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ORIGINAL ARTICLE

Correlation Between Serum Zinc Levels and Severity of Acute Diarrhea in Children

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ABSTRACT

Background: Acute diarrhea is one of the major causes of morbidity and mortality in children under the age of five years of age especially in developing countries. Zinc plays a vital role in immune functions, the mucosal integrity of the intestines and enzyme functions. The predisposition to infections and the duration of time in diarrhea has been associated with zinc deficiency.

Place and Duration of Study: The study was carried out in the paediatric medicine department of The Children's Hospital Lahore from November 2022 to April 2023.

Objective: To determine the correlation between the intensity of serum zinc and the degree of acute diarrhea in children.

Methodology: A cross-sectional study was undertaken to examine paediatric patients (6 months to 5 years old) with acute diarrhea in a tertiary care hospital. The WHO sample size calculator formula was used to calculate the sample size. Consecutive sampling was used to enrol 120 patients. Informed consent was obtained and subsequently demographic and clinical data of each patient was recorded with the help of a structured proforma. The severity of the diarrhea in the patients was identified by the number of stools/days, degree of dehydration (as per the WHO guidelines) and period of the illness. Standardized laboratory procedures were used to measure serum zinc levels in the venous blood samples of each patient taken under aseptic conditions. Clinical examination based their division of the patients as mild, moderate and severe diarrhea. All the data collected were typed and calculated using appropriate statistical software. The connection between zinc in serum, and the severity of diarrhea in patients was determined by applying the relevant statistical tests with a p-value of less than 0.05 as the statistically significant value.

Results: A total of 120 patients were included in the study. Mean serum zinc level was also significantly less in children with severe diarrhea, as opposed to mild and moderate ones ($p < 0.05$). The serum zinc levels showed negative relationship with the severity of diarrhea necessitating that reduced levels of zinc were correlated with the severity of the disease and the duration of diarrhea.

Conclusion: Acute diarrhea is a highly severe disease whose severity is greatly linked to low serum levels of zinc in children. The use of zinc assessment and supplementation has the potential to be instrumental in the decreased disease burden and better clinical outcomes.

Keywords: Serum zinc, acute diarrhea, children, dehydration, severity, pediatrics, deficiency, correlation

INTRODUCTION

Acute diarrhea is a societal issue of high public health concern and is currently one of the highest morbidity and mortality causes in children under five years old in the whole word. Global health estimates are that there are millions of cases of diarrheal disease every year, a large percentage of which lead to hospitalization and death especially in developing countries. Children are especially vulnerable since they possess an underdeveloped immune system, malnutrition state, and are deprived of clean water, sanitation[1]. The acute diarrhea is typically regarded as the loss of three or more loose, liquid diarrhea within a day, and a span of less than 14 days, and is usually caused by viral, bacterial or parasitic infections.

Acute diarrhea can begin with mild and self-limiting episodes and go to severe and life-threatening cases which are indicated by dehydration, electrolyte imbalance, and malnutrition[2]. The most important complication and one of the leading causes of death among children with the disease is dehydration[3]. The diarrheal episodes are affected by different factors, such as age, nutritional status, immune response and the deficiencies of micronutrients. Of these, zinc deficiency has achieved a lot of focus given its large contribution in immune systems and gastrointestinal health[4].

Zinc is a crucial trace element which is critical in many biological functions such as cellular development, immunity, as well as the integrity of the intestinal mucosa[5]. The normal operation of enzymes and proteins that aid in digestion and absorption is very important. In low- and middle-income nations, Zinc deficiency is very high, and this is mostly because of poor food consumption, absorption and loss of the nutrient during sickness[6]. Zinc deficiency may cause children to have poor immune response, be more prone to infections and take longer to heal diseases like diarrhea.

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Various research has shown that zinc supplementation can decrease the length, severity and incidence of diarrheal episodes in children[7]. The World Health Organization (WHO) and UNICEF recommend zinc supplementation as a routine therapy to acute diarrhea, in addition to oral rehydration therapy. Zinc is thought to repair intestinal epithelia, enhance absorption of water and electrolytes and enhance immune responses toward enteric pathogens. Although all these benefits have been established, the correlation between baseline serum zinc levels with severity of acute diarrhea is a field that needs to be researched[8].

