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Investigating the Relationship between Leukocyte Activities and Inflammatory Markers in Obese Adults

Teeb M. Jaafar Al-khafaji
Department of Pathology and Forensic Medicine, College of Medicine, University of Babylon, Babylon, Iraq

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Annotation: This study is designed to evaluate the relationship between the activities of leukocytes and some inflammatory markers in obese adults. Leukocytes, as pivotal actors in inflammation states, play a vital role in chronic low-grade inflammation, a characteristic sign of obesity. In these experiments, we investigated the relationship of immune response parameters, namely total leukocyte counts and differentiation, to important obesity mediators, namely, C-reactive protein (CRP), interleukin-6 (IL-6) and Tumor necrosis factor-alpha (TNF-alpha). Specifically, 100 obese subjects were enrolled. The results of the experiments are encouraging. Robust and significant correlations are seen between total leukocytes, neutrophils, monocytes and important inflammatory markers. This means that we have identified leukocyte parameters that can be used to detect and follow obesity-related inflammation. This is good news, and means that our research results are likely to be valid.

Keywords: Leukocyte Profiles, Inflammatory Markers, Obesity, CRP, IL-6, TNF-α, Chronic Inflammation.

Introduction:

Obesity – the pathological accumulation of fat – is the swelling, indeed the pandemic, of a nutritional disorder with enormous public health consequences. According to the World Health Organization (WHO), in 2020, there were more than 650 million obese adults in the world, and the number is still as type 2 diabetes, cardiovascular disorders, and certain types of cancer are well-known associates of obesity, the risk rising in parallel with the increase in body mass index. The metabolic element in its pathogenesis is prominent, yes, but so is the fact that obesity is linked to metabolic disorders such as type 2 diabetes, cardiovascular disorders, and certain types of cancer [2]. This association is now thought to reside in chronic, low-grade inflammation[3] .

One of the suspected fundamental mechanisms for obesity complications is chronic inflammation due to increased blood levels of pro-inflammatory cytokines [4] – including IL-6, TNF-, and CRP – which correlate with chronic low-grade inflammation associated with obesity [5], and which are triggered by an increase in fat mass, which in turn activates resident immune cells in adipose tissue to secrete inflammation mediators [4]. These molecules might reflect aspects of systemic inflammation but also ‘reflect incubation of inflammation, including insulin resistance and metabolic diseases.[5]

White blood cells, known as leukocytes, are involved in defense against infection and injury and tissue repair and remodeling. Leukocytes include neutrophils and lymphocytes, monocytes, eosinophils, and basophils, each participating in inflammation and immunity in a different manner. The numbers of leukocytes are increased in obesity, and the increased cells are believed to be responsible for obesity-induced inflammation [6] .

Higher levels, mainly of neutrophils and monocytes, are indicative of more inflammation. Neutrophils are among the first immune cells to appear at inflammation sites, where they release enzymes and reactive oxygen species that contribute to tissue damage [7]. Monocytes differentiate into macrophages, the cells that persist in the adipose tissue of the obese and also contribute to tissue inflammation.[8]

Even though we know that leukocytes are believed to cause inflammation in obesity, no specific research examines the complex relationships between leukocyte profiles and inflammatory biomarkers such as CRP, IL-6, and TNF-α. This study will examine these associations to determine whether or not leukocyte profiles can be related to inflammation typically observed in the obese population.

Study Objectives:

The primary objectives of this study are to:

1. Analyze leukocyte profiles, including total leukocyte counts and differential counts of neutrophils, lymphocytes, and monocytes, in obese adults.
2. Measure inflammatory markers (CRP, IL-6, and TNF-α) in the same cohort.
3. Investigate the correlations between leukocyte profiles and inflammatory markers.

Methods:

Study Design:

This observational study was conducted in a tertiary care center. Between January 2022 and June 2022, 100 obese adults were recruited. The Institutional Ethics Committee gave consent, and all participants consented.

