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Obesity Profile of Lahore District: Risk Factors And Inflammatory Mediators

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Abstract
An increasing public health concern is obesity, which is particularly common in Pakistan's urban areas and other developing nations. This cross-sectional study looked at 1301 people in Lahore to determine the prevalence of obesity and the metabolic and inflammatory markers that are linked to it in Lahore District, Pakistan. Overall, the rates of underweight, normal BMI, overweight, and obesity were 19.14%, 24.2%, 38.91%, and 17.75%, respectively. The age group of 26–39 years old had the highest obesity rate, with a notable gender difference of 60.12% for men and 39.88% for women. Significant variations were observed in the cholesterol levels between obese and normal-weight subjects (261 ± 2.8 mg/dL versus 163 ± 3.17 mg/dL), according to the study. Additionally, leptin resistance was shown by lower soluble leptin receptor levels (13.8 ± 0.432 ng/mL) and higher leptin levels (33.8 ± 1.26 ng/mL) in the obese participants. Obese people had considerably higher levels of inflammatory markers, such as TGF-β, TNF-α, CRP, IL-6, and IL-8, indicating a condition of chronic low-grade inflammation. Particularly, there was a noticeable increase in CRP (4.68 ± 0.285 mg/dL), IL-8 (29 ± 3.19 pg/mL), and IL-6 (16.2 ± 0.925 pg/mL). These results highlight the significance of managing inflammatory and metabolic pathways in obesity. The report emphasizes how urgently focused efforts are needed to reduce obesity and the health problems associated with it in the people of Lahore. Gaining insight into how inflammatory indicators and leptin signaling interact in obesity may help develop preventative and treatment methods that are more successful.

Keywords: Obesity, pro-inflammatory mediators, CRP, ESR, leptin and leptin receptor.

Introduction

Obesity is an emerging public health problem, and is prevalent in developing countries, especially the urban areas (Jaacks et al., 2019; Prentice, 2006). High rates of obesity and overweight are a concern due to implication for health in developed and developing countries including Pakistan (Asif et al., 2020; Satti & Khalid, 2019). In Lahore, Pakistan many factors e.g. trend of urbanization along with associated sedentary lifestyle; physical inactivity status etc., may promote development and progression of obesity from simple state to overweight and thereafter towards pathologic states of obesity (undoubtedly linked with other risk factors like hypertension, dyslipidemia, diabetes mellitus etc.) at relatively younger age signifying the need to look into the problem promptly especially when effective preventive strategies could be planned in any population. Obesity is defined as the accumulation of an excessive amount of body fat and is frequently measured by body weight (BW) categories through Body Mass Index (BMI), and can categorize people in normal BMI, overweight or obese (Moltrer et al., 2022; Owusu-Banahene et al., 2018). The condition is more than just the result of lifestyle choices, being closely tied to multiple biological processes and inflammation (Gasmi et al., 2021; Guerreiro et al., 2022; Lustig et al., 2022).

Leptin, a hormone secreted by adipocytes and known to suppress hunger and to induce energy expenditure is an essential element in the regulation of energy balance (Friedman, 2019; Seth et al., 2021). Under normal physiological conditions, leptin binds to its receptors in the hypothalamus which induces anorexia and reduces food intake. Nonetheless, in obesity, activity in the leptin signaling pathway is typically blunted, despite high circulating leptin levels (Childs et al., 2021; Perez-Leighton et al., 2024). In this resistance the messages that come to the brain that we already eat, are not properly received by it and we continue eating and gaining weight. In the blood, leptin is bound by the soluble leptin receptor, which reduces the availability of free leptin to its receptors and changes in levels has effects on downstream leptin signaling (Bordo, 2023; Grannell et al., 2021; Pan & Myers Jr, 2018; Seth et al., 2021).

