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ASSESSMENT OF BIOCHEMICAL PARAMETERS AS INDICATORS OF PROTEIN ENERGY MALNUTRITION IN TURKISH CHILDREN: A COMPREHENSIVE AND RETROSPECTIVE STUDY

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Abstract: This study aims to address this research gap by meticulously analyzing the biochemical parameters of children aged 0-59 months diagnosed with Protein Energy Malnutrition (PEM) within the confines of a state hospital over a two-year period. This study is a retrospective study evaluating the biochemistry and hormone laboratory findings of 302 children aged 0-59 months who were diagnosed with Protein Energy Malnutrition between the years 2020-2022 in the pediatric health and diseases clinic of Iğdır State Hospital. This study investigated the distribution of various biochemical parameters in children diagnosed with protein-energy malnutrition (PEM) and explored their significance within this context. The findings, based on reference values, revealed substantial proportions of children with abnormal values for iron, immunoglobulin (IgM and IgA), liver enzymes (ALT and AST), creatinine, CRP, and vitamin D. Gender-based differences were observed for calcium, IgM, Folate, and TSH, with notable variations between male and female children. Correlations between age and various parameters were identified, underscoring the complex interplay between developmental stages and biochemical values. The study highlights the importance of addressing deficiencies, potential complications, and demographic influences in managing PEM. The absence of demographic data integration in existing studies serves as a limitation, emphasizing the need for comprehensive research in this domain. Overall, these insights contribute to a deeper understanding of biochemical dynamics in children with PEM, aiding targeted interventions for improved health outcomes.

Keywords: Protein-energy malnutrition, Turkish children, Biochemical parameters, Podiatry

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1. Introduction

Malnutrition is a general term and it most often refers to undernutrition resulting from inadequate consumption, poor absorption or excessive loss of nutrients (Ashok et al., 2020).

Inadequate access to food sources and inability to meet daily energy needs lead to malnutrition, also known as nutritional deficiency. Malnutrition is a serious public health problem in different parts of the world, especially in developing countries (Onal et al., 2016). More than 33% of deaths among 0-5 year olds are related to malnutrition (WHO, 2011; UNICEF 2013). The socio-economic status of the family and access to food also has an impact on the occurrence of malnutrition. The most basic indicators of exposure to malnutrition for a long time are; short stature, retardation in growth and development according to age (Elkholy et al., 2012). Preschool children are defined by health professionals as a vulnerable group affected by malnutrition, which is often referred to as malnutrition in the community (Waly, 2014).

It is stated that health problems such as malnutrition and iron deficiency are seen in children aged 0-5 in our country. It was determined that malnutrition developed in 30% of the children in the Eastern Anatolia Region, and 3% of these children had severe malnutrition (Kilic et al., 2004). Protein-Energy Malnutrition (PEM) is a predominant form of malnutrition in developing countries, primarily impacting children between the ages of 6 months and 5 years. This condition arises from insufficient intake of proteins and/or calories, leading to various clinical manifestations that reflect the severity and type of malnutrition (Acar, 2012). PEM is well defined in terms of clinical features; however, its pathophysiology is still not fully understood. In recent studies, free radicals are involved in the pathogenesis of PEM. It has been suggested that the pathogenesis of edema and anemia, commonly found in children with Protein Energy Malnutrition, is due to an imbalance between the production of free radicals and their safe elimination (Thakur et al., 2004; Jain et al., 2013).Clinical findings of Protein Energy Malnutrition; It varies according to the duration and severity of nutritional deficiency, the quality of the diet, and personal factors (age, infection). While the diagnosis can be made easily in severe malnutrition, it can be difficult to diagnose in moderate or mild patients. In this case, the diet taken by the patient should be controlled, energy needs should be determined, anthropometric measurements and biochemical parameters should be evaluated (Benjamin, 1989; Figueroa, 1993; Gulec, 2011).

Moderate anemia is common in children with PEM. The most common cause of anemia in children with PEM is iron deficiency. Clinical signs of iron deficiency are found in two out of three children with PEM in India (Singh, 2004). Mild protein deficiency, which causes 15-20% reduction in muscle mass, may sometimes not cause a significant reduction in weight and arm circumference. As the protein and energy deficit increases, the decrease in muscle mass and other symptoms become more pronounced (Singh, 2004).