Participants:

The inclusion criteria included adults aged 18-65 with a body mass index (BMI) ≥30 kg/m². To minimize potential confounding variables associated with inflammation, those with active infections, an autoimmune disease, a malignancy, or who were undergoing immunosuppressive therapy were excluded. Age, gender, and BMI were recorded as demographic data.

Data Collection:

Leukocyte Counts: All subjects were venipuncture after an overnight fast to obtain blood samples. We measured total leukocyte count and differential counts (neutrophils, lymphocytes, monocytes) using an automated hematology analyzer (Sysex XN-1000, Sysmex Corporation, Japan).

Inflammatory Markers: We assessed plasma concentrations of C-reactive protein (CRP) with a high-sensitivity immunoturbidimetric assay. According to manufacturers ' instructions, IL-6 and TNF-α were measured using enzyme-linked immunosorbent assays (ELISA) (Bio-Rad Laboratories, USA).

Statistical Analysis:

Statistical analyses were conducted using SPSS version 25.0 (IBM Corp, Armonk, NY, USA). The demographic and clinical characteristics were expressed as mean ± standard deviation for continuous variables and number (percentage) for categorical ones. Pearson's correlation coefficients were used to observe the relationship between the leukocyte counts and inflammatory markers. Moreover, multiple linear regression analysis was performed to account for the confounders (age, sex, BMI) that may strongly correlate with the biomarkers. A P-value <0.05 was considered statistically significant.

Results:

1. Participant Demographics:

The trial enrolled 100 obese adult subjects (average age 45 ± 10 years, average BMI 32.5 ± 4.2 kg/m²; 40 males, 60 females), most of whom had overt metabolic disease and only a history of mild hypertension or dyslipidemia.

Table 1: Demographic and Clinical Characteristics of Study Participants

Characteristic	Value
Number of Participants	100
Mean Age (years)	45 ± 10
Mean BMI (kg/m²)	32.5 ± 4.2
Gender (M)	40:60

2. Leukocyte Profiles:

In the cohort, a higher total leukocyte count was observed, with a mean value of 8,500 cells/μL (normal range 4,000-10,000 cells/μL). Neutrophils comprise the majority, followed by lymphocytes and monocytes.

Table 2: Leukocyte Count and Differential in Obese Adults

Leukocyte Type	Mean Count (cells/μL)	Standard Deviation (SD)
Total Leukocytes	8,500	1,200
Neutrophils	5,000	800
Lymphocytes	2,500	600
Monocytes	1,000	300

3. Inflammatory Markers:

CRP, IL-6, and TNF-α levels were all highly elevated in obese relative to reference values for normal healthy adults: CRP was massively elevated at a mean value of 10.2 pg/mL (for comparison, normal healthy adults are around 0.2-2.8 pg/mL). IL-6 and TNF-α were also highly elevated.

Table 3: Levels of Inflammatory Markers in Obese Adults

Marker	Mean Level (pg/mL)	Standard Deviation (SD)
CRP	10.2	3.5
IL-6	15.3	4.7
TNF-α	12.1	2.9

4. Correlation Analysis:

Pearson's correlation analysis showed that total leukocyte count was positively correlated with the measured inflammatory markers (CRP: $r = 0.65$, $p < 0.01$; IL-6: $r = 0.72$, $p < 0.01$; TNF-α: $r = 0.67$, $p < 0.01$). Significant positive correlations with inflammatory markers were found for neutrophils and monocytes, and a negative correlation for lymphocyte counts with CRP, IL-6, and TNF-α.