The association between the level of serum zinc and the severity of acute diarrhea is valuable in enhancing clinical control and prevention interventions[9]. The low serum levels of zinc can not only predispose children to more serious disease, but it may also delay recovery and expose them to more complications[11]. The zinc status determination of paediatric patients with diarrhea could therefore come in handy during the disease prognosis and guide certain interventions[10].

In third world countries such as Pakistan where malnutrition and micronutrient deficiencies are widespread, such an exploration of this correlation is more urgent[12]. Early recognition of children at risk of severe cases of diarrhea because of zinc deficiency can aid in the provision of timely and effective management measures, such as zinc supplementation and nutrition. Moreover, this kind of research is relevant in the policy of the public health in terms of decreasing the burden of diarrheal diseases in the vulnerable populations[13].

Hence, the aim of the study is to investigate the association between serum zinc levels and the severity of acute diarrhea in

children to further the knowledge of the importance of micronutrients in the development of the disease and contribute to the better healthcare results in paediatrics.

OBJECTIVE: This study aims to establish the relationship between zinc levels in serum and severity of acute diarrhea in children who are aged between 6 months and 5 years. It aims to establish the connection between decreased zinc levels and the extent, length and dehydration of disease which can assist in establishing the clinical importance of zinc status to diarrhea disease in children.

METHODOLOGY

The study was done in paediatric medicine department of The Children's Hospital Lahore from November 2022 to April 2023. Paediatric patients aged 6 months to 5 years with symptoms of acute diarrhea (three or more loose or watery stools daily) less than 14 days were included in the study. WHO sample size calculator was used to determine the sample and 120 patients were recruited through the process of consecutive sampling. Following informed consent taken by parents or legal guardians, all patients were clinically evaluated and recorded with a structured proforma. Demographic data, such as age, gender, and nutritional status was noted. Clinical examination was the history of the disease, frequency of stool, diarrhea duration and the assessment of dehydration based on WHO (no dehydration, a bit of dehydration, and serious dehydration). Blood of each patient was collected under aseptic conditions in order to identify the levels of serum zinc through the standard laboratory procedures. They were careful in handling and processing of samples to prevent contamination and final accuracy of results. The patients were grouped into mild, moderate and severe diarrhea groups, according to the frequency of stool, the period of illness and the extent of dehydration. The statistical software, SPSS, was used to enter and analyse the data Demographic and clinical characteristics were summarized using the descriptive statistics, and the inferential statistics was used to evaluate the relationship between the serum levels of zinc and the severity of diarrhea. A significant value was the p-value that was less than 0.05.

INCLUSION AND EXCLUSION CRITERIA

INCLUSION CRITERIA: The study consisted of children aged between 6 months and 5 years with acute diarrhea of less than 14 days. Only patients who were informed consent by their parents or guardians were enrolled. Eligible children had either mild, moderate or severe levels of dehydration as well as no previous zinc supplementation during the current illness. Clinically stable patients who could have their serum sampled were taken to make sure that serum zinc levels were accurately evaluated.

EXCLUSION CRITERIA: Children who had chronic diarrhea of a duration of over 14 days, underlying chronic conditions like renal, hepatic or metabolic conditions and children who were already under zinc supplementation were excluded. Also, patients who were also severely ill and required an intensive care, and those whose parents or guardians declined to provide consent were not included in the study.

DATA COLLECTION: A structured and pre-tested proforma was used to gather data in this study. At the time of admission, every patient, who fit the inclusion criteria, was carefully assessed. Demographic data (age, gender and nutrition status) were obtained. Clinical data, length of diarrhea, stool frequency, vomiting, fever and dehydration symptoms were collected through history taking and physical examination. The level of dehydration was measured based on the WHO guidelines and was categorized as no dehydration, a bit of dehydration, or severe dehydration. The serum levels of zinc were measured using a venous blood sample under aseptic conditions on each patient. The samples were all taken in trace element-free tubes to prevent contamination and subject to immediate processing in the hospital laboratory by standardized biochemical methods. Strict quality control measures were adhered to in order to guarantee reliability and accuracy of results. All the data were duly entered and then imported into statistical programs to analyse them. Privacy This was achieved by assigning various identification numbers to all patients. Data validation was carried out to minimize the errors and guarantee consistency. To further analyze the data obtained, the data were then categorized depending on the severity of the diarrhea (mild, moderate and severe). Proper documentation and record keeping have ensured that the data collected were complete, accurate and suitable to statistical analysis of the correlation between serum zinc and severity of the disease.