In Kenya and Nairobi, most children with clinically defined rickets are younger than 2 years old and have been associated with rickets, acute malnutrition and developmental delay. When the biochemical characteristics indicating the risk of rickets in children with varying degrees of acute malnutrition were examined, it was determined that there was a relationship between subclinical malnutrition, vitamin D deficiency and severe weight loss (Edwards et al., 2014; Jones et al., 2018).

The existing literature lacks comprehensive investigations into the utilization of biochemical indicators for detecting mild forms of malnutrition, with a predominant focus on elucidating the biochemical alterations associated with severe malnutrition. This study aims to address this research gap by meticulously analyzing the biochemical parameters of children aged 0-59 months diagnosed with Protein Energy Malnutrition (PEM) within the confines of a state hospital over a two-year period. By shedding light on the biochemical intricacies of mild malnutrition, this research contributes to a more holistic understanding of malnutrition's spectrum and its potential implications for early detection and intervention strategies.

2. Materials and Methods

2.1. Study Population and Design

This is a retrospective study in which biochemistry and hormone laboratory findings (Iron, UIBC, TIBC, Calcium, Glucose, IgM, Sodium, Potassium, IgA, ALT, AST, Creatinine, CRP, Ferritin, Folate, T4, TSH, and Vitamin B12) are evaluated. Iğdır State Hospital Pediatric Health and Diseases Polyclinic between 2020 and 2022, belonging to 302 children aged 0-59 months who were diagnosed with Protein Energy Malnutrition (Vitamin D). Necessary permissions were obtained from the relevant institution to conduct the research and obtain data.

The demographic characteristics of the children included in our study are as follows (Table 1).

Table 1. Distribution of demographic characteristics of included children in the study

Variables		n	%
Sex	Female	157	52.0
	Male	145	48.0
Age (Mean±SD)		3.85±1.843	
Total		302	100

Inclusion criteria:

1. Aged 0-59 months,
2. Diagnosed between these dates,
3. Had common laboratory findings,
4. Did not have any other chronic diseases.

Exclusion criteria:

1. Having a different accompanying chronic disease,
2. Children with missing laboratory findings were not included in the study.

2.2. Statistical Analysis

A descriptive analysis of the characteristics was conducted, presenting the outcomes through descriptive tables detailing means, standard deviations (SD), and percentages, as applicable. Significance was determined at a P-value threshold of less than 0.05. The statistical computations were carried out utilizing SPSS for Windows, version 23 (IBM Corpn., Armonk, NY, USA).

3. Results

The present study aimed to investigate the distribution of various biochemical parameters among children diagnosed with protein-energy malnutrition (PEM). The findings provide valuable insights into the prevalence of abnormal values for different biomarkers, shedding light on the significance of these parameters in the context of PEM.

Table 2 presents the distribution of biochemical parameters among the children included in the study, based on reference values. In the case of the iron parameter, 33.8% (102) of the children exhibited values below the reference range, while 64.9% (196) fell within the reference range, and 1.3% (4) had values exceeding the reference range. The data reveal that a considerable proportion of children with PEM, approximately 33.8%, exhibited iron values below the reference range. Remarkably, the investigation of the Unsaturated Iron-Binding Capacity (UIBC) parameter revealed that 3.6% (11) of the children exhibited values below the reference range, while the majority, comprising 94.4% (285) of the cohort, fell within the reference range, and 2% (6) had values above the reference range. Similarly, the analysis of the Total Iron-Binding Capacity (TIBC) parameter showed that 2.3% (7) of the children had values below the reference range, 97% (293) fell within the reference range, and 0.7% (2) had values above the reference range. On the other hand, ferritin parameter, 7.9% (24) of the children had values below the reference range, 90.7% (274) fell within the reference range, and 1.3% (4) had values above the reference range.

Table 2. Distribution of biochemical parameters of children included in the study according to reference values

Biochemical Parameters	Below the Reference Value		Within the Reference Range		Above the Reference Value	
	n	%	n	%	n	%
Iron	102	33.8	196	64.9	4	1.3
UIBC	11	3.6	285	94.4	6	2.0
TIBC	7	2.3	293	97.0	2	0.7
Calcium	6	2.0	295	97.7	1	0.3
Glucose	26	8.6	255	84.4	21	7.0
IgM	22	7.3	280	92.7	-	-
Sodium	34	11.3	266	88.1	2	0.7
Potassium	1	0.3	285	94.4	16	5.3
IgA	71	23.5	219	72.5	12	4.0
ALT	-	-	300	99.3	2	0.7
AST	-	-	267	88.4	35	11.6
Creatinin	297	98.3	5	1.7	-	-
CRP	-	-	168	55.6	134	44.4
Ferritin	24	7.9	274	90.7	4	1.3
Folate	7	2.3	295	97.7	-	-
Free T4	15	5.0	286	94.7	1	0.3
TSH	9	3.0	289	95.7	4	1.3
Vitamin B12	13	4.3	264	87.4	25	8.3
Vitamin D	214	70.9	88	29.1	-	-

Subsequent statistical analysis demonstrated no statistically significant difference between the UIB, TIBC, and ferritin parameters in the cohort of children under investigation.

