ORIGINAL RESEARCH REPORT

Complete blood profile of children diagnosed with asymptomatic urinary tract infection: oral nutritional supplement (ONS) intervention

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Article Info

ABSTRACT

Background: Young children are at high risk of urinary tract infections (UTI) that present as asymptomatic non-specific signs without clinical presentation. UTIs put children at risk of malnutrition, and thus early diagnosis, nutritional management, and medication are important. The administration of oral nutritional supplements (ONS) with an energy intake of 400 kcal/day is thought to be an effective strategy to provide balanced nutritional needs.

Objectives: This study aims to investigate the clinical symptoms and growth pattern of young children with UTIs and with clinical symptoms of poor feeding and growth faltering who received medical treatment and nutritional intervention for three months.

Methods: A cross-sectional analytical study was conducted from January 2019 to December 2020 at the outpatient installation unit of Husada Utama Hospital. Subjects were children aged one to five years old, with the main complaint of poor feeding and constant weight gain. UTIs were identified according to the urine culture results. If the count exceeded 100,000 cfu/ml, it was determined as a urinary tract infection.

Results: A total of 37 children were enrolled in this study and received diet advice, ONS, and medication. The proportion of boys was higher than girls in this study (21 to 16, respectively). Undernutrition was experienced by 14 subjects (37.84%) who were stunted or severely stunted (13 subjects or 35.14%), underweight or severely underweight (seven subjects or 18.92%), and wasted (four or 10.81%). It was shown that ONS improves mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH) significantly, and slightly increased haemoglobin though there was no significant difference. White blood cell (WBC) and lymphocyte levels reduced after ONS intervention.

Conclusion: Nutritional intervention with ONS improves erythropoiesis (MCV and MCH) but reduces WBC and lymphocytes in children with UTIs.

Keywords: growth faltering; hemoglobin; malnutrition; urinary tract infection; white blood cell; urine culture

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Highlights

1. Undernutrition occurred to 155 million children under five years old; wasting occurred to 52 million children under five years old; and severe wasting occurred to 17 million children.
2. Undernutrition is caused by insufficient nutrient intake to meet the child’s nutrient for maintaining his/her growth and development.
3. Urinary tract infection (UTI) is one of the causes of undernutrition in young children due to insufficient nutritional intake.

BACKGROUND

Neonates and infants are at high risk of urinary tract infection (UTI) during the first year of life due to their immature immune system (Chang and Shortliffe, 2006). Up to 8% of children had at least one UTI, and up to 30% experienced recurrent UTIs during their first years of life (Simões e Silva et al., 2020) which led to severe bacterial infection. The incidence of UTIs among girls was 3-7%, while among boys it was 1-2% (Cataldi et al., 2010). A child is determined to have a UTI if the colonization of pathogens along their urinary tract (Chang and Shortliffe, 2006) if UTI is measured as $>10^5$ CFU/ml (Pryles, 1957). This can initially be proven through bagged urine collection as the most practical and non-invasive method. However, this method does not entirely prove UTIs due to having the highest rate of contaminants (Davies, 2004). Accurate diagnosis is important to ensure proper medical treatment and reduce the risk of kidney damage because young children are at risk of renal damage (Bergman et al., 1999).

In neonates and young children, UTI symptoms appear with no clinical presentation and are non-specific, such as poor feeding, anorexia or loss of appetite, and growth faltering (Chang and Shortliffe, 2006; Habib, 2012; World Health Organization, 2005). As a result, most parents and caregivers are not aware of this disease, and it is quite challenging for clinicians to diagnose this disease, especially in limited clinical settings such as in developing countries. Children with UTIs often have indistinguishable conditions because of bacteraemia but have more frequent feeding problems than non-bacteraemia patients because bacteraemia leads to severe inflammatory reactions (Honkinen et al., 2000) which places them at high risk of malnutrition.

Poor feeding leads to a significant reduction in nutritional intake, which will influence malnutrition and developmental delays in children (Millward, 2017). This is especially true during the first two years of age, in which children grow and develop rapidly. In this phase, early diagnosis, nutritional management, and medication are important. The administration of oral nutritional supplements (ONS) (100 kcal energy and 2.6 g protein per 100mL) with an energy intake of 400 kcal/day is thought to be an effective strategy to provide balanced nutritional needs (Kareem et al., 2021). This combination contains both macro- and micronutrients that are sufficient to meet the daily nutritional needs of those at risk of malnutrition (Ui Dhuibhir et al., 2019). This is intended to increase nutritional intake due to insufficiency in diets to meet daily nutritional requirements (Collins et al., 2019), particularly protein and calories (Lo et al., 2019), needed for accelerating children’s growth. The growth refers to accelerated weight gain to return to the normal growth channel after a period of active weight faltering (Jackson, 1990). For this purpose, the calories required are above the calories needed for energy expenditure, and a higher minimum protein intake is required (Whitehead, 1977).

