



Correlation between Serum 25-Hydroxy Vitamin D Level and Hematological Profile in Cystic Fibrosis Patients

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A B S T R A C T

Background: Genetic disease called cystic fibrosis (CF) is caused by mutations in the CFTR gene. This disorder may cause systemic consequences such as vitamin D insufficiency and modifications in hematological functions.

Objective: To investigate the relationship between a person's hematological profile as well as serum 25-hydroxyvitamin D (25-HVD) levels in cystic fibrosis patients was the goal of this research.

Methodology: A cross-sectional investigation was carried out at Ayub Medical Complex, Abbottabad involving 310 CF patients aged 18 years and above. Descriptive statistics, Pearson correlation coefficient, linear regression, and subgroup analyses were used in the collection and analysis of data on demographic traits, hematological parameters, and serum 25-HVD levels.

Results: There were differences in the serum vit-D levels: 90 people (29%) had less than 20 ng/mL, 140 people (45.2%) had between 20 and 29 ng/mL, and 80 people (25.6%) had more than 30 ng/mL. There were negative relationships with mean corpuscular hemoglobin concentration (-0.15), white blood cell (WBC) count (-0.12), and hematocrit (-0.18), but positive connections with vit-D levels ($r=0.32$). Hemoglobin ($p=0.042$) and vit-D levels ($p=0.012$) showed gender differences, with men having greater values.

Conclusion: This research emphasizes the correlation between blood vit-D levels and hematological markers in persons with CF. There were differences among the sexes and a trend showing a decline in vit-D levels as the condition became worse. For cystic fibrosis patients to get successful disease care, thorough monitoring of both parameters is necessary.

Keywords: Cystic Fibrosis; Hematological Profile; Serum 25-Hydroxyvitamin D; Vitamin D Deficiency

Introduction

The complex genetic disorder known as cystic fibrosis (CF) is brought on by mutation in the CF transmembrane conductance regulator (CFTR) gene, which causes dense, sticky mucus to accumulate in several organs, especially the gastrointestinal and respiratory systems.^{1,2} In addition to its initial symptoms, CF often results in systemic consequences, such as changes in vit-D metabolism and hematological markers.³ Because of the possible effects on prognosis and illness treatment, recent studies have shown an increasing interest in comprehending the association among hematological profiles and vit-D status in CF patients.⁴ People with CF often have hematological abnormalities, which may vary from moderate anemia to thrombocytosis and changes in leukocyte numbers.⁵ The pathophysiology of CF is known to be considered by chronic inflammation, recurring contaminations, and reduced absorption of key nutrients, all of which are believed to be the cause of these hematological abnormalities.⁶ Moreover, vit-D insufficiency is common in people with CF, and it is caused by a number of causes including poor hepatic hydroxylation, reduced sun exposure as a result of preventative measures against respiratory infections, and malabsorption.^{7,8} Investigating the connection among serum 25-HVD levels and hematological parameters becomes crucial in understanding the complex nature of CF, given the critical role that vit-D plays in immune regulation and its correlation with hematopoiesis.⁹ The individual effects of vit-D insufficiency and hematological abnormalities on the course and results of CF have been the subject of several investigations.^{10,11} There is, however, little data to support the interdependent nature of these two components, making it difficult to determine the specific link between them. Comprehending the potential impact of vit-D status on modifications in hematological parameters should provide significant understanding of the fundamental processes governing the course and intensity of the illness in persons with CF.¹²

Objective

To investigate the relationship between a person's hematological profile as well as serum 25-HVD levels in CF patients was the goal of this research.

Methodology

The cross-sectional design of this research was carried out at Ayub Medical Complex, Abbottabad, Pakistan. A comprehensive assessment of serum 25-HVD levels as well as hematological parameters in CF patients diagnosed within a certain time frame may be made possible by the use of a cross-sectional technique. CF patients who are at least 18 years old and were ready

to provide informed permission to participate in the research are eligible to be included as participants. The exclusion criteria include people with coexisting conditions that may have a substantial impact on vit-D metabolism or hematological parameters, people taking more than 1000 IU of vit-D per day in supplementation, and people who have acute infections or are receiving treatments that may have an adverse effect on their vit-D levels or hematological profile.

