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THE PHYSIOLOGICAL AND PHARMACOLOGICAL ROLE OF VITAMIN D IN IMMUNE MODULATION AND INFECTION OUTCOMES AMONG MALNOURISHED PEDIATRIC PATIENTS IN LOW-INCOME SETTINGS

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ABSTRACT

Background: To assess the 'physiological and pharmacological role of Vitamin D in immune modulation and to determine its association with infection outcomes' among malnourished pediatric patients.

Methods: A cross-sectional study was conducted at the Department of Pediatrics, Hayatabad Medical Complex, Peshawar, from January 2023 to January 2024. A total of 73 malnourished children aged 6 months to 10 years were enrolled. Anthropometric indices, serum 25(OH)D, calcium, phosphate, alkaline phosphatase, hemoglobin, and C-reactive protein were measured. Infection outcomes including respiratory and diarrheal episodes, hospital stay, recurrent infections, and mortality were recorded. Statistical analysis was performed using SPSS version 26 with significance set at $p < 0.05$.

Results: 'Vitamin D deficiency was detected in 61.6% (n=45) of participants'. Deficient children had significantly lower weight-for-age Z-scores (−2.9 ± 0.8 vs. −2.3 ± 0.7, p = 0.02) and MUAC (11.5 ± 1.1 cm vs. 12.2 ± 1.0 cm, p = 0.03). Biochemically, deficiency was associated with lower calcium levels (8.2 ± 0.7 vs. 8.8 ± 0.6 mg/dL, p = 0.01), higher alkaline phosphatase (320 ± 85 vs. 270 ± 74 U/L, p = 0.03), and elevated CRP positivity (53% vs. 29%, p = 0.04). Clinically, acute respiratory infections (64% vs. 36%, p = 0.01), diarrheal illnesses (56% vs. 32%, p = 0.03), longer hospital stays (7.2 ± 2.1 vs. 5.9 ± 1.8 days, p = 0.04), and recurrent infections (47% vs. 25%, p = 0.02) were significantly more frequent among deficient children.

Conclusion: Vitamin D deficiency was highly prevalent among malnourished children and significantly associated with increased infectious morbidity and prolonged hospitalization. Early

detection and supplementation strategies may improve immune function and reduce infection burden in resource-limited pediatric populations.

Keywords: Vitamin D, Immune modulation, Malnutrition, Pediatric infections, Low-income settings, Pakistan

INTRODUCTION

Malnutrition remains one of the leading causes of morbidity and mortality among children in low- and middle-income countries. It is estimated that nearly half of under-five deaths globally are linked to undernutrition, with Pakistan being one of the most affected regions in South Asia. Children who are malnourished not only suffer from stunted growth and impaired cognitive development but also have a substantially higher risk of infections such as pneumonia and diarrhea, which remain the foremost killers in this age group (1-3).

Vitamin D, traditionally recognized for its role in bone mineralization and calcium-phosphate homeostasis, has gained increasing attention for its immunomodulatory effects. Beyond skeletal health, Vitamin D regulates innate and adaptive immune responses by influencing macrophage activity, T-cell differentiation, and production of antimicrobial peptides such as cathelicidin and defensins. Deficiency in Vitamin D has been associated with heightened susceptibility to respiratory infections, gastrointestinal diseases, and poor recovery outcomes in children (4-6).

In low-resource settings, multiple factors contribute to Vitamin D deficiency. Limited dietary intake, inadequate sunlight exposure due to cultural clothing practices, darker skin pigmentation, and lack of fortified foods all play a role. When combined with protein-energy malnutrition, these deficiencies may further weaken immune responses and prolong the course of infectious illnesses. Evidence from global studies has shown that ‘Vitamin D supplementation can reduce the incidence of acute respiratory tract infections, particularly in individuals with baseline deficiency’. However, there is limited data from South Asia, where malnutrition and Vitamin D deficiency frequently coexist (7-9).

