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ORIGINAL ARTICLE

Comparison of serum selenium levels in anaemic and non-anaemic Pakistani children.

Fatima Babar[1], Huma Abdul Shakoor[2], Sundas Ali[3], Shazia Anwar[4], Qurrat-ul-Ain Akhlaq[5], Zahra Rashid Khan[6]

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ABSTRACT… Objective: To compare the serum selenium levels in anemic and non-anemic Pakistani children. **Study Design:** Case-control Prospective study. **Setting:** PAEC General Hospital, Islamabad, Pakistan. **Period:** 1st March 2022 to 31st August 2022. **Methods:** A case control study was conducted wherein comparison of Selenium levels in anemic and non anaemic Pakistani children was investigated. Age, serum selenium level and haemoglobin were the quantitative variables of this study and were subjected to median and standard deviation. Severity of anemia, mean being qualitative (ordinal) variables were expressed in terms of percentages. Bar graph and tables were used to display results. Chi square test was applied to compare both the groups. Odd ratios were also calculated. A total of 60 samples from anemic and control population were selected using consecutive non-probability sampling method. Selenium levels of the serum were determined using atomic absorption spectrometry. SPSS 19 version software was used for data analysis. **Results:** The findings in this study indicated that 33% of cases were Selenium deficient, while 27% among controls had low Selenium levels. ($p=0.57$). **Conclusion:** This study showed no association of selenium deficiency with anaemia.

Key words: Anaemia, Serum Selenium, Trace Elements.

INTRODUCTION

Anemia poses a significant health challenge for infants and children across various regions globally. Likewise, in nations undergoing development, such as Pakistan, moderate to severe anemia is notably common among children under five years old.[1] In South Asia, the occurrence of anemia stands at 52% among children below the age of five. Additionally, within the subset of seven countries in the South Asian region, Pakistan exhibits the second-highest prevalence of anemia among this age group, at 53%. Moreover, the prevalence slightly tilts towards males, with 54.2% affected compared to 53.1% among females.[2,3]

Anemia is frequently linked with deficiencies in trace elements.[3] Among numerous mineral micronutrients, such as calcium, cobalt, copper, magnesium, molybdenum, selenium, and zinc, there is evidence indicating their association with hematological parameters.[4] During erythropoiesis, hemoglobin is susceptible to oxidative damage. Selenium (Se) acts as an antioxidant through selenoproteins, guarding against erythrocyte breakdown. Changes in Se levels typically correlate with various pathological conditions linked to oxidative stress. Se deficiency is associated with heightened hemoglobin denaturation, increased methemoglobin content, elevated protein carbonyls, lipid peroxidation, the formation of Heinz bodies, and enhanced erythrocyte osmotic fragility. The Forkhead transcription factor (FoxO3a) is notably abundant in erythroid cells and crucial for maintaining the hematopoietic stem cell pool. Se status plays a critical role in erythrocyte equilibrium by regulating FoxO3a localization, which is vital for counteracting oxidative stress in erythroid cells. Erythrocyte Se concentration correlates with hospital mortality in patients with septic shock. Furthermore, erythrocyte Se levels can serve as

1. MBBS, FCPS (Haematology), Consultant Pathology, Begum Hasina Memorial Medical Complex Wah Cantt.
2. MBBS, FCPS (Haematology), Principal Medical Officer Pathology, PAEC General Hospital, Nilore, Islamabad.
3. MBBS, FCPS (Haematology), Medical Officer Pathology, Shaheed Zulfiqar Ali Bhutto Medical University (SZABMU), Pakistan Institute of Medical Sciences, (P.I.M.S) Islamabad.
4. MBBS, FCPS (Haematology), Consultant Hematologist Pathology, Islamabad Medical Complex, Islamabad.
5. MBBS, FCPS (Haematology), Consultant Pathology, Wah General Hospital, Wah Cantt, Pakistan.
6. MBBS, FCPS (Haematology), Associate Professor Pathology, NUST School of Health Sciences, Islamabad.

Correspondence Address:
Dr. Sundas Ali
Department of Pathology
Shaheed Zulfiqar Ali Bhutto Medical University (SZABMU), Pakistan Institute of Medical Sciences, (P.I.M.S) Islamabad.
sundasali243@gmail.com

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a prognostic indicator of mortality in individuals experiencing septic shock.[5]

Enzymes containing selenium are referred to as selenoenzymes, with one of the most crucial being glutathione peroxidase. Glutathione functions as an antioxidant, safeguarding red blood cells by reducing hydrogen peroxide and oxygen radicals, as well as maintaining protein sulfhydryl groups in a reduced state. Moreover, it shields hemoglobin from oxidation within erythrocytes. It is also thought to induce the up-regulation of heme oxygenase-1, facilitating the release of $Fe2+$ from heme molecules and actively removing intracellular iron. Glutathione executes its role through the catalysis of the selenoenzyme glutathione peroxidase.[6]

Deficiencies in micronutrients result from various factors, including insufficient intake, genetic predispositions, and infectious diseases, among others.[7] Selenium is a vital trace element found naturally in the diet, commonly sourced from cereals, meat and fish. Its bioavailability is typically higher in non-vegetarian diets compared to vegetarian diets. In developing nations, poor dietary quality is closely linked with inadequate selenium intake.[8]

