosis, rubella, cytomegalovirus and syphilis were all negative. Lumbar puncture was only done 5 days after starting second cycle of acyclovir after obtaining parental consent. CSF PCR was negative for both VZV and HSV, probably due to commencement of acyclovir. Mother serum viral immunology for herpes and varicella infection shows positive for VZV IgG.

Though baby had progress well without further reactivations and was discharged at day 61 of life, he had shown obvious grow failure of the head especially during the first 4 weeks of life. The head circumference and also weight remain static below tenth percentile (Figure 6 & 7).
Discussion

Congenital HSV-2 infection is a very rare but severe disease of high morbidity and mortality despite prompt treatment. Infant who acquires intrauterine HSV infection may present with typical clinical triad of cutaneous, ophthalmological and neurological manifestations as illustrated by our case. The cutaneous manifestations can be in the form of active lesions, scarring, cutis aplasia, skin pigmentation (hypo & hyperpigmentation) and erythematous rash. Ophthalmological manifestations may take the form of microophthalmia, retinal dysplasia, optic atrophy and chorioretinitis whilst neurological manifestations namely microcephaly, encephalomalacia, hydranencephaly, intracranial calcifications [4, 5].

This case also demonstrates that the amount of damage caused by intrauterine HSV-2 infection to the foetus and the probability of frequent reactivation which leads to high morbidity, prolong duration and high cost needed in managing this case. The mother with HSV-2 infections infant can be asymptomatic at the time of delivery as seen in this case.

Therefore awareness among health care workers on the increasing prevalence of genital HSV infection which may lead to the increased incidence in the neonatal herpes plays a very important role in the screening and management, especially on the treatment decisions for early antiviral initiation and also appropriate timing for discontinuation. High index of suspicion and prompt treatment still remain the most important role, as early screening and treatment of these pregnant mothers not only improve the babies outcomes but also cost effective.

Not all HSV infections are easily diagnosed at birth as in our case, which makes early antiviral initiations impossible. There are also those milder cases of congenital HSV-2 infections which maybe under diagnosed and left untreated. Therefore health care workers need to be aware of the probability of HSV infections in the pregnant mothers.
to initiate early treatment, even though there is lack of skin lesions.

Conclusion

In conclusion, attention should be focused on prevention of maternal-foetal transmission as well as on early management of infected pregnant mother, as these will not only be more cost effective but also improve infant outcome. Further studies are needed to monitor HSV-2 trends and effective strategies to prevent HSV infection in our country.

Acknowledgement

The author would like to thank the director of Health Malaysia for permission to published this paper

Abbreviations

CSF (Cerebrospinal Fluid)  
CXR (Chest X-ray)  
HIV (Human Immunodeficiency Virus)  
HSV-2 (Herpes Simplex Type – 2)  
IgG (Immunoglobulin G)  
NICU (Neonatal Intensive Care Unit)  
VZV (Varicella Zoster Virus)

References


CASE REPORT

PEUTZ-JEGHERS SYNDROME ANAEMIA AS ONLY PRESENTATION

Pancham Kumar, Ashok Garg, Ambika Sood

Department of Paediatrics Indira Gandhi Medical College, Shimla, Himachal Pradesh, 171001, India

Abstract

Peutz-Jeghers syndrome (PJS) is a rare autosomal dominant genetic disease manifesting as mucocutaneous pigmentation and multiple polyps in gastrointestinal tract. We report this case of PJS as it is a rare entity with our patient having a unique presentation of severe anaemia only without any gastrointestinal complaints.

Keywords: Peutz-Jeghers Syndrome, Anaemia, Intestinal Polyposis

Corresponding Author: Dr. Pancham Kumar, Department of Paediatrics, Indira Gandhi Medical College, Shimla, Himachal Pradesh, 171001, India
Tel: +91-9418452827
Email: panchamdr@gmail.com

Introduction

Peutz-Jeghers syndrome (PJS) is a rare inherited disease that is characterized by gastrointestinal polyps in association with pigmentation affecting skin and mucous membranes. PJS has autosomal dominant inheritance. Patients with PJS have an increased risk of developing cancers compared with the general population in addition to the various problems which pertain to the intestinal polyposis.