Regarding the calcium parameter, 2% (6) of the children had values below the reference range, 97.7% (295) fell within the reference range, and 0.3% (1) had values above the reference range. For sodium parameter, 11.3% (34) of the children had values below the reference range, 88.1% (266) fell within the reference range, and 0.7% (2) had values above the reference range. As for potassium parameter, 0.3% (1) of the children had values below the reference range, 94.4% (285) fell within the reference range, and 5.3% (16) had values above the reference range. Statistical analysis demonstrated no statistically significant difference between the calcium, sodium and potassium parameters in the cohort of children under investigation.

For glucose parameter, 8.6% (26) of the children had values below the reference range, 84.4% (255) fell within the reference range, and 7% (21) had values above the reference range. Statistical analysis demonstrated no statistically significant difference between the glucose parameter in the cohort of children under investigation.

In the case of IgM parameter, 7.3% (22) of the children had values below the reference range, and 92.7% (280) fell within the reference range. With respect to IgA parameter, 23.5% (71) of the children had values below the reference range, 72.5% (219) fell within the reference range, and 4% (12) had values above the reference range. The data indicate that a proportion of children with PEM had IgM (7.3%) and IgA (23.5%) values below the reference range. These immunoglobulins play a crucial role in the immune response, defending the body against infections and diseases. Lower than normal IgM and IgA levels could increase the susceptibility of these children to infections and hinder their recovery process.

ALT parameter was within the reference range for 99.3% (300) of the children, and 0.7% (2) had values above the reference range. As for AST parameter, 88.4% (267) of the children had values within the reference range, and 11.6% (35) had values above the reference range. Liver enzymes ALT and AST were within the reference range for the majority of children with PEM, indicating that liver function was relatively preserved. However, a small percentage (0.7%) had elevated ALT levels, and 11.6% had elevated AST levels. Liver dysfunction could further exacerbate the health challenges faced by children with PEM. Identifying the underlying causes of these enzyme elevations and providing necessary interventions are crucial to ensure hepatic health and support overall recovery.

In the case of creatinine parameter, 98.3% (297) of the children had values below the reference range, and 1.7% (5) fell within the reference range. Most children with PEM (98.3%) had creatinine values below the reference range.

For CRP parameter, 55.6% (168) of the children had values within the reference range, and 44.4% (134) had values above the reference range.

For folate parameter, 2.3% (7) of the children had values below the reference range, and 97.7% (295) fell within the reference range. Serum free T4 parameter showed that 5% (15) of the children had values below the reference range, 94.7% (286) fell within the reference range, and 0.3% (1) had values above the reference range. In terms of TSH parameter, 3% (9) of the children had values below the reference range, 95.7% (289) fell within the reference range, and 1.3% (4) had values above the reference range. As for vitamin B12 parameter, 4.3% (13) of the children had values below the reference range, 87.4% (264) fell within the reference range, and 8.3% (25) had values above the reference range. Statistical analysis demonstrated no statistically significant difference between these parameters in the cohort of children under investigation.

Vitamin D parameter showed that 70.9% (214) of the children had values below the reference range, and 29.1% (88) fell within the reference range. Protein-energy malnutrition (PEM) is commonly linked to inadequate intake of vitamin D.

The analysis results, presented in Table 3, compare the mean values of biochemical parameters based on the genders and ages of the included children. The table reveals statistically significant differences (P<0.05) in the mean values of Calcium, IgM, Folate, and TSH parameters between male and female children.