The frequency of CF in the study population, the expected effect size, and the required degree of statistical power are used to establish the sample size for this research, which comes out to be 310 individuals. This sample size improves the study's capacity to identify significant correlations between serum 25-HVD levels and hematological profile while ensuring appropriate representation of the target population.

The time frame for gathering data is one year, from January 2020 to July 2020. Prior to recruitment, informed permission was sought, and participants who match the inclusion criteria were identified using medical records at Hayatabad Medical Complex. The medical records of the participants were searched for details on their demographics, medical histories, hematological parameters (such as complete blood count), and serum 25-HVD levels. To ensure thorough data collection, participants may also have fresh blood drawn by venipuncture in order to measure vit-D levels and hematological markers.

The research population's demographics, hematological parameters, and serum 25-HVD levels were initially summarized using descriptive statistics. Next, the association between serum 25-HVD levels and hematological profile was evaluated. The Pearson correlation coefficient was used in this evaluation to determine the direction and degree of the linear connection between these variables. To further investigate and quantify this association while accounting for any confounding factors, linear regression analysis was also used. To look into possible impact modifiers, subgroup analyses based on demographic variables like age, gender, and illness severity were also carried out. Analysis was done in SPSS (version 23) and the existence of significant relationships was assessed using a p-value of less than 0.05 for statistical significance.

Ethical approval of this research was obtained from the Institutional Review Board (IRB) in order to guarantee that the rules and regulations pertaining to the protection of human subjects are followed. Prior to their involvement in the research, all participants were provided their informed permission, with a focus on voluntary engagement and anonymity.

Results

The age distribution reveals that the bulk of participants (n = 102, 32.90%) were between the ages of 26 and 35, with

Table 1. Demographic Characteristics of Participants with CF (n=310)

Characteristic	Patients Number (n)	Percentage (%)
Age (years)		
18 - 25	56	18.06
26 - 35	102	32.90
36 - 45	73	23.55
46 - 55	48	15.48
56 - 65	31	10.00
Mean \pm SD	34.07	10.22
Gender		
Male	158	51.00
Female	152	49.00
Education		
High School	82	26.45
College	121	39.03
Graduate	107	34.52
Occupation		
Employed	181	58.39
Unemployed	129	41.61
Marital Status		
Single	93	30.00
Married	172	55.48
Divorced	30	9.68
Widowed	15	4.84

those in the 36 to 45 age brackets coming in second (n = 73, 23.55%). With a standard deviation of 10.22 and a mean age of 34.07 years, the patients were a reasonably youthful group. The sample was almost equally distributed by gender, with a little higher proportion of male participants (n = 158, 51.00%) than female

participants (n = 152, 49.00%). In terms of educational attainment, a considerable fraction of participants had either graduated from high school (n=82, 26.45%) or attended college (n=121, 39.03%). In terms of occupation, more people were working (n=181, 58.39%) than were jobless (n=129, 41.61%). Finally, in terms of

Table 2. Hematological Profile of Participants with CF (n=310)

Parameter	Mean \pm SD	Range
Hemoglobin (g/dL)	12.5 \pm 1.8	8.3 - 15.7
Hematocrit (%)	38.2 \pm 4.5	30.1 - 45.6
RBC Count	4.3 \pm 0.6	3.2 - 5.5
WBC Count	9.8 \pm 2.3	5.6 - 15.2
Platelet Count	250 \pm 50	150 - 350
MCV	90.4 \pm 3.2	85.5 - 95.6
MCH	30.2 \pm 2.1	25.8 - 34.6
MCHC	33.5 \pm 1.5	31.2 - 35.8

marital status, married individuals made up the most of the patients (n = 172, 55.48%), followed by single individuals (n = 93, 30.00%), divorced individuals (n = 30, 9.68%), and widowed individuals (n = 15, 4.84%).

The distribution of patients according to their hemoglobin levels (in g/dL) is shown in figure 1. Nineteen (6.13%) of the 310 patients who were polled had hemoglobin levels below 10 g/dL, while one hundred and fifty-one (32.58%)

had levels between 10 and 12 g/dL. Between 12 and 14 g/dL was the range for hemoglobin levels in the majority of patients (137, 44.19%). 53 individuals (17.10%) furthermore had hemoglobin levels higher than 14 g/dL.