The correlation between selenium deficiency and anemia has been explored in various investigations. For instance, a study conducted by Qing Zhou, utilizing data from National Health and Nutrition Examination Survey (NHANES) database 2003–2004 involving a total of 2,902 individuals in a cross-sectional study, concluded that elevated serum selenium levels were associated with increased serum iron levels, mean corpuscular hemoglobin concentration (MCHC), and hemoglobin levels, along with a reduced risk of anemia. They found out that as serum selenium levels increased, there was a significant reduction in the likelihood of anemia observed, with this effect plateauing at a threshold of 138 ng/ml ($p < 0.001$).[9] A study conducted in Tokyo concluded that serum selenium concentration displayed a positive correlation with packed cell volume. The study participants showed a significant positive association between serum selenium concentration and packed cell volume (PCV) ($p=0.016$).[4] Observations from cross-sectional studies involving children in rural Vietnam and healthy individuals in Iran revealed the presence of selenium-deficient individuals.[10,11] Consequently, this study was undertaken to investigate the potential role of selenium as a causal or contributory factor to anemia among Pakistani children.

METHODS

This case-control study was carried out at PAEC General Hospital Islamabad, Pakistan, from March 2022 to August 2022 after ethical approval (IRB/1099-21-2-22). The patients were selected by non-probability consecutive sampling. All patients meeting the inclusion criteria were included in the study after taking an informed consent. Cases included children of both sexes with hemoglobin level less than normal for age and gender as per WHO guidelines. Controls were children with normal hemoglobin levels. However patients taking selenium supplements, on parenteral nutrition, diagnosed haematological disorders causing bone marrow failure i.e. leukemias, lymphomas and those with acute blood loss were excluded from study and not included in both cases and controls. Children less than 6 months of age were also excluded. A history performa was filled in isolation. Blood was collected in plain tubes and EDTA tubes for determination of trace elements and hemoglobin samples respectively. Children were divided into anaemic and non anaemic groups on basis of their hemoglobin levels according to age. Serum selenium levels were estimated by Graphite furnace atomic absorption spectrometry. EDTA samples were assessed for haemoglobin estimation by automatic hematology analyzer XN-1000. Controls and cases were then grouped according to their Hemoglobin levels.

RESULTS

A total of 60 blood samples of pediatric population were included in the study. Samples were categorized as cases and controls by non-probability consecutive sampling. Each group included 30 subjects. As there were no follow up visits; therefore, none of the subjects dropped out or were lost at any point in the study.

Among both cases and controls, 16 (53%) were males, while 14 (47%) were females subjects in both the groups, male: female ratio being 1.3:1 (Figure-1). The age among both groups ranged from 6 months to 5 years. Mean age among cases and controls were 2.0 ± 1.2 years. Maximum patients were in 2-3 years of age.

Regarding selenium levels, among anemics (cases), 67% had normal selenium status and 33% were deficient. Among controls, 73% had normal selenium and 27% showed selenium deficiency. (Figure-2)

Normal Se levels differed in different age groups therefore both cases and controls were further sub grouped into less than 2 years, 2 to 3 years and 4 to 5 years. (Table-I)

Anemia was further categorized into mild, moderate and severe depending upon hemoglobin levels. Among the total anemic patients, 30% were mildly anemic, 63% had moderate anemia and 7% had severe anaemia. Regarding selenium deficiency, 17% were deficient among mild anemics and 17% in moderately anemics. None were deficient in severely anemics. (Table-II). Of cases, 2(7%) had normochromic normocytic anemia while rest of the deficient 9(30%) had microcytic anemia. (Table-II).There was no significant difference among cases and controls (p- value 0.57). (Table-III)

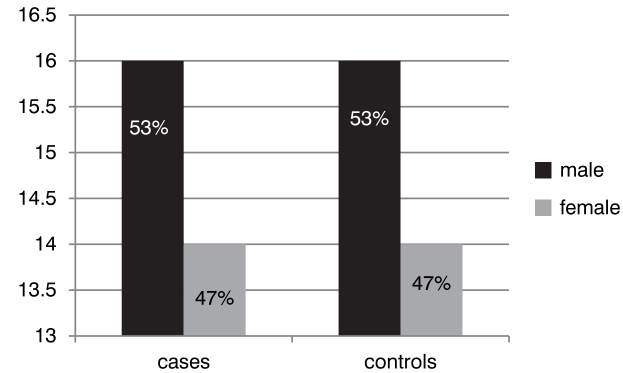

Figure-1. Gender distribution among cases and controls (n= 30 in each group)