Moreover, upon examining the relationship between the ages of the children and the values of biochemical parameters, several noteworthy correlations were observed (P<0.05). There was a positive and low-level correlation between age and Iron, a negative and low-level correlation between age and UIBC, and another negative and low-level correlation between age and Calcium. Additionally, a positive and moderate-level correlation between age and Sodium, and a negative and low-level correlation between age and Potassium were found. Furthermore, the analysis indicated a positive and low-level correlation between age and IgA, a negative and low-level correlation between age and ALT, and a negative and moderate-level correlation between age and AST. Moreover, there was a positive and moderate-level correlation between age and Creatinine, and a negative and low-level correlation between age and CRP. Additionally, age showed a negative and moderate-level correlation with Folate, a positive and low-level correlation with Free T4, and a negative and low-level correlation with TSH. Lastly, age displayed a negative and low-level correlation with Vitamin D. It is crucial to establish diagnostic criteria that can be applied universally across different ages and developmental stages, as this is an essential requirement for accurately assessing the prevalence of rickets. Nonetheless, no significant relationships were found between age and the remaining parameters (P>0.05).

Table 3. Comparison of mean values of biochemical parameters based on the sex and age of the included children

Biochemical Parameters	Female X±SD	Male X±SD	Total X±SD	P^T	Age^r
Iron	55.23±31.73	56.84±31.13	56.00±31.40	0.656	0.218*
UIBC	253.17±67.77	247.01±60.19	250.21±64.21	0.406	-0.147*
TIBC	322.08±62.38	315.75±62.55	319.04±62.44	0.379	0.063
Calcium	9.89±0.46	9.76±0.47	9.83±0.47	0.013*	-0.143*
Glucose	87.87±12.62	88.81±12.83	88.32±12.71	0.521	-0.060
IgM	63.81±31.50	76.71±32.13	70.00±32.40	0.000*	-0.015
Sodium	138.02±3.56	138.27±2.91	138.14±3.26	0.506	0.310*
Potassium	4.38±0.36	4.43±0.45	4.40±0.41	0.247	-0.136*
IgA	64.19±54.80	69.02±55.36	66.51±55.03	0.448	0.196*
ALT	14.40±7.32	14.38±5.08	14.39±6.33	0.977	-0.218*
AST	28.98±8.95	30.64±6.94	29.78±8.08	0.073	-0.371*
Creatinine	0.35±0.12	0.36±0.12	0.36±0.12	0.789	0.557*
CRP	2.58±4.56	2.79±5.32	2.68±4.93	0.711	-0.133*
Ferritin	49.36±36.68	41.17±47.21	45.43±42.19	0.092	-0.021
Folate	11.83±4.43	10.78±4.15	11.33±4.33	0.036*	-0.304*
Free T4	1.26±0.19	1.27±0.17	1.26±0.18	0.799	0.212*
TSH	2.34±1.20	2.05±0.83	2.20±1.05	0.015*	-0.180*
Vitamin B12	458.74±196.95	470.71±251.06	464.49±224.26	0.644	-0.019
Vitamin D	24.12±11.56	26.86±14.29	25.43±12.99	0.066	-0.206*

*= P<0.05, r= Pearson correlation, T= Independent samples t-test.

4. Discussion

Distribution of biochemical parameters among the children included in the study, based on reference values. The data reveal that a considerable proportion of children with PEM, approximately 33.8%, exhibited iron values below the reference range. This finding highlights the high prevalence of iron deficiency in this vulnerable population. The majority of studies indicated that iron deficiency was the leading cause of anemia in patients with protein-energy malnutrition (Said et al., 1975; Nkrumah et al., 1988; Borelli et al., 2004). In a study conducted it was revealed that 97% of the participants in the experimental group had anemia, and approximately 67% of them had low serum iron level. Iron deficiency can exacerbate the consequences of PEM, leading to impaired growth, compromised immune function, and cognitive deficits. Proper management of iron deficiency becomes crucial in these children to support their recovery and overall health. Remarkably, the investigation of the Unsaturated Iron-Binding Capacity (UIBC) parameter revealed that 3.6% of the children exhibited values below the reference range, while the majority, comprising 94.4% of the cohort, fell within the reference range, and 2% had values above the reference range. Similarly, the analysis of the Total Iron-Binding Capacity (TIBC) parameter showed that 2.3% of the children had values below the reference range, 97% fell within the reference range, and 0.7% had values above the reference range. On the other hand, ferritin parameter, 7.9% of the children had values below the reference range, 90.7% fell within the reference range, and 1.3% had values above the reference range. Subsequent statistical analysis demonstrated no statistically significant difference between the UIB, TIBC, and ferritin parameters in the cohort of children under investigation. Although the differences between the studies are thought to be due to the sample taken, it is noteworthy that conditions such as iron deficiency aggravate the consequences of PEM (Borelli et al., 2004).

