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Serum Total IgE, Allergen-Specific IgE and Interleukin-37 in Adults with Bronchial Asthma: A Case–Control Study from Baghdad, Iraq

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ABSTRACT

Background: Immunoglobulin E (IgE) drives type 2 inflammation in allergic asthma, whereas interleukin-37 (IL-37) has been proposed as an endogenous restraint on airway inflammation.

Objectives: To quantify serum total IgE, allergen-specific IgE and IL-37 in adults with asthma and relate them to haematological indices.

Methods: In this hospital-based case–control study conducted in Baghdad from November 2025 to March 2026, 60 adults with physician-diagnosed asthma and 40 self-reported healthy, non-atopic controls were enrolled by consecutive sampling. Total IgE and IL-37 were measured by enzyme-linked immunosorbent assay.

Results: Total IgE and IL-37 were non-normally distributed and are therefore reported as medians with interquartile ranges (IQRs). Both were higher in patients with asthma than in controls: total IgE, 351.80 (200.20–546.90) versus 68.23 (48.22–82.52) IU/mL ($P < 0.0001$), and IL-37, 127.20 (101.50–173.30) versus 67.36 (45.36–80.15) pg/mL ($P < 0.0001$). Eosinophil and basophil percentages were higher and monocyte percentage was lower after Bonferroni correction. Total IgE showed nominal positive monotonic correlations with monocytes ($r_s = 0.384$, $P = 0.003$) and lymphocytes ($r_s = 0.333$, $P = 0.010$), and nominal inverse correlations with eosinophils ($r_s = −0.329$, $P = 0.011$), neutrophils ($r_s = −0.326$, $P = 0.012$) and basophils ($r_s = −0.281$, $P = 0.031$). None of these IgE correlations remained significant after Bonferroni correction for 55 correlations (adjusted threshold $P < 0.0009$).

Conclusions: Adults with asthma in Baghdad had higher total IgE, IL-37, eosinophil percentage and basophil percentage than the selected controls, together with a locally distinctive aeroallergen-sensitisation pattern. The IL-37 elevation may be consistent with a possible counter-regulatory response.

Keywords: Asthma; Immunoglobulin E; Interleukin-37; Allergens; Eosinophils

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INTRODUCTION

Asthma is a chronic inflammatory airway disorder defined by variable respiratory symptoms—including wheeze, dyspnoea, chest tightness and cough—together with fluctuating expiratory airflow limitation [1]. The Global Burden of Disease study estimated 260.5 million prevalent cases and 436,190 deaths in 2021, with morbidity concentrated in low- and middle-income settings where diagnostic and therapeutic resources are constrained [2,3]. Disease arises from interactions among genetic susceptibility, environmental exposure and immune dysregulation, culminating in persistent inflammation and bronchial wall remodelling [1].

The dominant immunological axis in allergic asthma is type 2 inflammation. Allergen presentation activates T helper 2 lymphocytes and group 2 innate lymphoid cells, releasing interleukin (IL)-4, IL-5 and IL-13, which drive B-cell class switching to immunoglobulin E (IgE), eosinophil recruitment, mucus hypersecretion and airway hyperresponsiveness [4]. Total IgE thus provides an accessible surrogate of systemic atopic activation, whereas allergen-specific IgE defines the sensitisation profile that underlies symptom triggering, guides environmental avoidance and determines eligibility for allergen immunotherapy and anti-IgE therapy [5,6]. Because aeroallergen exposure is shaped by climate and vegetation, sensitisation patterns cannot be extrapolated between countries; arid Middle Eastern environments favour *Chenopodiaceae* and *Amaranthaceae* weed pollens alongside house dust mites and cockroach allergens [7,8].

Counterbalancing these pathways, IL-37 has emerged as a distinctive anti-inflammatory member of the IL-1 family. It signals through the IL-18 receptor α-chain together with the decoy co-receptor SIGIRR/IL-1R8, and intracellularly via Smad3, suppressing nuclear factor-κB and mitogen-activated protein kinase signalling [9,10]. In murine allergic airway disease, IL-37 reduces eosinophilic infiltration, mucus production, Th2 and Th17 responses and remodelling, and antagonises the alarmins IL-1β and IL-33 [10–12]. Human data are discordant: several studies report reduced circulating IL-37 in asthma and allergic rhinitis, indicating deficient endogenous restraint [13–15], whereas others describe elevated IL-37 in asthma and other active inflammatory states, interpreted as a compensatory surge [16,17]. Direction of change may therefore depend on disease phase, treatment, age and assay platform, and remains unresolved in adult Middle Eastern populations, with sparse and mutually inconsistent Iraqi reports [15,16].

Three gaps motivated the present work: the concurrent behaviour of total IgE, allergen-specific IgE and IL-37 has rarely been assessed in one adult cohort; the aeroallergen spectrum of adults with asthma in Baghdad has not been characterised with a standardised multi-allergen immunoblot panel; and the relation of IL-37 to conventional type 2 markers remains uncertain. This case–control study therefore measured serum total IgE, specific IgE against 20 inhalant allergens, IL-37 and complete blood-count parameters in adults with bronchial asthma and selected controls from Baghdad. It also evaluated the observed associations among these measures without presuming that correlation, or its absence, demonstrates a regulatory mechanism.

MATERIALS AND METHODS

Study design, setting and period

A hospital-based, observational case–control study was conducted at the Specialized Allergy Center of the Al-Rusafa Health Directorate, Baghdad, Iraq, between November 2025 and March 2026. Laboratory work was carried out in the immunology laboratories of the Iraqi Center for Cancer and Medical Genetic Research, Mustansiriyah University. The study was reported in accordance with the Strengthening the Reporting of Observational Studies in

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Epidemiology (STROBE) recommendations for case–control studies [18].

Participants and eligibility criteria

One hundred adults were enrolled by consecutive non-probability sampling: 60 patients with bronchial asthma and 40 self-reported healthy controls. Cases were aged 18 years or older and had a diagnosis recorded by the treating physician as meeting Global Initiative for Asthma (GINA) criteria, including spirometric evidence of variable expiratory airflow limitation [1]. Controls were recruited during the same period from hospital attendees and staff. Control eligibility required no known asthma, allergic rhinitis, atopic dermatitis, urticaria or food allergy, no first-degree family history of atopy, and no condition listed in the general exclusion criteria. The term "self-reported healthy" indicates that eligibility was established by structured history rather than by spirometric, allergy-test or laboratory screening.

Participants in either group were excluded for autoimmune or connective-tissue disease, current or previous malignancy, immunodeficiency, acute infection within the preceding four weeks, chronic renal or hepatic disease, pregnancy or lactation, smoking, or receipt of systemic corticosteroids, immunosuppressive agents or biological therapy within four weeks, because these factors may modify circulating IgE or IL-1-family cytokines. Patients with chronic parasitic infection were also excluded. For this study, non-exacerbating outpatient status was operationally defined as routine outpatient assessment with no acute infection, no acute severe exacerbation requiring emergency treatment and no systemic corticosteroid use during the preceding four weeks. A validated asthma-control score and a longer prespecified stability interval were not recorded; therefore, the cohort should not be interpreted as uniformly well-controlled asthma.