‘Given this background, the present study was designed to evaluate the physiological and pharmacological role of Vitamin D in immune modulation and to investigate its association with infection outcomes in malnourished pediatric patients admitted to a tertiary care hospital in Peshawar’. By identifying the extent of deficiency and its clinical impact, this study seeks to provide evidence for simple, cost-effective interventions that may help reduce infection-related morbidity among vulnerable children in low-income settings.

METHODOLOGY

This was a hospital-based cross-sectional observational study conducted at the Department of Pediatrics, Hayatabad Medical Complex, Peshawar. The study was carried out over a one-year period from January 2023 to January 2024. The primary objective was to evaluate the ‘physiological and pharmacological role of Vitamin D in immune modulation and its association with infection outcomes among malnourished pediatric patients in a low-income setting’. Ethical approval for the study was obtained from the Institutional Review Board of Hayatabad Medical Complex, Peshawar. Informed written consent was taken from parents or guardians before enrollment. Confidentiality of all participants was ensured by coding identifiers and restricting data access to the research team.

‘A total of 73 malnourished children aged between 6 months and 10 years were enrolled\’. Malnutrition was defined and classified according to the World Health Organization (WHO) growth standards using Z-scores for weight-for-age (WAZ), height-for-age (HAZ), and weight-for-height (WHZ). Only patients presenting with moderate to severe malnutrition were considered eligible.

Inclusion Criteria

- Children aged 6 months to 10 years.
- Clinically diagnosed moderate to severe malnutrition based on WHO Z-scores or MUAC <12.5 cm.

- Availability of consent from parents or legal guardians.

Exclusion Criteria

- Children on long-term corticosteroid or anticonvulsant therapy known to affect Vitamin D metabolism.
- Patients with chronic illnesses such as congenital heart disease, chronic kidney disease, or advanced liver disease.
- Children already receiving Vitamin D supplementation within the last three months.
- Cases with incomplete clinical or laboratory data.

All eligible children admitted to the pediatric unit during the study period were screened and those fulfilling the criteria were recruited consecutively. After obtaining written informed consent from parents or guardians, detailed demographic and socioeconomic data were recorded, including age, sex, residence (urban/rural), parental education, and monthly household income.

Nutritional assessment was performed through anthropometric measurements: weight (kg) using a digital scale, height/length (cm) with a stadiometer, and mid-upper arm circumference (MUAC) using a standard non-stretchable tape. 'WHO Anthro software was used to calculate Z-scores for weight-for-age, height-for-age, and weight-for-height'.

Clinical history was taken regarding breastfeeding status, dietary intake, vaccination, frequency of respiratory or diarrheal illnesses, hospital admissions, and prior episodes of recurrent infections. A general physical examination was conducted to look for clinical features of rickets or other micronutrient deficiencies.

Venous blood samples were collected under aseptic technique for biochemical analysis. Serum 25-hydroxy Vitamin D [25(OH)D] was measured using chemiluminescent immunoassay. Levels <20 ng/mL were considered deficient, 20–30 ng/mL insufficient, and >30 ng/mL sufficient. Other biochemical investigations included serum calcium, phosphate, alkaline phosphatase, hemoglobin, and 'inflammatory markers such as C-reactive protein (CRP)'.

The main outcome measures were the frequency of acute respiratory tract infections, diarrheal episodes, recurrent infections within six months, mean duration of hospital stay, and mortality. These outcomes were assessed through patient records, caregiver interviews, and follow-up data where available.

