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ORIGINAL ARTICLE

Association Between Serum Interleukin-6 Levels and Left Ventricular Diastolic Dysfunction in Obese Adults

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ABSTRACT

Background/Aim: Obesity is associated with low-grade systemic inflammation and may contribute to left ventricular diastolic dysfunction (DD). Interleukin-6 (IL-6) is a pro-inflammatory cytokine implicated in cardiovascular disease. This study aimed to evaluate the association between raised serum IL-6 levels and left ventricular diastolic dysfunction in obese adults.

Methods: This comparative cross-sectional study included 134 adults aged 18–50 years who were recruited between December 2024 and February 2026. Participants were divided into an obese group (n = 67) and a normal-weight control group (n = 67). Clinical assessment, anthropometric measurements, serum IL-6 determination, and transthoracic echocardiographic assessment of diastolic function were performed. Logistic regression analysis was used to identify factors associated with DD.

Results: DD was more prevalent among obese participants than controls (35.8% vs. 4.5%, $p < 0.001$). Median serum IL-6 levels were significantly higher in obese individuals than controls (6.9 vs. 1.2 pg/mL, $p < 0.001$) and in obese participants with DD than in those without DD (11.4 vs. 5.6 pg/mL, $p < 0.001$). In a limited two-variable logistic regression model, body mass index (OR 1.62, 95% CI 1.06–2.42; $p = 0.02$) and log-transformed IL-6 levels (OR 1.53, 95% CI 1.05–2.23; $p = 0.03$) remained mutually associated with DD. Exploratory ROC analysis showed an AUC of 0.812 for IL-6.

Conclusion: Obesity was associated with a higher prevalence of DD. Serum IL-6 levels were significantly higher in obese participants and remained associated with DD after mutual adjustment for body mass index in the limited two-variable model.

Key words: Obesity; Left ventricular diastolic dysfunction; Interleukin-6; Echocardiography; Inflammation.

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INTRODUCTION

Obesity has become a major public health concern because of its increasing global prevalence and its strong association with cardiometabolic morbidity and cardiovascular disease [1, 2]. Even in younger adults without overt cardiovascular disease, obesity is increasingly recognized not only as a metabolic disorder but also as a condition associated with structural and functional cardiac changes [3, 4].

Diastolic dysfunction (DD) is characterized by impaired myocardial relaxation, increased ventricular stiffness, and elevated left ventricular (LV) filling pressures despite preserved systolic function [5, 6]. Excess adiposity has been associated with adverse cardiac remodeling and impaired LV diastolic function, particularly when obesity is accompanied by abnormal fat distribution or other cardiometabolic risk factors [3, 4, 7]. Doppler echocardiography and tissue Doppler imaging remain key non-invasive methods for evaluating LV diastolic function [5, 6].

The prevalence and clinical significance of DD are influenced by age, obesity, hypertension, diabetes mellitus, and LV remodeling. In younger adults without major cardiovascular risk factors, clinically relevant DD is less common, whereas its frequency increases with increasing age and cardiometabolic burden [4–6]. Therefore, evaluating early diastolic abnormalities in relatively young obese individuals without major comorbidities may help identify subclinical cardiac dysfunction before overt cardiovascular disease develops.

The association between obesity and DD is complex and involves both hemodynamic and inflammatory mechanisms. Obesity is associated with increased preload, afterload, cardiac output, and LV mass, in addition to chronic low-grade systemic inflammation [2, 3]. Adipose tissue functions as an active endocrine organ and releases adipokines and pro-inflammatory cytokines, including tumor necrosis factor-α, interleukin-6 (IL-6), and interleukin-1β, which may contribute to metabolic and cardiovascular dysfunction [8–10]. Among these inflammatory mediators, IL-6 has received increasing attention because of its association with cardiovascular risk, adverse cardiac remodeling, and heart failure phenotypes [9–11]. Experimental evidence suggests that IL-6-related signaling may contribute to obesity-induced diastolic dysfunction through inflammatory and myocardial remodeling pathways [12]. However, clinical studies specifically examining circulating IL-6 levels and early DD in otherwise healthy obese adults without major confounding conditions remain limited.

Therefore, the present study aimed to evaluate the association between serum IL-6 levels and LV diastolic dysfunction in obese adults compared with normal-weight controls after excluding major cardiovascular and metabolic comorbidities.

