Kufa Medical Journal | Vol. 22, No. 1, 2026

Original article | DOI: https://doi.org/10.36330/kmj.v22i1.24043

p-ISSN: 1993-517X
e-ISSN: 2709-4464

Diagnostic Utility of Serum Thymic Stromal Lymphopoietin, Immunoglobulin E, and Vitamin D3 as a Combined Biomarker Profile in Pediatric Bronchial Asthma: A Case-Control Study in Iraq

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ABSTRACT

Background: *Thymic stromal lymphopoietin (TSLP), Immunoglobulin E (IgE), and Vitamin D3(Vit D3) play critical roles in asthma pathogenesis, but their combined diagnostic utility in pediatric populations remains under-evaluated. Objective: to investigate the diagnostic role of serum TSLP, IgE, and vitamin D3 in pediatric bronchial asthma. Hypothesis: TSLP and IgE levels are increased, while vitamin D3 levels are decreased in asthmatic children compared with healthy controls.. **Methods**: A case-control study included 60 asthmatic children and 60 healthy controls in Karbala, Iraq. Serum levels of TSLP, total IgE, and 25(OH)Vitamin D3 were quantified using ELISA. Diagnostic performance was assessed via ROC curve analysis, and independent risk factors were determined using multivariate logistic regression. **Results**: Asthmatic children exhibited significantly higher serum IgE (512.1 vs. 178.7 ng/mL, P<0.001) and TSLP (500.0 vs. 239.5 ng/L, P<0.001), but lower Vitamin D3 (17.0 vs. 28.2 ng/mL, P<0.001) compared to controls. Both IgE and TSLP increased progressively with asthma severity. Total serum IgE demonstrated the highest diagnostic accuracy (AUC=0.933), followed by TSLP (AUC=0.902) and Vitamin D3 (AUC=0.819). In multivariate analysis, elevated BMI (aOR=1.528, P=0.014) and total serum IgE (aOR=1.013, P=0.006) emerged as the strongest independent predictors of asthma. **Clinical Implications:** the findings of this study carry significant clinical implications. The excellent diagnostic performance of total serum IgE (AUC = 0.933) and TSLP (AUC = 0.902) suggests their utility as robust biomarkers for asthma phenotyping and severity stratification in the Iraqi pediatric population.* **Conclusion:** *The combined assessment of elevated IgE, increased TSLP, and Vitamin D deficiency offers a valuable biomarker profile for pediatric asthma. These findings highlight the TSLP-IgE inflammatory axis and suggest a potential immunomodulatory role for Vitamin D3.*

Keywords: Thymic Stromal Lymphopoietin (TSLP), Vitamin D Deficiency, Pediatric Allergy.

Article Information

Received: April 30, 2026; Revised: May 24, 2026; Online June, 2026 y

INTRODUCTION

Bronchial asthma is one of the most prevalent chronic non-communicable diseases globally, affecting an estimated 260 to 300 million individuals and causing approximately 1,000 deaths daily [1, 2]. It imposes a disproportionate health burden on the pediatric population, where it ranks as the most common chronic childhood disease, leading to significant morbidity, school absenteeism, and healthcare expenditure [3]. According to the Global Initiative for Asthma (GINA) 2024 report, the global prevalence of childhood asthma continues to rise, particularly in developing regions undergoing rapid urbanization [1]. In the Middle East, the prevalence of childhood asthma is notably high; a recent meta-analysis reported an asthma prevalence of 16.22% among children and adolescents in Iraq, making it one of the highest in the Eastern Mediterranean Region [4]. Despite advances in standard-of-care pharmacotherapy, achieving optimal asthma control remains a substantial challenge, necessitating a deeper understanding of the underlying molecular and immunological mechanisms driving the disease in specific populations. The purpose of our research project was to assess total serum IgE levels, TSLP, and 25-OH-vitamin D3 levels in children from Iraq suffering from bronchial asthma; additionally, we compared the measurements with healthy controls who do not have asthma. We were also interested in whether there are any correlations among these

three measurements, and if there is a correlation between any of these three measurements with the severity of asthma

METHODS

This study was designed as an observational case-control study to evaluate the serum levels of total immunoglobulin E (IgE), thymic stromal lymphopoietin (TSLP), and 25-hydroxyvitamin D3 in children diagnosed with bronchial asthma compared to controls group without asthma. The research was conducted in strict adherence to the ethical principles outlined in the Declaration of Helsinki. Prior to enrollment, written informed consent was obtained from the parents or legal guardians of all participating children after a thorough explanation of the study's objectives, procedures, and potential risks.

Study Population and Setting

Participants were recruited from the outpatient respiratory clinics and inpatient wards of the Children's Teaching Hospital in Karbala, Iraq. The sample collection period extended from July 2025 to January 2026. A total of 120 children aged 5–15 years were enrolled and categorized into two groups: the case group consisted of 60 children with bronchial asthma, and the control group without asthma comprised 60 age- and sex-matched apparently healthy children who attended the hospital for routine check-ups or minor non-inflammatory conditions.

Inclusion and Exclusion Criteria

Children aged 5–15 years with a confirmed diagnosis of bronchial asthma, established by consultant pediatric pulmonologists according to the 2024 Global Initiative for Asthma (GINA) guidelines[1], that participants in the asthma group are stratified into mild, moderate, and severe categories by sing, symptom and (GINA) guidelines . Participants in both groups were excluded if they had other chronic respiratory diseases (such as cystic fibrosis or bronchiectasis), autoimmune disorders, or congenital anomalies, as well as those with active acute systemic or respiratory infections at the time of recruitment. Additionally, children who had received systemic corticosteroids, immunosuppressive, or immunomodulatory therapy within four weeks prior to enrollment, or whose parents or legal guardians declined to provide informed consent, were excluded.