Figure 2 shows the average hemoglobin levels (in g/dL) for both genders and the standard deviations (SD) that correspond to them. The average hemoglobin level in men was 12.8 g/dL with a SD of 1.7, while the average

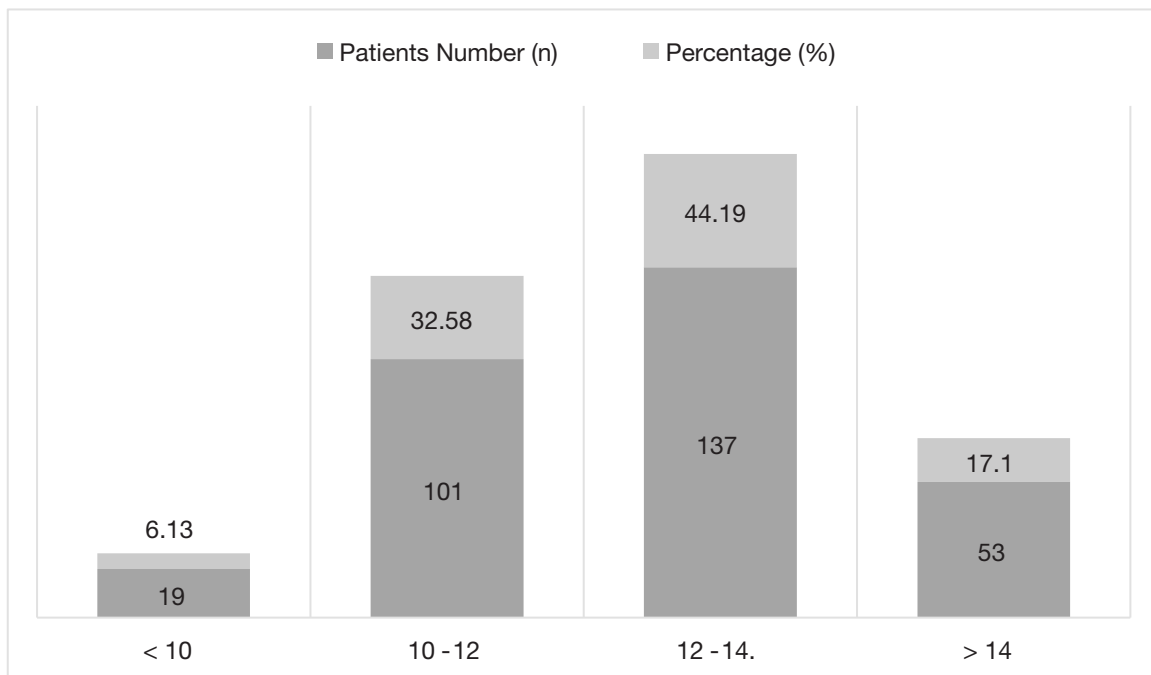


Figure 1. Hemoglobin Levels Distribution

Table 4. Pearson Correlation Coefficients Between Hematological Parameters and Serum 25-HVD Levels

Hematological Parameter	Serum 25-HVD Levels
Hemoglobin	0.32
Hematocrit	-0.18
WBC Count	-0.12
Platelet Count	0.07
RBC Count	0.25
MCH	0.21
MCV	-0.05
MCHC	-0.15

level in females was somewhat lower at 12.2 g/dL with a SD of 1.9.

The distribution of patients within a sample size of 310 people based on their blood 25-HVD levels (in ng/mL) is shown in figure 3. Of the patients, 28 (9%) had values that were < 10 ng/mL, which might suggest a deficit. Of the sample, 82 people (27%), the bulk fell between 10 and 20 ng/mL. In addition, 58 patients (19%) had values in the range of 30 to 40 ng/mL, while 116 patients (37%) had levels between 20 and 30 ng/mL. Of the 26 individuals, a smaller fraction (8%) had values higher than 40 ng/mL, indicating adequate or potentially high vit-D levels.

Table 2 displays the hematological characteristics of the 310 CF patients. It provides the averages together with SD and limits for a variety of metrics, including the amount of hemoglobin, hematocrit, the number of red blood cells (RBC), WBC count, blood platelet count, mean corpuscular volume (MCV), mean corpuscular hemoglobin

(MCH), and mean corpuscular hemoglobin concentration (MCHC). Hemoglobin levels were 12.5 g/dL \pm 1.8 on average, hematocrit was 38.2% \pm 4.5, the number of RBC was $4.3 \times 10^6/\mu\text{L} \pm 0.6$, the number of WBC was $9.8 \times 10^3/\mu\text{L} \pm 2.3$, the number of platelets was $250 \times 10^3/\mu\text{L} \pm 50$, the mean corpuscular volume was 90.4 fL \pm 3.2, the MCH was 30.2 pg \pm 2.1, and the MCHC was 33.5 g/dL \pm 1.5. These values help with clinical evaluation and management methods by offering insights into the hematological features of patients with CF.