Case Presentation

A twelve-year-old female presented with progressive shortness of breath, paleness of the body and easy fatigability for last three months and swelling of the feet developing over last one week. Her dietary intake was adequate. On examination she was well preserved with normal vitals. She had severe pallor, pedal oedema extending up to the legs and hyper pigmented macules over the face and lips (Figure 1).
There was no lymphadenopathy, icterus, clubbing, cyanosis or superficial and deep bleeds with a normal jugular venous pressure. Cardiovascular system examination had a short systolic murmur with normal heart sounds. On investigations her haemoglobin was 4.1gm/dL. Peripheral blood film showed a microcytic, hypochromic picture with corrected reticulocyte count of 1.1% and no abnormal/immature cells or parasites. Red cell distribution width was 15.8%. The total leukocyte, differential leukocyte, platelet counts and erythrocyte sedimentation rate were within normal limits. Antinuclear antibodies and direct Coombs’ test were negative. Her renal and hepatic function tests, ultrasonographic, doppler and echocardiography studies were normal. Serum iron studies were reported as iron 23ug/dL, transferrin saturation 5%, total iron binding capacity 433ug/dL suggesting iron deficiency. Stool examination was negative for parasites but positive for occult blood. Endoscopy and colonoscopy were done in view of occult blood in stools which showed three polyps in antral region, scalloped folds in the second part of duodenum and a large simple polyp at the hepatic flexure (Figure 2).
Histopathological examination of the polyps showed polypoidal structure lined by normal colonic mucosa with variably sized gland with smooth muscle bundles having racemose appearance (Figure 3).
Few glands were cystically dilated having intraluminal eosinophilic secretions. Final diagnosis of severe anaemia due to gastrointestinal blood loss as a consequence of intestinal polyps part of Peutz-Jeghers syndrome was kept. Polypectomy was done and patient was discharged on iron. On follow-up after 3 months her haematocrit increased towards age appropriate levels with serum iron studies being reported as normal. Repeat stool testing showed no gross or occult blood. She is doing well with a normal haematocrit and no blood in stools for last six months. Family screening could not be performed due to the financial constraints of the family.

**Discussion**

Peutz-Jeghers syndrome named after Augustine’s Peutz and Harold Joseph Jeghers is also known as hereditary intestinal polyposis syndrome. It is an autosomal dominant genetic disease manifesting as benign hamartomatous polyps in the gastrointestinal tract and melanotic macules on the skin, especially on the lips and oral mucosa [1]. Its incidence is approximately 1 in 25,000 to 300,000 births [2].
The main criteria for clinical diagnosis of PJS are:

1. Family history of Peutz-Jeghers syndrome.

2. Mucocutaneous manifestations include appearance of melanocytic macules (pigmented spots). They are tan, dark brown or bluish black flat patches of 1 to 5 mm in size present in 95% of the patients. These lesions usually appear before 5 years of age. They may fade after puberty and are seen over the mouth, lips, gums, inner lining of the mouth, eyes, hands and feet, fingers and toes, anus and genital areas. Localization in the oral mucosa is typical of patients with PJS and does not happen with other types of dermatologic pigmented lesions.

3. Gastrointestinal manifestations which include benign hamartomatous polyps found in the gastrointestinal tract having a 15-fold increased risk of developing intestinal cancer compared with the general population. They manifest as anaemia, rectal bleeding, abdominal pain, obstruction, and/or intussusception. A rectal polyp may be found during a rectal examination or may prolapse.

Clinical diagnosis is established when 2 out of the above 3 features are present and 90-100% of these patients have a mutation in the tumour suppressor gene STK11/LKB1 located on chromosome 19 for which molecular genetic testing is available [3]. A cumulative risk for all cancers by age 30 years is 5% and rises up to 85% by the age of 70 years [4].

In investigative workup, complete blood cell (CBC) count, iron studies and faecal occult blood are directed to detect any faecal blood loss and its consequences. Various imaging studies and endoscopic studies have a role in diagnosis and treatment. Multiple polyps and a large mass at hepatic flexure on contrast barium and endoscopic studies are seen in PJS. Histological examination of polyps shows extensive smooth muscle arborization throughout the polyp giving the appearance of pseudoinvasion, because some of the epithelial cells are surrounded by the smooth muscle. Various tumour markers like cancer antigen (CA)-19-9 and CA-125 testing is indicated every year starting at age 18 years, and CA 19-9 is indicated every 1-2 years starting at age 25 years [5].

### Treatment

Management includes resection of symptomatic and large polyps and surveillance for cancers. Resection of the polyps is required only if serious bleeding or intussusceptions occurs. Various modalities for resection are enterotomy for removing large and single nodules, resection of short lengths of heavily involved intestinal segments and snaring the polyps during colonoscopy if they are within reach.

Pharmacological agents like cyclooxygenase (COX) inhibitors, mammalian target of rapamycin (mTOR inhibitors; sirolimus) and RAD001 (everolimus) has been under trial for PJS.

Surveillance guidelines for early detection of cancer are [6]:

- Small bowel radiography, esophagogastroduodenoscopy and colonoscopy every 2 years
- Computed tomography or magnetic resonance imaging of the pancreas, ultrasound of the pelvis (women) and testes (men) yearly
- Mammography (women) from age 25 and papanicolaou (Pap) test every year
Conclusion

PJS should be suspected in any patient with mucocutaneous pigmentation and gastrointestinal features. It can rarely present as anaemia without any gastrointestinal symptoms as in our patient. It needs more attention because of the complications related to polyps and its association with the cancers.

Acknowledgement

The author would like to thank Department of Paediatrics IGMC Shimla India for all the help, the patient and family members for their cooperation.

References