RESULTS

A total of 120 paediatric patients were included in the study, with a mean age of 2.3 ± 1.2 years. Among them, 65 (54.2%) were male and 55 (45.8%) were female. Clinically, 40 (33.3) individuals were diagnosed with mild diarrhea, 45(37.5) with moderate, and 35 (29.2) with severe diarrhea. The mean serum zinc of mildly diarrhea patients was significantly greater than the moderate diarrhea patients and the severe diarrhea patients. The lowest mean serum zinc levels were found in children with severe diarrhea. Statistical analysis showed that there existed a significant negative association between concentration of zinc in serum and severity of the diarrhea ($p < 0.05$) that is, the lower the levels of the zinc in the serum the more severe the diarrhea and duration of the illness. Moreover, the patients who were severely dehydrated showed considerably lower levels of serum zinc as compared to the ones who were not dehydrated or those who were partially dehydrated. These results indicate that zinc deficiency can be one of the factors that promote the intensity and duration of acute diarrhea in children.

Table 1 shows the demographic features of the study sample of 120 paediatric patients. The average age of the children was 2.3+/-1.2 years which means that majority of the respondents were toddlers. A slightly higher percent of males (54.2) was observed as compared to females (45.8). This distribution shows that an equal representation of the two sexes was used in the study though a bit on the male side. The age range and gender distribution gives a pertinent background on the study population and makes the results on the serum zinc levels and diarrhea severity applicable to young children in such an age range.

Table 2 shows the number of patients in terms of acute diarrhea severity. The highest number of patients was in moderate category (37.5) then there were mild cases (33.3) and severe cases (29.2). This means that most children were hospitalized with moderate symptoms. However, the number of patients with severe was also high, which also highlights the clinical significance of acute diarrhea in the severe group. The distribution shows that there is variability in the way the disease is manifested and supports the need to assess and treat the disease early to prevent the occurrence of mild or moderate cases into severe cases.

Table 3 shows how the level of diarrhea is associated with the level of serum zinc. Highest levels of serum zinc were observed in children with mild diarrhea (85.4 µg/dL), and a gradual decline in children with moderate and severe diarrhea (70.6 µg/dL and 55.3 µg/dL respectively). This negative pattern of decline shows a negative relationship between disease severity and the levels of zinc. The findings suggest that inadequate serum zinc might be one of the factors that result in worsening of clinical conditions in children. It also highlights the importance of zinc in the intestinal health and immune system that underpins the use of zinc in minimizing the severity and complications of acute diarrhea.

Table 4 shows the mean serum zinc levels according to dehydration status in children with acute diarrhea. Children with no dehydration had the highest mean serum zinc level (88.2 µg/dL), while those with some dehydration had lower levels (72.5 µg/dL), and patients with severe dehydration had the lowest mean level (54.1 µg/dL). This pattern indicates that serum zinc levels decrease as dehydration becomes more severe. The findings suggest that zinc deficiency may be associated with poor fluid balance and worsening clinical condition. It supports the view that adequate zinc levels are important in reducing complications of acute diarrhea.

Table 5 presents the relationship that exists between serum levels of zinc and diarrhea severity in children. This correlation coefficient was -0.62 meaning that the relationship between the two variables was moderate to strong, negative. This implies that the more the diarrhea severity, the lower the serum zinc levels. The p-value was below 0.05 which indicated that the relationship was statistically significant. These results indicate low serum zinc levels are associated with more serious diarrheal disease in children. Thus, zinc deficiency can have a significant role in exacerbating the clinical situation of children with acute diarrhea.