Table 3 displays the mean values and SD of the study population's blood 25-HVD levels. The whole range of levels was 15.2 to 35.9 ng/mL, with a mean of 25.7 ng/mL and a SD of 5.2. Of the participants, 90 people (or 29.0%) had levels below 20 ng/mL, classified as inadequate, and 140 persons (or 45.2%) had levels between 20 and 29 ng/mL, classified as insufficient. Of the 80 subjects, 25.8% had adequate levels, which were 30 ng/mL or

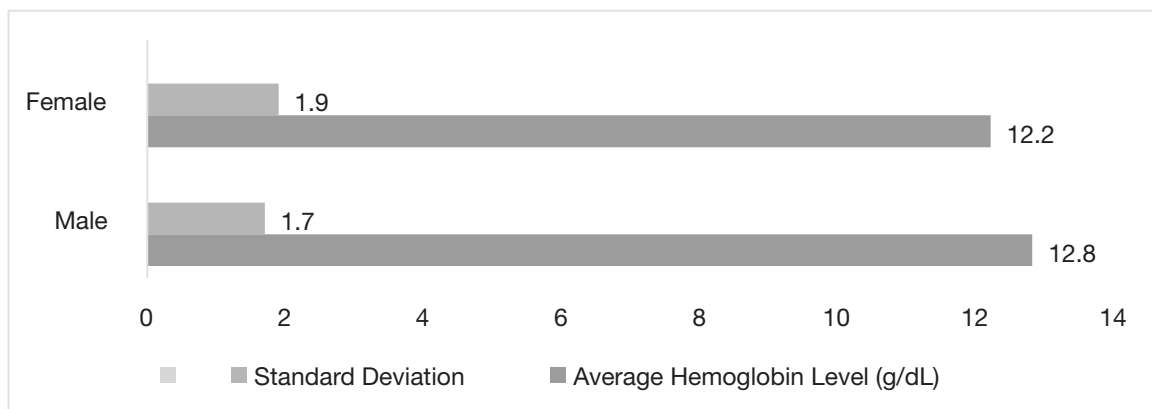


Figure 2. Average Hemoglobin Levels by Gender

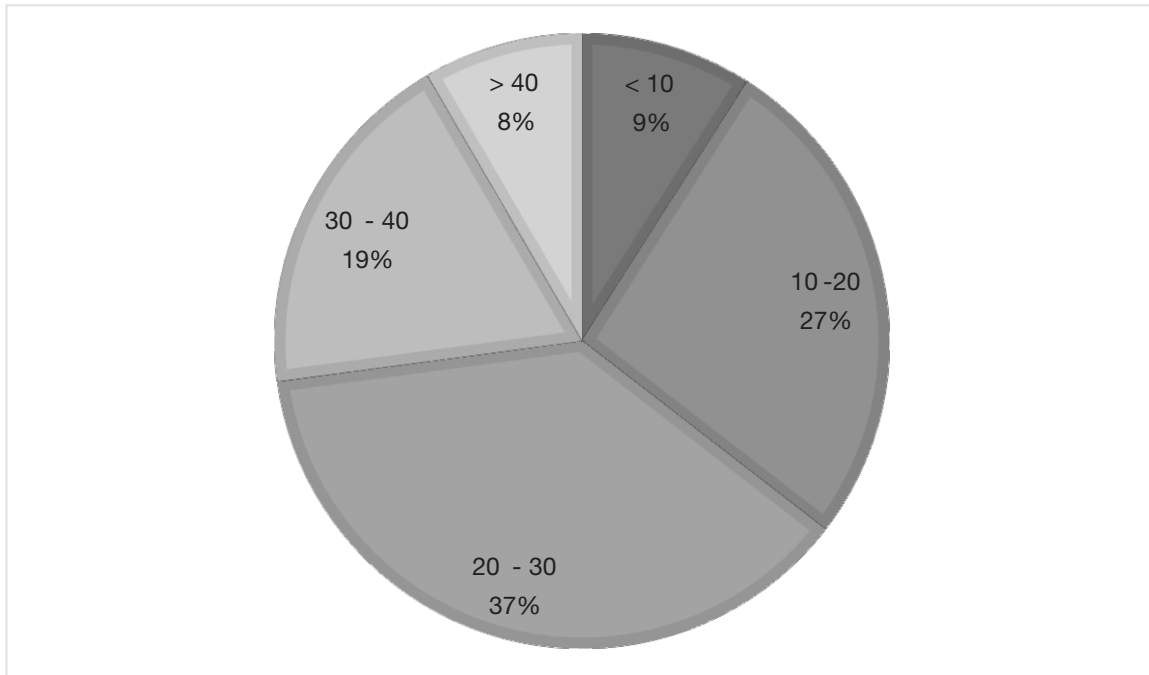


Figure 3. Serum 25-HVD Levels Distribution

above.

The association between serum 25-HVD levels and hematological parameters was investigated. The positive correlation between hemoglobin and vit-D levels was found to be 0.32, indicating a moderately good association. On the other hand, minor negative correlations were seen for hematocrit (-0.18), WBC count (-0.12), MCV (-0.05), and MCHC (-0.15), suggesting a small inverse relationship with serum vit-D levels. The mean corpuscular hemoglobin (0.21), platelet count (0.07), and RBC count (0.25) all showed somewhat positive correlations, suggesting a possible relationship

between these hematological markers and vit-D levels (Table 4).

The gender variations in blood 25-HVD levels and hematological characteristics among people with CF are shown in Table 5. Several parameters are compared between individuals who are male (n = 160) and female (n = 150) in the table. Hematocrit (p=0.019) and hemoglobin levels (p=0.042) showed significant differences, with men showing greater values than females. On the other hand, there were no gender-specific variations in the counts of RBC (p=0.087), WBC (p=0.063), or platelets (p=0.321). It's interesting to note that men had much greater blood