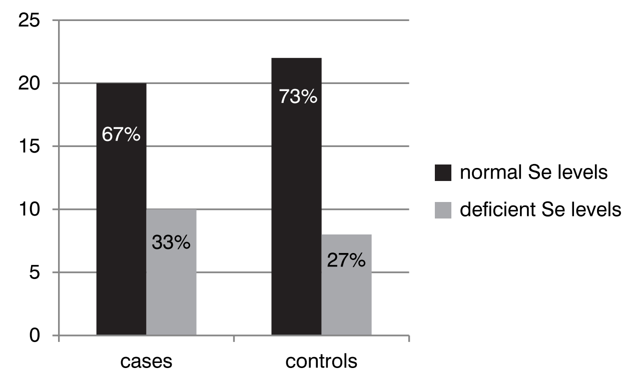

Figure-2. Selenium deficiency among cases and controls (n = 30 in each group)

Age	Normal Value	Cases				Controls				Total (% of Total)
		Normal Se		Low Se		Normal Se		Low Se		
		Male	Female	Male	Female	Male	Female	Male	Female	
<2yrs	16-71mcg/L	5	3	1	0	6	3	0	0	18(30%)
2-3yrs	40-103mcg/L	3	6	4	1	5	6	2	1	28(46.67%)
4-5yrs	55-134mcg/L	1	2	2	2	2	0	1	4	14(23.33%)
Total		9	11	7	3	13	9	3	5	60 (100%)

Table-I. Se levels with respect to age & gender. (n= 30 in each group)

Severity of Anemia	Serum Selenium Levels	
	Normal	Deficient
Mild	5 (17%)	5(17%)
Moderate	13 (43%)	5(17%)
Severe	2 (6%)	0

Table-II. Severity of anaemia and selenium deficiency

Group	Selenium Deficiency		Chi Square	P-Value	Odd Ratio
	Yes	No			
Cases	10(33%)	20(67%)	0.317	0.57	1.375
Controls	08(27%)	22(73%)			

Table-III. Difference of serum selenium levels among anemic and non-anemic children

DISCUSSION

Anemia persists as a significant global public health concern, particularly prevalent in developing nations. Its impact is particularly pronounced among children under the age of five (CU5), women of reproductive age (WRA), and pregnant women, given their increased requirement for iron. Among children, anemia contributes to compromised physical and cognitive development, diminished academic performance, and reduced productivity in adulthood.[2] While iron deficiency stands as the most prevalent cause of anemia, it's important to note that anemia can also arise from deficiencies in other micronutrients such as selenium. Selenium deficiency manifests in various outcomes, including oxidative damage, immunological complications, susceptibility to cancers, and thyroid abnormalities. Moreover, selenium deficiency can lead to gastrointestinal disturbances, impairing the absorption of other micronutrients like iron, magnesium, and zinc.[12]

In the present study, the association between selenium deficiency and anemia was investigated. Interestingly, there was no significant disparity in selenium status observed between the cases and controls. Specifically, 33% of cases and 27% of controls were found to be deficient in selenium, with a calculated p-value of 0.57, indicating insignificance. Numerous human studies across different age groups, including primary school-aged children (6 to 9 years old), adolescent girls (11 to 17 years old), and adults aged 65 years and older, have revealed associations between low serum selenium concentrations and the presence of anemia. Additionally, statistically significant links between low serum selenium levels and the development of anemia have been noted in various pathological conditions, such as chronic kidney disease and pulmonary tuberculosis. However, contrasting these findings, studies involving patients with iron deficiency anemia (IDA) and control subjects have demonstrated no significant relationship between serum selenium levels and hemoglobin concentration, similar to our study.[12]

In contrast, in a study conducted in Pakistan among primary school children, out of 73 children identified with selenium deficiency, 55 (36.7%) were found to be anemic, while the remaining 18 (12%) children were non-anemic. Serum selenium levels were notably lower in anemic children compared to non-anemic ones. The association between selenium levels and anemia was found to be statistically significant, with a p-value of less than 0.01.[13] In current study patients with age less than 2 years were not deficient or mildly deficient with only 1 case of deficiency. However, in 4-5 years group majority were deficient in both groups of cases and controls. This finding may be incidental or due to the fact that breast milk is a good source of selenium. Regarding gender majority of the subjects that entered the study were males being 16(53%) among cases and controls. Among cases majority were males who were selenium deficient while among controls majority of deficient children were females and were among the age group of 4-5 years. In our study, mild, moderate, and severe anemia were observed in 30%, 63%, and 7% of the participants, respectively. Among those with mild anemia, 17% had normal selenium levels while another 17% were selenium deficient. Similarly, among moderately anemic individuals, 43% had normal selenium levels, and 17% had low selenium levels. Interestingly, none of the severely anemic individuals were found to be selenium deficient. It's worth noting that this observation may be purely incidental, as only two patients were identified as having severe anemia. These findings suggest that no significant difference was noted in selenium levels between anemic and non-anemic Pakistani children.

CONCLUSION

The above findings suggest that no significant difference was observed in selenium levels in anemic and non-anemic Pakistani children.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Fatima Babar	Study conception, Study design, Data collection, Data analysis.	
2	Huma Abdul Shakoor	Data collection, Data analysis.	
3	Sundas Ali	Data analysis, literature search, result interpretation.	
4	Shazia Anwar	Draft manuscript preparation.	
5	Qurrat-ul-Ain Akhlaq	Literature search.	
6	Zahra Rashid Khan	Manuscript draft preparation.	