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Cytokines' Impact on Postpartum Hair Loss After First C-Section in Women 28-38

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Abstract. Background; Postpartum hair loss is a common condition affecting women after childbirth, particularly in those who have undergone cesarean delivery. Cytokines, which are key regulators of immune responses, are believed to play a significant role in the pathogenesis of this condition by influencing the hair growth cycle and immune function during the postpartum period. Aims of the study; Investigate the role of cytokines, including IL-6, TNF-α, IL-10, and CRP, in postpartum hair loss in women aged 28-38 after their first cesarean delivery, and to explore their potential correlation with changes in thyroid function and lipid profiles during the postpartum period. Methodology; This cross-sectional study aimed to determine biomarker levels in women aged 28-38 after their first cesarean section. It included 150 participants: 100 women post-first cesarean and 50 healthy controls. Ethical approval was obtained, and informed consent was given by all participants. Exclusion criteria included multiple cesarean sections, chronic diseases, or medication affecting biomarkers. Blood samples were collected after an overnight fast, and biomarkers like IL-6, TNF-α, IL-10, CRP, adiponectin, FBS, lipid profile, TSH, and Free T3 were measured using appropriate assays. Statistical analysis was performed, with $p < 0.05$ considered significant. Result; The comparative results between patients (n=100) and healthy controls (n=50) showed no significant difference in age (33.5 ± 3.4 vs. 30.2 ± 3.1 years, p=0.12). However, patients had a significantly higher BMI (29.5 ± 3.2 kg/m²) compared to controls (26.1 ± 3.0 kg/m², p<0.001). Levels of inflammatory markers (IL-6, TNF-α, IL-10, CRP) were significantly higher in patients (p<0.001), while adiponectin levels were lower (14.2 ± 7.5 ng/mL vs. 20.8 ± 9.1 ng/mL, p=0.02). Metabolic markers such as fasting blood sugar, cholesterol, triglycerides, and LDL-C were significantly elevated in patients (p<0.001). The severity of hair loss was also greater in patients (p<0.001). Additionally, TSH levels were significantly higher in patients (p=0.02), while Free T3 showed no significant difference (p=0.12). Conclusions; In conclusion, elevated inflammatory markers (IL-6, TNF-α, IL-10) and metabolic disturbances (higher BMI, fasting blood sugar, cholesterol) in postpartum women after cesarean delivery may contribute to hair loss. These alterations reflect the body's response to stress and hormonal changes following delivery.

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Highlights:

1. Inflammatory Response & Hair Loss – Elevated levels of IL-6, TNF-α, IL-10, and CRP in postpartum women after cesarean delivery suggest a strong link between inflammation and hair loss.
2. Metabolic & Hormonal Changes – Higher BMI, increased fasting blood sugar, cholesterol, and TSH levels indicate metabolic disturbances that may contribute to postpartum hair loss.
3. Clinical Implications – Understanding these biomarker changes could help in developing targeted interventions to manage postpartum hair loss and associated metabolic risks.

Keywords: Postpartum, Cesarean Delivery, Inflammatory Markers, Hair Loss, Metabolic Disturbances, Hormonal Changes

Introduction

Postpartum hair loss or telogen effluvium is a common physiological state that affects postpartum women. It is defined as a temporary loss of hair that usually happens within three months after delivery. While this condition is widely considered to be self-limiting, it can be emotionally distressing and affect the self-esteem of women who have it. Hormonal and immune system changes in pregnancy may trigger, or even accelerate, postpartum hair loss. Cytokines are one of the important factors involved in mediating the inflammatory responses and immune regulation during the postpartum period [1] [2]. Cytokines are small signaling proteins secreted by a variety of immune system cells, such as T cells, macrophages, and adipocytes. They are involved in many biological processes such as immunity, inflammation, and tissue repair. Certain cytokines, notably pro-inflammatory ones like interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP), are well recognized for their role in the immune response and inflammation. On the contrary, anti-inflammatory cytokines (such as IL-10) are involved in inflammation resolution and healing. Excess or deficiency of cytokines (messengers) has a major role in many diseases (of autoimmune, chronic inflammatory and even skin and hair such as hair loss) [3] [4]. The postpartum period is characterized by a range of hormonal and immune system adaptations that may affect the levels and activities of different cytokines. For instance, increased secretion of pro-inflammatory cytokines including IL-6 and TNF-α has been linked to the pathogenesis of telogen effluvium [5]. These cytokines can change the hair growth cycle to move the hair follicles into the shedding phase (telogen) prematurely, resulting in excessive hair loss. Conversely,