Data Collection and Clinical Assessment

A structured, pre-tested questionnaire was administered via face-to-face interviews with the parents or guardians to collect comprehensive sociodemographic and clinical data. The collected variables included age, sex, residence (urban or rural), passive smoking exposure, household pet exposure, and a detailed family history of asthma or atopy. Clinical symptoms such as the presence of shortness of breath, wheezing, cough, food allergies by guide line (Cushing et al., 2022), and susceptibility to environmental triggers (e.g., cold air and dust) were systematically recorded.

Anthropometric measurements, including weight and height, were obtained using standard calibrated equipment. Body Mass Index (BMI) was calculated as weight in kilograms divided by the square of height in meters (kg/m^2). The BMI values were then interpreted using the World Health Organization (WHO) BMI-for-age growth reference standards for children and adolescents aged 5–19 years [14].

Blood Sample Collection and Processing

Under complete aseptic conditions, five milliliters (5 mL) of venous blood were drawn from the antecubital vein of each participant using sterile disposable syringes.

Biochemical Analysis

The serum concentrations of the selected biomarkers were quantitatively determined using commercially available Enzyme-Linked Immunosorbent Assay (ELISA) kits manufactured by Bioassay Technology Laboratory (BT LAB, Shanghai, China), based on the sandwich ELISA principle. All assays were performed strictly according to the

manufacturer's provided protocols. The intra-assay coefficient of variation (CV) was < 8%, and the inter-assay CV was < 10% for all three kits.

Serum thymic stromal lymphopoietin (TSLP), total immunoglobulin E (IgE), and 25-hydroxyvitamin D3 [25(OH)D3] levels were quantified using commercially available ELISA kits (BT LAB, Shanghai, China; Cat. No. E0426Hu, E0188Hu, and E1543Hu, respectively), following the manufacturer's instructions.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics, Normality was assessed using the Shapiro–Wilk test. Normally distributed data were expressed as mean ± SD and compared using the student's t-test, while comparisons across ≥3 groups were performed using one-way ANOVA followed by Tukey's HSD test.

RESULTS

Demographic and Clinical Characteristics

Table 1 shows comparable age and sex distribution between asthma patients and controls (P = 0.718 and 0.708), confirming appropriate matching. However, BMI was significantly higher in the asthma group (P = 0.001). Asthma patients were more frequently urban residents (P = 0.040) and had higher exposure to passive smoking, as well as a greater prevalence of positive family history (both P < 0.001). No significant difference was observed in pet exposure (P = 0.265). Clinical symptoms (dyspnea, wheeze, and cough) were significantly more common in the asthma group (all P < 0.001). Additionally, food allergy and sensitivity to environmental triggers (cold air and dust) were markedly higher among asthma patients (all P < 0.001).

Table 1: Comparison of Demographic and Clinical Characteristics Between Patients with Asthma and Controls without Asthma.

Parameters	Asthma Group (n=60)	Control Group (n=60)	P-value
Age (years), Mean ± SD	9.27 ± 2.79	9.53 ± 3.16	0.718 (NS)
- 5-8 years, N (%)	26 (43.3%)	26 (43.3%)	
- 9-11 years, N (%)	18 (30.0%)	15 (25.0%)	
- 12-15 years, N (%)	16 (26.7%)	19 (31.7%)	
Sex, N (%)			0.708 (NS)
- Male	38 (63.3%)	35 (58.3%)	
- Female	22 (36.7%)	25 (41.7%)	
BMI (kg/m²), Mean ± SD	19.58 ± 5.73	16.61 ± 2.18	**0.001****
- Underweight (<18.5), N (%)	35 (58.3%)	51 (85.0%)	
- Normal (18.5-24.9), N (%)	16 (26.7%)	9 (15.0%)	
- Overweight (25-29.9), N (%)	5 (8.3%)	0 (0.0%)	

Parameters	Asthma Group (n=60)	Control Group (n=60)	P-value
- Obese (≥30), N (%)	4 (6.7%)	0 (0.0%)	
Passive Smoking Exposure, N (%)			**<0.001*** **
- Exposed	36 (60.0%)	17 (28.3%)	
- Not Exposed	24 (40.0%)	43 (71.7%)	
Residence, N (%)			**0.040***
- Urban	42 (70.0%)	30 (50.0%)	
- Rural	18 (30.0%)	30 (50.0%)	
Household Pet Exposure, N (%)			0.265 (NS)
- Yes	28 (46.7%)	21 (35.0%)	
- No	32 (53.3%)	39 (65.0%)	
Family History of Asthma, N (%)			**<0.001*** **
- Positive	32 (53.3%)	8 (13.3%)	
- Negative	28 (46.7%)	52 (86.7%)	
Shortness of Breath, N (%)			**<0.001*** **
- Yes	54 (90.0%)	0 (0.0%)	
- No	6 (10.0%)	60 (100.0%)	
Wheezing, N (%)			**<0.001*** **
- Yes	37 (61.7%)	0 (0.0%)	
- No	23 (38.3%)	60 (100.0%)	
Cough, N (%)			**<0.001*** **
- Yes	44 (73.3%)	0 (0.0%)	
- No	16 (26.7%)	60 (100.0%)	

Parameters	Asthma Group (n=60)	Control Group (n=60)	P-value
Food Allergy, N (%)			**<0.001*** **
- Yes	27 (45.0%)	3 (5.0%)	
- No	33 (55.0%)	57 (95.0%)	
Cold Air Trigger, N (%)			**<0.001*** **
- Yes	46 (76.7%)	0 (0.0%)	
- No	14 (23.3%)	60 (100.0%)	
Dust Trigger, N (%)			**<0.001*** **
- Yes	45 (75.0%)	0 (0.0%)	
- No	15 (25.0%)	60 (100.0%)	

NS: Not Significant (P > 0.05); * P < 0.05; ** P < 0.01; *** P < 0.001. Continuous variables are expressed as Mean ± SD and compared using the Independent samples t-test. Categorical variables are expressed as N (%) and compared using the Chi-Square test or Fisher's Exact test.

