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Prospective Analysis of Pre-Operative Nutritional Indices and Micronutrients Affecting Outcome in Children Undergoing Surgery

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ABSTRACT

Background: Optimum nutrition is necessary for a child's growth, development and recovery from illness or disease. This study has analysed pre-operative nutritional indices and micronutrients affecting outcome in children undergoing surgery.

Methods: In a prospective observational cohort study at a tertiary pediatric surgery center, 186 children aged three months to 17 years and planned for major elective surgery were recruited. Height for age, weight for age, mid-arm circumference, and triceps skin fold thickness were measured. Blood samples were drawn for albumin, prealbumin, transferrin, iron, ferritin, vitamin B12, zinc, folate, calcium, and vitamin D. The development of nutritional-associated complications were recorded too.

Results: Stunting was seen in 42.9%, while 28.2% needed blood transfusion, 7.1% required total parenteral nutrition, and 2.2% needed ventilator support. Totally, 19.5% developed wound infection and 8.7% required redo surgery. An association of zinc with incidents [OR=0.826, 95% CI: (0.708, 0.964)], folate with the need for transfusion [OR=0.92, 95% CI: (0.85, 0.99)], and serum iron with a need for total parenteral nutrition [OR=0.98, 95% CI: (0.95, 1.00)] was noticed. Triceps skin fold thickness was correlated with the length of stay and underweight with a need for transfusion, while stunting had no impact on outcomes.

Conclusion: The prevalence of malnutrition in children undergoing surgery was significant. Zinc was associated with adverse outcomes; while folate with the need for a blood transfusion. Underweight and triceps skin fold thickness had predictive potential. It seems that pre-operative identification and correction of these micronutrients deficiency before surgery may help in improving the outcomes.

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Introduction

Optimum nutrition is necessary for a child's growth, development and recovery from illness or disease. Nutrition in paediatric surgical patients does play a vital role in early recovery and outcome. Malnutrition is high among pediatric surgical patients particularly; patients undergoing gastrointestinal (GI) surgery due to anorexia, dietary restriction, malabsorption, increased intestinal losses or altered nutrient requirements. Moreover, the hypermetabolic state induced by surgical stress and postoperative restriction of oral intake can exaggerate malnutrition which results in reduced immunity and stress resistance (1). This can be regarded as a risk factor for complications such as infection, poor wound healing, GI tract bacterial overgrowth, prolonged hospital stays and mortality. Postoperative complications are an independent determinant of the length of hospital stay and healthcare costs for surgical patients. Reducing postoperative complications can thus potentially shorten the length of hospital stay, reduce healthcare costs, and improve patients' quality of life. While malnutrition is commonly regarded as a condition associated with low-income countries, the prevalence of malnutrition among hospitalized children in higher-income countries has been found to range from 6.1% to 35% (2, 3) and is hence a global phenomenon (4). The prevalence of undernutrition among children under five years of age in India is reported to be 35.7%, according to the national family health survey 4 (5). However, there is no data available regarding the prevalence of undernutrition in infants and children undergoing surgery.

Moreover, the data on the severity of micronutrient deficiency and its impact on this group remained limited. Though the evaluation of nutritional status forms the general part of the examination, there is a need to be more consensus on the predictive value of each test (6). There is a paucity of literature on assessing the role of nutrition, the method of screening, and nutrition-related complications in children undergoing surgery, especially from the Indian subcontinent. Hence, we sought to assess the prevalence of the impact of pre-operative nutritional status and micronutrient deficiency on children undergoing surgery. We sought to evaluate the relationship between pre-operative subjective examination, anthropometric assessment, and the micronutrient levels on post-surgical outcomes.

Materials and Methods

This prospective observational cohort study was performed at a tertiary hospital, the Department of Pediatric Surgery from January 2018 to January 2022 after appropriate ethical approval and CTRI registration (CTRI/2019/03/018036). The Advanced Center for Research at Rajiv Gandhi University of Health Sciences, Bangalore, funded this study (17M046). Children aged three months up to 17 years were included. Only children planned for major elective surgery and requiring admission for more than 48 hours were enrolled into the study. Children requiring emergency surgery, cancer-related surgery, day-care surgery, and minor urological conditions were excluded from the study. Those children with features of severe malnutrition were excluded from the study as they would not be deemed fit for elective surgical repair and received nutritional rehabilitation. This included those children with severe scores on Subjective Global Assessment (SGA) scoring. Basic demographic details, diagnosis, and type of surgery were documented.