Table 1: Demographic Characteristics of Patients (n = 120)

Variable	Frequency (n)	Percentage (%)
Age (Mean ± SD)	2.3 ± 1.2 yrs	—
Male	65	54.2%
Female	55	45.8%

Table 2: Distribution of Patients According to Severity of Diarrhea (n = 120)

Severity Level	Frequency (n)	Percentage (%)
Mild	40	33.3%
Moderate	45	37.5%
Severe	35	29.2%
Total	120	100%

Table 3: Mean Serum Zinc Levels by Severity of Diarrhea

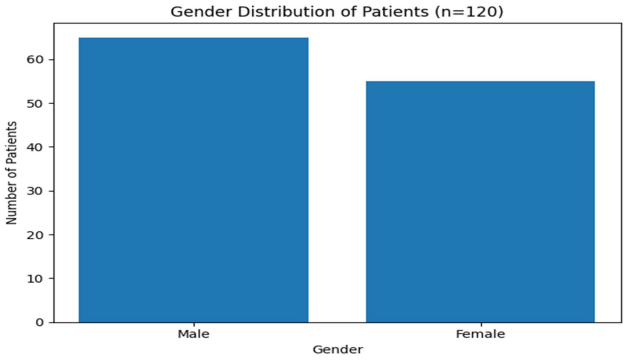
Severity Level	Mean Serum Zinc Level (µg/dL)	Standard Deviation
Mild	85.4	± 8.2
Moderate	70.6	± 7.5
Severe	55.3	± 6.9

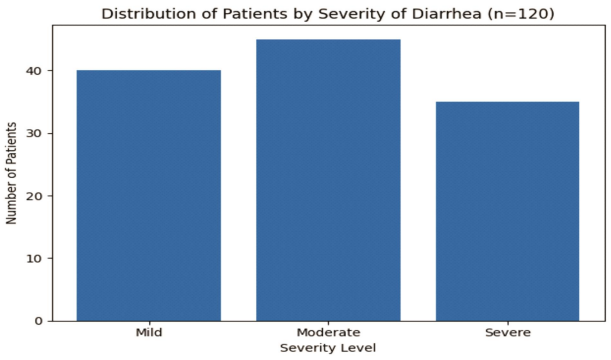
Table 4: Serum Zinc Levels According to Dehydration Status

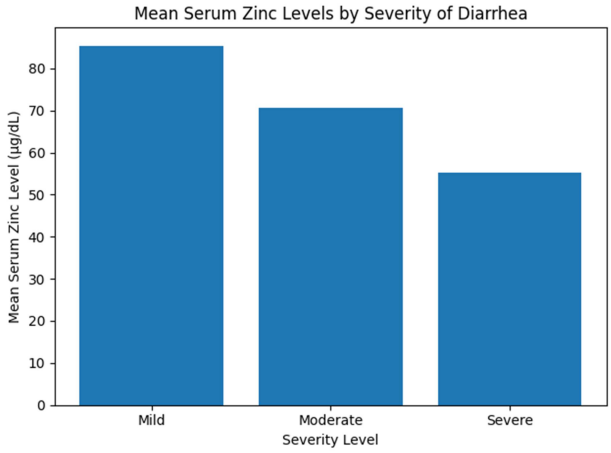
Dehydration Status	Mean Zinc Level (µg/dL)	Standard Deviation
No Dehydration	88.2	± 7.8
Some Dehydration	72.5	± 6.9
Severe Dehydration	54.1	± 6.5

Table 5: Correlation Between Serum Zinc Levels and Severity of Diarrhea

Variable	Correlation Coefficient (r)	p-value
Serum Zinc vs Severity	-0.62	< 0.05







DISCUSSION

The current study was carried out to ascertain the relationship between the level of zinc in serum and the severity of acute diarrhea in children 6 months to 5 years of age14. The results revealed a strong negative relationship between zinc levels in serum and severity of the disease, which implied that the lower the zinc levels, the more severe diarrheal episodes15. This is in line with past studies that indicate the critical importance of zinc in preserving intestinal integrity, immune system and general child health16.

In the paper, children with a more severe diarrhea showed significantly lower serum zinc levels in comparison to mild and moderate diarrhea (IKEJIAKU et al., 2022. This pattern implies that zinc deficiency can not only pre-dispose children to diarrhea but also lead to the development of the disease and its intensity17. Zinc has been reported to increase intestinal epithelial regeneration, water and electrolytes absorption, and intestinal permeability18. Thus, zinc deficiency can interfere with these protective mechanisms and cause more severe and prolonged manifestations of diseases.

The correlation between poor serum zinc concentrations and dehydration condition in this study also supports the importance of zinc in fluid balance and gastrointestinal functioning. Severely dehydrated children were found to contain considerably low amounts of zinc as compared to those with no or mild dehydrations. This could be attributed to zinc losses in cases of diarrheal episodes and insufficient dietary intake of the affected children. Also, zinc deficiency can enhance intestinal damage, thus enhance fluid loss and lead to dehydration.