Sample size considerations

The sample size was determined by the number of eligible consecutive attendees during the predefined recruitment window. Post hoc evaluation indicated that the achieved design (60 cases versus 40 controls, two-sided $\alpha = 0.05$) provides 80% power to detect a standardised difference of approximately 0.58 standard deviations and above 99% power for the differences observed in total IgE, IL-37 and eosinophil percentage; the study was therefore well powered for the primary biomarker comparisons.

Clinical and anthropometric assessment

Demographic data, symptom history, disease duration, family history of atopy and current medication were recorded on a structured case-report form during direct interview. However, participant-level medication records were not available in an analysable dataset for the present report; class-level frequencies. Weight and height were measured in light clothing without footwear, and body mass index (BMI) was calculated as weight in kilograms divided by height in metres squared.

Blood sampling and processing

Five millilitres of venous blood were withdrawn from the antecubital vein under aseptic conditions. Two millilitres were dispensed into dipotassium ethylenediaminetetraacetic acid tubes for complete blood count, performed within two hours of collection. The remaining three millilitres were delivered into plain gel separator tubes, allowed to clot at room temperature for 20 to 30 minutes and centrifuged at 3,000 revolutions per minute for 10 minutes. Serum was separated, inspected for haemolysis, aliquoted into sterile Eppendorf tubes and stored at −20 °C. Repeated freeze–thaw cycles were avoided and all samples of a given analyte were assayed in a single batch to eliminate inter-assay variability. To minimize measurement bias, all serum samples were coded before laboratory analysis, and laboratory personnel performing the biomarker assays were blinded

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to participants' clinical status throughout the study.

Complete blood count

Total leucocyte count, differential percentages of neutrophils, lymphocytes, monocytes, eosinophils and basophils, and haemoglobin concentration were measured on an automated haematology analyser operated under the manufacturer's daily quality-control protocol with commercial control material at three levels. Differential results are reported as relative percentages, as recorded in the routine laboratory report.

Determination of serum total IgE

Serum total IgE was quantified by a quantitative solid-phase enzyme-linked immunosorbent assay (ELISA) kit (Dr. Fooke Laboratorien GmbH, Neuss, Germany) according to the manufacturer's instructions. Diluted samples, calibrators and controls were incubated in microwells coated with anti-human IgE antibody; after washing, bound IgE was detected with a horseradish peroxidase-conjugated anti-IgE antibody and tetramethylbenzidine substrate, the reaction stopped and absorbance read at 450 nm. All samples were assayed in duplicate and results expressed in international units per millilitre.

Determination of serum IL-37

Serum IL-37 was measured with a commercial sandwich ELISA kit (MyBioSource, San Diego, CA, USA) according to the manufacturer's protocol. Standards, controls and samples were added to microwells pre-coated with a monoclonal anti-human IL-37 antibody, incubated with a biotin-conjugated detection antibody and then streptavidin–horseradish peroxidase, developed with tetramethylbenzidine, stopped with sulphuric acid and read at 450 nm. Samples were analysed in duplicate. Concentrations are reported in picograms per millilitre (pg/mL), the unit used for the human IL-37 kit calibration and output. Samples exceeding the highest standard were diluted in kit diluent and re-assayed with the dilution factor applied.

Detection of allergen-specific IgE

Allergen-specific IgE was determined by the Polycheck Allergy multiparameter immunoblot system (Biocheck GmbH, Münster, Germany), in which individual allergen extracts are immobilised as discrete lines on a test strip. Serum was incubated with the strip and bound specific IgE visualised with an enzyme-labelled anti-human IgE antibody and chromogenic substrate; band intensity was quantified by a dedicated scanner against reference calibration and assigned to conventional semi-quantitative classes. A concentration of 0.35 kU/L or greater (class ≥ 1) was regarded as positive sensitisation. The panel comprised 20 inhalant allergens relevant to the local environment: tree pollens (olive, *Olea europaea*, T09; cypress, *Cupressus sempervirens*, T23), grass pollens (Bermuda grass, *Cynodon dactylon*, G02; Timothy grass, *Phleum pratense*, G06; rye, *Secale cereale*, G12), weed pollens (mugwort, *Artemisia vulgaris*, W06; plantain, *Plantago lanceolata*, W09; goosefoot, *Chenopodium album*, W10; Russian thistle, *Salsola kali*, W11), house dust mites (*Dermatophagoides pteronyssinus*, D01; *Dermatophagoides farinae*, D02; *Blomia tropicalis*, D201), animal epithelia (cat, E01; dog, E02/E05; camel, E17), moulds (*Penicillium notatum*, M01; *Cladosporium herbarum*, M02; *Aspergillus fumigatus*, M03; *Alternaria alternata*, M06) and the insect allergen *Blattella germanica* (I06).

Statistical analysis

Data were compiled in Microsoft Excel and analysed using GraphPad Prism version 10.0 (GraphPad Software, Boston, MA, USA). The distribution of each continuous variable was examined separately in each group by the Shapiro–Wilk test, supplemented by histograms and quantile–quantile plots. Body mass index and neutrophil, lymphocyte and monocyte percentages satisfied the normality criterion in both groups and are summarised

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as mean ± standard deviation; these variables were compared by the unpaired two-tailed Student t-test. Age, total leucocyte count, basophil percentage, eosinophil percentage, haemoglobin, total IgE and IL-37 deviated from normality in at least one group and are summarised as median with interquartile range (IQR); these variables were compared by the Mann–Whitney U test. Categorical allergen-specific IgE results are expressed as frequencies with percentages and were compared by the Fisher exact test because controls contained zero positive observations. Allergen-specific IgE was analysed as sensitisation rather than as a diagnostic test for asthma; sensitivity and specificity were therefore not calculated. Associations among the 11 continuous variables were quantified by Spearman rank correlation coefficients (r_s), which assess monotonic association. Cohen's d was calculated for normally distributed variables. For skewed variables, the patient-to-control ratio of medians is reported only as a descriptive fold change and not as a standardised effect size; confidence intervals for these ratios were not estimated. Three prespecified families were corrected separately by Bonferroni adjustment: 11 between-group continuous-variable comparisons ($P < 0.0045$), 20 allergen comparisons ($P < 0.0025$), and 55 pairwise correlations among 11 variables ($P < 0.0009$). Results with unadjusted $P < 0.05$ that did not meet the relevant corrected threshold are described as nominal. Statistical notation was standardised as follows: ns, $P \geq 0.05$; * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$; and **** $P < 0.0001$.

RESULTS

Demographic and Laboratory Characteristics of the Study Groups

The groups were comparable in age and body mass index. Median age was 34.00 years (IQR 32.00–36.00) in controls and 36.00 years (IQR 33.00–37.00) in patients ($P = 0.0844$). Mean body mass index was 26.48 ± 1.95 and 26.89 ± 1.91 kg/m², respectively ($P = 0.3044$; Cohen's $d = 0.21$). Patients with asthma had higher total IgE and IL-37 concentrations than controls (Table 1). Median total IgE was 351.80 IU/mL (IQR 200.20–546.90) in patients versus 68.23 IU/mL (IQR 48.22–82.52) in controls, a descriptive 5.2-fold difference ($P < 0.0001$). Median IL-37 was 127.20 pg/mL (IQR 101.50–173.30) versus 67.36 pg/mL (IQR 45.36–80.15), a descriptive 1.9-fold difference ($P < 0.0001$). Both comparisons remained significant at the Bonferroni-adjusted threshold for 11 continuous-variable comparisons ($P < 0.0045$; Figure 1).