MATERIALS AND METHODS

Study design and population

This single-center comparative cross-sectional study was conducted at Azadi Teaching Hospital in Kirkuk, Iraq, between December 2024 and February 2026. The study included 134 adults aged 18–50 years and was designed to evaluate the association between serum interleukin-6 (IL-6) levels, obesity, and left ventricular diastolic dysfunction (DD).

Participants were divided into two groups according to body mass index (BMI). Participants with a BMI of 18.5–24.9 kg/m^2 served as the normal-weight control group (n = 67), and participants with a BMI $\geq$30 kg/m^2 comprised the obese group (n = 67). No participant in the control group had a BMI below 18.5 kg/m^2; therefore, all controls were within the normal adult BMI range. Individuals with overweight (BMI 25.0–29.9 kg/m^2) were excluded to maintain clear group separation and reduce misclassification bias [1].

All participants provided written informed consent after approval from the institutional ethics committee. Eligible participants were consecutively recruited from inpatient and outpatient departments. Normal-weight participants served as controls, whereas obese participants were categorized as cases.

Inclusion and exclusion criteria

Eligible participants were men and women aged 18–50 years who were willing to participate and provide written informed consent. Participants were excluded if they had hypertension, defined as systolic blood pressure $\geq$140 mmHg, diastolic blood pressure $\geq$90 mmHg, or a previous diagnosis [13]; diabetes mellitus, defined as HbA1c $\geq$6.5%, fasting blood glucose $\geq$126 mg/dL, or a previous diagnosis [14]; congenital, valvular, or ischemic heart disease; LV ejection fraction <50%; regional wall-motion abnormalities; atrial fibrillation; inflammatory or autoimmune disorders; dyslipidemia, defined by previous diagnosis or total cholesterol $\geq$240 mg/dL [15]; use of anti-inflammatory drugs or steroids; or increased inflammatory markers such as erythrocyte sedimentation rate. Participants were categorized by BMI rather than by outcome, and DD was evaluated as an outcome variable within each group.

Clinical and anthropometric assessment

A detailed medical history and physical assessment were obtained from every participant. Standardized methods were used to measure height and body weight. BMI was calculated as weight in kilograms divided by height in meters squared [1]. According to standard adult BMI classification, BMI 18.5–24.9 kg/m^2 was considered normal weight, BMI 25.0–29.9 kg/m^2 was considered overweight, and BMI $\geq$30 kg/m^2 was considered obesity [1]. After five minutes of seated rest, blood pres-

sure was measured using a calibrated sphygmomanometer; the mean of two measurements obtained at least 30 seconds apart was recorded [13]. Twenty-six participants (16 with obesity, nine with overweight, and one with BMI <25 kg/m^2) were classified as having newly diagnosed hypertension and were excluded from the current study.

Biochemical measurements

Venous blood samples were collected between 7:00 and 8:00 AM after an overnight fast of 8–12 hours. Serum IL-6 levels were measured using a commercial enzyme-linked immunosorbent assay kit (Quantikine IL-6, R&D Systems, Minneapolis, MN, USA) according to the manufacturer's instructions. The assay sensitivity was 0.7 pg/mL, and the detection range was 1.1–300 pg/mL. No significant cross-reactivity has been reported between this kit and other cytokines. The typical laboratory reference range is 0–5 pg/mL.

Before analysis, blood samples were promptly chilled to 4 °C, separated by centrifugation at 4 °C for 10 minutes at 3000 rpm, and stored at −20 °C until analysis. Fasting blood glucose and total serum cholesterol were measured from a clot activator tube.

Echocardiographic assessment

Transthoracic echocardiographic examinations were performed by multiple experienced sonographers following a standardized protocol and using a commercially available ultrasound system (Vivid S70N.SN; 330860YP8; assembled in Japan, August 2019). All operators were blinded to participants' BMI category and serum IL-6 levels to minimize measurement bias. Echocardiographic measurements were obtained according to current guideline recommendations. Formal intra-observer and inter-observer reproducibility assessments were not performed.