The conclusion drawn in this paper aligns with the suggestions of both the world health organization (WHO) and the UNICEF, which recommend the use of zinc supplementation in the treatment of acute diarrhea. Several clinical trials have demonstrated that zinc supplementation helps decrease the severity and duration of diarrhea, and the risk of recurrence. The present study underlines these suggestions by showing a definite correlation between the deficiency in zinc and the severity of the disease, which makes zinc a significant element of clinical practice19.

Zinc deficiency is a significant issue of concern, especially to the public health of developing countries like Pakistan . Micronutrient deficiencies in children are caused by poor nutritional status, poor dietary access to balanced diets and frequent infections20. Dietary interventions and supplementation programs to treat zinc deficiency might have a great impact on the burden of diarrheal diseases and enhance child survival rates.

Nonetheless, there are some limitations of this study. As a cross-sectional study, it fails to provide a causal relationship of zinc deficiency and the severity of diarrhea. Besides, the research was

carried out in one facility and with a small sample size, which could be a weakness in terms of generalizability of the findings. Dietary intake, socioeconomic status, and other micronutrient deficiencies were not adequately considered, which may affect serum levels of zinc.

Regardless of these shortcomings, the research sheds a lot of light on the correlation between serum zinc level and severity of acute diarrhea in children . It underlines the importance of early zinc status evaluation and promotes the use of zinc supplementation as a vital part of diarrhea treatment. Further research with larger samples and longitudinal studies is suggested to investigate this relationship further and determine causality .

CONCLUSION

The conclusion of this research is that serum zinc levels and severity of acute diarrhea in children have a strong negative relationship. Reduced levels of zinc were linked to severity of the disease, duration of illness, and levels of dehydration. These results indicate that zinc plays a key role in preserving intestinal functions and immune response in children. The findings justify the clinical significance of early detection of zinc deficiency and zinc supplementation during the treatment of acute diarrhea. Zinc is also beneficial in lessening the severity and the period of the disease, as well as preventing recurrence. Zinc deficiency in developing countries where malnutrition is prevalent can greatly decrease the burden of diarrheal diseases. Altogether, zinc status may be improved by appropriate nutrition and supplementation to increase recovery, decrease complications, and help to achieve better health outcomes in children with acute diarrhea.

