RESEARCH ARTICLE

Frequency of vitamin D deficiency in children with iron deficiency anaemia and factors associated with vitamin D deficiency

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Abstract

Objective: To evaluate vitamin D deficiency in children with iron-deficiency anaemia, and to identify the risk factors for such deficiency.

Method: The cross-sectional study was conducted at the Children's Hospital, Pakistan Institute of Medical Sciences, Islamabad, Pakistan, from October 2021 to March 2022, and comprised children aged 1-5 years who had been diagnosed with iron-deficiency anaemia. Quantitative variables, like age, height, weight, gender, socioeconomic status and sibling status, were controlled by stratification. Data was compared to assess the risk factors of vitamin D deficiency among the subjects. Data was analysed using SPSS 22.

Results: Of the 236 children with iron-deficiency anaemia, 159(67.5%) also had vitamin D deficiency; 95(59%) girls and 65(41%) boys. Overall, 104(65.4%) subjects were aged 4-5 years and 55(34.6%) were aged 1-3 years. Vitamin D deficiency had significant association with female gender, older age, height and weight <5th centiles, educated parents, low to middle socioeconomic status, urban residence and higher number of siblings ($p<0.05$).

Conclusion: The prevalence of vitamin D deficiency among children with iron-deficiency anaemia was found to be high.

Key Words: Anaemia, IDA, Vitamin D deficiency, Micronutrients deficiency, Risk factors.

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Introduction

Iron deficiency anaemia (IDA) in children adversely affects their wellbeing, especially the cognitive development.[1] Global IDA prevalence in children aged <5 years is 16.42%,[2] and that of vitamin D deficiency is 15.7%.[3] According to a 2018 nutrition survey, IDA prevalence in children <5 years in Pakistan was 28.6% and vitamin D deficiency was 13.7%.[4]

Vitamin D reduces pro-inflammatory cytokines, and is also involved in the direct suppression of hepcidin messenger ribonucleic acid (mRNA) transcription, and that may be the reason it has an association with anaemia in chronic diseases. Vitamin D also supports erythropoiesis, and, thus, has a protecting role in anaemia.[5]

After iron deficiency, vitamin D deficiency is the next most common deficiency in preschool children.[6] Vitamin D plays an important role in both innate and adaptive arms of the immune system. Vitamin D deficiency has been associated with multiple rheumatological conditions, such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and dermatomyositis. It is also associated with autoimmune diseases, like type 1 diabetes, multiple sclerosis, inflammatory bowel disease, psoriasis and hepatitis. It is also related to certain allergies, like food allergies, asthma, cancer, and behavioural disorders, like autism spectrum disorder.[7,8] Vitamin D deficiency caused increased susceptibility to respiratory tract infections (RTIs), including pneumonia and bronchiolitis.[9,10] It was observed that patients with significantly lower vitamin D levels were predisposed to developing severe coronavirus diseases-2019 (COVID-19).[11]

The current study was planned to estimate the frequency of vitamin D deficiency in children with IDA, and to identify the risk factors associated with such deficiency.

Subjects and Methods

The cross-sectional study was conducted at the Children's Hospital, Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan, from October 2021 to March 2022. After approval from the institutional ethics review committee, the sample size was calculated using the World Health Organisation (WHO) calculator with level of significance 5%, anticipated population 67% and absolute precision 6%.[12] The sample was raised using consecutive non-probability sampling technique. Those

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included were children aged 1-5 years who had been diagnosed with IDA with haemoglobin (Hb) ≤11g/dl and serum ferritin ≤15ng/ml.[13] Children having serum vitamin D level <20ng/ ml were labelled as vitamin D deficient.[14] Children already taking iron or vitamin D supplements, those diagnosed with certain haematological conditions, like thalassemia, leukaemia, glucose-6-phosphate dehydrogenase deficiency (G6PD), and severe systemic illnesses were excluded.

After taking written, informed consent from the parents/guardians, data was collected on a predesigned proforma, and all the patients were subjected to serum vitamin D estimation. All investigations were done at a single laboratory to exclude variations.

The association of vitamin D deficiency was explored in relation to age, gender, height, weight, socioeconomic status (SES), educational level, residential status, and number of siblings. Families with income less than Pakistani rupees (PKR) 30,000 were taken as low SES, PKR 30,000 to PKR 80,000 middle SES, and <PKR 80,000 as high SES. Parents with studied up to matriculation were considered uneducated, while those with intermediate or more qualification were labelled as educated.

Data was analysed using SPSS 22. Data was expressed as frequencies and percentages or as mean ± standard deviation, as appropriate. Post stratification chi-square test was used when appropriate. Univariate and multivariate logistic regression analyses were applied. P≤0.05 was considered significant.