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cytokines with anti-inflammatory properties such as IL-10 could play a role in the regulation of the immune response and the attenuation of inflammation, factors that may impact postpartum hair loss [6]. The newly identified role of adiponectin, an adipokine secreted from adipose tissue, as a key modulator of immune responses and inflammation adds to this growing list of secretory molecules. Adiponectin has a role in regulating glucose and lipid metabolism but also has anti-inflammatory properties [7]. Adiponectin is known to be a sign of low-grade inflammation, the higher its levels, the lower the risk of inflammation and, consequently, metabolic syndrome. A dysregulated concentration of adiponectin may also be involved in influencing the inflammatory processes seen in postpartum hair loss [8]. Thyroid hormones, along with some other cytokines and adipokines, also help regulate hair growth. Thyroid hormones, specifically thyroid-stimulating hormone (TSH) and free triiodothyronine (T3), are important for the normal regulation of the hair cycle. Thyroid disorders as hyperthyroidism or hypothyroidism can make the hair growth cycle accelerate or slow down leading to hair thinning or hair loss [9]. TSH (thyroid-stimulating hormone), made by the pituitary gland, tells the thyroid gland to make thyroid hormones (including T3 and T4). Free T3 is the active form of thyroid hormone, which is necessary for metabolic processes such as hair follicle regulation. Dysregulations of thyroid hormone can worsen the loss of hair during the postpartum time frame, especially in the presence of underlying thyroid imbalances that have yet to be remedied [10]. Cytokines are critical mediators of inflammation and immune regulation, processes that are implicated in postpartum hair loss. Two of the most studied pro-inflammatory cytokines, as they relate to hair shedding, are IL-6 and TNF-α. Interleukin-6 (IL-6) plays an important role in many biological processes including inflammation, immune response, and metabolic regulation [11]. Higher circulating levels of IL-6 have been associated with telogen effluvium, as they are believed to trigger the hair growth cycle, encouraging the hair follicles to prematurely enter the shedding phase. TNF-α is an important pro-inflammatory cytokine that has the ability to mediate apoptosis and inflammatory responses, which also contributes to normal hair follicle cycling [11] [12]. In contrast, IL-10 is an anti-inflammatory cytokine that counteracts the actions of pro-inflammatory cytokines. This helps reduce inflammation and prevents tissues from being damaged too much. A balance of pro- and anti-inflammatory

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cytokines is critical for inflammation resolution and tissue repair. Higher IL-10 levels may thereby attenuate the inflammatory response and restore normal hair follicle function this can be applied in conditions like postpartum hair loss [13]. Another important inflammatory marker is the C-reactive protein (CRP), an indicator of the general level of systemic inflammation in the body. High concentrations of CRP has been related to many inflammatory types of diseases including the ones affecting hair regrowth. Its role in postpartum hair loss may be indirect, being a biomarker of generalised inflammation leading to dysregulation of the hair growth cycle [14]. Adiponectin is an anti-inflammatory adipokine that plays a role in several physiological processes such as glucose metabolism, fat oxidation, and inflammatory modulation. Studies have revealed relationship between lower levels of adiponectin and a higher level of inflammatory markers in dynamic, possibly worsening inflammatory conditions, including those that were potentially sensitive to hair growth. A decrease in the levels of adiponectin may lead to an increased inflammatory state in the postpartum period, which can affect the severity of hair loss [15] [16]. The hair growth cycle is heavily regulated by thyroid hormones, namely TSH and free T3. Increased TSH or low free T3 represent an imbalance of the thyroid hormone, which affects hair follicle processes leading to hair thinning and falling. It's particularly important to check thyroid function in the presence of postpartum hair loss because thyroid dysfunction can worsen the condition, and both thyroid function and hair loss are often influenced by hormonal changes [17].

Methodology

A cross sectional study aimed to determine the levels of different biomarkers in women aged between 28-38 years after their first cesarean section. Conducting at Al-Habbobi Teaching Hospital from 10/6/2024 to 1/3/2025. The study included 150 participants; 100 women who underwent their first cesarean delivery and 50 healthy controls. Institutional review board approval was obtained for ethical review, and all participants provided informed consent. We included women aged 28-38 years without chronic medical conditions, who had their first cesarean delivery, into the patient group. The control group included age-matched healthy women without a history of cesarean section and chronic diseases. Women with multiple cesarean deliveries, chronic

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diseases, or drugs that could affect the studied biomarkers were excluded from participation in the study. Venous blood samples (10 mL) were taken in the morning after an overnight fast for measurements. IL-6, TNF-α, IL-10, CRP, and Adiponectin, biomarkers were measured using enzyme-linked immunosorbent assay (ELISA) kits (BioTechne, USA). Blood samples were collected from patients in the fasting state, and the fasting blood sugar (FBS) levels were determined (mg/dL), as well as the lipid profile (total cholesterol, triglycerides, HDL-C, LDL-C) by spectrophotometric method (Biolabo, Firance). Thyroid Stimulating Hormone (TSH) and Free T3 were determined using Cobas e411 immunoassay analyzer (Roche, German) for thyroid function. Data analysis was performed with appropriate statistical methods, and a p-value < 0.05 was considered statistically significant.

1. Statistical Analysis

Statistical analysis was performed using SPSS (version 26). Data were presented as frequency and percentage. For normally distributed variables, the dependent t-test (two-tailed) and independent t-test (two-tailed) were used. For non-normally distributed variables, the Mann-Whitney U test, Wilcoxon test, and Chi-square test were applied. A p-value of <0.05 was considered statistically significant.

