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Malaria and Urinary Tract Infections among Children Under five Years with Malnutrition at a District Hospital in Ghana

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ABSTRACT

Background: Malnutrition is a major cause of morbidity and mortality in children under five years. This study aimed to evaluate malaria and urinary tract infections among children under five years of age with malnutrition.

Materials & Methods: This cross-sectional study was carried out on 189 children under five years with malnutrition. Their weight and height were measured using standard scales. Weight to height/length (wasting), weight to age (underweight), and height/length to age (stunting) ratios were computed using WHO growth charts. Clinical features were assessed. Blood smear, rapid diagnostic test for malaria, as well as urine dipstick test were done to detect those with malaria and urinary tract infections.

Findings: About 80.95% of participants had marasmus, and 11.64% had marasmic kwashiorkor, while 7.41% had kwashiorkor. Also, 23.70 and 62.42% of participants had moderate and severe malnutrition, respectively; in addition, 21.69 and 2.12% were moderately and severely stunted, respectively. Regarding underweight (weight to age), 50.26 and 4.76% were moderately and severely underweight, respectively. Also, 15.87% of participants had a positive blood smear for malaria, and 19.58% had a positive rapid diagnostic test for malaria, while 20.11 and 20.63% had positive results for nitrite and leukocyte esterase activity in urine dipstick test, respectively.

Conclusion: Malaria and urinary tract infections are common among children with malnutrition and could be diagnosed using simple laboratory tests such as rapid diagnostic tests and urine dipstick tests in health facilities without laboratory support in resource-limited countries.

Keywords: Children, Malaria, Malnutrition, Urinary tract infection.

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Introduction

Malnutrition is defined as the mismatch between nutrients intake and energy expended and the demand for more nutrients to ensure growth and perform other physiological functions [1]. The World Food Program (WFP) also defines malnutrition as a state in which individuals' physical function is impaired to the point that they could no longer maintain bodily processes and functions required, such as growth, pregnancy, lactation, physical work, resistance to diseases, and recovery [2].

Malnutrition makes an individual more prone to infections, which in turn contribute to malnutrition, resulting in a vicious cycle. Poor dietary intake leads to weight loss, low immunity, mucosal damage, invasion by pathogens, and impaired growth and development in children [3]. The development of the infant's immune system during the first 1000 days of life is so sensitive that any imbalance in nutrition or prolonged inadequate nutrition leads to immunodeficiency that makes the infant more susceptible to infections [4]. Malnutrition is caused by disordered nutrient assimilation and characterized by recurrent infections and chronic inflammation, implying an underlying immune defect. It is considered as the most important risk factor for illness and death among malnourished children. Both the innate and adaptive arms of the immune system have been consistently demonstrated to be impaired in children with malnutrition [3, 5].

Malnutrition in children is complicated by infections such as malaria, diarrhoea, pneumonia, and urinary tract and respiratory infections [6, 7]. Malaria infection is common among children treated for uncomplicated severe acute malnutrition and may lead to stunting [8]. Shikur et al. (2016) [9] showed that children who were severely wasted had higher odds of malarial infection. Fevang et al. (2018) [10] also found that children with marasmus were more infected with malaria, while those with kwashiorkor were found to have significantly lower levels of *Plasmodium falciparum* parasitaemia. However, the prevalence of malaria in children under five years without malnutrition has decreased consistently from 27% in 2014 to 21 and 14% in 2016 and 2019, respectively [11].

Children with severe acute malnutrition are more prone to urinary tract infection than well-nourished children due to decreased immunity. According to Rosli et al. (2008), [12] children with malnutrition are 2.6 times more likely to develop urinary tract infections compared to well-nourished children. Uwaezuoke (2016) [7] in a review article demonstrated that there is overwhelming evidence suggesting that children with malnutrition are highly susceptible to urinary tract infections. Furthermore, Uwaezuoke et al. (2019) [13] in another review and meta-analysis on data from 34 studies involving 3,294 malnourished children, found a pooled prevalence of 17% and a pooled odd ratio of 2.34 for urinary tract infections in 2,051 children with malnutrition (1,052 malnourished children versus 999 controls).