Obesity-related complications are mediated by inflammation. Inflammatory markers, such as interleukin-6 (IL-6), interleukin-8 (IL-8) and tumor necrosis factor-α (TNF-α), are elevated in obese people leading to a condition of constant low grade inflammation (Amaral et al., 2020; Phillips & Grayson, 2020; Vilotić et al., 2022). Such inflammatory response is also signified by an increase in C-reactive protein (CRP) levels and erythrocyte sedimentation rate (ESR). Moreover, obesity and its metabolic disorders are associated with transforming growth factor-β (TGF-β) and lipid abnormalities like increased cholesterol levels (Arias-de la Rosa et al., 2023; Leung et al., 2023).

Developing directed interventions necessitates understanding the connection between these inflammatory mediators and obesity. The aim of this study is to investigate the risk factors for, among other things, leptin and its receptor as major immune mediators of obesity in Lahore population in Pakistan with regard to interplay between these factors.

Methodology

Ethical Considerations

The Ethics Committee of The University of Lahore approved this study. All participants gave their consent with an assurance that their information would remain confidential while they had the right to withdraw at any time.

Study Design and Population

It is a Lahore District of Pakistan-based cross-sectional analysis. The sample population included 1301 participants who had been subjected to a Body Mass Index (BMI) checkup alongside other health parameters. Participants were chosen through the application of stratified random sampling in order to ensure even distribution across different demographics like age or sex.

Participant Recruitment

Participants were recruited from various healthcare facilities, community centers and public health campaigns. The inclusion criteria for selection was age of 30 years and above with informed consent given by an individual. Exclusion criteria involved people with chronic illnesses that did not relate to obesity such as late stage cancer or infectious diseases to avoid confusing factors.

Data Collection

Anthropometric Measurements

The weight was measured using a calibrated digital scale. Height was measured using stadiometer.
BMI was computed as: wt (kg)/ht (m^2). BMI categories were defined as follows:
Underweight: BMI less than 18.5 kg/m^2
Normal : 18.5-24.9 kg/m^2
Overweight: 25-29.9 kg/m^2
Obese: ≥30 kg/m^2, further classified into:
Class I – 30-34.9 kg/m^2
Class II – 35-39.9 kg/m^2
Class III - ≥40kg/m^2

Demographic and Medical History

Structured questionnaires were used to collect information about demographics such as age and gender; lifestyle factors like diet and physical activity; smoking status; medical history that contained co-morbidities such as diabetes mellitus hypertension cardiovascular disease only a few of the points that the authors made.

Biochemical Assessment

Blood Sample Collection

Fasting Blood Samples: Blood samples were collected after an overnight fast of at least 8 hours. Participants were instructed to avoid any food or drink, except water, during this period.

Venipuncture Procedure

Blood was drawn from the antecubital vein using a sterile technique. Approximately 10 mL of blood was collected into appropriate tubes for various assays.

Assessment of Cholesterol

Levels of cholesterol were measured using enzymatic colorimetric methods on automated analyzers.

Leptin and Soluble Leptin Receptor

Serum leptin levels and soluble leptin receptor concentrations were measured using Enzyme-Linked Immunosorbent Assay (ELISA) kits.
Samples were processed according to the manufacturer's instructions. The assays involved incubating the samples with specific antibodies and detecting the bound leptin or receptors using a colorimetric detection method.

Inflammatory Markers

Interleukin-6 (IL-6) and Interleukin-8 (IL-8): These cytokines were quantified using ELISA kits. The assays involved the capture of IL-6 and IL-8 from serum samples and subsequent detection using enzyme-linked secondary antibodies.

C-Reactive Protein (CRP)

CRP levels were measured using a high-sensitivity immunoassay. The test involved the use of monoclonal antibodies specific to CRP, with a detection system based on turbidity or nephelometry.

Erythrocyte Sedimentation Rate (ESR)
ESR was determined using the Westergren method. Blood was placed in a vertical tube, and the rate at which red blood cells settled was measured over one hour.
Transforming Growth Factor-B (TGF-β)
TGF-β levels were assessed using ELISA kits. The assay involved activation of latent TGF-β and subsequent detection using specific antibodies.

Tumor Necrosis Factor-A (TNF-α)
TNF-α levels were measured using ELISA kits. The process involved capturing TNF-α from serum samples and detecting it with enzyme-linked secondary antibodies.