Table 1. Demographic, haematological and immunological parameters in patients with asthma and controls.

Variable	Controls (n = 40)	Patients (n = 60)	Effect measure	P value
Age (years), median (IQR)	34.00 (32.00–36.00)	36.00 (33.00–37.00)	—	0.0844[2]
Body mass index (kg/m²), mean ± SD	26.48 ± 1.95	26.89 ± 1.91	d = 0.21	0.3044[1]
Leucocytes (×10⁹/L), median (IQR)	7.80 (6.47–8.86)	6.88 (5.87–8.45)	0.88×	0.0647[2]
Neutrophils (%), mean ± SD	55.60 ± 1.99	55.13 ± 5.15	d = −0.11	0.4702[1]
Lymphocytes (%), mean ± SD	33.93 ± 2.28	32.38 ± 4.29	d = −0.43	0.0292[1]
Monocytes (%), mean ± SD	7.60 ± 1.72	5.57 ± 2.65	d = −0.87	< 0.0001[1]
Basophils (%), median (IQR)	0.50 (0.30–0.65)	0.70 (0.40–0.90)	1.40×	0.0004[2]
Eosinophils (%), median (IQR)	2.40 (1.09–3.50)	6.00 (5.00–7.30)	2.50×	< 0.0001[2]
Haemoglobin (g/dL), median (IQR)	13.20 (12.45–13.80)	12.60 (11.90–13.50)	0.95×	0.0231[2]
Total IgE (IU/mL), median (IQR)	68.23 (48.22–82.52)	351.80 (200.20–546.90)	5.16×	< 0.0001[2]
IL-37 (pg/mL), median (IQR)	67.36 (45.36–80.15)	127.20 (101.50–173.30)	1.89×	< 0.0001[2]

1: unpaired Student t-test. 2: The Mann–Whitney U test. Cohen's d is shown for normally distributed variables. The Bonferroni-adjusted threshold for the 11 continuous-variable comparisons was $P < 0.0045$.

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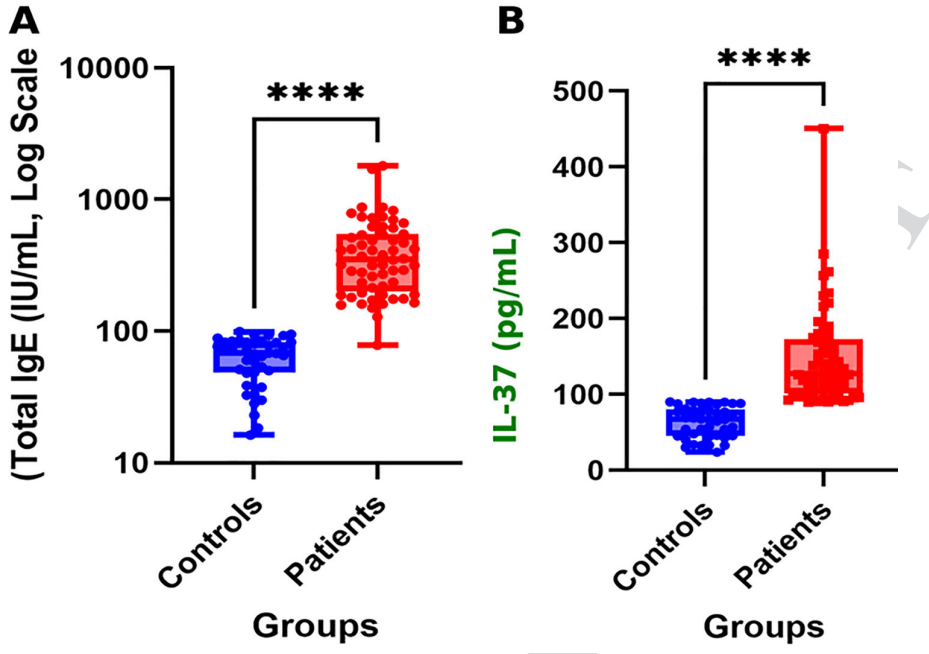


Figure 1. Serum concentrations of total immunoglobulin E and interleukin-37 in patients with asthma (n = 60) and controls (n = 40). (A) Total IgE (IU/mL), plotted on a logarithmic scale; (B) IL-37 (pg/mL). Box plots show the median and IQR, with whiskers extending to the minimum and maximum and individual observations superimposed. Groups were compared by the Mann–Whitney U test. **** P < 0.0001.

Table 2. Selected Spearman rank correlations among study parameters.

Variable pair	r_s	95% confidence interval	P value
Total IgE and monocytes (%)	0.384	0.14 to 0.58	0.003
Total IgE and lymphocytes (%)	0.333	0.08 to 0.54	0.010
Total IgE and eosinophils (%)	−0.329	−0.54 to −0.08	0.011
Total IgE and neutrophils (%)	−0.326	−0.54 to −0.08	0.012
Total IgE and basophils (%)	−0.281	−0.50 to −0.03	0.031
Neutrophils and lymphocytes (%)	−0.842	−0.90 to −0.75	< 0.0001
Neutrophils and monocytes (%)	−0.518	−0.68 to −0.30	< 0.0001

Nominal, unadjusted P values are shown. Fifty-five pairwise correlations were examined, giving a Bonferroni-adjusted threshold of P < 0.0009.

Among granulocytes, eosinophil percentage showed the largest relative difference, rising from a median of 2.40% (IQR 1.09–3.50) in controls to 6.00% (IQR 5.00–7.30) in patients (descriptive median ratio, 2.50; P < 0.0001). Basophil percentage increased from 0.50% (IQR 0.30–0.65) to 0.70% (IQR 0.40–0.90; median ratio, 1.40; P = 0.0004). Monocyte percentage decreased from 7.60 ± 1.72% to 5.57 ± 2.65% (P < 0.0001; Cohen's d = −0.87), whereas the decreases in lymphocyte percentage (P = 0.0292) and haemoglobin (P = 0.0231) were nominal. Total leucocyte count (P = 0.0647) and neutrophil percentage (P = 0.4702; Cohen's d = −0.11) did not differ significantly. After Bonferroni correction, only the between-group differences in eosinophils, basophils, monocytes, total IgE and IL-37 remained statistically significant (Figure 2).

