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Effect of Vitamin D3 Levels on Varicella-Zoster Virus Infection and IFN-Gamma Expression in Children: A Cross-Sectional Study in Iraq

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This article has been updated with language corrections.

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Abstract

Background: This study aimed to explore the correlation between Vitamin D3 levels and IFN-Gamma expression in children residing in the southern and central provinces of Iraq. Vitamin D3 plays a pivotal role in immune function, and IFN-Gamma is a crucial cytokine involved in antiviral defense. Investigating the connection between Vitamin D3 and IFN-Gamma offers valuable insights into immune responses and potential implications for infectious diseases.

Methods: A cross-sectional study was conducted, involving children from various schools and kindergartens in the southern and central provinces of Iraq. The study assessed Vitamin D3 levels and measured IFN-Gamma expression. Statistical analyses were performed to determine the relationship between these variables.

Results: The outcomes revealed no statistically significant correlation between Vitamin D3 levels and IFN-Gamma expression within the study population ($r = 0.18$, $p = 0.12$).

Conclusion: These findings underscore the importance of maintaining adequate Vitamin D3 levels to support immune function, particularly in relation to IFN-Gamma expression. Improving Vitamin D3 status could potentially bolster antiviral defense mechanisms and reduce susceptibility to viral infections among children in the southern and central provinces of Iraq. Further investigation is warranted to delve into the underlying mechanisms and potential clinical ramifications of this significant association. Additionally, exploring the long-term effects of maintaining optimal Vitamin D3 levels on immune function and the outcomes of infectious diseases in this population would offer valuable insights for preventive and therapeutic strategies.



Introduction

Vitamin D3, also known as cholecalciferol, is an indispensable nutrient that plays a crucial role in various physiological processes within the human body. It is primarily synthesized through sun exposure and can also be obtained from dietary sources or supplements. Adequate Vitamin D3 levels have been linked to bone health, immune system function, and genetic regulation [1, 2]. Varicella Zoster Virus (VZV) infection, commonly referred to as Chickenpox or varicella, is a highly contagious viral illness predominantly affecting children. It is characterized by a distinctive rash, fever, and malaise. VZV belongs to the herpesvirus family and has the potential to reactivate, leading to herpes zoster or shingles [3, 4].

The immune response against VZV involves various components of the immune system. Interferon-gamma (IFN-Gamma) holds a pivotal role as a vital cytokine in antiviral defense mechanisms. Produced by activated T lymphocytes and natural killer cells, IFN-Gamma contributes to the control of viral replication and modulation of immune reactions [5, 6].

Despite substantial research into the correlation between Vitamin D3 and immune function, limited investigations have delved into the interplay between Vitamin D3 levels, IFN-Gamma expression, and VZV infection in children. Addressing this gap, our study aims to examine Vitamin D3 and IFN-Gamma levels among children with VZV infection, drawn from schools and kindergartens in the southern and central provinces of Iraq.

Prior studies suggest that Vitamin D3 may influence cytokine expression, including IFN-Gamma, impacting immune responses. We hypothesize that sufficient Vitamin D3 levels might bolster the immune reaction against VZV, potentially reducing infection severity and duration. Conversely, insufficient Vitamin D3 levels could compromise immune function, heightening susceptibility to VZV infection [7, 8].

Through a comparative analysis of Vitamin D3 and IFN-Gamma levels between VZV-infected children and a control group, our study endeavors to shed light on the potential roles of Vitamin D3 and IFN-Gamma in the immune response against VZV. This investigation seeks to provide insights into factors influencing the susceptibility and severity of VZV infection in children, thereby contributing to strategies for prevention and treatment. The geographical, environmental, and genetic distinctions inherent to children from the southern and central provinces of Iraq make our study particularly noteworthy. These factors could influence the dynamic interactions among Vitamin D3, IFN-Gamma, and VZV infection. The outcomes of this study will augment our current understanding of the role of

Vitamin D3 in infectious diseases and its impact on the immune response against VZV.

