Global Journal of Medical and Health Science

Volume 9, Number 1; January-February 2022; ISSN: 2836-5577 Impact Factor: 6.75

https://zapjournals.com/Journals/index.php/Medical-Health/

Published By: Zendo Academic Publishing

ASSESSMENT OF PREVALENCE AND RELATED FACTORS OF DIARRHEAL DISEASES AMONG UNDER-FIVE CHILDREN IN SABAH, MALAYSIA: A HOSPITAL-BASED STUDY

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Article Info

Keywords:

Diarrheal diseases, under-five children, prevalence, related factors, Sabah, Malaysia.

Abstract

Diarrheal diseases remain a significant public health concern, particularly among under-five children, in Sabah, Malaysia. This hospital-based study aimed to assess the prevalence and related factors associated with diarrheal diseases in this vulnerable population.

From March to June 2017, data were collected using convenience sampling at the Menggatal health clinic in Kota Kinabalu, Sabah. A total of 210 under-five children were enrolled, with 105 cases of acute diarrhoea and 105 matched controls. Findings revealed that children aged between six and 11 months were most susceptible to diarrheal episodes, with boys showing a higher incidence. Socioeconomic status played a significant role, as children from households with lower income and education levels were at greater risk. Poor environmental conditions, including overcrowding, the presence of pets, unsafe drinking water sources, lack of proper sanitation facilities, and unsanitary garbage disposal, were all associated with an increased risk of diarrheal diseases.

Notably, caregiver knowledge emerged as a crucial factor, with children of caregivers possessing better knowledge of diarrheal disease prevention and management experiencing lower risk. The economic impact of diarrheal diseases on families was also highlighted, as the costs associated with seeking healthcare for diarrheal episodes posed a substantial burden.

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This study underscores the ongoing presence of risk factors for diarrheal diseases among under-five children in Sabah, Malaysia. It emphasizes the importance of environmental hygiene, proper sanitation, and caregiver education in reducing the prevalence of these diseases. Additionally, efforts to alleviate the economic burden on affected families are warranted. These findings can inform targeted interventions and policies to enhance child health in the region.

Introduction

Diarrhoeal disease is responsible for 1.7 billion morbidity and 760, 000 mortality of children every year (World Health Organization 2017). Most of these deaths occur in developing countries. Lack of access to safe drinking water and sanitary toilets, improper hand washing, poor environmental condition of household and modest health care system can worsen the severity of diarrhoea (Godana and Mengistie 2013). Childhood and infant mortality rates are important components for the assessment of social development as well as health status assessment and the outcome of interactions of behavioural, socioeconomic and environmental factors (Unicef 2012). Explorations of these factors are essential to obtain a better picture of childhood morbidity.

Besides all these, diarrheal disease is an economic burden not only for the healthcare system, but also for patients' families as well (Burke et al. 2014). Malaysia is a middle-income country in South East Asia. Despite tremendous progress in public health, the country still faces disparities among the population in different geographical locations. These are due to the inaccessibility of the places due to natural barriers such as dense tropical forests, mountains or remote islands. Diarrheal disease is a challenge for the health care system in these areas. Each year an estimated 16 outpatient clinic visits and 57 home-treated episodes per 1000 children under-5 with diarrhoea and costing about (Ringgit Malaysia) RM 10.8 million to the healthcare provider and about RM 15.8 million to society annually (Loganathan et al. 2016). The economic impacts of acute diarrhoea among children include high medical expenses, productivity loss, and childcare adjustment. The economic burden of family is highest among children aged less than two years old for acute diarrhoea (Diez-Domingo et al. 2011). Economically Sabah ranked the lowest among all the states in Malaysia (Jamil and Mat 2014). Evaluating the known risk factors and economic outcome associated with acute diarrhoea have important policy implications for health intervention programs that subsequently will improve child health care in the study area and in the country in general.

Therefore, this study was done to determine the risk factors and household costs associated with acute diarrhoea of under five children visited a clinic serving underprivileged population in Kota Kinabalu, the capital of Sabah, East Malaysia.