Data Analysis
Descriptive Statistics
It was done to calculate the prevalence of obesity, overweight and normal BMI. Another objective was to analyze distribution of obesity classes and gender proportions in the obese population. Also, age-specific prevalence rates were calculated.

Inferential Statistics
An unpaired t-test was used to compare the means of two independent groups (normal and obese). T-tests were used to compare differences in mean leptin levels, inflammatory markers, and lipid profiles across BMI categories.

Results
Assessment of Anthropometric Variables
The overall prevalence of obesity, overweight, normal, and underweight BMI among 1301 tested Lahore District, Pakistani population study subjects was 17.75%, 24.2%, 38.91%, and 19.14% respectively. Among 190 obese subjects, 66.6% had Class 1, 27.97% had Class 2, and 12.4% had Class 3 obesity. Among the obese, 60.12% and 39.88% were males and females. Obesity was highest among those aged 26-39. Overall, 34.8% of participants were young obese in the age group 18-25 years 45.9% of participants was adult (26-39), mature participant (40-54) were 16.79% and old participant (55 and above) were 11.81%. 13.58% presented one or more metabolic diseases, while the majority (86.42%) were free of any metabolic disease (Figure 1A-E).

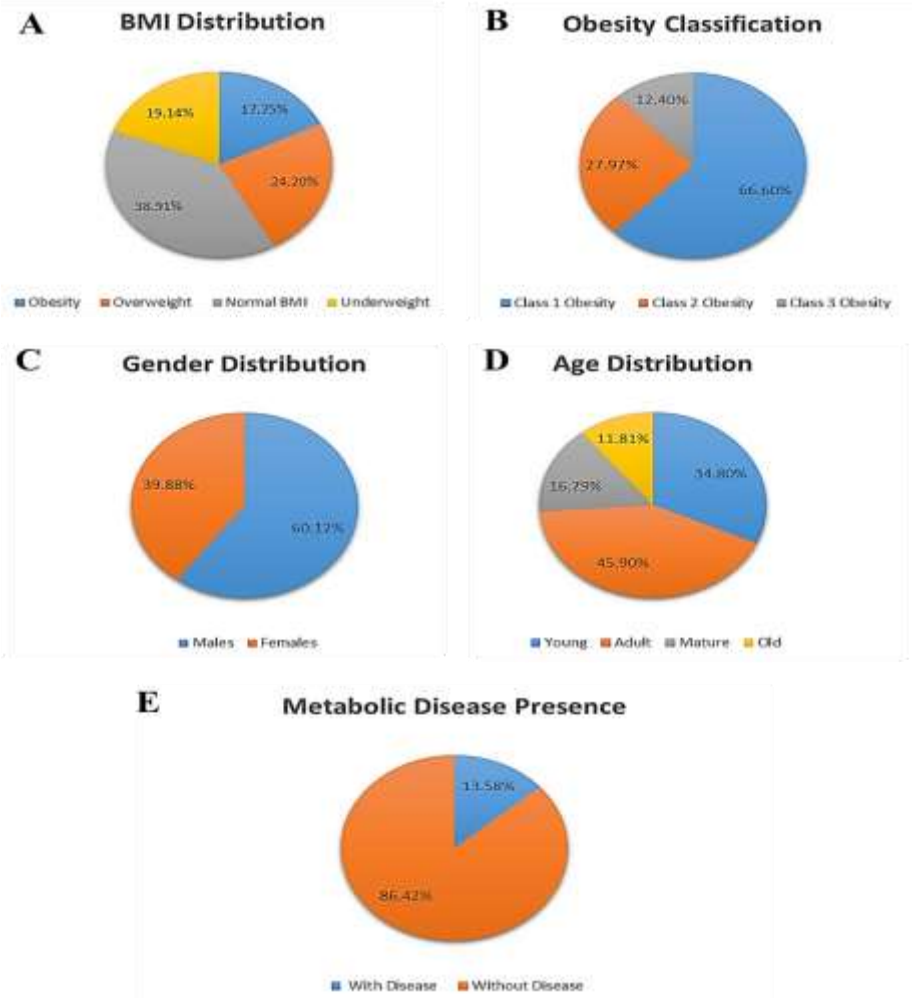

Figure 1: Distribution of Anthropometric variables among Study Population. A) BMI distribution showing the proportions of normal BMI, overweight, and obese individuals. **B)** Obesity classification illustrating the percentages of Class 1, Class 2, and Class 3 obesity among obese participants. **C)** Gender distribution among obese participants, indicating the proportions of males and females. **D)** Age distribution of obese participants across different age groups. **E)** Presence of metabolic diseases among obese participants, highlighting the percentage with and without metabolic diseases.