'Data were analyzed using Statistical Package for Social Sciences (SPSS) version 26'. 'Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages'. Comparison between Vitamin D deficient and sufficient groups was carried out using Student's t-test for continuous data and Chi-square test for categorical data. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Among the 73 malnourished pediatric patients enrolled, 45 (61.6%) were Vitamin D deficient, while 28 (38.4%) had sufficient Vitamin D levels. The mean age of children was comparable between the two groups (3.6 ± 1.2 vs. 3.9 ± 1.3 years, $p = 0.32$). Gender distribution showed no significant difference, with males slightly predominating in the deficient group (26 vs. 14). A higher proportion of children from rural areas were Vitamin D deficient (71.1% vs. 53.6%), though this trend did not reach statistical significance ($p = 0.18$). Socioeconomic status, however, demonstrated a significant association: the majority of deficient children belonged to low-income households (64% vs. 39%), whereas sufficient children were more evenly distributed across middle and higher socioeconomic brackets ($p = 0.04$).

Table 1. Demographic Characteristics of Malnourished Pediatric Patients (n=73)

Variable	'Vitamin D Deficient (n=45)'	'Vitamin D Sufficient (n=28)'	p-value
Age (years, Mean ± SD)	3.6 ± 1.2	3.9 ± 1.3	0.32
Sex (Male/Female)	26 / 19	14 / 14	0.48
Residence (Rural/Urban)	32 / 13	15 / 13	0.18
Socioeconomic status	Low 29 (64%), Middle 13 (29%), High 3 (7%)	Low 11 (39%), Middle 14 (50%), High 3 (11%)	0.04*

*Significant at $p < 0.05$

Nutritional profiling revealed that Vitamin D deficient children had significantly poorer anthropometric scores compared to their sufficient counterparts. The mean weight-for-age Z-score was markedly lower in the deficient group (−2.9 ± 0.8 vs. −2.3 ± 0.7, $p = 0.02$), indicating a higher prevalence of underweight status. Height-for-age Z-scores showed a trend toward greater stunting in deficient children, although this difference was not statistically significant ($p = 0.08$). Similarly, wasting assessed by weight-for-height Z-scores was more common in the deficient group but without significant difference ($p = 0.11$). Mid-upper arm circumference was notably lower among deficient children (11.5 ± 1.1 cm vs. 12.2 ± 1.0 cm, $p = 0.03$). Breastfeeding status did not differ significantly between groups ($p = 0.25$).

Table 2. Nutritional and Anthropometric Indicators (n=73)

Variable	Vitamin D Deficient (n=45)	Vitamin D Sufficient (n=28)	p-value
Weight-for-age Z-score (WAZ)	-2.9 ± 0.8	-2.3 ± 0.7	0.02*
Height-for-age Z-score (HAZ)	-3.1 ± 0.9	-2.7 ± 0.8	0.08
Weight-for-height Z-score	-2.5 ± 0.7	-2.1 ± 0.6	0.11
MUAC (cm)	11.5 ± 1.1	12.2 ± 1.0	0.03*
Breastfeeding status (Yes/No)	28 / 17	14 / 14	0.25

*Significant at $p < 0.05$

As expected, mean serum 25(OH)D levels were significantly lower among deficient children compared to those with sufficient Vitamin D (14.8 ± 3.2 vs. 32.6 ± 4.5 ng/mL, $p < 0.001$). Biochemical disturbances were also evident, with deficient children showing lower calcium levels (8.2 ± 0.7 vs. 8.8 ± 0.6 mg/dL, $p = 0.01$) and elevated alkaline phosphatase activity (320 ± 85 vs. 270 ± 74 U/L, $p = 0.03$), reflecting impaired bone metabolism. Phosphate values were slightly lower in the deficient group but did not differ significantly ($p = 0.24$). Hemoglobin levels trended lower in deficient children (9.8 ± 1.3 vs. 10.4 ± 1.2 g/dL, $p = 0.07$). Inflammatory activity, as indicated by C-reactive protein, was significantly higher in deficient children (53% vs. 29%, $p = 0.04$).