Figure 1 indicates that moderate asthma was the predominant category (40.0%), followed by mild (33.3%) and severe asthma (26.7%)

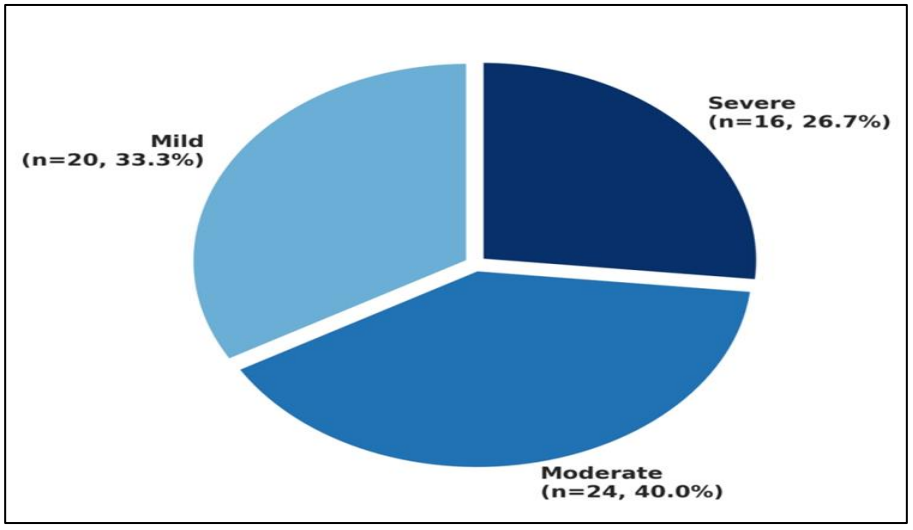

Figure 1. Distribution of asthma severity among the asthma group (n=60).

Moderate asthma was the most common category (40.0%, n=24), followed by mild asthma (33.3%, n=20) and severe asthma (26.7%, n=16).

Serum Biomarker Levels

Table 2 demonstrates significantly higher serum IgE and TSLP levels in the asthma group compared to controls (both P < 0.001).

Table 2. Serum Biomarker Levels in Asthma Patients and Healthy Controls

Parameter	Unit	Asthma Group (n=60)	Control Group (n=60)	P-value
Total Serum Immunoglobulin E (IgE) Mean ± SD	ng/mL	512.08 ± 218.89	178.66 ± 74.63	< 0.001***
Thymic Stromal Lymphopoietin (TSLP) Mean ± SD	ng/L	500.00 ± 201.69	239.51 ± 63.48	< 0.001***

*Data are expressed as Mean ± Standard Deviation (SD). Statistical comparison was performed using the **Independent samples t-test**. ***P < 0.001 indicates a highly significant difference*

Figure 2 shows that 25-hydroxyvitamin D3 levels were significantly lower in asthmatic children (P < 0.001), with median levels indicating deficiency in the asthma group and insufficiency in controls.