Correlations among immunological and haematological parameters

Among the 55 pairwise Spearman analyses, total IgE showed nominal positive monotonic correlations with monocyte percentage (r_s = 0.384, P = 0.003) and lymphocyte percentage (r_s = 0.333, P = 0.010), and

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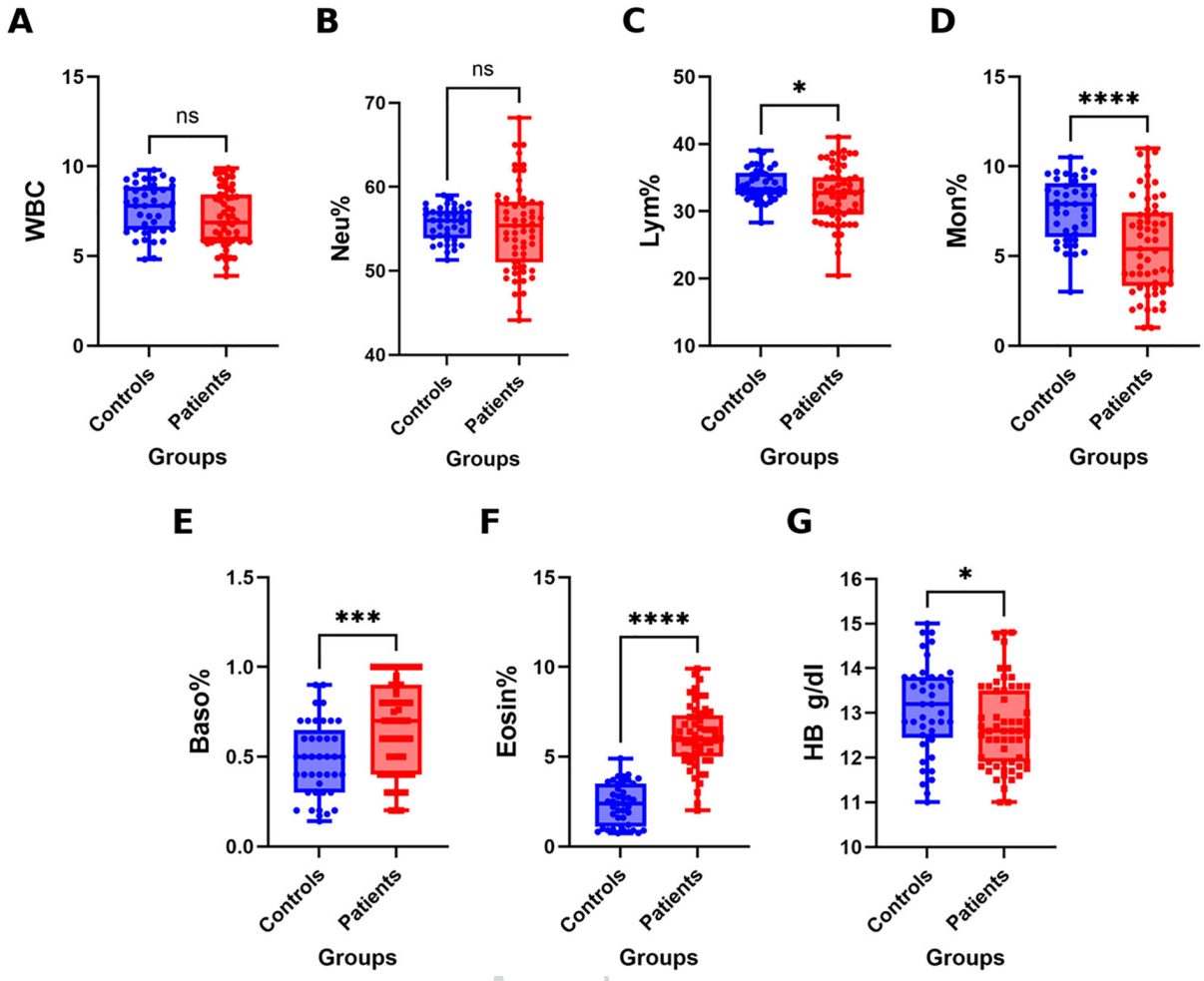


Figure 2. Haematological parameters in patients with asthma and controls. (A) Total leucocyte count; (B) neutrophils; (C) lymphocytes; (D) monocytes; (E) basophils; (F) eosinophils; (G) haemoglobin. Individual observations and box plots are shown. Normally distributed variables were compared by the unpaired Student t-test; non-normally distributed variables were compared by the Mann–Whitney U test. ns, $P \geq 0.05$; * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$; **** $P < 0.0001$.

nominal inverse correlations with eosinophil percentage ($r_s = -0.329$, $P = 0.011$), neutrophil percentage ($r_s = -0.326$, $P = 0.012$) and basophil percentage ($r_s = -0.281$, $P = 0.031$; Table 2). None of these IgE correlations remained significant at the Bonferroni-adjusted threshold of $P < 0.0009$. The neutrophil–lymphocyte ($r_s = -0.842$, $P < 0.0001$) and neutrophil–monocyte ($r_s = -0.518$, $P < 0.0001$) correlations remained significant after correction. Serum IL-37 showed no statistically significant monotonic association with age, body mass index, any leucocyte subset, haemoglobin or total IgE. Its weak inverse correlation with total IgE ($r_s = -0.24$) was not statistically significant ($P > 0.05$). Selected correlations are illustrated in Figure 3, and the full coefficient matrix is shown in Figure 4.

Allergen-specific IgE sensitisation patterns

Allergen-specific IgE was detected across all seven allergen categories in the patient group, whereas none of the selected non-atopic controls tested positive for any of the 20 allergens (Table 3). Grass and weed pollens predominated: Timothy grass and goosefoot were each recognised by 38 patients (63.3%), followed by Bermuda grass and rye (35 each, 58.3%), olive and cypress (31 each, 51.7%), mugwort (30, 50.0%), plantain (29, 48.3%) and Russian thistle (28, 46.7%). Among indoor

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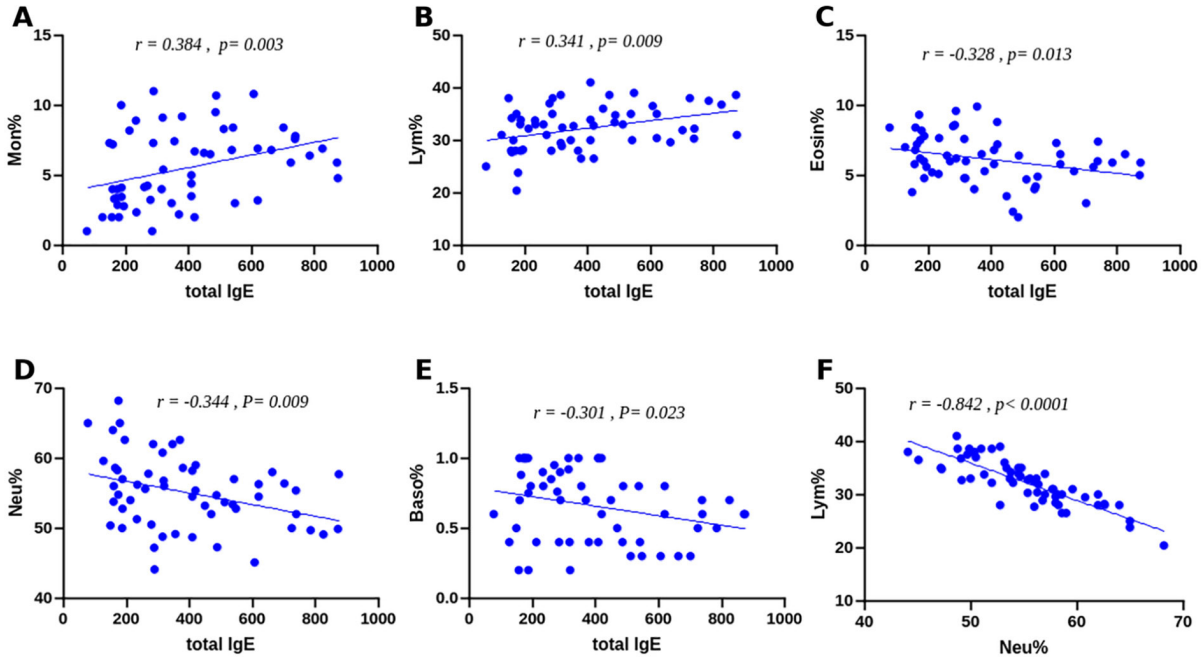