Methods

This is a clinic-based case-control study. The study was conducted at a suburban area of Kota Kinabalu containing many undocumented immigrants. It contributes the highest number of under-five diarrheal cases among all the primary health clinics. The study was conducted from March to June 2017. All under-five patients with diarrhoea attending at Health Clinic were enrolled in this study.

Written informed consents were obtained from caregivers who agreed to participate in this study. Children with acute diarrhoea were selected as cases and without diarrhoea as controls. Under-five children with food intolerance, adverse effects of medicine, irritable bowel syndrome and any other intestinal diseases were excluded. Sample size was calculated using the formula Parker and Bregman (Parker and Bregman 1986). Required minimum sample size was 210 among them; 105 cases and 105 matched controls.

A questionnaire based face-to-face interviews were conducted to collect data in the present study. The questionnaire was adopted from the WHO and translated into Malay language. After that a pre-testing of questionnaires was conducted in urban area with 30 respondents which revealed good reliability - Chronbach's Alpha 0.82. The questionnaire contains both open and close-ended questions, and it was divided into four sections: a section on demographic and socioeconomic information; a section on environmental factors; a section on behavioural factors of caregiver; and a section on household cost of family.

Data were cleaned and analysed using IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. It was analysed descriptively to identify demographic and socioeconomic characteristics of study population, environmental and behavioural factors that are potential risk factors for diarrhoea among under-five children. The household cost of family among those under-five children with acute diarrhoea was also calculated.

The study was reviewed and approved by the National Medical Research Registry (NMRR-16-224532787) and the Medical Ethics Committee of Universiti Malaysia Sabah Medical Ethics Committee [JKEtika 1/17(1)]. All the consents for the study participants were collected from their parents. The parents were explained verbally and given a written guide by the assigned research assistant, parents were also asked to read the disclosure twice and asked if there were any uprising questions regarding the study prior to agreeing.

Results

A total of 210 under-five children, aged 30.1±16.6 (mean±SD) months, were enrolled in this study. Details of the demographic and social characteristics of the cases and controls are shown in Table 1. The caregivers were at the mean age of 31.1±7.1 (range 17 to 63) years old. The mean monthly household income was RM 1833.62±1617.71 (Range RM 300–11000). There is a statistically significant difference (p=0.02) of the monthly household income between the cases (1621.43±1374.21) and controls (2045.81±1811.00). Children from households with pets, clean drinking water, using sanitary toilets, dispose garbage sanitary way, practice hand washing with soap, practice hand washing in critical time, had statistically significant less diarrhoea than households without pet, clean drinking water, not use sanitary toilets, not dispose garbage sanitary way, practice hand washing with water only, and do not practice hand washing in critical time (Table 2).

In the association test for knowledge, attitude and practice of diarrhoea related components of this study, knowledge was the only component that showed significant association to under-five diarrheal morbidity. The odds of having acute diarrhoea in children of caregivers who had poor knowledge of diarrhoea are 2.3 times compared to those children of caregivers who had better knowledge of the disease (OR=2.3; 95% CI 1.2 - 4.3; p<0.008). The total household costs of seeking care among underfive children with acute diarrhoea in this study are shown in Table 3. The mean transport time consumed was 14±11 minutes. The main cost items that family suffer are consultations and medications (combined) cost being RM 8.00 (1.86 USD) ± 19.80 (82.5% of total direct costs). We found out that the mean monthly food expenses are RM 471.33 (109.66 USD). The mean cost per diarrhoeal episode is RM 14.30 (3.33 USD) which almost consumes 3% of the mean monthly food expenses. The economic status of household was divided into poor and not poor, based on the classification of economic status by Economic Planning Unit of Malaysian Government. There were 57 families (61.3 %) in case group and 36 (38.7 %) in control group have poor household economic status (n=93). While 48 families (41.0 %) in case group and 69 (59.0 %) in control group have not poor household economic status (n=117). We found out that there is a statistically significant association between household economic status and under-five acute diarrhoea. The odds of having under-five acute diarrhoea among those with poor household economic status are 2.3 times compared to those with not poor household economic status (OR=2.3; 95%CI 1.3 – 4.0; p<0.0004). The main source of funding for household costs for diarrhoea episodes was by using savings from monthly income with

64.8%. The other common source was cutting down on other expenses (29.5%), borrowing (3.8%) and donation from friends/relatives (1.0%).