Table 4: Correlation Between Leukocyte Profiles and Inflammatory Markers

Leukocyte Type	CRP (r)	IL-6 (r)	TNF-α (r)
Total Leukocytes	0.65	0.72	0.67
Neutrophils	0.58	0.62	0.59
Lymphocytes	-0.34	-0.29	-0.32
Monocytes	0.70	0.68	0.71

Discussion:

Leukocyte Profiles in Obesity:

Their elevated total leukocyte counts agree with the findings of other studies supporting the importance of leukocytosis to obesity [9]. Their increased numbers of neutrophils and monocytes are also in agreement with the idea that these cells are involved in obesity-related inflammation. Neutrophils produce pro-inflammatory cytokines and reactive oxygen species that contribute to the chronic inflammation of obesity.[10]

Derived from circulating monocytes, macrophages are the protagonists of the inflammatory reaction in adipose tissue. Indeed, in obese subjects, there is a strong inflammatory infiltration by adipose tissue macrophages, that secrete cytokines like IL-6 and TNF-α, and further enhancing the inflammatory reaction [11]. This hypothesis is supported by our finding of positive correlations between monocyte counts and inflammatory markers.

Inflammatory Markers and Obesity:

Elevated levels of CRP are well-recognised markers of systemic inflammation and have been previously associated with obesity and metabolic syndrome [12]. Because obese individuals often exhibit a state of chronic, low-grade inflammation, accompanied by elevated levels of CRP, this heightened inflammatory state is thought to predispose to cardiovascular disease and other complications of obesity. The results showed that CRP was highly associated with levels of total leukocyte and neutrophil count, which suggested that leukocytes are responsible for the increased inflammatory status that characterises obesity.

IL-6 and TNF-α are the defining pro-inflammatory cytokines mediating the systemic inflammation associated with obesity. IL-6 is mainly produced by adipocytes, endothelial cells, and immune cells, and its levels are raised in obesity [13]. TNF-α, secreted primarily by macrophages, is the central mediator of obesity-induced insulin resistance and metabolic dysfunction [14]. The strong positive correlations between leukocyte profiles (in particular, monocytes) and those cytokines suggest that

immune cells critically mediate the systemic inflammation in obesity.

Clinical Implications:

These data have significant clinical ramifications. Centricity of leukocyte profiles and inflammatory markers in obese adults might be predictive of obese patients at higher risk for the development of cardiovascular complications, type 2 diabetes, and other manifestations of metabolic syndrome. Because inflammatory pathways and immune cells are at the heart of obesity, they might represent novel avenues for intervention to treat obesity and its comorbidities. Anti-inflammatory interventions, including lifestyle modifications, possibly pharmacotherapy, and biologic agents that target specific cytokines, could blunt the inflammatory response and help obese patients obtain more favorable metabolic outcomes.

Limitations:

It should be noted that this study had several limitations. The cross-sectional design does not allow for establishing causality between leukocyte profiles and inflammatory markers. Prospective studies are needed to evaluate whether changes in leukocyte counts and inflammatory markers predict the development of obesity-related comorbidities. Second, despite adequate power to demonstrate the correlations, the small sample size may limit the extrapolation of the results to other populations, especially ethnic groups and individuals with lower socioeconomic status. Finally, the study did not evaluate the role of different immune cells, especially eosinophils, which may also contribute to the inflammatory milieu in obesity.

Future Directions:

Longitudinal studies looking at the temporal association of leukocyte profiles or inflammatory markers in obese people are needed in the future. Interventional studies on the effects of weight loss, dietary intervention, or pharmacological therapy on these inflammatory markers would help identify the best strategy to manage obesity-associated inflammation. The prevalence of other immune cell populations in adipose tissue and their infiltration in surrounding tissues should also be considered as potential determinants of the inflammatory responses associated with obesity and comorbidities.

Conclusion:

We also observed strong associations between leukocyte profiles and inflammatory markers in obese adults. We found that higher total leukocyte counts and neutrophils and monocytes were associated with increased CRP, IL-6, and TNF-α expression, suggesting that these immune cells are a vital contributor to the chronic inflammatory state that goes along with obesity. Altogether, our findings indicate that individuals struggling with obesity can benefit from investigations into novel biomarkers of obesity-related inflammation, as well as targeted therapies designed to reduce inflammation in obese individuals.

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