Differential Expression of Cholesterol, Leptin, and Soluble Leptin Receptor in Obese Versus Normal-Weight Subjects

It was found in the population of Lahore that there were also significant differences in cholesterol levels between normal and obese persons. The average cholesterol level in healthy subjects was 163 ± 3.17 mg/dL. In contrast, obese people had significantly more cholesterol with a 261 ± 2.8 mg/dL value (Figure 2A). This large increase in cholesterol levels in the obese cohort serves to highlight how being obese places an individual at a significantly greater risk for dyslipidemia. An unpaired t-test was used to compare the means of two independent groups (normal and obese).

Obese subjects, however, exhibited marked changes in leptin and soluble leptin receptor levels, when compared to normal weight controls. Normal subjects had a value of mean leptin concentration of 9.11 ± 0.569 ng/mL. By contrast, obese participants showed an order of magnitude higher leptin level than the controls with a mean of 33.8 ± 1.26 ng/mL. Leptin is markedly increased in obese individuals presumably due to the combination of the high levels of leptin and severe obesity being studied. Being the case such pronounced overexpression of leptin among obese subjects most likely points towards the presence of leptin resistance, a typical hallmark of obesity where elevated leptin fails to efficiently mediate anorexigenic effects. An unpaired t-test to determine if the means of two independent groups are different (normal vs obese) Figure 2B.

The detailed results are illustrated in Figure 2C, and the soluble leptin receptor levels showed an inverse trend. Normal individuals were (21.1 ± 0.357 ng/mL) not obese as compared to average receptor levels in Obese individuals (13.8 ± 0.432 ng/mL). The decrease in soluble leptin receptor levels in obese individuals further contributes to leptin resistance by diminishing the bioavailability of functional leptin, exacerbating the metabolic dysregulation seen in obesity. An unpaired t-test was used to compare the means of two independent groups (normal and obese).