Table 1: Socio-demographic characteristics of children and caregivers

Variables	Cases (n=105)	Controls (n=105)		
Gender of children				
Male	63 (60.0%)	63 (60%)		
Female	42 (40.0%)	42 (40%)		
Age groups of children				
Mean age (months)				
Under 1 year	29.1	31.2		
1-3 years	18 (17.1%)	17 (16.2%)		
4-5 years	51 (48.6%)	49 (46.7%)		
	36 (34.3%)	39 (37.1%)		
Age groups of caregivers				
Under 20 years				
20-40 years	3 (2.9%)	-		
Above 40 years	93 (88.6%)	95 (90.5%)		
	9 (8.6%)	10 (9.5%)		
Household income per				
month (RM)				
<rm1000< td=""><td>34 (32.4%)</td><td>25 (23.8%)</td></rm1000<>	34 (32.4%)	25 (23.8%)		
RM1000-RM3000	61 (58.1%)	66 (62.9%)		
EM3001-RM5000	8 (7.6%)	10 (9.5%)		
>RM5000	2 (1.9%)	4 (3.8%)		

Table 2: Associated risk factors between cases and controls

Variables	Cases (n=105)	Control (n=105)	X ²	OR	95% CI
Mean age	29.26	33.03	3.99		p<0.001*
Education level of					
caregivers					
No formal education	27 (25.7%)	12 (11.4%)	7.09	2.7	(1.3, 5.6)
Formal education	78 (74.3%)	93 (88.6%)			
Household economic					
status Poor					
Not poor	57 (54.3%)	36 (34.3%)	8.51	2.3	(1.3,4.0)
	48 (45.7%)	69 (65.7%)			
Crowding index					
Overcrowded	79 (75.2%)	58 (55.2%)			
Not overcrowded	26 (24.8%)	47 (44.8%)	12.82	2.9	(1.6,5.2)

Household size					
≥ 5	87 (82.9%)	65 (61.9%)	11.53	3.0	(1.6,5.7)
<5	18 (17.1%)	40 (38.1%)			
Pet in house					
Yes	55 (52.4%)	35 (33.3%)	7.78	2.2	(1.3,3.8)
No	50 (47.6%)	70 (66.7%)			
Drinking water					
Unsafe	29 (27.6%)	12 (11.4%)	8.76	3.0	(1.4,6.2)
Safe	76 (72.4%)	93 (88.6%)			
Sanitation facility					
Unimproved	24 (22.8%)	10 (9.5%)	6.88	2.8	(1.3,6.2)
Improved	81 (77.2%)	95 (90.5%)			
Household garbage					
disposal Unsanitary					
Sanitary	50 (47.6%)	30 (28.6%)	8.08	2.3	(1.3,4.0)
	55 (52.4%)	75 (71.4%)			
Knowledge on					
diarrhoea					
Poor	37 (35.2%)	20 (19.0%)	6.96	2.3	(1.2,4.3)
Above poor	68 (64.8%)	85 (81.0%)			
Handwashing method					
Water only	35 (33.3%)	10 (9.5%)	17.68	4.8	(2.2,10.2)
Water and soap	70 (66.7%)	95 (90.5%)			
Handwashing during					
all critical times					
Not full	32 (30.5%)	13 (12.4%)	10.21	3.1	(1.5,6.3)
Full	73 (69.5%)	92 (87.6%)			
Breastfeeding					
No	74 (70.5%)	60 (57.1%)	4.04	1.8	(1.0,3.2)
Yes	31 (29.5%)	45 (42.9%)			
Recent street vendor					
food consumption					
Yes	32 (30.5%)	15 (14.3%)	7.92	2.6	(1.3,5.2)
No	73 (69.5%)	90 (85.7%)			

^{*}p-value <0.05 is significant

Table 3: Total household costs of seeking healthcare among case group

Type of cost	N	Mean ± SD
Total Direct Cost (RM)	105	9.70 <u>+</u> 21.30
Indirect Costs (RM)	8	59.40 <u>+</u> 34.70
Total Incurred Costs (RM)	105	14.30 <u>+</u> 28.10