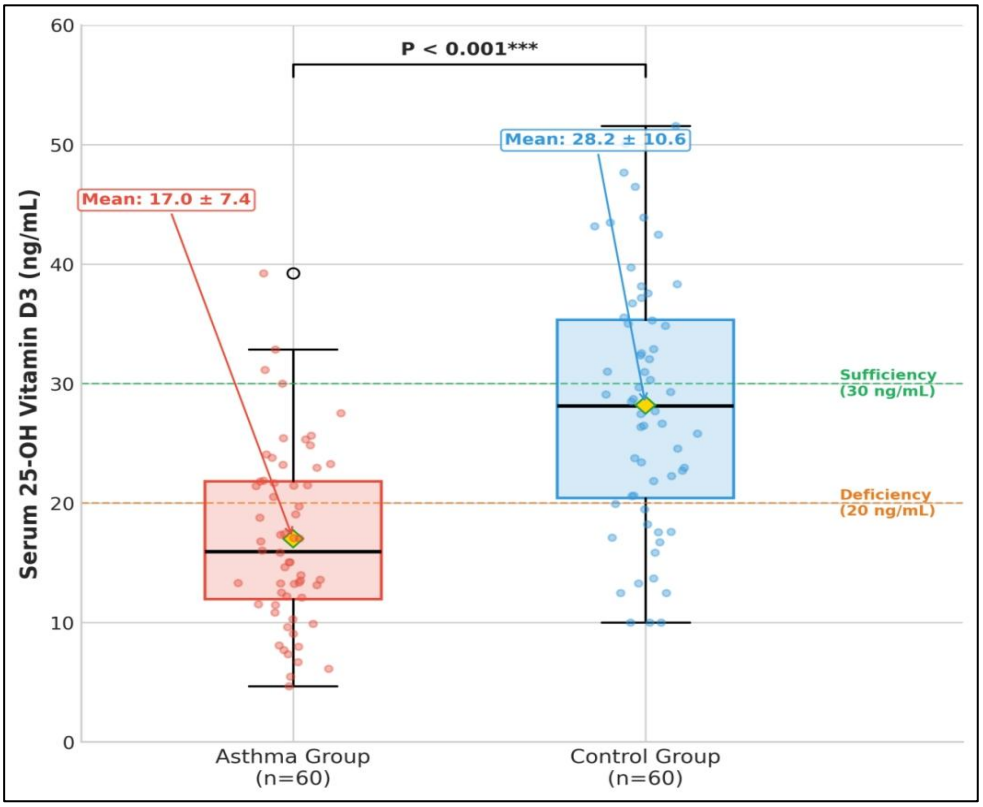

Figure 2. Comparison of serum 25-hydroxyvitamin D3 levels between asthma patients (n=60) and healthy controls (n=60).
Box plots show median (horizontal line), mean (diamond), interquartile range (box), and individual data points. Dashed lines indicate vitamin D deficiency (< 20 ng/mL) and sufficiency (≥ 30 ng/mL) cutoffs. Asthma patients showed significantly lower vitamin D3 levels (17.0 ± 7.4 ng/mL) compared to controls (28.2 ± 10.6 ng/mL). Independent samples t-test, P < 0.001

Serum Biomarker Levels by Asthma Severity

Table 3 shows significant differences in IgE and TSLP levels across asthma severity groups (P < 0.001). Both biomarkers increased progressively from mild to moderate to severe asthma, with all pairwise comparisons remaining significant (P < 0.05).

Table 3. Comparison of serum biomarker levels among asthmatic children classified by disease severity (Mild, Moderate, Severe).

Biomarker	Mild (n=20)	Moderate (n=24)	Severe (n=16)	P-value
Total Serum IgE (ng/mL) Mean ± SD	334.3 ±107.3 A	494.2 ± 132.3 B	708.9 ± 167.7 C	**< 0.001*** **
Serum Thymic Stromal Lymphopoietin (ng/L) Mean ± SD	360.4 ± 99.7 A	519.9 ± 109.4 B	717.6 ± 135.7 C	**< 0.001*** **

*Data are presented as mean ± SD. Different letters indicate significant differences among groups based on one-way ANOVA followed by Tukey's post hoc test (P < 0.05).*** P < 0.001 indicates highly significant differences.*

Inflammatory Biomarkers by Vitamin D Status

Table 4 shows that vitamin D–deficient asthmatic patients had significantly higher IgE and TSLP levels compared to non-deficient patients (P = 0.002 and 0.007, respectively).

Table 4: Comparison of inflammatory biomarkers (IgE, TSLP) based on Vitamin D status among asthmatic patients (n=60).

Biomarker	Vitamin D Deficient (< 20 ng/mL) (n = 39)	Vitamin D Non-Deficient (≥ 20 ng/mL) (n = 21)	Percentage Difference	*P*-value
Total Serum IgE (ng/mL) Mean ± SD	539.1 ± 173.2	385.0 ± 121.1	+ 40.0%	**0.002**
Serum TSLP (ng/L) Mean ± SD	555.9 ± 170.0	419.2 ± 150.2	+ 32.6%	**0.007**

Data are presented as Mean ± Standard Deviation (SD). Statistical significance was determined using independent samples t-test. Percentage difference represents the relative increase in the deficient group compared to the non-deficient group. A P-value < 0.05 is considered statistically significant

Correlation Between Serum Biomarkers

Figure (3) shows a strong positive correlation between IgE and TSLP levels (r = 0.773, P < 0.001), with higher values observed in more severe cases.