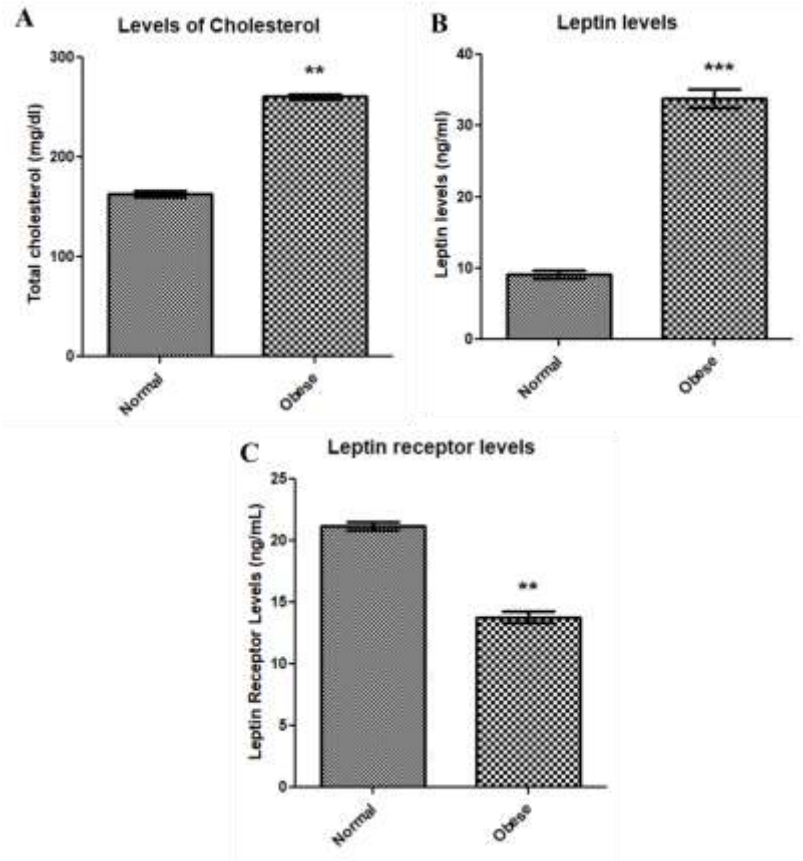

Figure 2: Cholesterol, leptin, and leptin-receptor levels. A) Difference in mean cholesterol levels (mg/dL) between normal and obese people group of Lahore city. B) Normal and obese people of the Lahore population mean leptin levels (ng/mL): C) A comparison of mean soluble leptin receptor levels (ng/mL) in normal and obese individuals in the Lahore population. The statistical analysis for comparing the values of the two groups was done using an unpaired t-test. Values are expressed as mean ± S.E.M. Where '*' indicates the level of significance. It appeared that the P value is accepted as <0. 05.

Levels of Inflammatory Markers in Normal and Obese Individuals

There was a various statistical difference between the normal and the obese group in the Lahore population concerning these inflammatory biomarkers. The inflammatory markers that were included in the study are IL-6, IL-8, CRP, ESR, TGF-β, and

TNF-α. The data that have been analyzed show the presence of this specific inflammatory response linked to obesity. Normal reference values of IL-6 in the human body were 5.71 ± 0.205 pg/mL. On the contrary, the rate of IL-6 in the bloodstream was significantly higher in the obese participants with a mean of 16.2 ± 0.925 pg/mL. This threefold increase in IL-6 among the obese subjects implies a high inflammatory state among these individuals since IL-6 is one of the potent cytokines involved in the inflammatory response and is also known to be related to insulin resistance and several metabolic disturbances. The mean IL-8 level in normal individuals was 8.75 ± 0.645 pg/mL. Obese subjects had significantly higher IL-8 levels of 29 ± 3.19 pg/mL. From this, the highly significant increase in IL-8 levels in obesity is consistent with the increase in the 'chemotactic activity' which increases the homing of the immune cells to the adipose tissue thereby escalating inflammation.

The mean CRP level in normal persons was 0.965 ± 0.0587 mg/dL, but the CRP level in obese individuals was substantially higher at 4.68 ± 0.285 mg/dL. A well-known indicator of systemic inflammation, higher CRP levels in obesity are suggestive of low-grade chronic inflammation, a risk factor for cardiovascular illnesses. Normal individuals had an ESR of 12.4 ± 0.969 pg/mL, while obese persons had an ESR of 20.6 ± 0.714 pg/mL. Given that ESR is a nonspecific indicator of inflammation, the elevated ESR in obese individuals further supports the existence of a continuous inflammatory process. Normal individuals exhibited mean TGF-β levels of 5.25 ± 0.290 pg/mL, but obese persons had higher levels of 8.41 ± 0.299 pg/mL. TGF-β plays a role in fibrosis and tissue remodeling; its elevated levels in obesity might be attributed to the expansion of adipose tissue and the fibrotic response. The mean TNF-α level in normal persons was 6.01 ± 0.302 pg/mL, while the levels in obese individuals were significantly higher at 14.5 ± 1.81 pg/mL. Strong pro-inflammatory cytokine TNF-α is involved in the etiology of insulin resistance and metabolic syndrome associated with obesity.