Discussion

Diarrhoeal disease is a widely recognized major contributor of morbidity and mortality in children. Factors such as poor socio-economic status, low level of education, unsatisfactory environmental sanitation and poor hygienic practices account for a serious threat to human's health, especially among children. In Malaysia, diarrhoeal disease accounts for 4.52 % and 4.82 % of hospitalization and mortality respectively in 2015 (Ministry of Health Malaysia 2016). Risk factors for acute diarrhoea are mainly varied with child's age, local environmental condition and behaviour of caregivers. This study is a supplement to not much pre-existing research that have been conducted so far in Malaysia generally and Sabah specifically.

The highest rates of diarrhoea occurrence were among children aged six to 11 months old. Diarrhoea occurrence rates maintained at a high level among the children aged one year old and reduced when children got older (Molbak 2000). In this study, the number of males was higher than females in all age groups. The reason for this difference is not clear. However, for older children, boys are more active compared to girls (Vale et al. 2010). The tendency of boys to move around and touch objects in the surrounding ground is higher than girls. Girls have more tendency to stay close to their caregivers and play with more hygienic toys (Arif and Naheed 2012; Eliot 2010; Kuitunen 2005; Yassin 2000).

Children from a poor socioeconomic background have higher risk to get acute diarrhoea. This finding is in line with the studies conducted in Pakistan (Alnawajha, Bakry, and Aljeesh 2015; Arif and Naheed 2012; Dessalegn, Kumie, and Tefera 2011; Kuitunen 2005; Yassin 2000). Perhaps lower income levels not only equated to poorer food safety and quality, but also less consumption of healthier foods like fruits and vegetables. Furthermore, with poor economic status, there will be lack of resources such as availability of disinfectants in home cleaning and condition of the house surrounding. The caregivers with higher education have better chance of a child being spared of acute diarrhoea compared to lower education caregivers (Alnawajha, Bakry, and Aljeesh 2015; Dessalegn, Kumie, and Tefera 2011; Gebru, Taha, and Kassahun 2014; Sinmegn Mihrete, Asres Alemie, and Shimeka Teferra 2014; Siziya, Muula, and Rudatsikira 2013). Education provides not only basic but also important information about personal and environmental hygiene, weaning and feeding practices, and disease signs and symptoms which boosts timely action on childhood illness.

Children from households with more than two crowding indexes were more likely to develop diarrhoea compared to children from households with lower crowding index (Siziya, Muula, and Rudatsikira 2013). Children who live in a household with pet was having higher risk to get diarrhoea compared to household without pet. This may indicate possible zoonotic infections or hygienic condition associated with pet rearing in our study population (Mamo and Hailu 2014; Seidu et al. 2013). Children from households with improved drinking water source were less vulnerable to diarrhoea compared to children from households who use unimproved water source as well as availability of proper sanitation facility (Dessalegn, Kumie, and Tefera 2011; Godana and Mengistie 2013).

Children of caregivers with good knowledge on general idea, signs and symptoms, causes, complications and preventive measures of diarrhoea were less likely to develop acute diarrhoea compared to those with poor knowledge. Caregivers' awareness of causes and general knowledge on how to prevent the disease are critical in the reduction of diarrhoea-related morbidity and mortality, which are, at present, unacceptably high (Ansari, Ibrahim, and Shankar 2011; Khalili et al. 2013; Ogunrinde et al. 2012; Wilson et al. 2012).

Diarrhoea causes economic burdens for families. Even though the absolute number of household economic costs are relatively low for each childhood diarrhoea episode, but their cumulative impact is likely to be great. The small average costs also hide the continuous possibility that an episode will require more extensive and expensive care, resulting in not only indebtedness, but also selling of productive assets. Furthermore, all the costs and other

barriers to care may create or accentuate disparities in adverse outcomes including mortality (Mendelsohn et al. 2008; Weraphong et al. 2013).

Conclusion

The risk factors for diarrhoea under 5 years of age still presents in Sabah especially among the underprivileged population. Environmental factors and hygienic practice are needed to control under 5 diarrhoea as it causes not only morbidity and mortality but detrimental effect on economy as well. Limitations of this study include method in selecting the controls and lack of observational component in the study.