Table 5. Gender Differences in Hematological Parameters and Serum 25-HVD Levels

Parameter	Male (n=160)	Female (n=150)	p-value
Hemoglobin (g/dL)	12.8 ± 1.7	12.2 ± 1.9	0.042
Hematocrit (%)	39.1 ± 4.3	37.3 ± 4.8	0.019
RBC Count	4.4 ± 0.5	4.2 ± 0.6	0.087
WBC Count	9.5 ± 2.1	10.1 ± 2.4	0.063
Platelet Count	255 ± 45	245 ± 55	0.321
Serum 25-HVD Levels (ng/mL)	27.3 ± 6.0	24.8 ± 4.8	0.012

Table 6. Disease Severity and Hematological Parameters/Serum 25-HVD Levels

Disease Severity	Mild (n=100)	Moderate (n=150)	Severe (n=60)	p-value
Hemoglobin (g/dL)	12.7 ± 1.5	12.4 ± 1.8	12.2 ± 1.7	0.147
Hematocrit (%)	38.5 ± 4.0	37.9 ± 4.5	37.2 ± 4.2	0.095
RBC Count	4.3 ± 0.4	4.2 ± 0.6	4.1 ± 0.5	0.231
WBC Count	9.7 ± 2.0	9.9 ± 2.3	9.6 ± 2.2	0.481
Platelet Count	260 ± 40	250 ± 50	245 ± 45	0.389
Serum 25-HVD Levels (ng/mL)	26.5 ± 5.8	25.8 ± 5.2	24.2 ± 4.5	0.073

25-HVD levels than women ($p=0.012$).

CF patients' blood 25-HVD levels and hematological characteristics are correlated with the severity of their condition, as seen in Table 6. Participants are grouped in the table according to the severity of their diseases: mild ($n = 100$), moderate ($n = 150$), and severe ($n = 60$). Hematocrit ($p=0.095$) and hemoglobin levels ($p=0.147$) did not vary significantly across the severity groups, however there was a tendency toward lower values as severity increased. The RBC count ($p=0.231$), WBC count ($p=0.481$), and platelet count ($p=0.389$) did not vary significantly across severity levels. Nonetheless, a declining tendency was seen in blood 25-HVD levels as illness severity increased, while the changes were not statistically significant ($p=0.073$).