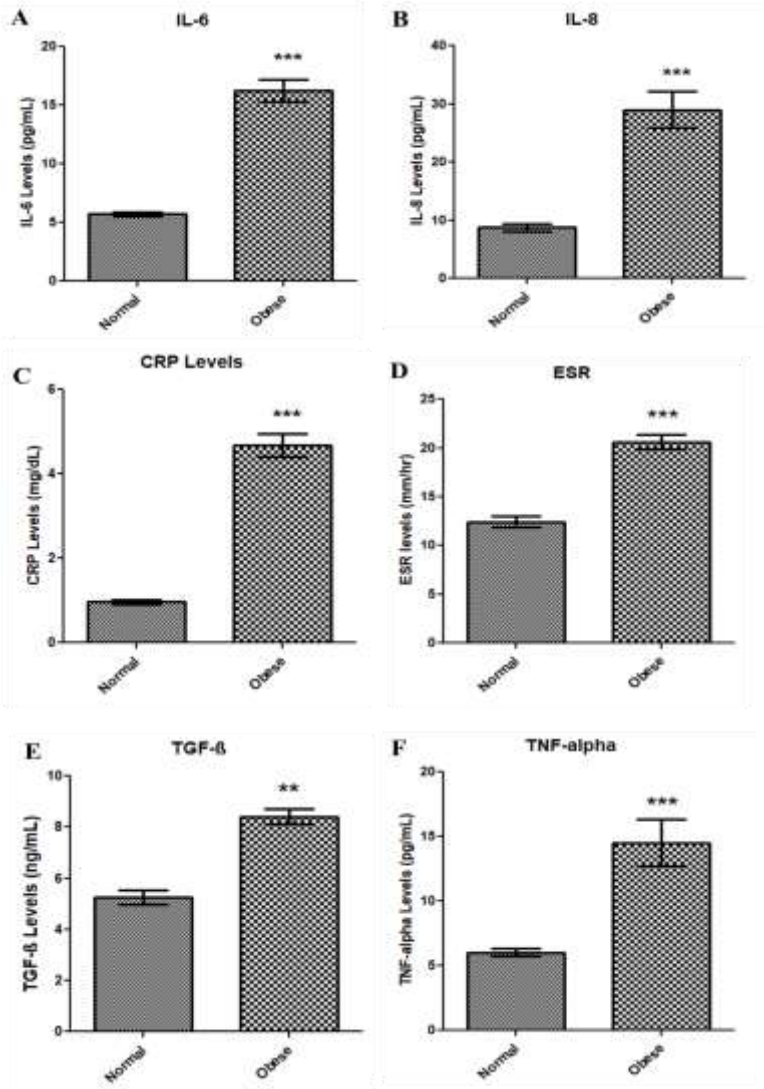

Figure 3: Inflammatory marker levels in normal and obese Lahori population. A) IL-6, B) IL-8, C) CRP, D) ESR, E) TGF-β, and F) TNF-α. The values were presented as mean ± SEM. The significance of the differences between groups was assessed using a t-test. When the p-value is less than 0.05, it indicates a statistically significant difference, shown by the asterisk (*).

Discussion

The current study looked at cholesterol levels, leptin signaling, a variety of inflammatory markers, and anthropometric factors to examine the metabolic and inflammatory profiles of normal and obese people in the Lahore population. The findings offer important new perspectives on the profound physiological changes linked to obesity.

An analysis of the anthropometric data showed that the research population's BMI categories varied widely. Among the 1301 people who were tested (Figure 1A-E), the general prevalence of obesity, overweight, normal weight, and underweight fell into different categories, with a significant percentage falling into the overweight and normal weight categories. Class 1 obesity accounted for the bulk of the 190 obese participants, with Class 2 and Class 3 obesity following. The gender distribution revealed that men were more likely than women to be obese (Cooper et al., 2021; Gregory et al., 2008). The age group of 26 to 39 was found to be the most obese, indicating a critical phase for the emergence and aggravation of obesity-related problems (Wrzosek et al., 2018). Although not as much, younger adults (18–25 years old) and middle-aged people (40–54 years old) also showed notable obesity rates. The lowest frequency of obesity was seen in the senior group (those 55 and older). Although metabolic illnesses were quite common among obese people, the majority did not have them, suggesting a window of opportunity for preventative care (Ogden et al., 2014; Zorena et al., 2020).

