Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 12s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Assessment Of Some Inflammatory Mediator's Role in Obese Males

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Cite this paper as: Hassan Y. Hassan, Mousa j. Mohammed, (2025) Assessment of Some Inflammatory Mediator's Role in Obese Males. *Journal of Neonatal Surgery*, 14 (12s), 420-424.

ABSTRACT

Obesity is a substantial issue that reduces the quality of life for numerous individuals and increases their susceptibility to various diseases. Inflammation plays a crucial role in the development of obesity and acts as a central factor for the interactions of cellular and humoral components inside adipose tissue. The research sought to investigate obesity-associated inflammatory markers, specifically IL-1α, IL-1β, TGF-Beta1, and TGF-Beta2, in individuals with obesity and healthy controls. The study featured a total of 160 patients, comprising 120 obese cases and 40 controls, conducted from January 2024 to June 2024. The samples underwent centrifugation (3000 g, 20 min), Subsequently, the serum was separated and preserved at -20°C. Serum from both the patient and control was subjected to enzyme-linked immunosorbent assays (ELISA) for (IL-1α, IL-1β, TGF-β1, and TGF-β2). The current study included 160 participants at various stages of obesity, indicating that the majority of overweight individuals were aged 20-30, comprising 30 subjects (83.33%). The recent findings indicated that the mean TGF-β2 was considerably highest in obese type II patients (274.8 ng/L). TGF-β1 was considerably higher ($P<0.05$) in obese type II participants, with a mean of 51.67 ng/L. Similarly, the levels of IL-1α and IL-1β did not demonstrate significant differences across the research groups, with $P>0.05$. The current study revealed that TGF-β1 and TGF-β2 may have a significant role in lipid metabolism, particularly in individuals with insulin resistance.

Keywords: *Obesity, BMI, TGF- β, MH, DII, DIL.*

1. INTRODUCTION

The incidence of overweight and obesity has increased markedly in recent decades. Obesity is strongly linked to several metabolic disorders, including: (Insulin resistance, atherogenic dyslipidemia, non-alcoholic fatty liver disease and metabolic syndrome) (1). Obesity and the metabolic syndrome are worldwide epidemics driven by an environment that encourages obesity. This is enabled by complex underlying pathophysiology, in which chronic inflammation acts as a crucial etiological and mechanistic element (2). Inflammation functions as an essential physiological defense mechanism; nonetheless, persistent or intense inflammation can result in disease. Persistent systemic and adipose tissue inflammation contributes to obesity-associated cardiovascular disease and type 2 diabetes mellitus (3). Excess weight and obesity induce a chronic inflammatory state since adipose tissue produces inflammatory biomarkers, which may affect pain pathways. Cytokines, such as interleukin-1β (IL-1β), IL-6, and tumor necrosis factor, may directly influence peripheral neurons through their receptors or indirectly by promoting prostaglandin production, which can activate or sensitize peripheral neurons, leading to increased pain perception. Cytokines are proposed to contribute to central pain mechanisms (4). Adipose tissue is insufficient in buffering dietary lipids, leading to ectopic fat accumulation in organs such the liver, heart, or skeletal muscles. Lipotoxicity in adipose tissue increases the generation of reactive oxygen species (ROS), and their excess causes cellular damage and promotes chronic inflammation (1,5). Stress and inadequate oxygenation induce apoptosis in adipocytes. This promotes the formation and activation of macrophages exhibiting an M1 (proinflammatory) phenotype, while diminishing the M2 (anti-inflammatory) phenotype. Proinflammatory cytokines, such as TNF-α, IL-6, and interleukin-1β (IL-1β), together with metabolites from injured cells, promote the translocation of HMGB-1 from the nucleus to the cytosol. This protein is recognized as a significant facilitator of inflammation at the site of damage. Thus, it is comprehensible that HMGB-1 levels are elevated in obesity and metabolic syndrome, as inflammation in these conditions, triggered by lipotoxicity and reactive oxygen species, leads to cellular damage and macrophage activation (1,6). Interleukin-1α (IL-1α), tumor necrosis factor-α (TNF-α), leptin, and transforming growth factor-α (TGF-α) are key adipokines that modulate inflammatory processes in individuals with obesity (7). Elevated TGF-β levels have been associated with impaired adipose tissue in individuals. Although TGF-β serves as an inhibitor of adipogenesis, its elevated expression in obese

adipose tissue suggests a possibly paradoxical role in metabolic control (8). Augmenting the synthesis and activity of IL-1α, both locally and systemically, precipitates insulin resistance (IR). Furthermore, elevated levels of TGF have been associated with obesity and its accompanying comorbidities, such as diabetes and dyslipidemia, indicating a potential role of adipokines in the metabolic mechanisms of obese individuals (7).