After appropriate written informed consent from the parent and the subject, anthropometric measurements and SGNA were performed on admission (7). In addition, the nutritional history, pre-operative diagnosis, and any pre-operative stress due to the disease were investigated. Anthropometric details including weight, height or length, head circumference, mid-arm circumference, and triceps skin fold thickness (TSFT) were provided. The Indian Academy of Paediatricians (IAP) adaptation of World Health Organization (WHO) growth charts were used to calculate the Z scores of weight for height and weight for age. Small babies were weighed when lying on a scale. Older children were weighed standing up with a digital weighing scale. Weight was recorded after the removal of all the child's clothes, except the underpants, before weighing. Height was measured with the child standing bare foot. Both heels were kept on the floor with the child's back pressed against a wall. Height was measured on stadiometer. Children under 2 years or 90 cm in length were evaluated with the child lying down using infantometer.

Measurements for mid upper arm circumference (MUAC) was performed with WHO tape, and the TSFT was measured with calibrated callipers. Children with a Z score of <2 for height for age were considered stunted. Pre-existing medical and surgical risk factors which would influence the outcome were documented.

At the time of induction for surgery, blood samples were drawn and sent for analysis of nutritional markers and micronutrients. Biochemical analyses were performed using standardized techniques. Cobas® 6000 analysers (series version-8.1) with software version - 05-02/06-02, from Roche Diagnostics were used for estimation of albumin, prealbumin, transferrin, ferritin, iron, vitamin B12, Zinc, folate, calcium, and Vitamin D. Serum albumin and iron were assessed using the colorimetric principle with ALB2 and Elecsys® kit Roche. Serum zinc was determined using the colorimetric principle with a Randox kit (Randox laboratories LTD, United Kingdom). Serum prealbumin and transferrin were evaluated using an immunoturbidimetric assay principle with PREA and TRSF2 kit respectively (Roche®). The competition principle using photomultiplier was used to assess serum folate, vitamin B12, vitamin D, and ferritin (Elecsys® kit Roche). ELISA principle was applied for the estimation of serum vitamin A and retinol binding protein with a microplate ELISA washer (Tulip Diagnostics Private Limited, India). VA ELISA kit and Human RBP4 ELISA kit from Elabscience, USA were utilized for estimation of vitamin A and retinol binding protein, respectively.

Children were followed up from the day of surgery till discharge and up to 30 days after surgery. During surgery, we documented the type of surgery, duration (surgical time only), need for blood transfusion, and any unrelated event. In the postoperative period, the need for ventilation, parenteral nutrition, additional blood transfusion, wound infection, or the development of other nutritional-associated complications like wound infection, dehiscence, anastomotic leak, intestinal obstruction, and redo surgery, if any were documented (1, 7). The time to start feeding and the length of hospital stay (LOS) were determined. Complications like occurrences of complications requiring readmission and surgery were recorded during one month's follow-up. Based on the duration of the surgery, the children were divided into three groups. Surgery duration of 45 mins-2 hours, 2-3 hours, 3-4 hours, and >4 hours. The effect of outcomes with each variable was calculated to assess their independent correlation.

All the statistical calculations were done using SPSS software (version 20, Chicago, IL, USA). Descriptive data were reported as frequency and percentages for reporting anthropometry and micronutrient deficiency. The Chi-square and Fisher's exact tests were used to analyse categorical variables. After checking for collinearity of independent quantitative variables, the variables were identified for developing a model for the outcome variables, i.e., incidents, redo surgery, blood transfusion, ventilation, LOS, undernutrition, TSFT, albumin, prealbumin, transferrin, duration of surgery (as categorical variables), zinc, folate, iron, calcium, and vitamin D.

Table 1: Characteristics of study population (n-186) showing gender distribution, surgery characteristics and duration of surgery.