For glucose parameter, 8.6% of the children had values below the reference range, 84.4% fell within the reference range, and 7% had values above the reference range. Statistical analysis demonstrated no statistically significant difference between the glucose parameter in the cohort of children under investigation.

In the case of IgM parameter, 7.3% of the children had values below the reference range, and 92.7% (280) fell within the reference range. With respect to IgA parameter, 23.5% of the children had values below the reference range, 72.5% fell within the reference range, and 4% (12) had values above the reference range. The data indicate that a proportion of children with PEM had IgM and IgA values below the reference range. These immunoglobulins play a crucial role in the immune response, defending the body against infections and diseases. Lower than normal IgM and IgA levels could increase the susceptibility of these children to infections and hinder their recovery process (Nielsen and Hejgaard, 2011).

ALT parameter was within the reference range for 99.3% of the children, and 0.7% had values above the reference range. As for AST parameter, 88.4% of the children had values within the reference range, and 11.6% had values above the reference range. Liver enzymes ALT and AST were within the reference range for the majority of children with PEM, indicating that liver function was relatively preserved. However, a small percentage (0.7%) had elevated ALT levels, and 11.6% had elevated AST levels. Liver dysfunction could further exacerbate the health challenges faced by children with PEM. Identifying the underlying causes of these enzyme elevations and providing necessary interventions are crucial to ensure hepatic health and support overall recovery.

In the case of creatinine parameter, 98.3% of the children had values below the reference range, and 1.7% fell within the reference range. A well-established characteristic of severe chronic renal failure is the spontaneous decrease in dietary protein intake (Kopple, 1999). There is some evidence suggesting that the reduction in protein intake initiates at an early stage of declining renal function (Ikizler et al., 1995). Malnutrition serves as a prognostic indicator for both morbidity and mortality (Soucie and McClellan, 1996). Most children with PEM (98.3%) had creatinine values below the reference range. Creatinine is a marker of kidney function, and low levels may signify impaired renal health in these individuals.

For CRP parameter, 55.6% of the children had values within the reference range, and 44.4% had values above the reference range. The data demonstrate that a significant proportion of children with PEM (44.4%) had CRP values above the reference range. CRP is an indicator of inflammation, and elevated levels suggest an ongoing inflammatory response in these children (Pepys and Hirschfield, 2003). Inflammation can exacerbate PEM's effects and hinder recovery. A study conducted by Sauerwein et al. demonstrated significantly elevated levels of C-reactive protein (CRP) in children with Protein-Energy Malnutrition (PEM) when compared to the control group (Sauerwein et al., 1997).

Vitamin D parameter showed that 70.9% of the children had values below the reference range, and 29.1% fell within the reference range. Protein-energy malnutrition (PEM) is commonly linked to inadequate intake of vitamin D. Additionally, certain individuals with apparently sufficient ultraviolet (UV) exposure may exhibit low serum vitamin D concentrations, attributed to variations in skin pigmentation levels (Binkley et al., 2007).Research investigations have consistently reported a significant prevalence of vitamin D deficiency among children with Protein-Energy Malnutrition (PEM) in comparison to control groups (Amira and Abdel, 2004).

Compare the mean values of biochemical parameters based on the genders and ages of the included children. The table reveals statistically significant differences ($p<0.05$) in the mean values of Calcium, IgM, Folate, and TSH parameters between male and female children. In a study focused on malnutrition among elderly residents in a nursing home, it was observed that the calcium levels were lower in male individuals. Conversely, in Uckun's (2016) investigation of severe short stature, no significant gender-based difference was identified in the TSH ratio. Specifically, female children exhibited higher mean values of Calcium and Folate, whereas male children had higher mean values of IgM and TSH. In a study carried out in Indonesia, it was observed that girls exhibit lower levels of vitamin D, possibly due to their reduced outdoor activities (Onal et al., 2016). In contrast to our findings, investigations into dietary calcium intake have revealed that only a quarter of adolescent girls manage to meet their daily calcium requirements (Chaki, 2017).