Patients and methods

The study featured a total of 160 patients, comprising 120 obese cases and 40 controls, conducted from January 2024 to June 2024. All instances having a documented history of obesity and a body mass index (BMI > 27). Patient data were collected from each participant following the acquisition of a signed consent form. Fasting venous blood samples (5 ml) were obtained from each participant. The samples were subjected to centrifugation (3000 g, 20 min.), following which the serum was extracted and preserved at -20°C. Serum from both the patient and control was subjected to enzyme-linked immunosorbent assays (ELISA) for IL-1α, IL-1β, TGF-Beta1, and TGF-Beta2, adhering to the manufacturer's instructions (SUNLUNG/Biotech, Ltd; China).

Statistical analysis

Statistical analysis was performed with GraphPad Prism (version 10.1, USA). Comparisons across the groups were performed utilizing One-Way ANOVA and/or Chi-square testing if required. A P value beyond 0.05 is considered non-significant, but a P value below 0.05 signifies considerable variation among groups.

2. RESULTS

The current study suggested that the majority of overweight individuals were in the age area of 20-30, including 30 participants (83.33%). In the case of obesity type-1, the biggest number of participants, 14 (73.68%), also belonged to the 20-30 age group. Conversely, for obese type-2, most individuals were in the 20-30 age bracket, totaling 3 participants (42.86%), as seen in Table 1. The BMI variation among the study population, as illustrated in Table 2, indicated that the mean BMI of the obese type II group was the highest (38.07), followed by obese type I (32) and overweight subjects (27.03). The current findings indicate that the mean TGF-β2 concentration was highest in obese type II people (274.8 ng/L) and lowest in overweight individuals (258.2 ng/L), with a significant difference between the categories ($P<0.05$). TGF-β1 was considerably enhanced ($P<0.05$) in obese type II participants, with a mean of 51.67 ng/L, compared to the other groups, as seen in Table 3. Similarly, the levels of IL-1α and IL-1β did not exhibit significant differences among the study groups, with $P>0.05$ for both. Minor variations were observed across the groups, with the highest concentration of IL-1α at 13.1 pg/ml reported in obese type 1 subjects, while a slight elevation of IL-1β at 9.4 pg/ml was noted in overweight individuals, as indicated in Table 4.

3. DISCUSSION

The interplay between adipose tissue and inflammation is complex and involves several cellular and humoral components. Macrophages are the principal cellular components involved in the chronic inflammation of obese adipose tissue, and their modulation is essential for the interaction between inflammatory and immune responses, possibly representing a critical factor in medical treatments for obese individuals (9,10). Obesity is frequently linked to a persistent, low-grade inflammatory condition that impacts the entire organism. This chronic inflammatory disorder disrupts the coordinated connection between the periphery and the brain, crucial for sustaining homeostasis via humoral, nutrient-mediated, immunological, and neural signaling pathways (11). The current study concurred with previous research indicating The impact of inflammatory mediators on the relationship between dietary insulin indices and the metabolic phenotypes of overweight and obese women (7). TGF-β serves as an inflammatory marker, with over 30 associated proteins identified as constituents of the TGF-β superfamily in mammals, predominantly located in liver tissue (12). The current data indicated that the mean TGF-β2 level was significantly elevated in obese type II subjects (274.8 ng/L). Our findings align with another study that reported a positive correlation between TGF-β levels and dietary carbohydrate intake. No substantial correlation was seen between inflammatory markers and total fat consumption. Nonetheless, a marginally significant negative correlation A correlation was seen between total fat consumption and TGF-β levels in the modified model. Thus, total dietary carbohydrate intake was associated with an elevated risk of inflammation, but total fat consumption showed no correlation with increased inflammation (13), Yadav et al., (14) who proposed that the TGF-β/Smad3 pathway plays a crucial role in the regulation of glucose and energy balance. Specifically, they demonstrated that the inhibition of TGF-β/Smad3 signaling enhances glucose and insulin tolerance, resulting in an improved metabolic profile. Another study indicated a positive correlation between TGF-β and BMI. Elevated concentrations of TGF-β in the bloodstream signify the severity of inflammation associated with obesity (15). TGF-β may contribute to cellular proliferation in addition to adipose tissue accumulation in adipocytes; hence, its increase in obese individuals may serve as a significant marker of fatty tissue production and deposition. Furthermore, our findings align with those of Fabregat and Caballero-Díaz studies (16), who argue