Echocardiographic assessment of LV dimensions, LV mass, LV ejection fraction, and diastolic function followed current chamber quantification and diastolic-function recommendations [5, 6, 16]. LV dimensions were measured from the parasternal long-axis view and indexed where appropriate for body size. LV ejection fraction was calculated using the biplane modified Simpson method [16]. LV diastolic function was assessed using mitral inflow velocity and mitral annular velocity from the apical four-chamber view [5, 6]. Transmitral flow was measured at the tips of the mitral valve leaflets using pulsed-wave Doppler. Early (E) and late (A) peak mitral inflow velocities were recorded, and the E/A ratio was calculated. Peak early diastolic velocities (E') were obtained using pulsed tissue Doppler imaging and then averaged.

Definition of diastolic dysfunction

DD was defined using three criteria: (i) E/A <0.7, indicating grade I impaired relaxation; (ii) E/A >0.7 and $\leq$1.5 with E' <7 cm/s or tricuspid velocity >2.8 cm/s, indicating grade II pseudonormal pattern; or (iii) E/A >1.5 with E' <7 cm/s, indicating grade III restrictive pattern [5, 6].

Statistical analysis

Statistical analysis was performed using SPSS version 20. The normality of continuous variables was assessed using the Shapiro–Wilk test and visual inspection of histograms. Normally distributed variables, including age, BMI, weight, height, heart rate, LV dimensions, LV mass, E, A, E/A ratio, E', and E/E' ratio, were expressed as mean $\pm$ standard deviation. Serum IL-6 levels showed a right-skewed non-normal distribution and were therefore presented as median and interquartile range (IQR). IL-6 values were log-transformed for regression analysis.

Between-group comparisons were performed using the independent-samples t-test for normally distributed continuous variables and the Mann–Whitney U test for non-normally distributed variables. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. For comparisons among more than two groups, one-way analysis of variance was used for normally distributed variables and the Kruskal–Wallis test for non-normally distributed variables, followed by appropriate post hoc analyses.

Logistic regression analysis was used to evaluate associations between BMI, IL-6, and DD, and results are reported as odds ratios (ORs) with 95% confidence intervals (CIs). Because only 27 participants had DD, the multivariable logistic regression model was intentionally limited to two predictors (BMI and log-transformed IL-6) to maintain an acceptable events-per-variable ratio and reduce overfitting. Age, sex, smoking status, heart rate, and LV mass index were evaluated descriptively but were not included in the final multivariable model. Receiver operating characteristic (ROC) curve analysis was used to assess the exploratory ability of IL-6 to discriminate between obese participants with and without DD. A p-value <0.05 was considered statistically significant.

Ethical approval

This study was approved by the Research Ethics Committee, College of Medicine, University of Kirkuk, with document number 58B on 14 October 2024. The study was conducted in compliance with the Declaration of Helsinki [17]. All participants provided written informed consent before participation.

RESULTS

Study population

A total of 134 participants were included and divided equally into a normal-weight control group (BMI 18.5–24.9 kg/m²; n = 67) and an obese group (BMI ≥30.0 kg/m²; n = 67). Baseline demographic, clinical, and structural echocardiographic characteristics are summarized in Table 1. Obese participants were slightly older than controls (41.59 ± 6.07 vs. 39.26 ± 6.58 years; $p = 0.03$). There were no significant differences between groups in sex distribution, smoking status, height, relative wall thickness, left ventricular ejection fraction, or heart rate. Body weight, BMI, serum IL-6 level, end-diastolic diameter, and LV mass were significantly higher in obese participants.

Table 1. Baseline clinical and echocardiographic characteristics of the study population by BMI category

Characteristic	Control BMI 18.5–24.9	Obese BMI ≥30.0	*p*
Demographic and clinical characteristics			
Age, years	39.26 ± 6.58	41.59 ± 6.07	**0.03**
Female, n (%)	33 (49.3)	38 (56.7)	0.39
Male, n (%)	34 (50.7)	29 (43.3)	–
Smoking, n (%)	21 (31.3)	28 (41.8)	0.19
Body weight, kg	52.61 ± 8.53	94.38 ± 10.21	**< 0.001**
Height, m	1.60 ± 0.08	1.60 ± 0.05	0.67
BMI, kg/m²	22.38 ± 1.44	36.78 ± 4.36	**< 0.001**
Serum IL-6, pg/mL	1.2 (0.8–1.6)	6.9 (4.8–9.5)	**< 0.001**
Structural echocardiographic characteristics			
End-diastolic diameter, cm	4.89 ± 0.27	5.36 ± 0.29	**< 0.001**
LV mass, g	169.4 ± 53.1	196.2 ± 47.8	**0.003**
Relative wall thickness	0.48 ± 0.11	0.51 ± 0.08	0.09
LV ejection fraction, %	63.1 ± 8.3	64.1 ± 5.9	0.43
Heart rate, beats/min	68.1 ± 11.3	71.2 ± 10.8	0.11