OBJECTIVE

This study investigated the clinical symptoms and growth patterns of young children with UTIs. These children showed clinical symptoms of poor feeding and growth faltering, and they received medical treatment and nutritional intervention for three months.
MATERIAL AND METHOD

Study design

This study is a cross-sectional analytical study that was conducted from January 2019 to December 2020 at the outpatient installation unit of a private hospital in Surabaya (Husada Utama Hospital), specifically focusing on the nutritional counseling unit. The main complaints were poor feeding and constant body weight gain. The inclusion criteria for subjects were that infants did not have genetic disorders such as cerebral palsy or Down syndrome, received breastfed milk as their main nutrition source during their first six months of life, and did not have any serious disease. Sample size was determined using total sampling during the period of study.

Feeding problem diagnosis and physical examinations were done by a paediatrician specializing in nutrition and metabolic syndrome with a nurse as a helper. Parts of the diagnosis and examinations were completed in accordance with the anamnesis of the parents/caregivers. The laboratory investigation included urine cultures, which were done in the same private hospital where the study was enrolled. UTIs were identified according to the urine culture results. Those with a count of >100,000 cfu/ml were determined to have a UTI (Coulthard, 2019; Pryles, 1957) and had to receive antibiotic medication according to the UTI consensus of the Indonesian Child Health Association (Ikatan Dokter Anak Indonesia, 2011). The subjects were given nutritional therapy, which involved dietary advice (enriched animal protein in the diet) and ONS to cover the calorie deficits when their oral diet could not meet the energy requirements.

Dietary recalls, calorie needs, and diet planning for the subjects were done by the child health medical doctor specializing in nutrition and metabolic disease. Nutritional status (weight-for-age or WAZ, length-for-age or LAZ, and weight-for-length or WLZ) was determined using WHO Anthro software.

Statistical analysis

The statistical analysis conducted in this study included normality, descriptive, and paired sample T-test/Wilcoxon tests.

Ethical clearance

This study was reviewed and declared to be ethically appropriate by the Health Research Ethics Committee of Universitas Airlangga, School of Medicine with approval number of 226/EC/KEPK/FKUA/2021 on October 4th, 2021.

RESULT

A total of 37 children aged 12 to 60 months and given 90 days of medication and nutritional intervention were enrolled in this study as shown in Table 1. The proportion of male children was higher than girls in this study (21 to 16 months old, respectively). The main complaints experienced by the children were of feeding difficulty and/or stagnant body weight gain for 2 to 36 months. Undernutrition was experienced by 14 subjects (37.84%) for being stunted/severely stunted (13 subjects or 35.14%), underweight/severely underweight (seven subjects or 18.92%), and wasted (four subjects or 10.81%). The age distribution ranged from 12 to 49 months old.

Bacteriological profile of the subjects included Staphylococcus haemolyticus (10), Staphylococcus epidermidis (1), Staphylococcus xylosus (1), Enteroxoccus faecalis (2), Escherichia coli (9), Morganella morganii (1), Proteus mirabilis (1), Klebsiella oxytuca (1), Shigella sonnei + Escherichia coli (1), Streptococcus agalactiae (1), Klebsiella pneumoniae (2), Staphylococcus sciuri (1), Staphylococcus simulans (1), Enterococcus faecalis + Proteus mirabilis (1), Klebsiella pneumoniae + Staphylococcus hominis (1), Staphylococcus spp. + Escherichia coli (1), Moranella morganii + Proteus mirabilis (1), and Staphylococcus haemolyticus + Klebsiella pneumoniae (1).
The effects of ONS intervention on the subjects are summarized in Table 2. It is shown that ONS improved subjects’ MCV and MCH significantly, and slightly increased their haemoglobin though there was no significant difference. White blood cells (WBC) and lymphocytes were reduced after ONS intervention. Other parameters such as platelets, MCHC, neutrophils, monocytes, eosinophils, and basophils showed no significant difference between pre- and post-intervention.
DISCUSSION

Adequate and appropriate nutrition is required for all immune cells to support immune functions. Activated immune systems have a huge energy requirement over basal energy expenditure from exogenous or endogenous sources with specific roles in the immune response, such as arginine, vitamin A, zinc (Hannigan, 1994), glutamine, fatty acids, vitamin D (Newsholme, 2021), vitamin C, and vitamin E. Due to this, sufficient nutrient intake is needed (Iddir et al., 2020). When a child experiences nutrient deficiency or undernutrition, it will lead to an immune deficiency and infections (Cunningham-Rundles et al., 2005).