Objevtives: This study was carried out to evaluate urinary tract infections and malaria among children with malnutrition at the Maternal and Child Health Hospital in Kumasi, Ghana.

Materials and Methods

Study Design: This prospective cross-sectional study was conducted in outpatient and inpatient clinics at the Maternal and Child Health Hospital (MCHH) in Kumasi, Ghana.

This study was performed on 200 children in the age range of 0 to 59 months with suspected malnutrition, referring to the hospital during the study period. During the assessment, three children were not

malnourished, and eight caregivers did not give informed consent; thus, 11 children were excluded from the study. The remaining 189 caregivers gave informed consent, and their children were recruited into the study. The study was conducted in the outpatient department (OPD) of the Nutritional Rehabilitation Center and the malnutrition ward at the Maternal and Child Health Hospital (MCHH) in Kumasi, Ghana.

MCHH is a district hospital with a capacity of 65 beds. The children ward has 33 beds. MCHH is a recognized center for the management and rehabilitation of children with malnutrition.

Criteria for diagnosing malnutrition were **s**evere wasting (weight-to-height ratio <70% or <-3 SD) and/or edema of both feet [13].

Study Procedure: The study was conducted during January 2, 2019 to April 30, 2019. Children with malnutrition in the age range of 0 to 59 months, who presented to MCHH were recruited. Recruitment was done in the ward and in the outpatient department (OPD) of the Nutritional Rehabilitation Center.

The types of malnutrition among participants were determined using weight to height/length (wasting), height to age (stunting), and weight to age (underweight) ratios and edema of both feet. These features were used to determine the types of malnutrition such as kwasiokor, marasmus, and marasmic/kwashiorkor.

Procedure for Measurement of Length: The length of participants less than two years of age was measured using an infantometer (seca 416). The infantometer was placed on a flat surface, and the participant was placed in a supine position. The head of the participant was positioned firmly against the cephalic end of the infantometer, and the knees were extended. The feet were fixed at right angles to the caudal end, and the length was recorded based on the nearest 0.1 cm.

Procedure for Measurement of Height: The height of participants over two years old was measured using a microtoise attached to a smooth, straight wall. They were made to stand erect, barefoot, with feet at right angles, and flat back against the wall. The headpiece of the "microtoise" was then gently lowered so that it touched the hair and made contact with top of the head. Height was recorded based on the nearest 0.1 cm.

Procedure for Measuring Weight: Children under five years of age, weighing less than 23 kilogram (kg), were weighted using toddlers weighing scale, while children under five years of age, who weighed more than 23 kg, were weighted using the adult analog weighing scale based on the nearest 0.1 kg.

Procedure for Rapid Diagnostic Test (RDT) and Blood Film Test for Malaria: Venous blood was collected from the dorsum of the palm or the cubital fossa. The identified area was thoroughly cleaned with 70% isopropyl alcohol. A tourniquet was then applied to make the vein engorge, and about one milliliter of blood was drawn with a needle and a syringe and transferred into a lithium heparinized tube.

One to two drops of blood were used in the rapid diagnostic test for malaria (parascreen for all *plasmodium* species, by Zephyr Biomedicals, India). The rapid diagnostic test for malaria was all done and read by one laboratory technician to eliminate inter-observer errors. The remaining blood sample was used in the blood film test for malaria parasites. Thick and thin films were made for each patient. Blood smears were stained with 3% Giemsa for 30 minutes. Two experienced laboratory technicians read the slides, and in case of any discrepancies, a third technician was employed for confirmation. A smear was judged to be negative if no parasites were observed after reviewing 100 high-power fields.