Moreover, upon examining the relationship between the ages of the children and the values of biochemical parameters, several noteworthy correlations were observed ($P<0.05$). There was a positive and low-level correlation between age and Iron, a negative and low-level correlation between age and UIBC, and another negative and low-level correlation between age and Calcium. In a study investigating malnutrition among children with cerebral palsy, no significant differences were observed in calcium levels across different age groups of children. While the traditional focus of iron supplementation has been on pregnant women and children under two years old, recent research suggests that the target group should also encompass all women of childbearing age, as well as preschool children and adolescents. Administering iron support to pregnant women with optimal iron stores enhances its effectiveness during pregnancy and mitigates the risk of iron deficiency in both the mother and the newborn post-delivery (UNICEF, 2013). Additionally, a positive and moderate-level correlation between age and Sodium, and a negative and low-level correlation between age and Potassium were found. Furthermore, the analysis indicated a positive and low-level correlation between age and IgA, a negative and low-level correlation between age and ALT, and a negative and moderate-level correlation between age and AST. Moreover, there was a positive and moderate-level correlation between age and Creatinine, and a negative and low-level correlation between age and CRP. Additionally, age showed a negative and moderate-level correlation with Folate, a positive and low-level correlation with Free T4, and a negative and low-level correlation with TSH. Lastly, age displayed a negative and low-level correlation with Vitamin D. The radiographic scoring method developed and validated by Thacher and colleagues was originally intended for use in children aged 12 months and older, who possessed independent mobility. However, in Nairobi, rickets affects a much younger age group and is often linked to a high frequency of motor developmental delay in these children (Thacher et al., 2002; Edwards et al., 2014; Munns et al., 2016). It is crucial to establish diagnostic criteria that can be applied universally across different ages and developmental stages, as this is an essential requirement for accurately assessing the prevalence of rickets. Nonetheless, no significant relationships were found between age and the remaining parameters.

The primary limitation of our discussion stems from the fact that nearly none of the studies carried out on children diagnosed with protein-energy malnutrition have compared their biochemical parameters with individual demographic information. Given that demographic data significantly influence these parameters, it becomes crucial to augment such research endeavors aimed at elucidating this matter.

5. Conclusion

In conclusion, the current study sought to explore the distribution of various biochemical parameters in children diagnosed with protein-energy malnutrition (PEM). The findings of this research provide valuable insights into the prevalence of abnormal biomarker values among these children, offering a comprehensive understanding of the role these parameters play within the context of PEM. The results revealed that a considerable proportion of children with PEM exhibited deficiencies in iron, an essential element crucial for growth, immune function, and cognitive development. It is essential to note that the diagnostic criteria for rickets need to be universally applicable, accounting for different age groups and developmental statuses. While this study has provided valuable insights into the biochemical profile of children with PEM, it is crucial to acknowledge the limitations. The absence of comprehensive demographic data integration in existing studies hinders a holistic understanding of the factors influencing these parameters. Future research endeavors should focus on bridging this gap, enabling a more comprehensive assessment of the intricate relationship between demographic variables and biochemical profiles in children diagnosed with PEM. In essence, this study contributes to our understanding of the intricate biochemical dynamics associated with protein-energy malnutrition in children. The findings underscore the need for targeted interventions addressing specific deficiencies and potential complications, aiming to improve the health outcomes and overall well-being of this vulnerable population.

Based on the obtained results, it is recommended that pediatric nurses focus their efforts on addressing protein-energy malnutrition and consider children within the context of nutritional disorders. Given its status as a significant public health concern, it holds paramount importance to impart education to families residing in rural areas about proper child nutrition practices.

Limitations and Strengths of the Study

The primary limitation of our discussion stems from the fact that nearly none of the studies carried out on children diagnosed with protein-energy malnutrition have compared their biochemical parameters with individual demographic information. Given that demographic data significantly influence these parameters, it becomes crucial to augment such research endeavors aimed at elucidating this matter.

The strengths of our study are anchored in the rigorous and comprehensive examinations and laboratory analyses conducted on the patient cohort from which our data were derived.

Author Contributions

The percentage of the author(s) contributions is presented below. All authors reviewed and approved the final version of the manuscript.

	E.G.	N.K.
C	70	30
D	70	30
S	50	50
DCP	70	30
DAI	60	40
L	60	40
W	50	50
CR	70	30
SR	80	20
PM	70	30
FA	50	50

C=Concept, D= design, S= supervision, DCP= data collection and/or processing, DAI= data analysis and/or interpretation, L= literature search, W= writing, CR= critical review, SR= submission and revision, PM= project management, FA= funding acquisition.

Conflict of Interest

The authors declared that there is no conflict of interest.

Ethical Approval/Informed Consent

This study was approved by Ethics Committee of Iğdır University (approval date: October 27, 2023, protocol code: E-37077861-900-119343,). Before collecting study data, written permissions were obtained from the relevant hospital (permission date: 19.01.2023).

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