The information showed that obese people had significantly higher cholesterol than people of normal weight (Figure 2A). This result is consistent with the known association between dyslipidemia, a disorder marked by elevated lipid levels and a known risk factor for cardiovascular illnesses, and obesity (Berberich & Hegele, 2022). Obese people have elevated cholesterol levels, which exacerbate atherosclerosis and raise the risk of cardiovascular events-related morbidity and death. This emphasizes the necessity of focused measures to control cholesterol levels in obese individuals, possibly involving dietary changes, exercise, and medication (Bovolini et al., 2021; Zokaei et al., 2020).

Adipocytes are the primary producers of the hormone leptin, which inhibits appetite and hence reduces food intake to maintain energy balance (Picó et al., 2022; Seth et al., 2021). According to the study, obese people had considerably greater leptin levels (Figure 2B), which is suggestive of leptin resistance, a condition in which raised leptin is unable to regulate hunger and energy expenditure (Liu et al., 2022). Concurrently, obese participants had considerably decreased levels of soluble leptin receptors (Figure 2C), which further exacerbated leptin resistance by lowering the hormone's bioavailability. These results demonstrate the intricate relationship between leptin signaling and obesity, indicating that treating obesity and related metabolic disorders may benefit from treatment approaches targeted at increasing leptin sensitivity (Obradovic et al., 2021; Pereira et al., 2021).

One important aspect of the metabolic dysfunction associated with obesity is inflammation. Several inflammatory markers were evaluated in the study, and the results showed that obese people had considerably higher levels of TGF-β, TNF-α, CRP, IL-6, and IL-8 than normal-weight controls (Figures 3A–F). Obese people had noticeably greater levels of these pro-inflammatory cytokines (Aliabadi et al., 2022; Hariharan et al., 2022). Insulin resistance has been linked to IL-6, which is known to be involved in the acute phase response (Al-Mansoori et al., 2022). Higher chemotactic activity is indicated by elevated IL-8 levels, which increases immune cell recruitment to fat tissue and exacerbates inflammation (Moghbeli et al., 2021; Uribe-Querol & Rosales, 2022).

CRP is a well-known indicator of systemic inflammation, and it was significantly greater among obese participants. Increased risk of cardiovascular illnesses is linked to obesity, which is characterized by persistent low-grade inflammation, which is indicated by elevated CRP levels (Khanna et al., 2022; Lund et al., 2020; Mouliou, 2023). The evidence of a continuous inflammatory process is further supported by the elevated ESR in obese persons. According to previously reported literature, elevated ESR indicates a heightened inflammatory state in obesity (Alende-Castro et al., 2021; Purdy & Shatzel, 2021). ESR is a nonspecific marker of inflammation. This cytokine is involved in fibrosis and tissue remodeling. The fibrotic response linked to the growth of adipose tissue may be reflected in the higher TGF-β levels in obese individuals, which could lead to metabolic disruptions (Kruszewska et al., 2022). TNF-α is a strong pro-inflammatory cytokine that plays a crucial role in the etiology of metabolic syndrome and insulin resistance associated with obesity. Its higher concentrations in obese people draw attention to the inflammatory environment that surrounds obesity (Al-Mansoori et al., 2022; Gasmi et al., 2021).

The study's notable changes in inflammatory markers, anthropometric factors, cholesterol, leptin, and other indicators highlight the complex nature of obesity and its systemic effects. The heightened inflammatory markers point to a chronic low-grade inflammatory state that predisposes people to a variety of additional health problems, such as type 2 diabetes and cardiovascular illnesses, in addition to the metabolic difficulties of obesity. To lessen the negative health effects of obesity, future research should concentrate on clarifying the underlying mechanisms causing these changes and creating focused therapies. This can involve investigating the effectiveness of leptin sensitizers, anti-inflammatory drugs, and lifestyle changes meant to lower body fat and enhance metabolic health. Furthermore, longitudinal research is required to comprehend the temporal dynamics of these indicators and their predictive significance for issues associated with obesity.

To sum up, this study offers a thorough understanding of the inflammatory and metabolic disorders linked to obesity in the people of Lahore. The results emphasize how critical it is to treat both the inflammatory and metabolic pathways for managing and preventing obesity and the health problems associated with it.

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Authors' Consent

All contributors have critically reviewed and approved this manuscript for publication.

Conflict of interest

The authors declare no conflict of interest.

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