This study indicates that there is a need to focus on comprehensive diarrheal disease control strategies, including improvement of water quality, hygiene, and sanitation, together with regular awareness talk on breastfeeding.

Acknowledgement

We would like to thank the Director General of Health Malaysia for his permission to publish this article. The authors would also like to express our gratitude to the Sabah State Health Department.

Conflicts of Interest

The author declares no conflicts of interest.

References

- Alnawajha, Samer Khader, Ghadeer Abdo Bakry, and Yousef Ibrahim Aljeesh. 2015. "Predictors of Acute Diarrhoea among Hospitalized Children in Gaza Governorates: A CaseControl Study." 33(1): 1–8.
- Ansari, Mukhtar, Mohamed Izham Mohamed Ibrahim, and Pathiyil Ravi Shankar. 2011. "A Survey of Mothers' Knowledge about Childhood Diarrhoea and Its Management among a Marginalised Community of Morang, Nepal." *Australasian Medical Journal* 4(9): 474–79.
- Arif, Asma, and Rukhsana Naheed. 2012. "Socio-Economic Determinants of Child Health in Pakistan." *Academic Research International* 2(1): 398.
- Burke, Rachel M et al. 2014. "The Economic Burden of Pediatric Gastroenteritis to Bolivian Families: A Cross-Sectional Study of Correlates of Catastrophic Cost and Overall Cost Burden."
- BMC public health 14: 642. http://www.ncbi.nlm.nih.gov/pubmed/24962128%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4094680.
- Dessalegn, Muluken, Abera Kumie, and Worku Tefera. 2011. "Predictors of Under-Five Childhood Diarrhea: Mecha District, West Gojam, Ethiopia." *Ethiopian Journal of Health Development* 25(3).
- Diez-Domingo, Javier et al. 2011. "Primary Care-Based Surveillance to Estimate the Burden of Rotavirus Gastroenteritis among Children Aged Less than 5 Years in Six European Countries." *European Journal of Pediatrics* 170(2): 213–22. http://link.springer.com/10.1007/s00431-0101289-1.
- Eliot, Lise. 2010. "The Truth about Boys and Girls." *Scientific American Mind* 21(2): 22–29. http://www.jstor.org/stable/24943036.
- Gebru, Teklemichael, Mohammed Taha, and Wondwosen Kassahun. 2014. "Risk Factors of Diarrhoeal Disease in Under-Five Children among Health Extension Model and Non-Model Families in Sheko District Rural