Gender	
Male	102
Female	84
Age (mean)	
3 months-2 years	82
2 years-5 years	44
5 years-12 years	45
12 years-18 years	15
Primary surgical procedures	
Posterior Saggital Anorecto Plasty, Pull through, colostomy closure, colostomy, bowel resection and anastomosis	93
Excision of cysts (mesenteric cyst, duplication cyst), mesenteric lymph node biopsy)	7
Cholecystectomy	4
Kasai's portoenterostomy	3
Choledochal cyst	9
Shunt procedure for Extra hepatic portal vein obstruction	12
Cardiomyotomy and fundoplication	5
Splenectomy	3
Malrotation	2
Drainage procedures for chronic pancreatitis	4
Other abdominal surgeries	16
Thoracic procedures	3
Urological procedures (Exstrophy Epispadias Complex repair, bladder augmentation, urethral stricture repair, hypospadias)	25
Duration of surgery	
45 min-2 hours	61
2 hours-3 hours	46
3 hours-4 hours	24
>4 hours	55
Total	186

Results

Out of 186 children who fulfilled the inclusion criteria, 172 were available for final analysis. Table 1 shows the baseline demographics, including the type of surgical procedures and duration of surgery. Seventy-six percent of the children who underwent surgery were undernourished, while stunting and underweight were 41.5 % and 59.5 %, respectively. TSFT was below normal in 19% of the children (Table 2). Prealbumin was the most common nutritional marker deficiency, while among micronutrients, vitamin D deficiency was the highest seen, followed by iron and zinc. multiple micronutrient deficiencies (>3) were demonstrated in 30 children (18.29%, Table 2). Events documented during the study period were highlighted in Figure 1.

Fifty (28.2%) children needed a blood transfusion, 36 children developed wound infection (19.5%), 13 (7.1%) children required total parenteral nutrition (TPN), and 4 (2.2%) needed ventilator support. The average length of hospital stay was 6.2 days. The time to start feeding was 3.7 days. A total of 20 (11%) incidents were observed in our study, including the follow-up period. Redo surgery in the postoperative period was necessary in 16 (8.7%), while four were

Table 2: Prevalence of malnutrition and micronutrient deficiencies in study population.

Variable	Number (%)
Anthropometric. Parameters	
1. Stunting	
Z score less than -2	73 (41.5)
2. Undernourished (MUACZ)	
Z score less than -2	86 (76.8)
3. Underweight	
Z score less than -2	91 (59.5)
4. TSFT	
Low	32 (19.1)
5. Nutritional markers	
Albumin	83 (45.35)
Prealbumin	106 (60.22)
Transferrin	24 (13.11)
Ferritin	34 (18.68)
6. Micronutrient	
Iron	109 (59)
Vitamin B12	51 (28.02)
Calcium	31 (17)
Zinc	34 (21.65)
Folate	31 (19.21)
Vitamin D	111 (63.79)

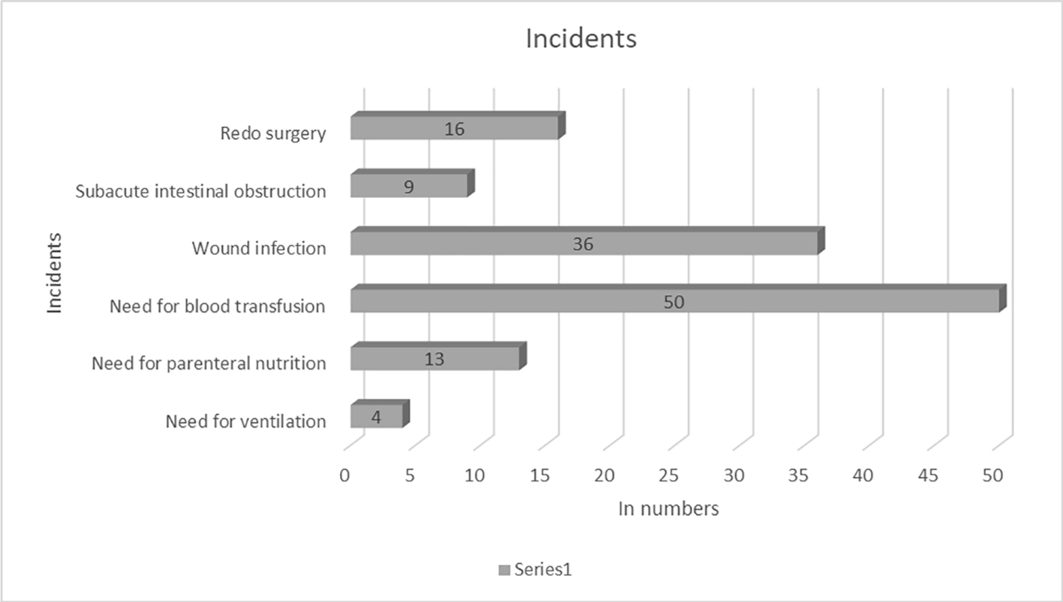

Figure 1: Events documented during the study period.