Urine sample collection for urine dipstick test: Caregivers were given clean sample bottles to collect mid-stream urine from participants for urine dipstick testing. Participants under six months were encouraged to breastfeed, and those older than six months were given water or fruit juice to drink to help them void freely and easily. In situation where urine sample collection was difficult, urethral catheterization was done under aseptic conditions to obtain urine. Xylocaine gel was used as a lubricant to prevent or reduce urethral abrasion and also to serve as a local anesthesia.

The urine sample was collected into a clean sample bottle and tested using combi-10 urine dipstick, which detects nitrite and leukocyte esterase activity as well as other parameters. Patients whose urine sample was positive for nitrite, leukocyte esterase activity, or both were classified positive for urine dipstick test and hence diagnosed with urinary tract infections. A positive nitrite or leukocyte esterase test indicates that a significant number of bacteria may be present in the participant's urine. The urine dipstick test was done by one laboratory technician to avoid inter-observer variability.

Statistical Analysis: Data collected by the case report forms were entered into Excel 2010 and analyzed using Stata software Version 14. Univariate analysis with point estimates were presented in frequencies and percentages. Fisher's exact test was used to assess differences in the means of continuous variables, and significant levels were assessed using a p <0.5.

Ethical Approval: The management of Maternal and Child Health Hospital gave us the authorization to conduct the study, and the Committee on Human Research, Publications, and Ethics of Kwame Nkrumah University of Science and Technology (KNUST) gave ethical approval for the study protocol (reference number: CHRPR/AP/081/19).

Findings

Demographic characteristics of participants: Table 1 presents the demographic information of children with malnutrition, including age, sex, registration status of National Health Insurance Scheme (NHIS), and tribe of participants. The median age of participants was 14 months (IQR: 9-20). The youngest child was two months old, and oldest one was 59 months old. About 88.88% of children were up to 24 months old. More than half of the participants (55.5%) were male. Most participants (84.13%) were registered under the NHIS, while 11.64% were not registered, and 4.23% were registered, but their registration status was expired. The major tribe was Akan, accounting for 71.43% of participants.

Nutritional status of children: Table 2 demonstrates the types of malnutrition including wasting, underweight, and stunting. Marasmus was the commonest type of malnutrition, accounting for 80.95% of participants recruited, while marasmic/kwashiorkor and kwashiorkor accounted for 11.64 and 7.41% of participants, respectively. Children aged over 21 months were at higher risk of developing kwashiorkor than marasmus (approximately 16 months) and marasmic kwashiokor (over 14 months) as depicted in Figure 1. Based on weight to height/length (wasting) ratio, 13.87 and 62.42% of participants with a mean age of 16 months were diagnosed with mild and severe malnutrition, respectively, whilst 23.70% of them with a mean age of 13 months were diagnosed with moderate malnutrition. Based on weight to age (underweight) ratio, 32.28 and 4.76% of children were mildly and severely underweight, whilst based on height to age (stunting) ratio, 2.12% were severely stunted as depicted in Figure 2.

Table 1) Demographic characteristics of malnourished children

Variables	Category	Frequency N (%)
Age (months)	0-12	84 (44.44)
	13-24	84 (44.44)
	25-36	15 (7.94)
	37-48	3 (1.59)
	49-59	3 (1.59)
Sex	Male	103 (55.5)
	Female	86 (45.5)
National health insurance	Access	159 (84.13)
	No Access	22 (11.64)
	Expired	8 (4.23)
Tribe	Akan	135 (71.43)
	Mole-Dagomba	10 (5.29)
	Ewe	6 (3.17)
	Ga-Adangbe	4 (2.12)
	Guan	3 (1.59)
	Others	31(16.40)

Table 2) Nutritional status of participants

Variables	Category	Frequency N (%)
Type of malnutrition	Kwashiokor	14 (7.41)
	Marasmus	153 (80.95)
	Marasmic Kwashiokor	22 (11.64)
Weight to height/length (wasting)	Severe	108 (62.42)
	Moderate	41 (23.70)
	Mild	24 (13.87)
Weight to age (underweight)	Severe	9 (4.76)
	Moderate	95 (50.26)
	Mild	61 (32.28)
	Normal	24 (12.70)
Height to age (stunting)	Severe	4 (2.12)
	Moderate	41 (21.69)
	Mild	67 (35.45)
	Normal	77 (40.74)