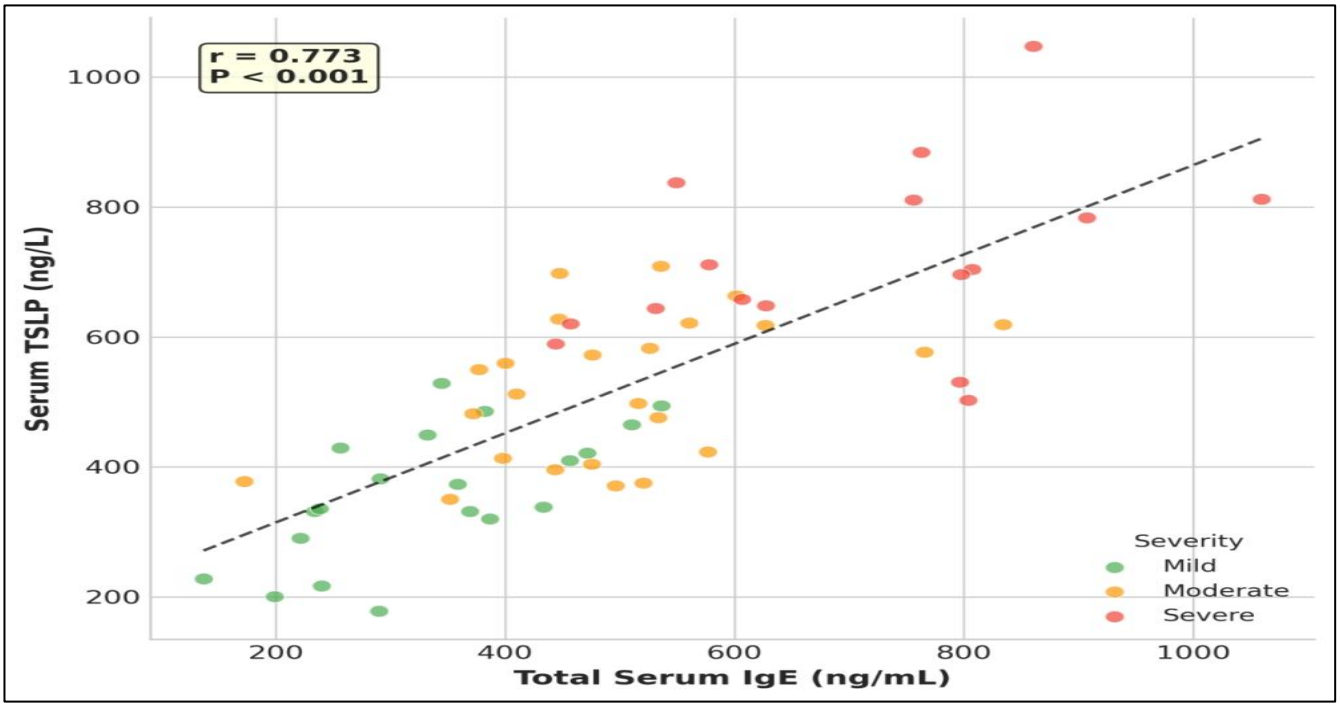

Figure 3. Scatter plot showing the positive correlation between total serum IgE (ng/mL) and serum TSLP (ng/L) in asthmatic children (n = 60), color-coded by disease severity.

Spearman correlation coefficient r = 0.773, P < 0.001. This correlation supports the role of TSLP in promoting IgE class-switching via dendritic cell activation and Th2 polarization.

Diagnostic Performance of Serum Biomarkers

Table 5 and Figures 5–7 demonstrate that IgE showed the highest diagnostic accuracy (AUC = 0.933, P < 0.001), with high sensitivity (85.0%) and specificity (95.0%). TSLP also exhibited excellent performance (AUC = 0.902, P < 0.001), with perfect specificity (100.0%) but lower sensitivity (70.0%), supporting its role as a confirmatory marker. Vitamin D3 showed good but lower accuracy (AUC = 0.819, P < 0.001), with moderate sensitivity and specificity; lower levels were associated with asthma.

Table 5: Diagnostic Performance of Biomarkers in Differentiating Asthma Patients from Healthy Controls (ROC Curve Analysis).

Biomarker	Cut-off Value	AUC (95% CI)	P-value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	Youden's J
Total Serum IgE (ng/mL)	≥ 325.8	0.933 (0.876–0.975)	< 0.001***	85.0	95.0	94.4	86.4	90.0	0.800
Serum TSLP (ng/L)	≥ 415.1	0.902 (0.838–0.952)	< 0.001***	70.0	100.0	100.0	76.9	85.0	0.700
Serum Vitamin D3 (ng/mL)	≤ 20.3	0.819 (0.734–0.890)	< 0.001***	80.0	75.0	76.2	78.9	77.5	0.550

Abbreviations: *ROC: Receiver Operating Characteristic; AUC: Area Under the Curve; CI: Confidence Interval; PPV: Positive Predictive Value; NPV: Negative Predictive Value; IgE: Immunoglobulin E; IL-33: Interleukin-33; TSLP: Thymic Stromal Lymphopoietin.* ***Statistical Note:*** *Cut-off values were determined using Youden's J statistic (Sensitivity + Specificity - 1) to maximize both sensitivity and specificity. *** P < 0.001 indicates a highly significant ability to discriminate between asthma patients and healthy controls. For Vitamin D3, values* below *the cut-off indicate asthma, while for all other biomarkers, values* above *the cut-off indicate asthma.*

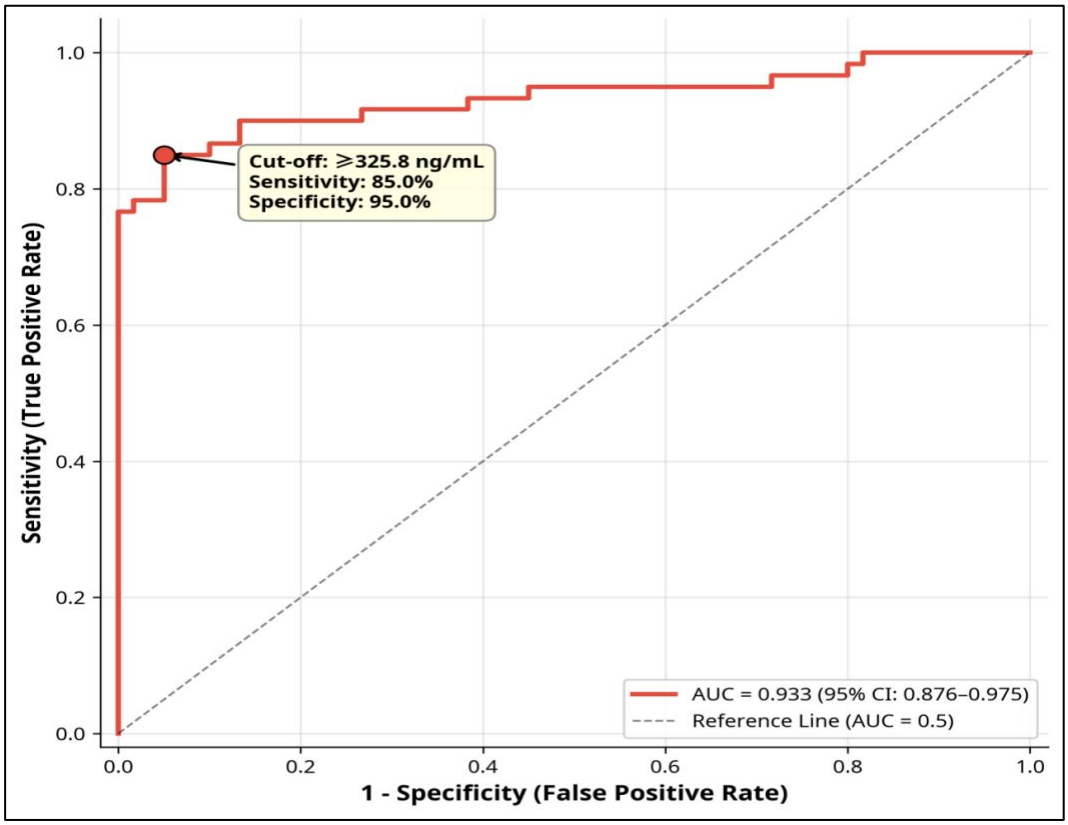

Figure 5: Receiver Operating Characteristic (ROC) curve for Total Serum IgE in distinguishing asthmatic children (n=60) from healthy controls (n=60). The area under the curve (AUC) was 0.933 (95% CI: 0.876–0.975; P < 0.001). The optimal cut-off value was ≥325.8 ng/mL (Youden's J statistic), yielding a sensitivity of 85.0% and specificity of 95.0%.