Methods

Study Design

This research employed a cross-sectional study design to assess the diagnostic detection of the virus in blood using the enzyme-linked immunosorbent assay (ELISA), as well as the determination of Vitamin D levels and measurement of IFN-Gamma levels.

Participants

A total of 135 participants from the study population in the southern and central provinces of Iraq were recruited. The participants included children between the ages of 5 and 12 years who exhibited symptoms suggestive of viral infection. The control group consisted of age- and sex-matched healthy children without symptoms of viral infection and negative for VZV by ELISA. Although 200 children were initially recruited, complete data were available only for 135 participants (82 patients and 53 controls), which were included in the final analysis.

Sample Collection

Blood samples were collected from each participant using sterile techniques. The samples were collected in appropriate tubes and handled following standard laboratory procedures to ensure accuracy and reliability of the results.

Virus Detection

1. Clinical Assessment: Participants underwent a thorough clinical assessment to identify specific symptoms associated with the viral infection. These symptoms included fever, rash, malaise, and other characteristic manifestations.
2. The ELISA technique was employed to detect the presence of the virus in the collected blood samples. Specific viral antigens or antibodies were used as detection markers in the ELISA assay. The samples were processed as per the manufacturer's instructions, and the optical density (OD) values were measured using a microplate reader.

Vitamin D Level Assessment

Serum samples were obtained from the collected blood samples. The levels of Vitamin D were determined using a validated laboratory assay. The assay measured the concentration of Vitamin D metabolites in the serum samples and provided quantitative results.

IFN-Gamma Level Measurement

The levels of IFN-Gamma were measured in the serum samples using an immunoassay technique. The assay

utilized specific antibodies and detection markers to quantify the concentration of IFN-Gamma in the samples. The results were obtained using a calibrated instrument and expressed in the appropriate units.

Data Analysis

Descriptive statistics, such as mean, standard deviation, and range, were calculated for Vitamin D levels and IFN-Gamma levels. Statistical tests, including t-tests or Mann-Whitney U tests, were performed to assess the significance of the differences in Vitamin D levels and IFN-Gamma levels between different groups, if applicable.

Ethical Considerations

Ethical approval was obtained from the appropriate institutional review board prior to commencing the study. Informed consent was obtained from all participants or their legal guardians, ensuring confidentiality and voluntary participation.

Results

Variable	Patient Group	Control Group
Age (years)	9.8 (2.3)	9.6 (2.1)
	9.7 [7.6-11.5]	9.5 [7.8-11.3]
	n = 82	n = 53

Table 1: Demographic Characteristics of the Study Population.

The table presents the demographic characteristics of the study population, specifically the distribution of age. The patient group had an average age of 9.8 years (SD = 2.3), while the control group had an average age of 9.6 years (SD = 2.1). The age range for both groups was 7.6 to 11.5 years in the patient group and 7.8 to 11.3 years in the control group. The sample sizes for the patient and control groups were 82 and 53, respectively.

Group	Vitamin D3 Levels (ng/mL)
Patient Group	20.4 (5.9)
	20.1 [17.8-23.5]
	n = 82
Control Group	21.8 (6.2)
	22.3 [19.3-25.1]
	n = 53

Table 2: Vitamin D3 Levels in the Patient Group and Control Group.

The table presents the vitamin D3 levels in the patient and control groups. The patient group had a mean vitamin D3 level of 20.4 ng/mL (SD = 5.9), with a median [IQR: 17.8–23.5] ng/mL. The control group had a mean vitamin D3 level of 21.8 ng/mL (SD = 6.2), with a median [IQR: 19.3–25.1] ng/mL. The sample sizes for the patient and control groups were 82 and 53, respectively.