managed conservatively. Underweight children had a higher incidence of blood transfusion [OR=1.41, 95% CI: (0.54, 3.67)] though they did not achieve statistical significance (Table 3). Iron deficiency was related to the need for TPN. The odds of need for TPN were lower for 1 unit increase in the average of iron [OR=0.98, 95% CI: (0.95, 1.00)] (Table 3). Prealbumin deficiency was closely related to the need for blood transfusion. Though it did not achieve statistical significance (Table 3). Albumin and transferrin had no impact on the occurrence of incidents, need for blood transfusion, ventilation, or redo surgery (Table 4). Zinc was directly related to outcomes. The odds of having incidents were

Table 3: Regression model for blood transfusion and for need of total parenteral nutrition.

Variable	Occurrence of blood transfusion		
	Number	**Unadjusted odds ratio**	**Adjusted odds ratio**
Underweight	124	2.04 (0.92, 4.51)	1.32 (0.49, 3.63)
Duration of surgery	124	2.15 (1.65, 2.78)	2.03 (1.45, 2.84)*
Pre-albumin	124	0.91 (0.84, 0.99)	0.92 (0.83, 1.02)
Folate	124	0.91 (0.85, 0.97)	0.92 (0.85, 0.99)*
Factor	Need for TPN		
	Number	**Unadjusted odds ratio**	**Adjusted odds ratio**
Iron	124	0.97 (0.95, 1.00)	0.98 (0.95, 1.00)
Vitamin B12	124	1.00 (1.00, 1.01)	1.00 (0.99, 1.01)

*Significant effect. The variables significant for the model blood transfusion are stunting (based on HAZ), underweight (based on WAZ), SGN, duration of surgery (as continuous variable), Pre-albumin (as continuous variable) and folate (as continuous variable). Multiple logistic regression model for blood transfusion. The variables being significant for the model of blood transfusion of stunting (based on height for age), underweight (based on weigh for age), duration of surgery (as continuous variable), pre-albumin (as continuous variable) and folate (as continuous variable).

Table 4: Logistic regression model for incidents and for redo surgery.

Variables in the equation		B	SE	Wald	df	Sig.	Exp(B)	95% CI for EXP (B)	
								Lower	**Upper**
Step1[a]	TSFT (mm)	0.134	0.100	1.801	1	0.180	1.144	0.940	1.392
	Albumin	-0.272	0.925	0.087	1	0.769	0.762	0.124	4.668
	Transferrin	-0.001	0.006	0.043	1	0.836	0.999	0.987	1.011
	Duration of surgery			3.663	3	0.300			
	Duration of surgery (2-3 hours)	1.050	1.102	0.907	1	0.341	2.857	0.329	24.789
	Duration of surgery (3-4 hours)	1.340	1.041	1.658	1	0.198	3.818	0.497	29.353
	Duration of surgery (>4 hours)	1.773	0.938	3.572	1	0.059	5.889	0.937	37.033
	Zinc	-0.191	0.079	5.860	1	0.015	0.826	0.708	0.964
	Folate	0.064	0.043	2.272	1	0.132	1.066	0.981	1.159
	Vitamin D	0.032	0.040	0.664	1	0.415	1.033	0.955	1.117
	Constant	-1.098	3.267	0.113	1	0.737	0.334		
Variable									
Step 1[a]	TSFT (mm)	0.012	0.102	0.014	1	0.905	0.988	0.809	1.207
	Albumin	0.235	0.807	0.085	1	0.771	1.265	0.260	6.150
	Transferrin	0.004	0.006	0.563	1	0.453	0.996	0.985	1.007
	Duration of surgery			2.538	3	0.468			
	Duration (2-3 hours)	-0.482	0.985	0.240	1	0.624	0.617	0.090	4.256
	Duration (3-4 hours)	0.742	0.888	0.699	1	0.403	2.100	0.369	11.962
	Duration (>4 hours)	0.796	0.773	1.060	1	0.303	2.217	0.487	10.088
	Zinc	0.011	0.064	0.029	1	0.866	1.011	0.892	1.146
	Folate	0.068	0.059	1.361	1	0.243	0.934	0.832	1.048
	Vitamin D	0.016	0.038	0.185	1	0.667	1.016	0.944	1.095
	Constant	1.941	3.10	0.392	1	0.531	0.144		

a. Variable(s) entered on step 1: TSFT (mm), Albumin, Transferrin, Duration of surgery, Zinc, Folate, Vitamin D, Tricep skin fold thickness (TSFT), Logistic regression co-efficient (B), Standard error (SE), Parameter estimate i.e. B/SE (Wald), Significance (Sig), Odds ratio [Exp (B)]. Confidence interval (CI), Degree of freedom (df).