Figure 3. Scatter plots of selected Spearman rank correlations. (A) Total IgE and monocytes; (B) total IgE and lymphocytes; (C) total IgE and eosinophils; (D) total IgE and neutrophils; (E) total IgE and basophils; (F) neutrophils and lymphocytes. Solid lines are visual guides; inferential results are based on monotonic Spearman rank associations. Coefficients and unadjusted P values are shown within each panel. The five total IgE correlations were nominal and did not remain significant after Bonferroni correction ($P < 0.0009$).

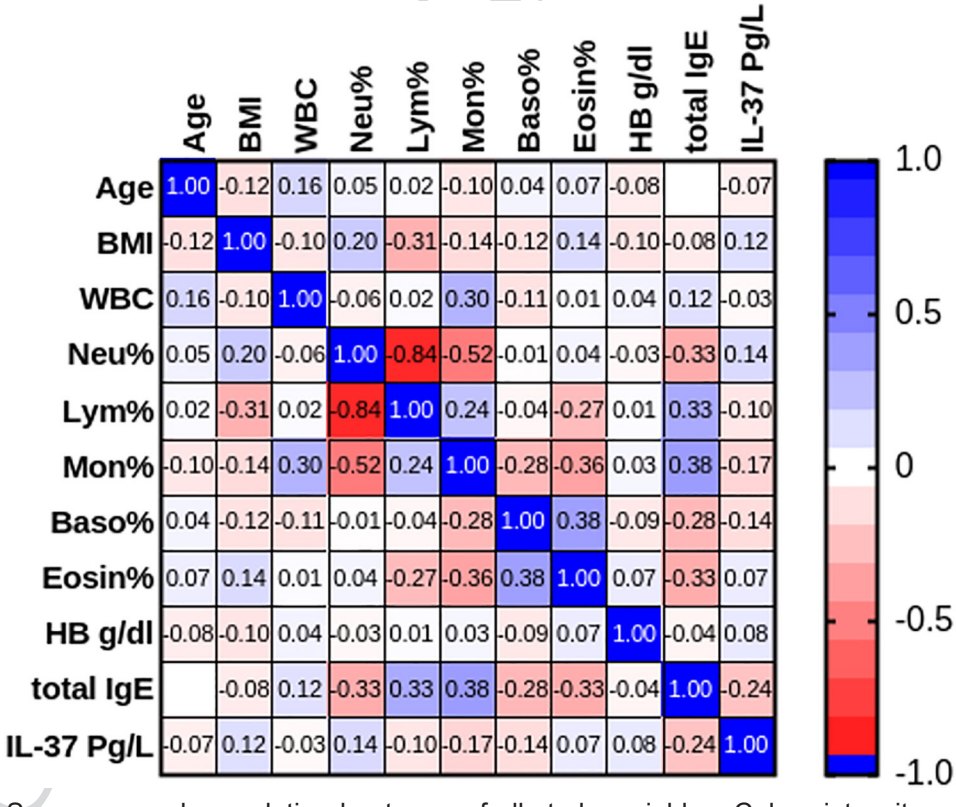


Figure 4. Spearman rank-correlation heat map of all study variables. Colour intensity encodes the magnitude and direction of each coefficient, with blue indicating positive and red indicating negative monotonic association according to the adjacent scale bar; numerical coefficients are printed within the cells. Inferential interpretation used the Bonferroni-adjusted threshold of $P < 0.0009$ for 55 correlations.

Table 3. Frequency of allergen-specific IgE positivity in patients with asthma and selected non-atopic controls.

Code	Allergen	Category	Positive patients (n = 60)	Positive controls (n = 40)	P value
G06	*Phleum pratense* (Timothy grass)	Grass pollen	38 (63.3%)	0 (0%)	< 0.0001
W10	*Chenopodium album* (goosefoot)	Weed pollen	38 (63.3%)	0 (0%)	< 0.0001
D01	*Dermatophagoides pteronyssinus*	House dust mite	37 (61.7%)	0 (0%)	< 0.0001
G02	*Cynodon dactylon* (Bermuda grass)	Grass pollen	35 (58.3%)	0 (0%)	< 0.0001
G12	*Secale cereale* (rye)	Grass pollen	35 (58.3%)	0 (0%)	< 0.0001
T09	*Olea europaea* (olive)	Tree pollen	31 (51.7%)	0 (0%)	< 0.0001
T23	*Cupressus sempervirens* (cypress)	Tree pollen	31 (51.7%)	0 (0%)	< 0.0001
W06	*Artemisia vulgaris* (mugwort)	Weed pollen	30 (50.0%)	0 (0%)	< 0.0001
W09	*Plantago lanceolata* (plantain)	Weed pollen	29 (48.3%)	0 (0%)	< 0.0001
D02	*Dermatophagoides farinae*	House dust mite	28 (46.7%)	0 (0%)	< 0.0001
W11	*Salsola kali* (Russian thistle)	Weed pollen	28 (46.7%)	0 (0%)	< 0.0001
D201	*Blomia tropicalis*	House dust mite	24 (40.0%)	0 (0%)	< 0.0001
I06	*Blattella germanica* (cockroach)	Insect	22 (36.7%)	0 (0%)	< 0.0001
E02/E05	Dog epithelium and dander	Animal epithelium	14 (23.3%)	0 (0%)	0.0006
M06	*Alternaria alternata*	Mould	14 (23.3%)	0 (0%)	0.0006
E01	Cat epithelium	Animal epithelium	12 (20.0%)	0 (0%)	0.0015
E17	Camel epithelium	Animal epithelium	8 (13.3%)	0 (0%)	0.0202
M02	*Cladosporium herbarum*	Mould	5 (8.3%)	0 (0%)	0.0813
M03	*Aspergillus fumigatus*	Mould	4 (6.7%)	0 (0%)	0.1477
M01	*Penicillium notatum*	Mould	3 (5.0%)	0 (0%)	0.2727