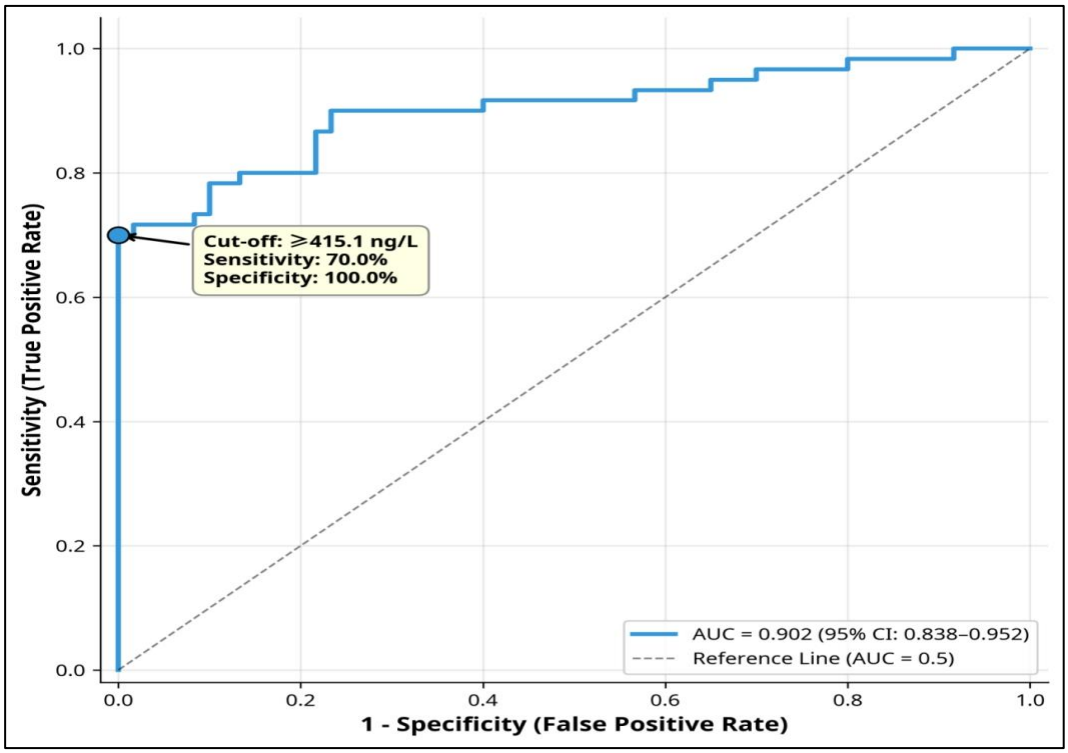

Figure 6: Receiver Operating Characteristic (ROC) curve for Serum TSLP in distinguishing asthmatic children (n=60) from healthy controls (n=60). The area under the curve (AUC) was 0.902 (95% CI: 0.838–0.952; P < 0.001). The optimal cut-off value was ≥415.1 ng/L (Youden's J statistic), yielding a sensitivity of 70.0% and specificity of 100.0%.