Table 3. Biochemical and Laboratory Parameters (n=73)

Variable	'Vitamin D Deficient' (n=45)	'Vitamin D Sufficient' (n=28)	p-value
Serum 25(OH)D (ng/mL)	14.8 ± 3.2	32.6 ± 4.5	<0.001*
'Serum Calcium (mg/dL)'	8.2 ± 0.7	8.8 ± 0.6	0.01*

'Serum Phosphate (mg/dL)'	3.7 ± 0.8	3.9 ± 0.7	0.24
Alkaline Phosphatase (U/L)	320 ± 85	270 ± 74	0.03*
Hemoglobin (g/dL)	9.8 ± 1.3	10.4 ± 1.2	0.07
CRP Positive (%)	24 (53%)	8 (29%)	0.04*

*Significant at $p < 0.05$

Clinical outcomes showed that Vitamin D deficiency was significantly associated with higher infection burden. Acute respiratory infections were more prevalent among deficient children (64% vs. 36%, $p = 0.01$), and diarrheal illnesses followed a similar pattern (56% vs. 32%, $p = 0.03$). Mean hospital stay was longer for deficient patients (7.2 ± 2.1 vs. 5.9 ± 1.8 days, $p = 0.04$), reflecting slower recovery. Recurrent infections within a 6-month follow-up were nearly twice as frequent in deficient children (47% vs. 25%, $p = 0.02$). Mortality was higher in the deficient group (9% vs. 4%), but the difference was not statistically significant ($p = 0.38$).

Table 4. Infection Outcomes and Clinical Parameters (n=73)

Outcome Variable	**'Vitamin D Deficient' (n=45)**	**'Vitamin D Sufficient' (n=28)**	**p-value**
Acute Respiratory Infections (%)	29 (64%)	10 (36%)	0.01*
Diarrheal Episodes (%)	25 (56%)	9 (32%)	0.03*
Mean Hospital Stay (days, ±SD)	7.2 ± 2.1	5.9 ± 1.8	0.04*
Recurrent Infections in 6 months	21 (47%)	7 (25%)	0.02*
Mortality (%)	4 (9%)	1 (4%)	0.38

*Significant at $p < 0.05$

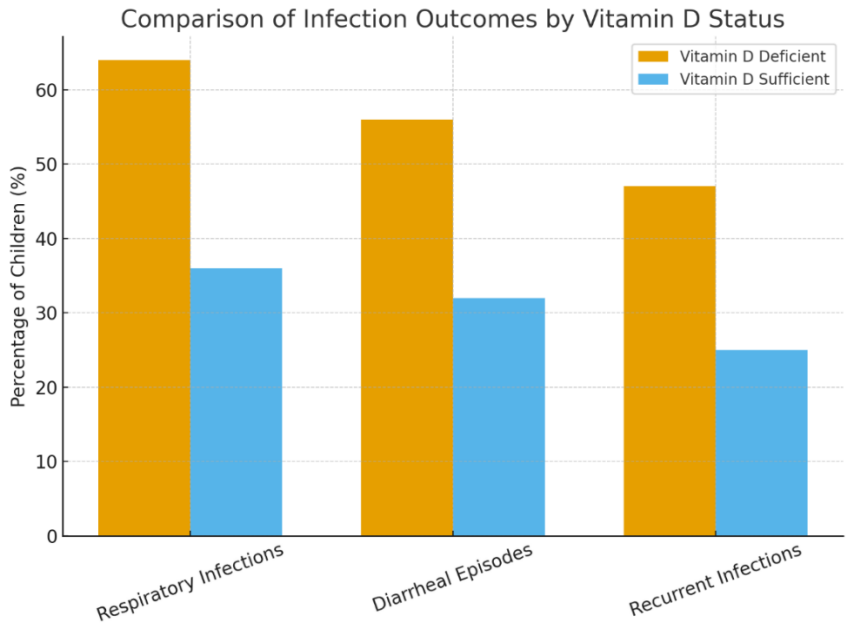

Figure 1: bar graph comparing infection outcomes between Vitamin D deficient and sufficient malnourished children. It shows higher rates of respiratory infections, diarrheal episodes, and recurrent infections among those who were Vitamin D deficient.