Results

Of the 85,000 patients who visited the outpatient department (OPD) during the study period, 1,000(%) anaemic patients were screened. Of them, 236(%) children of either gender aged 1-5 years were diagnosed with IDA. Among these children, 159(67.4%) had vitamin D deficiency (Figure).

Of the 159(67.5%) children with vitamin D deficiency, 95(59%) were girls and 65(41%) were boys. Overall, 104(65.4%) subjects were aged 4-5 years and 55(34.6%) were aged 1-3 years. Vitamin D deficiency had significant association with gender, age, height, weight, parents' education, SES, residence status and number of siblings (p<0.05) (Tables 1-2).

Table-1: Qualitative variables affecting vitamin D status.

Groups	Vitamin D Deficiency Frequency	Percentage	P-Value Chi-Squared	OR (95% CI), p-value
Gender				
Male	65	40.9%	0.048	0.68 (0.31 – 1.48), 0.34
Female	94	59.1%		
Residential Status*				
Rural	58	36.5%	0.001	0.47 (0.15 – 1.48), 0.20
Urban	101	63.5%		
Education Status **				
Educated	85	53.5%	0.001	0.11 (0.02 – 0.52). 0.006
Uneducated	74	46.5%		
Socioeconomic Status ***				
Low	67	42.1%	0.001	1.30 (0.48 – 3.50), 0.60
Middle	79	49.7%		
High	13	8.2%		

OR: Odds ratio, CI: Confidence interval.
*parents coming from villages with only a basic health unit (BHU) and no tertiary care hospital were labelled as coming from rural areas, while patients coming from a city having tertiary care hospitals were labelled as urban areas.
** Parents having matriculation and less education were labelled as uneducated, while those with intermediate or more qualification were labelled as educated.
*** parents having total income <Rs30,000 were labelled as a family with low socioeconomic status (SES), those between Rs30,000 and Rs50,000 as middle SES, and >Rs50,000 as high SES..

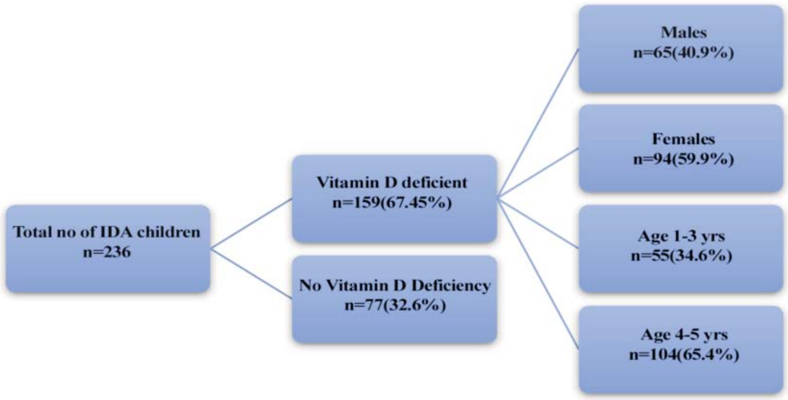

Figure: Frequency of vitamin D deficiency in iron-deficiency anaemia (IDA) children by gender and age category.

Univariate logistic regressions showed females had 1.7 times more chance of vitamin D deficiency than males (p=0.001). Children having height >90cm and weight >15kg had 3.3 times and 4.3 times more risk of having vitamin D deficiency, respectively (p=0.0001). Children from high SES background had highest risk of developing vitamin D deficiency (Table 3).

Multivariate analysis showed that age <3 years had a significant role in preventing vitamin D deficiency (p=0.0001), while gender and height groups did not show any significant relationships with vitamin D deficiency (p>0.05). Children with

Table-2: Quantitative variables affecting vitamin D status

Groups	Vitamin D Deficiency Frequency	Percentage	p Value Chi- Square
Age			
1-3 Years	55	34.6%	0.001
4-5 Years	104	65.4%	
Height			
≤ 10th centile	139	87.4%	0.001
> 10th centile	20	12.6%	
Weight			
≤ 5th centile	144	90.6%	0.001
> 5th centile	15	9.4%	
Number of Siblings			
1.00	4	2.5%	0.001
2.00	18	11.3%	
3.00	59	37.1%	
> 3.00	78	49.1%	

Table-3: Qualitative variables

	Descriptive Statistics N	Minimum	Maximum	Mean	Std. Deviation
Age	236	1.00	5.00	3.3254	1.35371
Height	236	59.00	105.00	84.5975	10.25396
Weight	236	5.00	20.00	12.8856	3.43815
Siblings	236	1.00	4.00	2.9237	1.02028

Table-4: Univariate variables affecting vitamin D status

S. No.	Variables	B	S.E.	Univariate Variables in the Equation Wald	df	Sig.	Exp(B)
1.	Age groups(1)	-.925	.284	10.580	1	.001	.397
2.	Gender(1)	.551	.280	3.875	1	.049	1.735
3.	Height groups(1)	1.206	.341	12.500	1	.000	3.341
4.	Weight groups(1)	1.470	.366	16.098	1	.000	4.347
5.	SES status			52.193	2	.000	
	SES status(1)	1.883	.557	11.443	1	.001	6.573
	SES status(2)	3.991	.605	43.563	1	.000	54.115
6.	Education status(1)	-2.766	.538	26.467	1	.000	.063

SES: Socioeconomic status.