Data are presented as mean ± SD, n (%), or median (IQR). Serum IL-6 was non-normally distributed and is presented as median (IQR). BMI, body mass index; IL-6, interleukin-6; IQR, interquartile range; LV, left ventricle; SD, standard deviation.

Echocardiographic parameters of diastolic function

Unadjusted comparisons of echocardiographic parameters of diastolic function are presented in Table 2. Compared with controls, obese participants had significantly higher peak E velocity, peak A velocity, and E/E′ ratio, and significantly lower E/A ratio and peak E′. Overall, diastolic dysfunction was identified in 27 of 134 participants (20.1%). The prevalence of diastolic dysfunction was significantly higher in obese participants than in controls (24/67, 35.8% vs. 3/67, 4.5%; $p < 0.001$).

Serum IL-6 levels according to obesity and diastolic dysfunction

Serum IL-6 levels differed significantly according to obesity and diastolic dysfunction status, as shown in Table 3. Median IL-6 was significantly higher in obese participants than in controls (6.9 [4.8–9.5] vs. 1.2 [0.8–1.6] pg/mL; $p < 0.001$). Within the obese group, participants with diastolic dysfunction had markedly higher IL-6 levels than those without diastolic dysfunction (11.4 [9.8–13.5] vs. 5.6 [5.2–6.0] pg/mL; $p < 0.001$).

Table 2. Echocardiographic parameters of diastolic function according to BMI category

Variable	Control BMI 18.5–24.9 kg/m²	Obese BMI ≥30.0 kg/m²	*p*
Peak E, cm/s	68.9 ± 10.2	72.9 ± 11.0	**0.03**
Peak A, cm/s	83.8 ± 12.5	93.1 ± 13.2	**< 0.001**
E/A ratio	0.88 ± 0.15	0.82 ± 0.14	**0.02**
Peak E′, cm/s	7.56 ± 1.10	7.10 ± 1.00	**0.01**
E/E′ ratio	9.8 ± 2.1	11.2 ± 2.4	**< 0.001**
DD, n (%)	3 (4.5)	24 (35.8)	**< 0.001**

Data are presented as mean ± SD or n (%). P-values were obtained using the independent-samples t-test for continuous variables and the chi-square test for categorical variables. BMI, body mass index; DD, diastolic dysfunction; SD, standard deviation.

Table 3. Serum IL-6 levels according to obesity and diastolic dysfunction status

Group	n	IL-6, median (IQR), pg/mL
Control group, BMI 18.5–24.9 kg/m²	67	1.2 (0.8–1.6)
All obese participants, BMI ≥30 kg/m²	67	6.9 (4.8–9.5)
Obese without DD	43	5.6 (5.2–6.0)
Obese with DD	24	11.4 (9.8–13.5)
Comparison	**Test**	***p***
Control vs. all obese participants	MWU	**< 0.001**
Obese with DD vs. obese without DD	MWU	**< 0.001**

IL-6 values are presented as median (IQR) because of non-normal distribution. No global four-group comparison was performed. BMI, body mass index; DD, diastolic dysfunction; IL-6, interleukin-6; IQR, interquartile range; MWU, Mann–Whitney U test.

Stratified analysis of serum IL-6 among obese participants

A stratified analysis was performed to examine whether serum IL-6 levels differed by sex or smoking status within obese participants with and without diastolic dysfunction. As shown in Table 4, IL-6 levels did not differ significantly by sex among obese participants without diastolic dysfunction ($p = 0.61$) or with diastolic dysfunction ($p = 0.74$). Similarly, no significant difference was observed between smokers and non-smokers among obese participants without diastolic dysfunction ($p = 0.56$) or with diastolic dysfunction ($p = 0.83$).