DISCUSSION

This study explored the relationship between Vitamin D status, immune modulation, and infection outcomes in malnourished pediatric patients admitted to Hayatabad Medical Complex, Peshawar. The results demonstrated that Vitamin D deficiency was highly prevalent among malnourished children and significantly associated with poor nutritional indices, biochemical abnormalities, and a higher burden of infectious morbidity.

In terms of demographics, most Vitamin D deficient children belonged to low-income households, reflecting the interplay between poverty, undernutrition, and micronutrient deficiencies. These findings are consistent with observations from Sub-Saharan Africa, where poverty-related dietary insufficiency and limited sunlight exposure were key predictors of Vitamin D deficiency (10). Similarly, studies highlighted socioeconomic disadvantage as a strong determinant of hypovitaminosis D in children (11-13).

Anthropometric analysis revealed that deficient children had significantly lower weight-for-age and MUAC compared to their Vitamin D sufficient peers. This supports the idea that Vitamin D not only influences bone metabolism but also interacts with energy and protein malnutrition pathways. studies reported comparable findings, linking Vitamin D deficiency to growth faltering and impaired muscle mass in malnourished children.

Biochemical findings in the present study showed reduced serum calcium and elevated alkaline phosphatase among deficient children, markers consistent with impaired bone turnover. These abnormalities align with studies where malnourished children with rickets demonstrated similar metabolic disturbances (14-16). ‘Additionally, the association between Vitamin D deficiency and elevated C-reactive protein observed here mirrors evidence from European pediatric cohorts, suggesting an immune-inflammatory pathway linking hypovitaminosis D to heightened susceptibility to infections’ (17, 18).

Most importantly, infection outcomes in this study highlighted the protective role of Vitamin D. Children with deficiency experienced more frequent acute respiratory infections, diarrheal diseases, prolonged hospital stays, and higher recurrence of infections. Several studies support this association. Studies concluded that ‘Vitamin D supplementation reduced the risk of respiratory tract infections, particularly in individuals with baseline deficiency’ (19). In low-income settings, research similarly demonstrated higher rates of pneumonia among Vitamin D deficient malnourished children. The present findings strengthen the argument that ‘Vitamin D deficiency acts as a modifiable risk factor for infection-related morbidity in vulnerable pediatric populations’.

Although mortality differences were not statistically significant in our cohort, the trend of higher mortality in Vitamin D deficient children suggests that larger studies with longer follow-up may uncover stronger associations. This observation aligns with recent work, where hypovitaminosis D was linked with increased mortality risk in severely malnourished children(20).

Taken together, these findings indicate that Vitamin D deficiency is both a nutritional and immunological problem in malnourished children from low-resource settings. By affecting immune modulation, Vitamin D may influence susceptibility to common childhood infections and recovery outcomes. Addressing this deficiency, therefore, could serve as a cost-effective strategy to reduce infection-related morbidity in pediatric populations already burdened by malnutrition.

CONCLUSION

This study found that Vitamin D deficiency is highly prevalent among malnourished children and is significantly associated with impaired growth indices, altered biochemical markers, and increased susceptibility to infections such as respiratory and diarrheal illnesses. Deficient children also required longer hospital stays and had more recurrent infections ‘compared to those with adequate Vitamin D levels’.

The results emphasize the dual physiological and pharmacological role of Vitamin D in modulating immune responses and improving infection outcomes. In resource-limited settings, screening for Vitamin D deficiency and considering supplementation strategies may provide a simple, low-cost

intervention to improve child health and reduce the infection burden among malnourished populations.

Future 'multicenter studies with larger sample sizes and interventional designs are recommended to establish causality and assess the effectiveness of Vitamin D supplementation programs in reducing infection-related morbidity and mortality in low-income pediatric populations'.

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