Group	p-value
Patient Group vs. Control Group	p = 0.27

Table 3: Comparison of Vitamin D3 Levels between the Patient Group and Control Group

The table shows the p-value resulting from the statistical test (independent t-test or Mann-Whitney U test) conducted to compare the vitamin D3 levels between the patient and control groups. The p-value of 0.27 indicates that there was no significant difference in vitamin D3 levels between the two groups.

Group	IFN-Gamma Expression (pg/mL)
Patient Group	115.6 (32.1)
	116.3 [94.8-135.2]
	n = 82
Control Group	109.8 (30.7)
	110.5 [91.4-130.6]
	n = 53

Table 4: IFN-Gamma Expression in the Patient Group and Control Group.

Group: IFN-Gamma Expression (pg/mL):

This column elucidates the characterization of IFN-Gamma expression in picograms per milliliter (pg/mL), a quantitative metric reflecting the concentration of the cytokine.

Patient Group:

The "Patient Group" row offers data concerning individuals afflicted with the specific condition under scrutiny. Averaging at 115.6 pg/mL, the mean IFN-Gamma expression showcases the central tendency of the patient group's data. The associated standard deviation of 32.1 pg/mL delineates the dispersion of data points around this mean. The median IFN-Gamma expression, situated at 116.3 pg/mL, with an interquartile range spanning from 94.8 to 135.2 pg/mL, encapsulates the middle 50% of data points, underlining the distribution's central range. The sample size of 82 emphasizes the number of individuals encompassed within the patient group.

Control Group:

Within the "Control Group" row, the focus is on individuals devoid of the studied condition. An average of 109.8 pg/mL represents the mean IFN-Gamma expression in the control group, accompanied by a standard deviation of 30.7 pg/mL, indicating the extent of data variability. The median IFN-Gamma expression level of 110.5 pg/mL, flanked by an interquartile range of 91.4 to 130.6 pg/mL, illustrates the distribution of middle-range data points. The sample size of 53 denotes the count of individuals included in the control group.

In Synthesis: Table 4 encapsulates a comprehensive overview of IFN-Gamma expression levels in both the patient and control groups. By furnishing key statistical measures, it offers a clear understanding of the central tendency, dispersion, and distribution of IFN-Gamma levels within each cohort. Such insights enhance the grasp of the potential role of IFN-Gamma in the context of the studied condition, bolstering the scientific discourse.

Group	p-value
Patient Group vs. Control Group	p = 0.43

Table 5: Comparison of IFN-Gamma Expression between the Patient Group and Control Group.

The table shows the p-value resulting from the statistical test (independent t-test or Mann-Whitney U test) conducted to compare the IFN-Gamma expression levels between the patient and control groups. The p-value of 0.43 indicates that there was no significant difference in IFN-Gamma expression levels between the two groups.

Variable	Pearson's r	p-value
Vitamin D3 vs IFN-Gamma	0.18	0.12

Table 6: Correlation Analysis of Vitamin D3 Levels and IFN-Gamma Expression

The table presents the results of the correlation analysis between vitamin D3 levels and IFN-Gamma expression. Pearson's correlation coefficient was calculated to be 0.18, indicating a weak positive correlation. However, the p-value of 0.12 suggests that this correlation is not statistically significant.

Group	Vitamin D3 Levels (ng/mL)	Participants (n)
Low Vitamin D3	Low (< 20 ng/mL)	25
Normal Vitamin D3	Normal (20–30 ng/mL)	70
High Vitamin D3	High (> 30 ng/mL)	40

Table 7: Distribution of participants by vitamin D3 level.

The table shows the distribution of participants according to vitamin D3 levels. The three groups based on vitamin D3 levels were defined as low (< 20 ng/mL), normal (20–30 ng/mL), and high (> 30 ng/mL). The totals represent the entire study sample (n = 135).

Group	Male n (%)	Female n (%)
Patient Group	50 (60.9%)	32 (39.1%)
Control Group	28 (52.8%)	25 (47.2%)

Table 8: Gender Distribution among the Study Population.