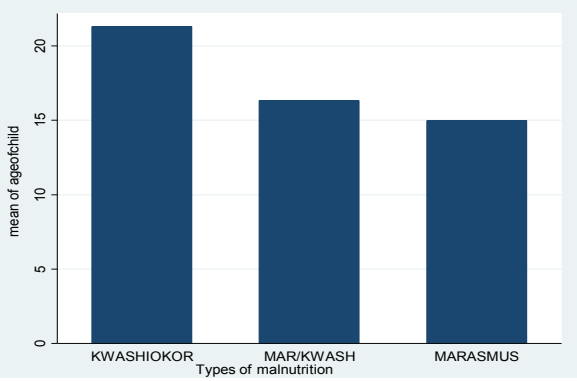

Figure 1) Average age distribution of the malnourished children

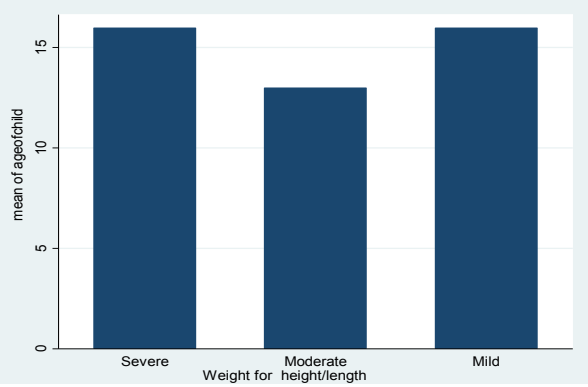

Figure 2) Distribution of children's age on Z-score

Infections among children with malnutrition: For infections, 15.87% of participants had positive blood smears for malaria, while 19.58% tested positive for malaria using RDT: also, 20.11 and 20.63% had positive nitrite and leukocyte esterase tests, respectively as presented in Table 3. Data were presented in frequency and percentage. Fewer children with kwashiorkor had malaria compared to marasmic/kwasiokor and marasmus. Proportions were compared using Fisher's exact test.

Discussion

Infections are more common among children with malnutrition than among well-nourished peers because nutrition is an important factor in the development of immunity, especially in children [3, 4]. Furthermore, infections cause extensive systemic immune activation triggering the release of specific cytokines, which cause fever, nausea, hypophagia, and cachexia and worsen or cause malnutrition [3, 15]. Cytokines also affect the production of insulin and insulin-like growth factor 1, leading to growth retardation [15]. Malnutrition in children is complicated by infections such as malaria, diarrhoea, pneumonia, as well as urinary tract and respiratory infections [6, 7]. In this study, 15.87 and 19.58% of malnourished children were diagnosed with malaria by means of microscopy using blood smear test and rapid diagnostic test for malaria, respectively. The prevalence of malaria in children under five years without malnutrition has decreased consistently over time from 27% in 2014 to 21 and 14% in 2016 and 2019, respectively [11].

Children with marasmus (28/37) in this study were more likely to have malaria compared to those with kwashiorkor (3/37). Shikur et al. (2016) [9] found out that most malnourished-children had malaria compared to well-nourished children. Fevang et al. (2018) [10] also found lower parasitemia in children with kwashiorkor compared to those with marasmic kwashiorkor and marasmus. The reason for the lower prevalence of malaria infection in children with kwashiorkor seems to be an excess amount of prooxidants leading to the production of excess free radicals. Furthermore, it has been found that the concentration of free fatty acids is high in children with kwashiorkor and, therefore, the erythrocyte membrane is prone to peroxidation [10].