Logistic regression analysis of factors associated with diastolic dysfunction

Univariate and multivariable logistic regression analyses are presented in Table 5. In univariate analysis, BMI and log-transformed IL-6 were significantly associated with diastolic dysfunction. In the limited two-variable multivariable model, BMI and log-transformed IL-6 remained mutually associated

Table 4. Stratified serum IL-6 levels among obese participants by sex and smoking status

Stratum	Category	n	Without DD IL-6, median (IQR), pg/mL	*p*	With DD IL-6, median (IQR), pg/mL	*p*
Sex	Male	29	5.7 (5.3–6.2)	0.61	11.2 (9.5–13.0)	0.74
	Female	38	5.5 (5.1–6.0)		11.6 (10.0–13.8)	
Smoking	Smoker	28	5.8 (5.2–6.3)	0.56	11.5 (9.7–13.4)	0.83
	Non-smoker	39	5.9 (5.4–6.7)		11.6 (9.7–13.8)	

Values are presented as median (IQR). The n column represents the total number of obese participants in each sex or smoking category, not the number within each DD subgroup. P-values were obtained using the Mann–Whitney U test. For sex, p-values compare male versus female participants within each DD stratum. For smoking status, p-values compare smokers versus non-smokers within each DD stratum. DD, diastolic dysfunction; IL-6, interleukin-6; IQR, interquartile range.

Table 5. Logistic regression analysis of factors associated with left ventricular diastolic dysfunction

Variable	Univariate OR (95% CI)	*p*-value	Adjusted OR[a] (95% CI)	*p*-value
BMI, kg/m²	1.93 (1.31–2.83)	**0.001**	1.62 (1.06–2.42)	**0.02**
IL-6, log-transformed	1.67 (1.16–2.41)	**0.005**	1.53 (1.05–2.23)	**0.03**

[a] Adjusted ORs were obtained from a multivariable logistic regression model including BMI and log-transformed IL-6. Because only 27 participants had diastolic dysfunction, the multivariable model was restricted to these two predictors to reduce overfitting. Adjusted ORs are therefore mutually adjusted for BMI and IL-6 but not for age, sex, smoking status, heart rate, or LV mass index. BMI, body mass index; CI, confidence interval; IL-6, interleukin-6; LV, left ventricle; OR, odds ratio.

with diastolic dysfunction after adjustment for each other. Each 1 kg/m² increase in BMI was associated with higher odds of diastolic dysfunction (adjusted OR 1.62, 95% CI 1.06–2.42; $p = 0.02$), and higher log-transformed IL-6 was also associated with higher odds of diastolic dysfunction (adjusted OR 1.53, 95% CI 1.05–2.23; $p = 0.03$).

Exploratory ROC analysis and IL-6 cutoff classification

ROC analysis was performed as an exploratory assessment of the ability of serum IL-6 to discriminate between obese participants with and without diastolic dysfunction. IL-6 showed good discriminative performance, with an AUC of 0.812 (95% CI 0.768–0.856; $p < 0.001$). The optimal cutoff identified within this cohort was 8.9 pg/mL, with sensitivity of 95.8% and specificity of 62.8%. The corresponding ROC curve is shown in Figure 1. Because the cutoff was derived and evaluated in the same sample and was not externally validated, these findings should be interpreted as exploratory.

The classification of obese participants according to the exploratory ROC-derived IL-6 cutoff is shown in Table 6. Among the 24 obese participants with diastolic dysfunction, 23 were classified as IL-6 positive and one was classified as IL-6 negative. Among the 43 obese participants without diastolic dysfunction, 27 were classified as IL-6 negative and 16 were classified as IL-6 positive.

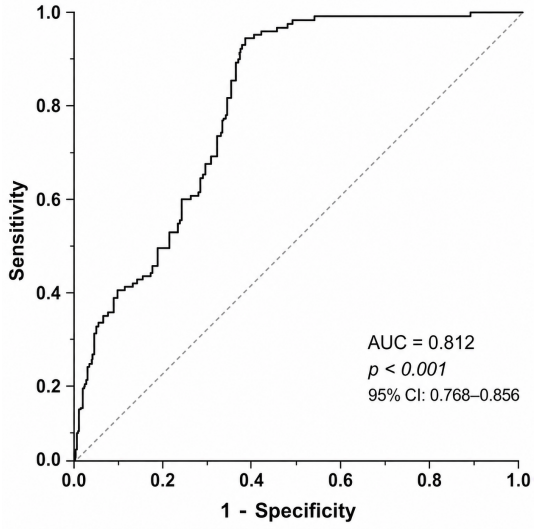

Figure 1. Receiver operating characteristic curve for serum IL-6 in discriminating obese participants with and without diastolic dysfunction.