Positivity was defined as allergen-specific IgE ≥ 0.35 kU/L (class ≥ 1) by the Polycheck Allergy immunoblot system. Groups were compared by the Fisher exact test, with a Bonferroni-adjusted threshold of P < 0.0025 for 20 allergen comparisons. Allergens are ordered by decreasing frequency of sensitisation among patients.

allergens, *Dermatophagoides pteronyssinus* was detected in 37 patients (61.7%), *Dermatophagoides farinae* in 28 (46.7%), *Blomia tropicalis* in 24 (40.0%) and *Blattella germanica* in 22 (36.7%). Animal epithelia were less frequent: dog in 14 patients (23.3%), cat in 12 (20.0%) and camel in eight (13.3%). Among moulds, only *Alternaria alternata* met the Bonferroni-adjusted threshold (14, 23.3%; P = 0.0006); *Cladosporium herbarum* (5, 8.3%; P = 0.0813), *Aspergillus fumigatus* (4, 6.7%; P = 0.1477) and *Penicillium notatum* (3, 5.0%; P = 0.2727) did not differ significantly from controls. After correction for 20 comparisons (P < 0.0025), all comparisons with unadjusted P < 0.05 remained significant except camel epithelium (P = 0.0202), which was nominal only.

Aggregate sensitisation pattern by allergen category

Grouping allergens into biologically related categories highlighted the overall sensitisation profile of the patient cohort (Table 4). Pollens were the predominant source of sensitisation, with the nine pollen allergens recognised by 46.7% to 63.3% of patients, followed by house dust mites (40.0% to 61.7%), cockroach (36.7%), animal epithelia (13.3% to 23.3%) and moulds (5.0% to 23.3%).

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Table 4. Summary of allergen-specific IgE sensitisation by allergen category among patients with asthma.

Allergen category	Allergens tested	Range of sensitisation	Most frequent allergen (%)	Allergens meeting P < 0.0025
Grass pollen	3	58.3% to 63.3%	Timothy grass (63.3%)	3 of 3
Weed pollen	4	46.7% to 63.3%	Goosefoot (63.3%)	4 of 4
Tree pollen	2	51.7%	Olive and cypress (51.7%)	2 of 2
House dust mite	3	40.0% to 61.7%	*D. pteronyssinus* (61.7%)	3 of 3
Insect	1	36.7%	*Blattella germanica* (36.7%)	1 of 1
Animal epithelium	3	13.3% to 23.3%	Dog (23.3%)	2 of 3
Mould	4	5.0% to 23.3%	*Alternaria alternata* (23.3%)	1 of 4

Percentages denote the proportion of the 60 asthmatic patients with allergen-specific IgE of 0.35 kU/L or greater.

DISCUSSION

This case–control study yielded three principal findings. First, patients with asthma had higher serum total IgE, eosinophil percentage and basophil percentage than controls, a pattern consistent with type 2 inflammation. Second, serum IL-37 was higher in patients, but it showed no statistically significant monotonic association with the measured inflammatory or haematological indices. Third, sensitisation was most frequent to wind-borne grass and Chenopodiaceae weed pollens and to house dust mites.

The magnitude of IgE elevation is consistent with the established position of IgE as a central effector immunoglobulin in allergic asthma. Allergen-driven T-helper-2 activation and the resulting IL-4 and IL-13 signalling promote class switching to IgE, which sensitises mast cells and basophils through the high-affinity FcεRI receptor and initiates mediator release that contributes to bronchoconstriction, mucosal oedema and airway remodelling [4,19]. The concurrent eosinophilia is also consistent with the IL-5-dependent eosinophil maturation and mobilisation characteristic of type 2-high asthma [5,6]. Nevertheless, this study did not include clinical phenotyping sufficient to determine eligibility for anti-IgE or anti-IL-5 treatment. The increase in basophil percentage is biologically plausible because basophils express FcεRI and contribute histamine and IL-4 to the allergic cascade [19].

The behaviour of IL-37 in our cohort is the most notable and most contested finding, since a substantial body of evidence supports the opposite direction of change. Charrad and colleagues reported reduced IL-37 in serum and induced sputum of asthmatic children, inversely related to tumour necrosis factor-α, IL-1β, IL-6 and IL-17A, and showed that recombinant IL-37 suppressed these mediators in vitro [13]. Zhang and co-workers documented serum concentrations of 48.15 ± 8.49 pg/mL in asthmatics versus 98.59 ± 21.83 pg/mL in healthy participants [14]. Most directly relevant to our setting, Ahmed and Ad'hiah, working in Baghdad, found lower median IL-37 in allergic rhinitis (105.9 pg/mL) and asthma (88.1 pg/mL) than in controls (180.2 pg/mL), with an area under the receiver operating characteristic curve of 0.897 for asthma [15], and a further Iraqi study at the same centre reported reduced IL-37 across allergic rhinitis, asthma and urticaria [20]. Experimental work supports a deficiency model: IL-37 requires IL-18Rα and IL-1R8 to attenuate allergic airway inflammation in mice [9], counterbalances the alarmins IL-1β and IL-33 [10], and suppresses airway inflammation and remodelling by inhibiting nuclear factor-κB and STAT3 signalling [11].

The higher IL-37 concentration observed in this cohort is not without precedent. Elevated IL-37 has been described in a regional asthma cohort that also reported increased IL-38 [16], and in Iraqi women with rheumatoid arthritis, in whom serum IL-37 rose with

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disease activity [17]. Counter-regulatory elevations have also been reported in other inflammatory diseases [21]. Experimental evidence indicates that pro-inflammatory stimuli can induce IL-37 transcription [12,23]. Accordingly, the present finding may be consistent with a possible reactive or counter-regulatory response. This interpretation remains a hypothesis: the cross-sectional design, single measurement and absence of receptor or signalling measurements cannot determine whether IL-37 was induced by inflammation, insufficient to restrain it, or mechanistically unrelated to the measured asthma features.

Several methodological factors may contribute to differences among studies. Age structures differ because some reports examined children or mixed populations, whereas the present cohort included adults; Ahmed and Ad'hiah also observed age-related variation [15]. Disease phase and treatment may be relevant, but the present study did not collect a validated control score or analysable inhaled-corticosteroid data and therefore cannot test these explanations. Assay heterogeneity is another concern because commercial IL-37 immunoassays differ in antibody pairs, isoform recognition and calibration. The unit in the present report has been corrected to pg/mL to match the manufacturer's human IL-37 calibration; the exact catalogue and lot-specific documentation should be checked against the original laboratory records before resubmission. In the absence of an international reference standard, comparisons of absolute concentrations across assays should remain cautious. Head-to-head studies using a common assay and parallel measurement of IL-18, IL-18 binding protein and IL-1R8 expression are needed to investigate the discrepancy.

No statistically significant monotonic correlation was detected between IL-37 and the measured immunological or haematological variables. This result indicates only that IL-37 did not show detectable monotonic co-variation with those measures in this sample. It does not establish biological independence, a distinct regulatory axis or the absence of more complex associations. Larger longitudinal studies with broader inflammatory profiling are required before mechanistic inferences can be made.