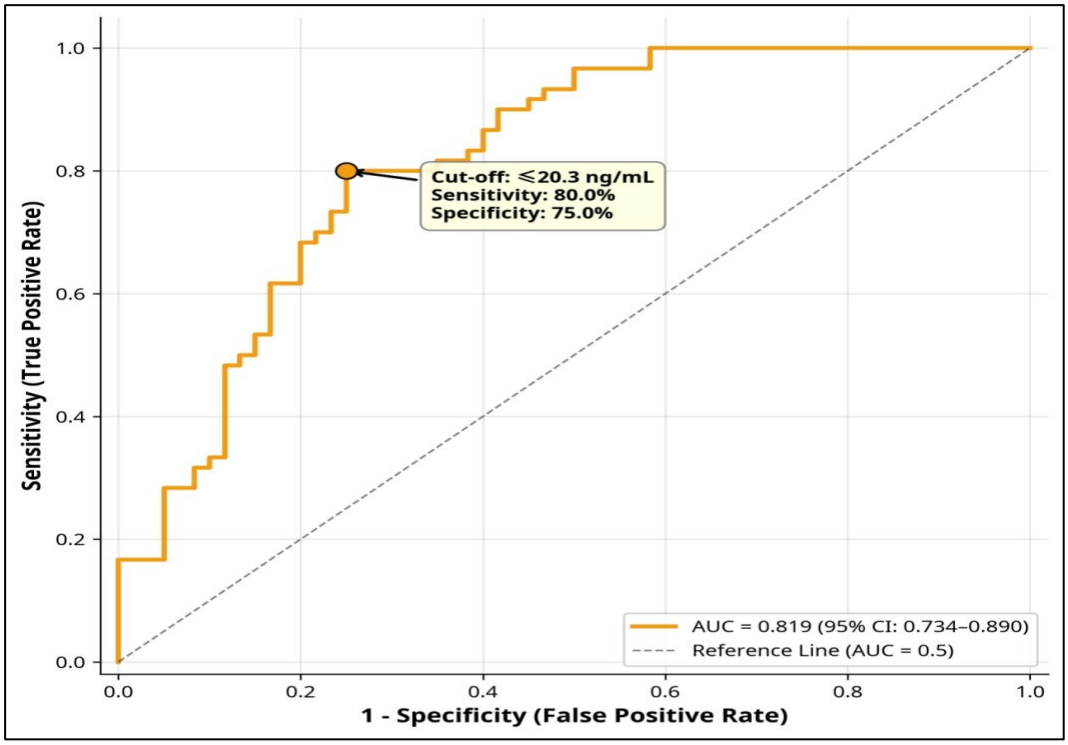

Figure 7: Receiver Operating Characteristic (ROC) curve for Serum Vitamin D3 in distinguishing asthmatic children (n=60) from healthy controls (n=60). The area under the curve (AUC) was 0.819 (95% CI: 0.734–0.890; P < 0.001). The optimal cut-off value was ≤20.3 ng/mL (Youden's J statistic), yielding a sensitivity of 80.0% and specificity of 75.0%.

Logistic Regression Analysis of Risk Factors

Table 6 shows that BMI, family history, passive smoking, urban residence, IgE, TSLP, and vitamin D3 were significant predictors in univariate analysis (all P < 0.05), while age, sex, and pet exposure were not. In the multivariate model, only BMI and IgE remained independent predictors (P = 0.033 and 0.016), whereas TSLP lost significance due to multicollinearity with IgE. The final model retained BMI and IgE as significant predictors, with vitamin D3 showing a non-significant protective trend. The final model demonstrated excellent performance (AUC = 0.972), high explanatory power (Nagelkerke R^2 = 0.866), and strong classification accuracy (95.8%), with good calibration (Hosmer–Lemeshow P = 0.176).

Table 6: Logistic Regression Analysis of Risk Factors for Bronchial Asthma — Univariate, Full Multivariate, and Final Parsimonious Models with Model Goodness-of-Fit Statistics

Variable	B	SE	Wald	OR/aOR	95% CI	P-value
Panel A: Univariate Logistic Regression Analysis						
Age (years)	0.015	0.038	0.16	1.015	0.944–1.091	0.693
Sex (Male)	0.367	0.394	0.87	1.444	0.665–3.136	0.353
BMI (kg/m²)	**0.251**	**0.076**	**10.85**	**1.285**	**1.107–1.491**	**0.001****
Family History (Positive)	**1.717**	**0.427**	**16.18**	**5.571**	**2.413–12.861**	**<0.001*****
Passive Smoking (Exposed)	**1.504**	**0.427**	**12.41**	**4.500**	**1.948–10.393**	**<0.001*****
Residence (Urban)	**0.865**	**0.437**	**3.93**	**2.375**	**1.009–5.591**	**0.048***
Total Serum IgE (ng/mL)	**0.012**	**0.002**	**25.42**	**1.012**	**1.008–1.016**	**<0.001*****
Serum TSLP (ng/L)	**0.016**	**0.003**	**25.40**	**1.016**	**1.010–1.022**	**<0.001*****

Variable	B	SE	Wald	OR/aOR	95% CI	P-value
Serum Vitamin D3 (ng/mL)	**–0.156**	**0.030**	**26.75**	**0.856**	**0.807–0.908**	**<0.001*** **
Panel B: Full Multivariate Model (All Significant Univariate Predictors)						
BMI (kg/m²)	**0.383**	**0.180**	**4.54**	**1.467**	**1.031–2.087**	**0.033***
Family History (Positive)	0.745	1.613	0.21	2.107	0.089–49.722	0.644
Passive Smoking (Exposed)	–1.574	1.644	0.92	0.207	0.008–5.195	0.338
Residence (Urban)	2.156	1.237	3.04	8.638	0.765–97.559	0.081
Total Serum IgE (ng/mL)	**0.014**	**0.006**	**5.80**	**1.014**	**1.003–1.025**	**0.016***
Serum TSLP (ng/L)	0.003	0.008	0.11	1.003	0.987–1.019	0.743
Serum Vitamin D3 (ng/mL)	–0.114	0.061	3.53	0.892	0.792–1.005	0.060
Panel C: Final Parsimonious Model (After Backward Elimination)						
BMI (kg/m²)	**0.424**	**0.173**	**6.02**	**1.528**	**1.089–2.144**	**0.014***
Total Serum IgE (ng/mL)	**0.013**	**0.005**	**7.42**	**1.013**	**1.004–1.022**	**0.006****
Serum Vitamin D3 (ng/mL)	–0.084	0.051	2.75	0.919	0.832–1.015	0.097
Panel D: Model Summary and Goodness-of-Fit						
–2 Log-Likelihood	40.63					
Chi-Square (Model)	125.72 (P < 0.001)					
Cox & Snell R^2	0.649					
Nagelkerke R^2	0.866					
Overall Classification Accuracy	95.8% (115/120)					
Sensitivity	93.3% (56/60)					
Specificity	98.3% (59/60)					
AUC (ROC)	0.972					
Hosmer-Lemeshow Test	$\chi^2 = 8.95$, P = 0.176					

*Abbreviations: B, regression coefficient; SE, standard error; OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval; BMI, body mass index; IgE, immunoglobulin E; TSLP, thymic stromal lymphopoietin; AUC, area under the curve; ROC, receiver operating characteristic. * P < 0.05; ** P < 0.01; *** P < 0.001. Bold rows in Panels A, B, and C indicate statistically significant predictors (P < 0.05).*

Panel A presents univariate analysis; variables with P < 0.05 were entered into the full multivariate model (Panel B).