Enteric infections, such as *Shigella*, have a negative effect on growth (Jackson, 1990), and so do UTIs (Malaki et al., 2011). UTIs caused by *Escherichia coli* (*E. coli*) are the most common types of infections (Lee et al., 2018). *E. coli* colonize by attaching to the bladder’s epithelium, followed by bacterial invasion and replication. It forms a compact aggregate with biofilm-like properties in urothelial epithelial cells (Zagaglia et al., 2022). *E. coli* is considered one of the microorganisms most commonly responsible for infections (sepsis, neonatal meningitis, pneumonia, bacteremia, and diarrhoea) (Ali et al., 2018) and coinfections with other pathogens. It has a negative association with delta WLZ and WAZ in infants aged 0-6 months (Lima et al., 2018).

It is well known that, in neonates and young children, UTIs are present with non-specific symptoms such as slow weight gain, feeding difficulties, irritability, vomiting, and refusal of foods with a sickly appearance. Children with unexplained fever or growth faltering must undergo UTI examination procedures, including a qualitative urine culture to establish the diagnosis (Tokan and Kari, 1999). Urinalysis components useful in predicting UTIs include WBC and bacteria, with sensitivity and specificity varying between 73% to 83% in predicting infection (Menni et al., 2021). In the adult population, WBC has a 62.7% sensitivity and 100% specificity in predicting UTIs (Mohanna et al., 2021). In the paediatric setting, WBC with a cut-off value of >12,000/ml has 56% and 88% sensitivity and specificity, respectively.

Nutritional intervention increases the red blood cell count, and especially the haemoglobin patterns, in malnourished children (Barroso et al., 2022). Vitamin B7 supplementation (600-700 µg/kg body weight) has been found to improve the red blood cells, haematocrit, and haemoglobin of Japanese quail (Hamza Yasser Al-Awadi and Abdul-Lateef Ali Al-Nadawi, 2020), which is in line with this study’s findings. Another study using iron supplementation also supports these findings as it observed an improvement in MCV and MCH in female adolescents after intervention (Rezaedian et al., 2014). Another study combined vitamin A and EPO supplementation in children with anaemia, and the intervention improved iron-deficient erythropoiesis (including MCV) without changing iron store (ferritin) (Zimmermann et al., 2006).

WBC varies depending on age. Children aged 1-5 years were observed to have higher WBC than other populations (8.9 x 10^3/mm^3) (McGrath et al., 1982). WBC has consequences both when it is too low or too high, and thus maintaining a normal WBC is important. When it is low, it has been linked to inadequate immune response. It has even been associated with nutritional deficiencies, long-term use of medication, and immune dysfunction. When it is high, it has been linked to chronic inflammation. WBC has also been found to be modulated by nutritional status (Hernández et al., 2021) and nutritional intake (Menni et al., 2021).

It has been found that high vegetable intake (green vegetables) lowers WBC (Menni et al., 2021). Another study observed the effects of nutritional supplementation enriched with fish oil, high protein and leucine, and specific oligosaccharides in adults for one week. This was able to increase the subjects’ EPA percentage within their WBC and increase their proinflammation cytokine production (Faber et al., 2011), as well as alter their leukocyte function (Hamza Yasser Al-Awadi and Abdul-Lateef Ali Al-Nadawi, 2020). A study in young adults showed that WBC is strongly associated with age, gender, race, and BMI. In addition to that, the increment of diet components such as dietary copper, iron, and vitamin K were found to decrease WBC. Meanwhile, the increment of vitamin B1 in the diet was found to increase WBC (Balkaransingh et al., 2013). After intervention on malnourished children, there was a
significant decrease in their leukocytes (p = 0.04) and lymphocytes (p < 0.01) (Barroso et al., 2022), which is in line with this study’s results. Although there was a decrease in leukocytes, their value was still in the normal range (5,000 to 12,000/mm³). Leukocytes are an important marker in investigating subclinical inflammations to produce pro-inflammation markers (Barroso et al., 2022).

**Strength and Limitations**

This study did not investigate cytokines as the immune response against the parasite.

**CONCLUSION**

Nutritional intervention with oral nutrition supplement (ONS) improves erythropoiesis (MCV and MCH) but reduces WBC and lymphocytes in children with UTIs.

**Acknowledgment**

None.

**Conflict of Interest**

All authors have no conflict of interest.

**Ethical Clearance**

The study was reviewed and declared to be ethically appropriate by the Health Research Ethics Committee of Universitas Airlangga, School of Medicine with approval number 226/EC/KEPK/FKUA/2021 on October 4th, 2021.

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None.

**Author Contribution**

Nur Aisiyah Widjaja was responsible for data collection, data analysis, and drafting. Meta Herdiana Hanindita was responsible for supervising the study and proofreading the manuscript.

**REFERENCES**


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