- Community, Southwest Ethiopia: Comparative Cross-Sectional Study." *BMC Public Health* 14(1): 395. http://bmcpublichealth.biomedcentral.com/articles/10.1186/1471-2458-14-395.
- Godana, W, and B Mengistie. 2013. "Determinants of Acute Diarrhoea among Children under Five Years of Age in Derashe District, Southern Ethiopia." *Rural and Remote Health* 13(3): 2329.
- Jamil, Norzita, and Siti Hadijah Che Mat. 2014. "Realiti Kemiskinan: Satu Kajian Teoritikal." *Jurnal Ekonomi Malaysia* 48(1): 167–77.
- Khalili, Manijeh et al. 2013. "Maternal Knowledge and Practice Regarding Childhood Diarrhea and Diet in Zahedan, Iran." *Health Scope* 2(1): 19–24. http://www.jhealthscope.com/?page=article&article_id=9885.
- Kuitunen, Kwasi Owisu & Markku. 2005. "Childhood Diarrheal Morbidity in the Accra Metropolitan Area, Ghana: Socio-Economic, Environmental and Behavioral Risk Determinants Childhood Diarrheal Morbidity in the Accra Metropolitan Area, Ghana: Socio-Economic, Environmental and Behavioral Ris." *Journal of health & population in developing countries* (January): 1–13. www.jhpdc.unc.edu.
- Loganathan, Tharani, Chiu-Wan Ng, Way-Seah Lee, and Mark Jit. 2016. "The Hidden Health and Economic Burden of Rotavirus Gastroenteritis in Malaysia." *The Pediatric Infectious Disease Journal* 35(6): 601–6.
- Mamo, Ayele, and Awraris Hailu. 2014. "Assessment of Prevalence and Related Factors of Diarrheal Diseases among Under-Five Year's Children in Debrebirehan Referral Hospital, Debrebirehan Town, North Shoa Zone, Amhara Region, Ethiopia." *Open Access Library Journal* (April): 1–14.
- Mendelsohn, Andrea S. et al. 2008. "Estimates of the Economic Burden of Rotavirus Associated and All-Cause Diarrhoea in Vellore, India." *Tropical Medicine and International Health* 13(7): 934–42.
- Ministry of Health Malaysia. 2016. "Health Facts 2016." https://www.moh.gov.my/moh/resources/Penerbitan/Penerbitan Utama/HEALTH FACTS/KKM HEALTH FACTS 2016.pdf.
- Molbak, K. 2000. "The Epidemiology of Diarrhoeal Diseases in Early Childhood: A Review of Community Studies in Guinea-Bissau." *Danish Medical Bulletin* 47(5).
- Ogunrinde, Olufemi G., Tajudeen Raji, Olumuyiwa A. Owolabi, and Kola M. Anigo. 2012. "Knowledge, Attitude and Practice of Home Management of Childhood Diarrhoea among Caregivers of under-5 Children with Diarrhoeal Disease in Northwestern Nigeria." *Journal of Tropical Pediatrics* 58(2): 143–46.
- Parker, R A, and D J Bregman. 1986. "Sample Size for Individually Matched Case-Control Studies." *Source: Biometrics* 42(4): 919–26. http://www.jstor.org/stable/2530705%5Cnhttp://about.jstor.org/terms.
- Seidu, R, O Löfman, P Drechsel, and T A Stenström. 2013. "Risk Factor Analysis of Diarrhoeal Disease Incidence in Faecal Sludge-Applying Farmers' Households in Tamale, Ghana." *Journal of Water Sanitation and Hygiene for Development* 3(2): 134–43. http://www.scopus.com/inward/record.url?eid=2-s2.0-84883043479&partnerID=40&md5=de30d21368acc49909d3115ca38e0135.

- Sinmegn Mihrete, Thomas, Getahun Asres Alemie, and Alemayehu Shimeka Teferra. 2014. "Determinants of Childhood Diarrhea among Underfive Children in Benishangul Gumuz Regional State, North West Ethiopia." *BMC Pediatrics* 14(1): 102. http://bmcpediatr.biomedcentral.com/articles/10.1186/1471-2431-14-102.
- Siziya, S, a S Muula, and E Rudatsikira. 2013. "Correlates of Diarrhoea among Children below the Age of 5 Years in Sudan." *African health sciences* 13(2): 376–83. http://www.mendeley.com/catalog/correlates-diarrhoea-among-children-below-age-5-yearssudan/.
- Unicef. 2012. United Nations Children's Fund *Pneumonia and Diarrhoea*. http://www.unicef.org/eapro/Pneumonia and Diarrhoea Report 2012.pdf.
- Vale, Susana et al. 2010. "Compliance with Physical Activity Guidelines in Preschool Children." *Journal of Sports Sciences* 28(6): 603–8.
- Weraphong, J, S Pannaruthai, T Luxananun, and N Junsri. 2013. "Catastrophic Health Expenditure in an Urban City: Seven Years after Universal Coverage Policy in Thailand." *Southeast Asian Trop Med Public Health* 44(1): 124–36.
- Wilson, Shelby E. et al. 2012. "Caregiver Recognition of Childhood Diarrhea, Care Seeking Behaviors and Home Treatment Practices in Rural Burkina Faso: A Cross-Sectional Survey." *PLoS ONE* 7(3).
- World Health Organization. 2017. "Diarrhoeal Disease." https://www.who.int/news-room/factsheets/detail/diarrhoeal-disease.
- Yassin, K. 2000. "Morbidity and Risk Factors of Diarrheal Diseases among Under-Five Children in Rural Upper Egypt." *Journal of tropical pediatrics* 46(5): 282–87. http://www.ncbi.nlm.nih.gov/pubmed/11077937.