The nominal inverse correlations between total IgE and circulating eosinophil, basophil and neutrophil percentages appear paradoxical because patients as a group had higher eosinophil and basophil values. Relative differential percentages impose a closed-sum constraint: expansion of one subset necessarily reduces the proportion assigned to others, even when absolute counts do not fall. This constraint may contribute to the observed patterns and to the strong reciprocal correlation between neutrophils and lymphocytes ($r_s = -0.842$). Biological compartmentalisation between blood and airway tissue is another possible explanation, but it was not measured. Because none of the total IgE correlations survived Bonferroni correction, these associations should be treated as exploratory rather than as established biological relationships. A recent Iranian study similarly found no positive correlation between serum IgE and blood or nasal eosinophil counts [24].

This distinction between relative and absolute values is essential when comparing our haematological findings with the wider literature. Analyses of the National Health and Nutrition Examination Survey, encompassing more than 48,000 participants, showed that absolute leucocyte, neutrophil, monocyte and lymphocyte counts were all higher in asthma, and that the neutrophil-to-lymphocyte and monocyte-to-lymphocyte ratios were positively associated with asthma prevalence and all-cause mortality [25]. The apparent contradiction is largely resolved by recognising that we report proportions within an unchanged total leucocyte count, underlining the recommendation that future studies report absolute counts. The modest reduction in haemoglobin is compatible with the mild anaemia of chronic inflammation

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described in persistent asthma, in which interleukin-6-driven hepcidin induction restricts iron availability, although iron studies were not performed and this remains inferential.

The sensitisation profile identified here is characteristic of an arid Middle Eastern setting and carries direct clinical implications. The high frequencies for goosefoot (*Chenopodium album*, 63.3%) and Russian thistle (*Salsola kali*, 46.7%) reflect the ecological dominance of *Chenopodiaceae* and *Amaranthaceae* in the region. In Kuwait, *Salsola* pollen was the single most common sensitiser, affecting 76.7% of 451 patients with respiratory allergy, with *Chenopodium album* implicated in 57.6% [7]. Among asthmatic children in eastern Saudi Arabia, *Salsola kali* sensitisation reached 48% alongside house dust mite in 54% [8]. Our findings therefore corroborate the regional pattern while indicating that grass pollens, particularly Timothy and Bermuda grass, contribute at least equally in central Iraq.

House dust mite sensitisation in 61.7% of our patients is comparable to the 54% reported in Saudi children [8] and the 37.5% recorded in Kuwait [7], but appreciably exceeds the 13.9% found in an Egyptian asthmatic cohort [26], a difference plausibly related to housing density, indoor humidity and the use of evaporative cooling. Sensitisation to *Blattella germanica* in 36.7% of patients is consistent with the 33.2% and 22.3% reported for American and German cockroach in Kuwait [7] and exceeds the 18.9% documented in Egypt [26], identifying cockroach allergen as a modifiable indoor exposure that is frequently neglected in local practice. Conversely, mould sensitisation was infrequent apart from *Alternaria alternata*, mirroring the low fungal reactivity described in arid climates where low ambient humidity limits sporulation [7,8].

No control participant tested positive for any allergen in the panel; however, this finding reflects the deliberate selection of a particularly non-atopic comparator group and is likely to exaggerate the contrast relative to the general population. Allergen-specific IgE indicates sensitisation, not asthma: sensitisation may occur without asthma, and asthma may occur without sensitisation to the tested allergens.

Clinical implications

The findings are hypothesis-generating. They describe differences in total IgE, IL-37, blood-cell percentages and allergen sensitisation between selected groups, and they identify aeroallergens that were frequent in this Baghdad sample. The study did not test diagnostic performance, phenotyping accuracy, the effectiveness of avoidance measures, eligibility for immunotherapy or biologic treatment, or patient outcomes. IL-37 should therefore be regarded as a research analyte in this context rather than a clinically validated biomarker or therapeutic target.

Strengths and limitations

The principal strengths of this study are the concurrent measurement of total IgE, a 20-allergen specific IgE panel, IL-37 and complete blood counts in the same participants; the distribution-driven selection of statistical tests; the recruitment of a non-emergency adult outpatient cohort from one specialised centre; and the distinction between standardised effect sizes for normally distributed variables and descriptive median ratios for skewed variables.

Several limitations must be acknowledged. The cross-sectional case–control design precludes causal inference and cannot establish whether higher IL-37 preceded, accompanied or followed inflammation. The sample of 100 participants from one centre was recruited by consecutive non-probability sampling, which limits generalisability and precluded reliable stratification by sex, severity or control status. Controls were selected to have neither a personal history of allergic disease nor a first-degree family history of atopy; this particularly non-atopic comparator group may exaggerate between-

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group differences in total IgE and allergen-specific IgE and does not represent the source population. Control health status was based on structured history rather than objective respiratory or allergy testing. Medication frequencies, especially inhaled corticosteroid exposure, were not available in analysable form; residual treatment confounding of eosinophils, IgE and IL-37 is therefore possible. Leucocyte data were relative percentages rather than absolute counts. Both biomarkers were measured once, and the IL-37 assay lacked cross-platform validation and an international reference standard. Finally, IL-18, IL-18 binding protein and IL-1R8 were not measured, which limits mechanistic interpretation.

Future work should use longitudinal, multicentre designs with population-representative controls, complete spirometry, validated control and severity measures, quantitative medication exposure, absolute blood-cell counts, standardised or cross-validated IL-37 assays, and concurrent assessment of the IL-18/IL-1R8 axis. Such studies would permit treatment-adjusted analyses and evaluation of temporal and mechanistic hypotheses.

CONCLUSIONS

Adults with bronchial asthma in Baghdad exhibit a pronounced IgE-mediated, eosinophil- and basophil-rich immunological profile, with median total IgE elevated more than fivefold above healthy controls. Serum IL-37 was concurrently and significantly increased yet showed no linear dependence on IgE or any leucocyte subset, a pattern most consistent with a compensatory regulatory response which may be insufficient to fully counterbalance established allergic inflammation. Sensitisation was dominated by Timothy grass and goosefoot pollen and by *Dermatophagoides pteronyssinus*, with cockroach allergen a substantial additional contributor and moulds a minor one. Combined assessment of total IgE, a locally tailored allergen-specific IgE panel and IL-37 therefore characterises asthma more completely than any single marker, supports evidence-based avoidance and immunotherapy planning in central Iraq, and highlights the IL-37 axis as potential target for future therapeutic investigation.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE.

The study protocol was reviewed and approved by the Institutional Review Board of the Iraqi Center for Cancer and Medical Genetic Research, Mustansiriyah University, Baghdad, Iraq (Approval No. ICCMGR/29, 2026;). Administrative permission was granted by the Al-Rusafa Health Directorate, Baghdad. All procedures were performed in accordance with the ethical standards of the institutional research committee and the 1964 Declaration of Helsinki and its later amendments. Written informed consent was obtained from every participant before enrolment and blood sampling.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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AUTHORS' CONTRIBUTIONS

R.A.A., T.A.H., R.A.M. and R.R.M. conceived and designed the study, recruited participants, performed the laboratory immunoassays, curated the dataset, conducted the statistical analysis and drafted the manuscript. R.A.A. and T.A.H. supervised the study, contributed to the design and methodology, verified the analytical procedures, critically revised the manuscript for intellectual content and provided scientific and administrative oversight. All authors read and approved the final manuscript and agree to be accountable for all aspects of the work.