Table 6. Exploratory ROC performance and IL-6 cutoff classification

A. ROC performance of serum IL-6					
Variable	**AUC**	**95% CI**	**Cutoff, pg/mL**	**Sensitivity**	**Specificity**
IL-6	0.812	0.768–0.856	8.9	95.8%	62.8%
B. Classification according to the IL-6 cutoff of 8.9 pg/mL					
IL-6 status	**DD present**	**DD absent**	**Total**		
Positive	23	16	39		
Negative	1	27	28		
Total	24	43	67		

ROC analysis was exploratory. The ROC p-value was < 0.001. The IL-6 cutoff was derived and evaluated within the same obese cohort and was not externally validated. AUC, area under the curve; CI, confidence interval; DD, diastolic dysfunction; IL-6, interleukin-6; ROC, receiver operating characteristic.

DISCUSSION

In this comparative cross-sectional study, we evaluated the association between systemic inflammation, reflected by serum IL-6 level, obesity, and LV diastolic function in a relatively young population free of major comorbidities. The main findings were that obese participants had more impaired diastolic function than controls; serum IL-6 levels were higher in obese participants and in those with DD; and BMI and log-transformed IL-6 remained mutually associated with DD in a limited two-variable logistic regression model. In exploratory ROC analysis, IL-6 showed good discrimination between obese participants with and without DD within this study cohort.

Our findings are consistent with previous research showing an association between obesity and impaired LV diastolic function [3, 4, 7]. Compared with several previous studies of younger or community-based populations, the prevalence of DD among obese participants in the present study was relatively high at 35.8%. Shemirani et al. reported an association between obesity and LV diastolic function in young individuals, while other contemporary studies have highlighted the relationship between adiposity, LV remodeling, and later-life cardiac functional changes [3, 4, 7]. Differences in DD prevalence across studies may be related to differences in population characteristics, study design, obesity severity, exclusion criteria, and echocardiographic definitions.

Strict exclusion of confounding diseases such as heart disease, diabetes, and hypertension may have helped isolate the association between obesity and DD; however, geographic, ethnic, and cardiometabolic variation may also have contributed to the observed prevalence. In addition, combined Doppler and tissue Doppler parameters may improve the detection of subclinical diastolic impairment. Nevertheless, the magnitude of the association between BMI and DD should be interpreted cautiously because of the limited sample size and small number of outcome events.

Median IL-6 levels in this study were 6.9 pg/mL in obese participants and 1.2 pg/mL in controls, representing an approximately six-fold difference. Previous evidence indicates that circulating IL-6 concentrations vary according to assay method, population characteristics, and metabolic phenotype, and that IL-6 levels are generally higher in adults with obesity or adverse metabolic profiles than in metabolically healthy non-obese individuals [18]. The low IL-6 level observed in the control group is also consistent with meta-analytic data showing that IL-6 concentrations in healthy individuals are usually in the low pg/mL range but vary across populations and laboratory methods [19]. Therefore, the IL-6 pattern observed in the present study is biologically plausible, although direct comparison with other studies should be made cautiously because of methodological differences.

The difference in IL-6 levels between obese participants with and without DD (11.4 vs. 5.6 pg/mL) was one of the main findings. This finding supports an association between higher circulating IL-6 levels and the presence of DD. Previous reviews have described IL-6 as an inflammatory mediator linked to cardiovascular risk and cardiac remodeling pathways [9, 10]. Experimental evidence has suggested that IL-6-related signaling may contribute to obesity-induced diastolic dysfunction, while clinical studies in heart failure with preserved ejection fraction have reported associations between IL-6 and adverse cardiac phenotypes [11, 12, 20, 21]. However, the present study did not assess myocardial fibrosis, ventricular stiffness, inflammatory signaling pathways, or longitudinal cardiac outcomes. Therefore, our findings demonstrate an association but do not establish a causal role for IL-6 in the development of DD.