Table 5: Regression model for LOS.

Coefficients

Model		**Unstandardized coefficients**		**Standardized coefficients**	**t**	***p* value**
		B	**SE**	**Beta**		
1	(Constant)	7.886	1.511		5.220	0.000
	Zinc	-0.032	.042	-0.070	-0.761	0.448
	Folate	-0.001	0.031	-0.003	-0.036	0.971
	Vitamin D	0.019	0.025	0.069	0.741	0.460
	Pre-albumin	-0.020	0.048	-0.040	-0.423	0.673
	Transferrin	0.002	0.003	0.053	0.589	0.557
	TSFT (mm)	-0.175	0.065	-0.257	-2.677	0.009

Length of hospital stay (LOS), Logistic regression co-efficient (B), Standard error (SE), parameter estimate i.e. B/SE (t). The model is constructed using linear regression. The result shows that if all the other factors are adjusted, the average length of hospital stay is 1.25 lower for low TSFT, but is not statistically significant. After excluding the cases with LOS>20 (removed 9 cases), the variable LOS was approximately normally distributed. The model is constructed using linear regression.

significantly lower as the value of zinc increased [OR=0.826, 95% CI: (0.708, 0.964)]. Similarly, the odds of incidents were significantly lower for 1 unit increase in calcium [OR=0.34 95% CI: (0.13, 0.92)] (Table 4). Folate was related to the need for blood transfusion. The odds for blood transfusion were significantly lower as the value of folate increased [OR=0.92, 95% CI: (0.85, 0.99)] (Table 3). Vitamin D was the most common deficiency in our study group, and along with vitamin B-12, they did not have any impact on the surgical outcomes studied (Table 4). TSFT was associated with LOS. It was observed that when other variables in the model were adjusted for a unit increase in TSFT, the average LOS decreased by 0.175 units (Table 5). Stunting had no impact on outcomes. SGNA was not used in the final assessment as we excluded those children with severe scores from the study.

Discussion

In this study, we have identified the impact of micronutrient deficiency, nutritional markers, and anthropometry on outcomes in children undergoing major surgery. The prevalence of malnutrition in our study population was significant. Fifty-nine percent of our children were underweight, 41% were stunted, and 19% with TSFT. In the NFWS-4, the reported prevalence of underweight and stunting in India was 37.5% and 38%, respectively (5). The high incidence of underweight children in our study could be related to the underlying disease process with increased metabolic activity.

In our study, the most common micronutrient deficiency was vitamin D, followed by iron, vitamin B12, and zinc. Our finding is very similar to the findings of micronutrient deficiency in a recently published systematic review of micronutrient deficiency in India by Venkatesh *et al.* (8). Multiple micronutrient deficiencies were identified in 34% of our study group. Stunting was seen in about 42 % of our study population; however, it had no significant impact on the outcomes. There are varied findings on using height/age as an outcome marker. Secker *et al.* reported a statistically significant association between height for age and prolonged length of stay in children undergoing surgical procedures (7). Similar findings were reported by Toole *et al.* in their retrospective study on children undergoing surgery for congenital heart defects. Conversely, the moderate chronically-malnourished children in their series had better outcomes when compared to all groups, including the group that was not malnourished (9).

In our study, pre-operative weight-for-age was associated with a need for blood transfusion, though it did not achieve statistical significance. A similar association has not been reported with few studies reporting an association between underweight with postoperative outcomes (10). TSFT assessed the subcutaneous body fat distribution. The results of our study showed that the odds of having incidents were 1.14 times higher for lower values of TSFT. Also, children having higher TSFT had significantly reduced length of hospital stay when other variables in the model were adjusted for a unit increase in TSFT; 0.175 units decrease the average LOS. Radman *et al.* conducted a prospective study on children undergoing cardiac surgery. They reported that TSFT Z-scores were correlated with ICU length of stay, postoperative mechanical ventilation duration, and inotrope infusion (11). However, Secker *et al.* in their study of non-cardiac surgery patients reported no correlation between TSFT and postoperative clinical outcomes (6).