AVAILABILITY OF DATA AND MATERIALS

The datasets generated and analysed during the current study are available from the corresponding author on reasonable request, subject to institutional ethical and confidentiality requirements.

REFERENCES

1. Global Initiative for Asthma. Global strategy for asthma management and prevention: 2024 update. Fontana (WI): Global Initiative for Asthma; 2024. Available from: https://ginasthma.org/2024-report/
2. Zhang L, Zhang X, Zhang Y, Li Y, Wang Z, Zhao Y, et al. Global, regional, and national burden of asthma from 1990 to 2021: a systematic analysis for the Global Burden of Disease Study 2021. BMJ Open Respir Res. 2025;12(1):e003144. doi:10.1136/bmjresp-2024-003144
3. World Health Organization. Asthma: key facts. Geneva: World Health Organization; 2024. Available from: https://www.who.int/news-room/fact-sheets/detail/asthma
4. Hammad H, Lambrecht BN. The basic immunology of asthma. Cell. 2021;184(6):1469-85. doi:10.1016/j.cell.2021.02.016
5. Ansotegui IJ, Melioli G, Canonica GW, Caraballo L, Villa E, Ebisawa M, et al. IgE allergy diagnostics and other relevant tests in allergy, a World Allergy Organization position paper. World Allergy Organ J. 2020;13(2):100080. doi:10.1016/j.waojou.2019.100080
6. Froidure A, Mouthuy J, Durham SR, Chanez P, Sibille Y, Pilette C. Asthma phenotypes and IgE responses. Eur Respir J. 2016;47(1):304-19. doi:10.1183/13993003.01824-2014
7. Al-Mousawi MS, Lovel H, Behbehani N, Arifhodzic N, Woodcock A, Custovic A. Asthma and sensitization in a community with low indoor allergen levels and low pet-keeping frequency. J Allergy Clin Immunol. 2004;114(6):1389-94. doi:10.1016/j.jaci.2004.08.019
8. AlKhater SA. Sensitization to common aeroallergens in asthmatic children in the eastern region of Saudi Arabia. Saudi J Med Med Sci. 2017;5(2):136-41. doi:10.4103/1658-631X.204862
9. Lunding L, Webering S, Vock C, Schröder A, Baarsma HA, Königshoff M, et al. IL-37 requires IL-18Rα and SIGIRR/IL-1R8 to diminish allergic airway inflammation in mice. Allergy. 2015;70(4):366-73. doi:10.1111/all.12566
10. Schröder A, Lunding LP, Zissler UM, Vock C, Webering S, Ehlers JC, et al. IL-37 regulates allergic inflammation by counterbalancing pro-inflammatory IL-1 and IL-33. Allergy. 2022;77(3):856-69. doi:10.1111/all.15072
11. Huang N, Liu K, Liu J, Gao X, Zeng Z, Zhang Y, et al. Interleukin-37 alleviates airway inflammation and remodeling in asthma via inhibiting the activation of NF-κB and STAT3 signalings. Int Immunopharmacol. 2018;55:198-204. doi:10.1016/j.intimp.2017.12.010
12. Cao J, He K, Wang Y, Zhang L, Liu X, Chen H, et al. Interleukin-37 in respiratory diseases: molecular mechanisms and therapeutic potential. Front Immunol. 2025;16:1675791. doi:10.3389/fimmu.2025.1675791
13. Charrad R, Berraïes A, Hamdi B, Ammar J, Hamzaoui K, Hamzaoui A. Anti-inflammatory activity of IL-37 in asthmatic children: correlation with inflammatory cytokines TNF-α, IL-1β, IL-6 and IL-17A. Immunobiology. 2016;221(2):182-7. doi:10.1016/j.imbio.2015.09.009
14. Zhang L, Zhang J, Gao P. The potential of interleukin-37 as an effective therapeutic agent in asthma. Respir Res. 2017;18(1):192. doi:10.1186/s12931-017-0675-x
15. Ahmed MB, Ad'hiah AH. Reduced levels of interleukin-37 in serum of patients with allergic rhinitis or asthma. Rev Fr Allergol.

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2021;61(8):387-92. doi:10.1016/j.reval.2021.06.005
16. Algashami DA, Al-Mudhafar RH, Hadi NR. Interleukin-37 and interleukin-38 are elevated in patients with bronchial asthma: a case-control study. Gazz Med Ital Arch Sci Med. 2025;184(6):495-501. doi:10.23736/S0393-3660.25.05397-9
17. Bani-Wais DFN, Ad'hiah AH, Hussein SZ. Serum interleukin-37 levels are elevated in Iraqi women with rheumatoid arthritis. Egypt J Med Hum Genet. 2025;26:23. doi:10.1186/s43042-025-00793-6
18. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007;370(9596):1453-7. doi:10.1016/S0140-6736(07)61602-X
19. Gould HJ, Sutton BJ. IgE in allergy and asthma today. Nat Rev Immunol. 2008;8(3):205-17. doi:10.1038/nri2273
20. Kadhem AA, Ahmed AK, Hassan AS. The role of IL-37 in allergic rhinitis, asthma and urticaria diseases in samples of Iraqi patients. Iraqi J Sci. 2024;65(5):2456-64. doi:10.24996/ijs.2024.65.5.6
21. Xia L, Shen H, Lu J. Elevated serum and synovial fluid levels of interleukin-37 in patients with rheumatoid arthritis: attenuated the production of inflammatory cytokines. Cytokine. 2015;76(2):553-7. doi:10.1016/j.cyto.2015.06.005
22. Kamal A, Elshora A, Elsherbiny NM, Abdelrahman AM, Abdelaziz A. Serum interleukin 38 (IL-38) as a new potential biomarker of pediatric bronchial asthma. Egypt J Bronchol. 2022;16(1):41. doi:10.1186/s43168-022-00139-5
23. Nold MF, Nold-Petry CA, Zepp JA, Palmer BE, Bufler P, Dinarello CA. IL-37 is a fundamental inhibitor of innate immunity. Nat Immunol. 2010;11(11):1014-22. doi:10.1038/ni.1944
24. Torabizadeh M, Nasiri Amiri F, Sharifat M, Alavinejad P, Cheraghian B. Association of nasal and blood eosinophils with serum immunoglobulin E levels in patients with allergic rhinitis and asthma. Immun Inflamm Dis. 2024;12(11):e70057. doi:10.1002/iid3.70057
25. Ke J, Qiu F, Fan W, Wei S. Associations of complete blood cell count-derived inflammatory biomarkers with asthma and mortality in adults: a population-based study. Front Immunol. 2023;14:1205687. doi:10.3389/fimmu.2023.1205687
26. Ishak SR, Zaki MES, Abdel-Fattah MA, Ahmed EAE. Prevalence of common sensitizing aeroallergens in Egyptian asthmatic patients. World Allergy Organ J. 2020;13(1):100405. doi:10.1016/j.waojou.2020.100405

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