Both BMI and log-transformed IL-6 remained mutually associated with DD in a limited two-variable logistic regression model. The persistence of the association after mutual adjustment for BMI and IL-6 suggests that the observed relationship was not fully explained by BMI alone. However, the model was not adjusted for all possible confounders because only 27 participants had DD, and residual confounding cannot be excluded. Stratified analysis suggested that sex and smoking status did not significantly alter IL-6 levels within the obese group, but the ability to identify subtle subgroup

differences was limited by the small sample size.

Exploratory ROC analysis demonstrated good discrimination, with an AUC of 0.812. However, because the cutoff was derived and evaluated within the same cohort without external validation, these findings should be considered preliminary. Previous studies support the potential role of IL-6 as a biomarker related to cardiac dysfunction and HFpEF phenotypes [11, 22]. Nevertheless, the single-cohort design and absence of external validation limit the clinical applicability of the proposed cutoff. Additional prospective studies are needed to verify these findings and evaluate the clinical utility of IL-6 as a biomarker in obese individuals at risk of DD.

Because of the comparative cross-sectional design, the present findings should be interpreted as evidence of association rather than causation. Although experimental studies have proposed biological mechanisms linking IL-6 to obesity-related myocardial remodeling and impaired relaxation [12], the current study was not designed to evaluate these mechanisms directly.

The results suggest an association between higher systemic inflammatory activity, reflected by serum IL-6 levels, and DD in obesity. These findings highlight the importance of early identification and management of obesity to reduce the risk of subclinical cardiac dysfunction. However, interventional and longitudinal studies are required to determine whether inflammatory pathways, including IL-6-related pathways, are useful therapeutic or prognostic targets in obesity-associated cardiac dysfunction.

Several limitations should be considered when interpreting these results. First, temporal or causal relationships between IL-6 levels and DD cannot be inferred because of the cross-sectional design. Second, the single-center design and small sample size may limit generalizability. Third, overweight individuals (BMI 25.0–29.9 kg/m^2) were excluded to achieve clear group separation; although this may improve internal validity, it reduces external validity across the full BMI spectrum. Fourth, obesity was assessed only using BMI; waist circumference and waist-to-hip ratio, which better reflect visceral adiposity and cardiometabolic risk, were unavailable. Fifth, no a priori sample size or statistical power calculation was performed, and the study may have been underpowered for subgroup and multivariable analyses. Sixth, only 27 participants had DD, which may have reduced the stability of logistic regression and ROC analyses. Seventh, formal intra-observer and inter-observer reproducibility of echocardiographic measurements was not assessed. Eighth, residual confounding from unmeasured lifestyle factors, such as physical activity and diet, cannot be excluded. Finally, the ROC-derived IL-6 cutoff was internally derived and not externally validated, and IL-6 was measured at a single time point.

CONCLUSION

In this relatively young population without major comorbidities, obesity was associated with a higher prevalence of DD. Serum IL-6 levels were significantly higher in obese participants and remained associated with DD after mutual adjustment for BMI and IL-6 in a limited two-variable logistic regression model. These findings support an association between systemic inflammation and DD in obesity; however, prospective studies are required to establish causality and evaluate the clinical utility of IL-6 as a biomarker.

ETHICAL DECLARATIONS

Ethics approval and consent to participate

This study was approved by the Research Ethics Committee, College of Medicine, University of Kirkuk, with document number 58B on 14 October 2024. The study was conducted in compliance with the Declaration of Helsinki. Written informed consent was obtained from all participants before participation.

Consent for publication

Not applicable.

Availability of data and material

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Use of generative artificial intelligence

The authors used ChatGPT (OpenAI, San Francisco, CA, USA) solely to assist with English language editing, grammar correction, and improvement of manuscript readability. All scientific content, study design, data collection, statistical analyses, interpretation of results, and conclusions were performed exclusively by the authors. The authors reviewed and verified all AI-assisted edits and accept full responsibility for the accuracy and integrity of the manuscript.

Authors' contributions

All authors contributed to the literature review, study design, data collection, statistical analysis, and manuscript preparation. All authors read and approved the final version of the manuscript.

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