REFERENCES

1. Abd El-Ghaffar, Y. S., Shouman, A. E., Hakim, S. A., El Gendy, Y. G. A., & Wahdan, M. M. M. (2022). Effect of zinc supplementation in children less than 5 years on diarrhea attacks: a randomized controlled trial. Global Pediatric Health, 9, 2333794X221099266.
2. Abdul-Azeez, F., Abdulwahhab, S., & Ibraheem, M. (2020). The Impact of Serum Zinc Levels on Children with Acute Gastroenteritis. Iraqi Postgraduate Medical Journal, 20, 406-410.
3. Abolurin, O. O., Oyelami, O. A., & Oseni, S. B. (2020). A comparative study of the prevalence of zinc deficiency among children with acute diarrhoea in SouthWestern Nigeria. African Health Sciences, 20(1), 406.
4. Afolabi, O. F., Saka, A. O., Ojuawo, A., & Biliaminu, S. A. (2018). Serum zinc levels amongst under-five children with acute diarrhoea and bacterial pathogens. Nigerian Postgraduate Medical Journal, 25(3), 131-136.
5. Afolabi, O. F., Saka, A. O., Ojuawo, A., & Biliaminu, S. A. (2019). Serum zinc levels of hospitalized children with acute diarrhea differ by the isolated viruses. International journal of health sciences, 13(5), 4.
6. Afolabi, O. F., Saka, A. O., & Ojuwa, A. (2019). Serum Zinc Levels and Clinical Outcome of Hospitalized Nigerian Children with Acute Diarrhoea. Niger Delta Medical Journal, 3(1), 29-36.
7. Agarwal, A., Gupta, N. K., Upadhyay, A., Soni, R., Shah, D., & Jaiswal, V. (2018). Serum zinc levels as a predictor of severity of acute diarrhea. The Indian Journal of Pediatrics, 85(3), 179-183.
8. Barffour, M. A., Hinnouho, G.-M., Wessells, K. R., Kounnavong, S., Ratsavong, K., Sitthideth, D., Bounheuang, B., Sengnam, K., Chanhthavong, B., & Arnold, C. D. (2020). Effects of therapeutic zinc supplementation for diarrhea and two preventive zinc supplementation regimens on the incidence and duration of diarrhea and acute respiratory tract infections in rural Laotian children: A randomized controlled trial. Journal of Global Health, 10(1), 010424.
9. David, E. E., Yameen, M. A., Igwenyi, I. O., David, C. N., Nwobodo, V., & Ismail, A. K. (2022). Zinc Deficiency Elevates Fecal Protein, But Not Electrolyte and Short-Chain Fatty Acid, Levels in Enterotoxigenic Escherichia coli-Induced Diarrhea in Rats. Pediatric gastroenterology, hepatology & nutrition, 25(1), 79.
10. Dhingra, U., Kisenge, R., Sudfeld, C. R., Dhingra, P., Somji, S., Dutta, A., Bakari, M., Deb, S., Devi, P., & Liu, E. (2020). Lower-dose zinc for childhood diarrhea—A randomized, multicenter trial. New England Journal of Medicine, 383(13), 1231-1241.
11. Habibi, R., Hemati, M., Rezaei, M., & Daneshfar, A. (2019). Comparison of Baseline Serum Zinc Level in 1-5-Year-Old Children Hospitalized for Gastroenteritis with Children Hospitalized for Other Diseases at Dr. Mohammad Kermanshahi Hospital in Kermanshah.
12. Hassan, M., Younis, M. M. S., & Mohamed, H. (2021). Efficacy of oral zinc and probiotic on acute diarrhea in infancy. Al-Azhar J Pediatr, 24(2), 2114-2129.
13. Ikejiaku, U., Anochie, I., Nwolisa, E., Iregbu, F., & Amamilo, I. (2020). Serum Zinc Levels of Under Five Children with Diarrheal Disease. Journal of Advances in Medicine and Medical Research, 32(24), 1-10.
14. Jabeen, S., Shafique, T., Basharat, S., Khalil, A. A., Ali, M., & Saeed, M. (2021). Effect of Zinc Supplement on Severity of Acute Diarrhea Among Children Under Five Years of Age: Zinc Supplement on Severity of Acute Diarrhea among Children. Pakistan BioMedical Journal, 4(2), 143-149.
15. Park, Y., Son, M., Jekarl, D. W., Choi, H. Y., Kim, S. Y., & Lee, S. (2019). Clinical significance of inflammatory biomarkers in acute pediatric diarrhea. Pediatric gastroenterology, hepatology & nutrition, 22(4), 369-376.
16. Razeghi Jahromi, S., Moradi Tabriz, H., Togha, M., Ariyanfar, S., Ghorbani, Z., Naeeni, S., Haghighi, S., Jazayeri, A., Montazeri, M., & Talebpour, M. (2021). The correlation between serum selenium, zinc, and COVID-19 severity: an observational study. BMC infectious diseases, 21(1), 899.
17. Rerksuppaphol, L., & Rerksuppaphol, S. (2020). Efficacy of zinc supplementation in the management of acute diarrhoea: a randomised controlled trial. Paediatrics and International Child Health, 40(2), 105-110.
18. Wessells, K. R., Hinnouho, G.-M., Barffour, M. A., Arnold, C. D., Kounnavong, S., Kewcharoenwong, C., Lertmemongkolchai, G., Schuster, G. U., Stephensen, C. B., & Hess, S. Y. (2019). Impact of daily preventive zinc or therapeutic zinc supplementation for diarrhea on plasma biomarkers of environmental enteric dysfunction among rural Laotian children: a randomized controlled trial. The American Journal of Tropical Medicine and Hygiene, 102(2), 415.
19. Wongteerasut, A., & Pranweerapaibul, W. (2021). Does Serum Zinc Level Affect Severity of Acute Gastroenteritis Among Pre-School Thai Children? Pediatric Health, Medicine and Therapeutics, 481-489.
20. Yusuf, S., Soenarto, Y., Juffrie, M., & Lestariana, W. (2019). The effect of zinc supplementation on pro-inflammatory cytokines (TNF-α, IL-1 AND IL-6) in mice with Escherichia coli LPS-induced diarrhea. Iranian Journal of Microbiology, 11(5), 412.

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