Table-5: Multivariate variables affecting vitamin D status.

S. No. Variables	B	S.E.	Multivariate Variables in the Equation Wald	df	Sig.	Exp(B)
Step 1a						
Age groups(1)	-2.464	.488	25.448	1	.000	.085
Gender(1)	-.586	.386	2.302	1	.129	.557
Height groups(1)	1.004	.602	2.785	1	.095	2.730
Weight groups(1)	1.844	.646	8.160	1	.004	6.321
SES status			12.739	2	.002	
SES status(1)	-.865	1.085	.635	1	.425	.421
SES status(2)	.702	1.145	.376	1	.540	2.017
Education status(1)	-3.643	1.173	9.645	1	.002	.026
Residential status(1)	-.692	.563	1.513	1	.219	.500
Constant	1.857	1.285	2.086	1	.149	6.40

SES: Socioeconomic status.

weight >15kg were 6.3 times more at risk of developing vitamin D deficiency (p=0.004). Parental education had a significant association with vitamin D deficiency (p=0.002), while there was no significant relationship of SES and residential status with vitamin D deficiency (Table 4).

Discussion

The current study found that 67.4% children with IDA were also vitamin D deficient. Many studies have been conducted to establish a correlation between the two groups. Jin et al. evaluated 102 children aged 3-24 months and classified them into 3 groups; children with IDA, children who had iron deficiency but were not anaemic (ID), and controls. Vitamin D deficiency was present in 67% IDA children, 53% ID, and 29% controls.[12] Sharma et al. enrolled 263 children and classified them into 3 categories; deficient in vitamin D (VDD), insufficient vitamin D (VDI), and vitamin D sufficient (VDS). Anaemia was more predominant in VDD compared to VDS.[15] A recent study in Turkey on children between 6 months and 5 years of age showed that vitamin D levels were lower in those who were iron deficient or had IDA, and there was a direct correlation between Hb and vitamin D levels of the children.[16]

Lee JA et al. in South Korean children and adolescents found a significant association between IDA and vitamin D deficiency, showing that the incidence of both vitamin D deficiency and anaemia was higher in females,[17] which was similar to the current findings. Another study by Madar et al. did not find any improvement in Hb levels or iron status after supplementation with vitamin D 10µg or 25µg daily for 16 weeks.[18]

A study in Saudi Arabia showed that iron and vitamin D deficiencies were two most common micronutrient deficiencies found in children[19]. Like the current study, they also found that Vitamin D levels were higher in boys than girls.[19] It may be due to similarities in the cultural background where males are given priority over females, and they are served first and better food than females. Also, they are allowed to go outside which gives them better sun exposure than females. Another factor is that in Muslim countries, females cover their bodies, which means less sun exposure. The prevalence was higher in older age group (3 years and above), in a study by Nichols et al. in Jordan where deficiency of vitamin D was more among children aged >2 years.[20]

The current study showed that children who had weight below the 5th centile were more prone to developing iron and vitamin D deficiency. In contrast, Malden et al. exhibited that obese children were more predisposed to developing vitamin D deficiency compared to children with normal body mass index (BMI).[21]

The current study also looked for correlation with SES and the number of siblings. Vitamin D deficiency was found in higher percentages among low to middle SES and children with higher number of siblings. Studies conducted at India and China also found higher prevalence of vitamin D deficiency in lower SES group.[22,23] Voortman et al found no association of vitamin D deficiency with maternal education status.[24]

The current study also found higher prevalence of vitamin D among urban residents, which is in contrast to a study by Griffin et al which found vitamin D deficiency to be more in rural areas.[25]

No single study could be found in literature which covered all the risk factors that were explored by the current study.

The current study has limitations as it was done at a single centre study, and did not have a control group with children having normal iron levels.

In the light of the findings, routine screening of vitamin D deficiency in all children diagnosed with IDA is recommended.

Conclusion

Most IDA children also had concomitant vitamin D deficiency. Gender, age, height, weight, parental education, SES, residential status and number of siblings were significantly associated with vitamin D deficiency.

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Authors' Contributions

AAR: Data collection, study concept, design, drafting.
NH: Design, statistical analysis, drafting.
AF: Critically revision, final approval.
MN: Questionnaire design, data collection.
NW: Data interpretation, final drafting.
HBS: Literature search for discussion, drafting.