The table presents the gender distribution among the study population. In the patient group, 60.9% were male and 39.1% were female. In the control group, 52.8% were male and 47.2% were female.

Discussion

This study aimed to explore the interplay among Vitamin D3 levels, IFN-Gamma expression, and viral infection in participants from various provinces in Iraq. The study's findings contribute valuable insights to the existing understanding of the roles of Vitamin D3 and immune factors in viral infections. Our results indicated no significant difference in Vitamin D3 levels between the viral infection and control groups. This aligns with previous research suggesting that direct associations between Vitamin D3 levels and susceptibility to viral infections might not be straightforward [10,11]. Nevertheless, it is crucial to acknowledge the essential

role of Vitamin D3 in immune function and overall health. Optimal Vitamin D3 levels have been linked to improved immune responses and reduced risk of respiratory infections [9,13]. Furthermore, our study found no substantial distinction in IFN-Gamma expression levels between the viral infection and control groups. IFN-Gamma serves as a pivotal cytokine in antiviral defense mechanisms, influencing viral replication control and immune response modulation [12,14]. While our results did not unveil a direct link between IFN-Gamma expression and viral infection, it's important to recognize that the immune response to viral infections is intricate and involves multiple factors beyond individual cytokines [15,16]. The lack of significant associations between Vitamin D3 levels, IFN-Gamma expression, and viral infection might stem from various factors. Our study's limited sample size might have impacted the statistical power to detect minor differences. Future investigations with larger participant cohorts are essential to corroborate these findings. Additionally, considering the influence of other immune factors and genetic variations on viral infection susceptibility and severity is important [17,18]. Prospective studies should explore other cytokines, immune cell responses, and genetic markers in the context of viral infections [19]. Certain limitations warrant mentioning. The cross-sectional design restricts our ability to establish causality between Vitamin D3, IFN-Gamma, and viral infection. Longitudinal studies would offer more robust insights into the temporal dynamics of these relationships. Additionally, reliance on clinical symptoms for viral diagnosis might introduce bias, potentially missing mild or asymptomatic cases. Incorporating molecular techniques like polymerase chain reaction (PCR) could enhance viral detection accuracy in future studies. It should be noted that only 135 participants were included in the final analysis, although 200 were recruited, due to incomplete or missing data. This may limit the generalizability of the findings. Furthermore, the exclusion of 65 initially recruited children due to incomplete data may introduce selection bias, which should be considered when interpreting the results. Additionally, province-level infection data, including reported infection sources such as school or household, were not available within the analyzed cohort of 135 participants. While external reports from national or regional health authorities may provide such statistics, these were not collected or validated in our study population. Therefore, Tables 9 and 10 were omitted to avoid misinterpretation and ensure consistency with the described study design and sample size.

This study found no significant correlation between Vitamin D3 levels and IFN-Gamma expression ($r = 0.18$, $p = 0.12$). These findings indicate that, within this

cohort, Vitamin D3 levels did not demonstrate a measurable impact on IFN-Gamma production. However, further investigations with expanded sample sizes are imperative to validate and elucidate the mechanisms behind these findings. A comprehensive understanding of the connections between Vitamin D3, IFN-Gamma, and viral infections can guide strategies for preventing and managing viral infections in children.

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Ethical Approval

The data used in this study were anonymized and provided under the supervision of the Ministry of Health, Iraq, in accordance with ethical guidelines. Ethical approval for the study was obtained from the relevant authorities, ensuring compliance with ethical standards and protection of participant confidentiality.

Author Contributions

Maitham G. Yousif: Conceptualization, Methodology, Data Curation, Writing - Original Draft Preparation.
Fadhil G. Al-Amran: Conceptualization, Methodology, Investigation, Writing - Review and Editing.
Salman Rawaf: Data Analysis, Visualization, Writing - Review and Editing.
Dhiya Al-Jumeily: Conceptualization, Methodology, Supervision, Writing - Review and Editing.

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