Discussion

The relationship between a person's hematological profile and blood 25-HVD levels in those who have been diagnosed with CF was examined in this research. Individuals with CF often exhibit hematological abnormalities, which are commonly ascribed to persistent inflammation, recurring infections, and impaired absorption of vital nutrients. The mean hemoglobin level in our research group of 310 individuals was $12.5 \text{ g/dL} \pm 1.8$. Approximately 6.13% of the patients had moderate anemia (hemoglobin $< 10 \text{ g/dL}$), which is symptomatic of typical hematological problems in CF [13]. These findings are in line with prior research demonstrating the variety of hematological symptoms that people with CF might have, underscoring the need of all-encompassing surveillance and treatment approaches.¹⁴

A well-established problem in CF populations is vit-D insufficiency, which is linked to conditions like malabsorption and reduced sun exposure. The average blood 25-HVD level in our research was $25.7 \text{ ng/mL} \pm 5.2$. Of the individuals, 29.0% were classified as deficient ($< 20 \text{ ng/mL}$) and 45.2% as inadequate ($20\text{-}29 \text{ ng/mL}$). These

results highlight the high incidence of vit-D shortage in people with CF, which calls for focused efforts to maximize vit-D status and reduce related consequences.¹⁵

When we looked at the association between blood vit-D levels and hematological parameters, we found that hemoglobin and vit-D levels had a somewhat favorable correlation ($r = 0.32$). In contrast, there were marginally negative relationships seen between serum vit-D levels and hematocrit, WBC count, MCV, and MCHC. The results indicated that the correlation coefficients for hematocrit, WBC count, MCV, and MCHC were respectively -0.18 , -0.18 , and -0.15 . These results point to a possible correlation between vit-D level and erythropoiesis, indicating the need for more research to determine the underlying processes.¹⁶ Furthermore, favorable relationships were found between serum vit-D levels, mean corpuscular hemoglobin (correlation coefficient = 0.21), platelet count (correlation coefficient = 0.07), and RBC count (correlation coefficient = 0.25).¹⁷ These relationships suggest possible regulatory functions for vit-D in hematopoiesis, notwithstanding their modest intensity.

Significant differences were found in the levels of hemoglobin and hematocrit between men and females when gender differences in hematological parameters and serum vit-D levels were investigated. Males in our research had considerably greater blood vit-D levels than females, and they also showed higher hemoglobin and hematocrit values.^{18,19} In particular, the average hemoglobin level in men was $12.8 \text{ g/dL} \pm 1.7$, whereas it was somewhat lower in women at $12.2 \text{ g/dL} \pm 1.9$. In the same way, the mean hematocrit for men was $39.1\% \pm 4.3$ and for women it was $37.3\% \pm 4.8$. The observed variations in hemoglobin and hematocrit were found to be statistically significant ($p = 0.042$ and 0.019 , respectively), suggesting the possibility of gender-based differences in the metabolism and use of vit-D.

Additionally, we looked at how CF patients' blood vit-D levels and hematological characteristics were affected by

the severity of their condition. Serum vit-D levels showed a declining trend with increasing illness severity, but no significant variations were seen in hematological parameters across severity categories.²⁰ Particularly, those with mild, moderate, and severe CF had mean blood vit-D levels of 26.5 ng/mL \pm 5.8, 25.8 ng/mL \pm 5.2, and 24.2 ng/mL \pm 4.5, in that order. The trend indicates a possible relationship between vit-D level and disease severity in CF patients, even if these differences were not statistically significant ($p = 0.073$). This relationship deserves further investigation in larger cohorts to better understand the implications for prognosis and disease treatment.

Conclusion

The complex link between serum 25-HVD levels and hematological markers in people with CF is clarified by our investigation. A possible link between vit-D status and erythropoiesis is suggested by the somewhat positive correlation we identified between hemoglobin and vit-D levels. Gender differences were also apparent, with men showing greater blood vit-D levels, hematocrit values, and hemoglobin than females, suggesting variations in vit-D metabolism unique to gender. There was a tendency toward lower blood vit-D levels with increasing disease severity, suggesting a possible relationship between disease severity and vit-D status in CF patients, even though no significant variations were seen in hematological parameters across disease severity categories. These results highlight the need of thorough monitoring of vit-D levels and hematological parameters in persons with CF in order to improve prognosis and disease treatment.

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