Bacterial infections are more common among children with malnutrition than in normal controls [16]. Up to 20.11 and 20.63% of participants had positive results for nitrite and leukocyte esterase activity in urine dipstick test, respectively. Uwaezuoke et al. (2019) [13] in a review article found a pooled prevalence of 17% and a pooled odd ratio of

Table 4) Comparison of infection and type of malnutrition

Variables	Response Frequency, N (%)			Total	*P*-Value
	Kwashiokor	Mar/Kwa	Marasmus		
Malaria (blood film)					**.104**
Positive	2 (14.29)	7 (31.82)	21 (13.73)	30 (15.87)	
Negative	12 (85.71)	15(68.18)	132(86.27)	159 (84.13)	
Malaria (RDT)					**.540**
Positive	3 (21.43)	6 (27.27)	28 (18.30)	37 (19.58)	
Negative	11 (78.57)	16 (72.73)	125 (81.70)	152 (80.42)	
Urinalysis (Nitrite)					**.216**
Positive	1 (7.14)	7 (31.82)	30 (19.61)	38 (20.11)	
Negative	13 (92.86)	15 (68.18)	123 (80.39)	151 (79.89)	
Urinalysis (Leukocytes)					**.836**
Positive	2 (14.29)	5 (22.73)	32 (20.92)	39 (20.63)	
Negative	12 (85.71)	17 (77.27)	121 (79.08)	150(79.37)	

Table 3) Infections among children with malnutrition

Variables	Category	Frequency N (%)
Malaria (blood film)	Positive	30 (15.87)
	Negative	159 (84.13)
RDT for malaria	Positive	37(19.58)
	Negative	152 (80.42)
Urine culture	Positive	32 (16.93)
	Negative	157 (83.07)
Nitrite	Positive	38 (20.11)
	Negative	151(79.89)
Leukocyte esterase	Positive	39 (20.63)
	Negative	150 (79.37)
Urine sugar	Positive	12 (7.10)
	Negative	157 (92.90)

2.34 for urinary tract infection in children with malnutrition. Rosli et al. (2008) [12] in a similar study found out that 16.4% of children with malnutrition had urinary tract infection compared to 6.4% in well-nourished children. The difference in the proportion could be due to the fact that Rosli et al. (2008) [12] cultured bacterial isolates, while in this study, urinalysis was done using either nitrite or leukocyte esterase activity or both as a diagnostic test for urinary tract infection. However, comparable findings make it possible to use simple laboratory tools such as rapid diagnostic test for malaria and urine dipstick test to quickly diagnose malaria in district hospitals in Ghana and other low-income countries. To limit false-negative and false-positive results in nitrite and leukocyte esterase tests, caution was taken to ensure that clean catch urine was used in a clean bottle within two hours of collection. Participants with diabetes were excluded, and patients taking drugs such as cephalexin, nitrofurantoin, and vitamin C [17] were also excluded or asked to stop taking these drugs 72 hours before recruitment.

Conclusion

Malaria and urinary tract infections are not uncommon among children with malnutrition. Therefore, all children with severe malnutrition should be investigated for parasitic and bacterial infections. At the district and sub-district levels, simple laboratory tools such as rapid diagnostic test for malaria and urine dipstick test could be useful for such purposes.

Limitations of this study: There could be false-positive and false-negative results for nitrate and leukocyte in urine dipstick test, but this test could be an important guide in managing children with malnutrition in resource-limited settings because many first- and second-level hospitals in resource-limited countries including Ghana do not have well-resourced laboratories for doing culture and sensitivity test which is the gold standard. Furthermore, well-nourished peers were not compared because the study was a hospital based study.

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Ethical Permission: approval to conduct the study was obtain from the Committee on Human Research, Publication and Ethics of Kwame Nkrumah University of Science and Technology (CHRPE /AP/081/19).

Conflict of Interests: The authors declare that there is no conflict of interests.

Authors' contribution: Conceptualization: EA and RA, data curation: EA, IO and TOK, formal analysis: EA and TJA, Investigation: PT, methodology: PT, TJA and TOK, project administration: RA, supervision: EA and IO, writing of original draft: PT, TOK and RA, writing-review and editing: EA, RA, IO and TJA.

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