Panel C shows the final model after backward stepwise elimination retaining variables with the strongest independent associations. TSLP lost significance in the multivariate model due to strong multicollinearity with IgE (VIF = 28.0 and 33.3, respectively), which is biologically expected as both are epithelial-derived alarmins sharing the same inflammatory pathway. Panel D reports goodness-of-fit statistics for the final parsimonious model (Panel C).

DISCUSSION

The present study provides a comprehensive evaluation of the interplay between serum biomarkers (total IgE, TSLP, and 25-hydroxyvitamin D3) and demographic factors in the pathogenesis and severity of bronchial asthma among Iraqi children. Our primary findings demonstrate that asthmatic children exhibit significantly elevated levels of total serum IgE and TSLP, alongside markedly reduced levels of vitamin D3, compared to healthy controls. Furthermore, disease severity was positively correlated with IgE and TSLP, and inversely correlated with vitamin D3 status. In the multivariate analysis, body mass index (BMI) and total serum IgE emerged as the most robust independent predictors of asthma. These results not only corroborate the established immunological paradigms of asthma but also provide context-specific insights into the Iraqi pediatric population.

In our groups, BMI was significantly higher in asthmatic children and remained a strong independent predictor of asthma in the final parsimonious logistic regression model (aOR = 1.528). This finding aligns with a growing body of evidence linking obesity to asthma Ma et al [18]. demonstrated that elevated BMI and obesity-related adipokines, such as leptin, are intricately involved in childhood asthma, promoting systemic non-atopic inflammation. Similarly, Fang et al. [19] confirmed a significant positive association between BMI and asthma risk in pediatric populations. The mechanical effects of truncal obesity on lung compliance, coupled with the pro-inflammatory state induced by adiposity, likely contribute to this phenotype. Furthermore, our univariate analysis identified passive smoking and positive family history as significant risk factors. These observations are highly consistent with previous Iraqi studies; for instance, Al-Kubaisy et al. [20] and Alsamarai et al. [21] independently reported that family history of asthma and parental smoking are predominant risk factors for asthma development among children in Baghdad and other Iraqi governorates.

Our study revealed a profound elevation of total serum IgE in asthmatic children, which strongly correlated with disease severity. This is in agreement with the Iraqi study by Hameed et al. [22] conducted in Karbala, which reported highly significant differences in IgE levels between asthmatic patients and controls, noting that high IgE was related to asthma severity and eosinophil counts. The diagnostic utility of IgE in our study was exceptional, yielding an AUC of 0.933, which surpasses the diagnostic performance reported in several international cohorts, such as the study by Wang et al. [23], where tIgE showed an AUC of 0.835 for diagnosing childhood allergic asthma.

Crucially, we observed a strong positive correlation (r = 0.773) between serum TSLP and total IgE. Thymic stromal lymphopoietin (TSLP) is an epithelial-derived alarmin recognized as a master regulator of type 2 immunity [5]. Mechanistically, TSLP activates dendritic cells, upregulating costimulatory molecules and promoting Th2 differentiation, which subsequently drives IL-4 and IL-13 production, leading to IgE class-switching in B cells [24]. Our finding that TSLP levels increase in a dose-response manner with asthma severity is supported by Chorvinsky et al. [25], who linked higher pulmonary TSLP levels to clinical disease severity in children. However, in our multivariate logistic regression, TSLP lost its independent predictive significance due to strong multicollinearity with IgE. This statistical phenomenon perfectly reflects their biological relationship: TSLP is the upstream trigger that culminates in the downstream effector, IgE, meaning they share the same inflammatory pathway rather than acting as independent physiological variables.

A striking finding of the present study is the high prevalence of vitamin D deficiency among asthmatic children, with serum levels inversely correlating with total IgE (r = -0.631) and disease severity. This finding strongly resonates with multiple Iraqi studies. Al-Tuama et al. [12] found that 92% of asthmatic children in Kerbala were vitamin D insufficient, while Al-Shamsi [26] reported from Al Diwaniyah that serum 25-hydroxyvitamin D levels were markedly decreased as asthma severity increased. Furthermore, Al-Sharifi and Al-Ammar [13] concluded that vitamin D inadequacy is predominant among asthmatic kids living in Iraq.

The inverse relationship between vitamin D and IgE observed in our cohort highlights the immunomodulatory properties of vitamin D. Biologically, active vitamin D promotes the generation of IL-10-secreting T-regulatory cells and suppresses Th2 skewing. Consequently, vitamin D deficiency removes this inhibitory check, allowing exaggerated Th2 responses and enhanced IgE production [10, 27]. Our data support the hypothesis that correcting vitamin D deficiency could potentially mitigate the Th2-driven inflammatory cascade in pediatric asthma.

CONCLUSION

The combined assessment of elevated IgE, increased TSLP, and Vitamin D deficiency offers a valuable biomarker profile for pediatric asthma. These findings highlight the TSLP-IgE inflammatory axis and suggest a potential immunomodulatory role for Vitamin D3.

ACKNOWLEDGMENT

The authors would like to express their gratitude to the medical and nursing staff at the Children Teaching Hospital in Karbala, Iraq, for their invaluable assistance in patient recruitment and sample collection. We also thank all the children and their parents who participated in this study.

Ethical approval

The present study which is conducted by authors ((Zahraa Hazim Aziz1, Thikra Abdullah Mahmood) was approved by the local Department of medical microbiology committee.

Statement of Permission and Conflict of Interests

The others declare that there is statement of permission and conflict of interests

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