that TGF-β is a vital regulator across all stages of disease progression, from basic liver injury to cirrhosis and hepatocellular cancer, mediated by inflammation and fibrosis. Initial research suggests that sustained TGF-β expression in obesity is predominantly associated with advanced inflammatory stages and is considered a risk factor for serious diseases (17,18). The levels of IL-1α and IL-1β did not differ significantly among the study groups, with P>0.05 for both. Yet, slight variations were observed, with the highest concentration of IL-1α at 13.1 pg/ml reported in obese type 1 subjects, while a minor elevation of IL-1β was detected in overweight subjects at 9.4 pg/ml. Individuals with obesity exhibit elevated blood levels of interleukin-1 beta (IL-1β), which is generated by macrophages originating from adipose tissue. This pro-inflammatory cytokine modulates adipocyte proliferation and apoptosis, stimulates lipolysis, suppresses lipid production, and decreases blood lipids through autocrine and paracrine mechanisms (19). A recent study established that the metabolically healthy obesity (MH) phenotype in overweight and obese women is associated with dietary insulin index (DII) and dietary insulin load (DIL) intake, with IL-1β possibly affecting this correlation. Subsequent studies confirmed that IL-1 family genes have a role in the genetic propensity to obesity. The interaction between IL1B and IL1RN has been shown to correlate with both BMI and body fat percentage, with the rare T allele offering protection against increased levels (20).

4. CONCLUSION

In summary, the data presented indicate that TGF-β1 and TGF-β2 may significantly influence lipid metabolism, synthesis, and accumulation, especially in people exhibiting insulin resistance.

Ethical Approval

The study was conducted in complience with the ethical approval issued by kirkuk directorate of health (Document no. 2024/1/2 NAM1)

Financial support and sponsorship

This study was not supported by outside sources.

Conflicts of interest

The authors declare no conflict of

Table 1. The age group of the study groups

Age group	Overweight		Obese type I		Obese type II		Control	
	No.	%	No.	%	No.	%	No.	%
<20	2	5.00	1	2.50	4	10.00	3	7.50
20-30	30	75.00	22	55.00	16	40.00	17	42.50
31-40	4	10.00	8	20.00	12	30.00	9	22.50
41-50	2	5.00	7	17.50	7	17.50	6	15.00
>50	2	5.00	2	5.00	1	2.50	5	12.50
Total	40	100.00	40	100.00	40	100.00	40	100.00

Table 2. BMI distribution of the study groups

Boody mass index	Overweight	Obese type I	Obese type II	Control	*P* value
	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	
	27.03±1.23	32.0±1.26	38.07±1.73	21.81±1.52	<0.0001
Total	40	40	40	40	

	160	

Table 4: Inflammatory biomarkers levels among the study groups

Immunity variables	Overweight		Obese type I		Obese type II		Control		*P* value
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD	
TGF-Beta2 (ng/L)	258.20	52.26	266.50	48.16	274.80	29.51	263.80	56.11	**0.0037**
TGF-Beta1 (ng/L)	32.04	23.43	39.06	10.53	51.67	15.80	44.48	20.34	**0.0005**
IL-1 alpha (pg/ml)	13.00	2.45	13.16	3.18	12.43	1.24	12.80	2.84	0.8200
IL-1 beta (pg/ml)	9.40	2.74	8.32	2.24	9.23	0.68	9.25	3.05	0.4498
Total (n)	40		40		40		40		

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