In this study, serum albumin was not significantly associated with postoperative outcomes. Historically, serum albumin and prealbumin measurement were used as a marker for nutritional status. Rismala-Dewi *et al.* in their retrospective analysis of 201 children undergoing abdominal surgery reported that pre- and postoperative serum albumin levels of ≤3.00 g/dL were associated with a higher risk of postoperative sepsis and relaparotomy (12). Also, the median length of ICU stay was four days higher among them. Secker *et al.* in their prospective study on 175 children undergoing major thoracic or abdominal surgeries found that serum albumin results were correlated with infectious complications, antibiotic use, and length of stay (8).

In our study, it was observed that prealbumin was correlated with the need for blood transfusion. There was a 9% decrease in the odds of blood transfusion for one unit increase in prealbumin, though not reaching significance. Similar findings have not been reported earlier. Radman reported serum prealbumin levels were less than 12.1 mg/dL and were associated with a statistically significant increase in the duration of inotropic support postoperatively (11). Despite its historical utility, studies need to be more consistent in proving the utility of serum markers as determinants of a patient's nutritional status. Albumin and prealbumin are negative acute-phase proteins that are produced by the liver, while lacking specificity under acute metabolic stress and inflammation. Thus, it is affected by some of the same inflammatory states, such as infections and liver disease (11).

There were varying degrees of micronutrient deficiency in our study. Thirty-four percent were associated with multiple micronutrient deficiencies. The most common micronutrient deficiency in our study was vitamin D, which was identified in 63% of our children. However, this deficiency was not related to any adverse outcomes. Therefore, in a recent systematic review, the authors aimed to compare risks for diverse post-surgical outcomes with perioperative measures of vitamin D status in both adult and pediatric patients (13). Despite, several limitations due to the heterogeneous population and surgical procedures, they concluded that it would be advisable to test and or treat vitamin D deficiency before surgery.

Zinc is an essential micronutrient cofactor for many metalloenzymes required for cell membrane repair, cell proliferation, growth, and immune system function. The pathological effects of zinc deficiency include impaired immune function and compromised wound healing (14). In this study, serum zinc levels were significantly related to incidents. There was a 13% decrease in the odds of incidents for one unit increase in zinc. It was observed that the odds of having incidents were significantly lower as the value of zinc increases. Zinc deficiency was shown to significantly predict the survival outcome in solid malignancies, broadly consistent across subgroups postulating chemotoxicities due to impaired mucosal healing, compromising the dose intensity and subsequent outcomes (15-20).

Folate, also known as vitamin B9 and Vitamin B12 is involved in synthesizing nucleic acid, blood cells, and nervous tissue. Our study showed that folate level was significantly related to the need for blood transfusion. It was noticed that the odds of blood transfusion were significantly lower as the value of folate increased. There was a 10% decrease in the odds of the need for blood transfusion for one unit increase in folate. We found that iron deficiency was correlated with the need for TPN. The odds of the need for TPN were lower for a unit increase in the average of iron. No other literature reports on surgical outcomes were correlated with zinc, folate, iron, ferritin, vitamin B12, and calcium. Our study is the first reporting the relationship of these micronutrients with surgical outcomes.

In Summary, we evaluated the prevalence of malnutrition indices and micronutrient deficiencies on the impact of outcomes in children undergoing major surgery. We identified some markers which need further evaluation for establishing their predictive potential in children undergoing major surgeries. Serum zinc level and folate level were rated to incidents and need for transfusion, respectively. Stunting and routinely estimated markers like albumin individually did not impact the outcomes. In future studies, we hope to validate these findings of micronutrient deficiency and post-interventional outcomes in children undergoing surgery. The limitations of our study were that we excluded children from severe SGA groups. Furthermore, our study only assessed the association between the pre-operative variables and postoperative outcomes. Additionally, we did not correlate the micronutrient level with inflammatory markers which could alter the deficiency levels. Initial anthropometric assessment may help in identifying nutritionally at-risk children, who may benefit from nutritional rehabilitation interventions. By well-timed nutritional interventions in malnourished children, better surgical outcomes may be achieved.

Conclusion

The prevalence of malnutrition in children undergoing surgery was significant. Zinc was associated with adverse outcomes while, folate with the need for a blood transfusion. Underweight and triceps skin fold thickness had a predictive potential. Therefore, pre-operative identification and correction of these micronutrients deficiency before surgery may help in improving the outcomes.

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Conflict of Interest

None declared.

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