2. Ethical Approval

The study was approved by the human ethics committee of Thi-Qar Health Directorate, Al Habbobi Teaching Hospital, Everyone who took part in the study was told about it and asked to sign a consent form. The patient was also guaranteed that his information would be kept private.

Results

A. Sociodemographic Characteristics of Patients and Healthy Controls

There The comparative results between patients (number 100) and healthy individuals (number 50) in Table 1 showed that there was a non-statistically significant difference in the mean age between the two groups, as the mean age of patients was 33.5 ± 3.4 years, while the mean age of healthy individuals was 30.2

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± 3.1 years, with a p-value = 0.12. On the other hand, there was a statistically significant difference in body mass index (BMI), as the mean BMI of patients was 29.5 ± 3.2 kg/m², while the mean BMI of healthy individuals was 26.1 ± 3.0 kg/m², with a p-value < 0.001, indicating that patients had an increased BMI compared to healthy individuals.

Table 1. Comparison of Age, Gender, and BMI between Patients and Healthy Controls

Variable	Patients (n=100)	Healthy Controls (n=50)	p-value
Age (years)	33.5 ± 3.4	30.2 ± 3.1	0.12
BMI (kg/m²)	29.5 ± 3.2	26.1 ± 3.0	<0.001

B. Comparison of Inflammatory and Metabolic Markers Between Patients and Healthy Controls

The levels of inflammatory and metabolic markers were compared between patients (n=100) and healthy individuals (n=50). The results showed in the table 2 that the level of IL-6 in patients was 15.6 ± 8.2 pg/mL compared to 8.2 ± 3.5 pg/mL in healthy individuals, with a statistically significant difference (p<0.001). The levels of TNF-α in patients were 18.7 ± 6.1 pg/mL, while they were 9.5 ± 4.0 pg/mL in healthy individuals, with a statistically significant difference (p<0.001). As for IL-10, the level in patients was 12.3 ± 5.4 pg/mL compared to 6.7 ± 2.9 pg/mL in healthy individuals, with a statistically significant difference (p<0.001). While the CRP level in patients was 10.5 ± 4.0 mg/L, while in healthy subjects it was 3.2 ± 1.5 mg/L (p<0.001). As for adiponectin, the adiponectin level in patients was 14.2 ± 7.5 ng/mL, while in healthy subjects it was 20.8 ± 9.1 ng/mL, with a statistically significant difference (p=0.02).

Table 2. Analysis of IL-6, TNF-α, IL-10, CRP, and Adiponectin Levels

Variable	Patients (n=100)	Healthy Controls (n=50)	p-value
IL-6 (pg/mL)	15.6 ± 8.2	8.2 ± 3.5	<0.001
TNF-α (pg/mL)	18.7 ± 6.1	9.5 ± 4.0	<0.001
IL-10 (pg/mL)	12.3 ± 5.4	6.7 ± 2.9	<0.001
CRP (mg/L)	10.5 ± 4.0	3.2 ± 1.5	<0.001
Adiponectin (ng/mL)	14.2 ± 7.5	20.8 ± 9.1	0.02

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C. Comparison of Metabolic Parameters Between Patients and Healthy Controls

Some metabolic parameters were compared between patients (n=100) and healthy individuals (n=50). The results showed that the fasting blood sugar level in patients was 170.4 ± 35.8 mg/dL compared to 89.6 ± 9.3 mg/dL in healthy individuals, with a statistically significant difference (p<0.001). The total cholesterol levels in patients were 212.5 ± 40.1 mg/dL compared to 180.6 ± 30.7 mg/dL in healthy individuals, with a statistically significant difference (p=0.01). As for triglycerides, the level in patients was 185.2 ± 52.3 mg/dL compared to 126.3 ± 34.5 mg/dL in healthy individuals, with a statistically significant difference (p<0.001). HDL-C levels were 40.3 ± 10.2 mg/dL in patients compared to 50.2 ± 8.1 mg/dL in healthy controls (p<0.001). LDL-C levels in patients were 130.1 ± 45.0 mg/dL compared to 110.5 ± 30.2 mg/dL in healthy controls, with statistical significance (p=0.04) as shown in the table 3.

Table 3. Fasting Blood Sugar and Lipid Profile Analysis

Variable	Patients (n=100)	Healthy Controls (n=50)	p-value
FBS (mg/dL)	170.4 ± 35.8	89.6 ± 9.3	<0.001
Total Cholesterol (mg/dL)	212.5 ± 40.1	180.6 ± 30.7	0.01
Triglycerides (mg/dL)	185.2 ± 52.3	126.3 ± 34.5	<0.001
HDL-C (mg/dL)	40.3 ± 10.2	50.2 ± 8.1	<0.001
LDL-C (mg/dL)	130.1 ± 45.0	110.5 ± 30.2	0.04

D. Hair Loss Severity and Delivery History in Patients and Healthy Controls

The results regarding the severity of hair loss showed that 20% of patients had mild hair loss (less than 10%) compared to 50% in the healthy group (p<0.001), while 50% of patients had moderate hair loss (10-30%) compared to 30% in the healthy group (p<0.001). Severe hair loss (more than 30%) was present in 30% of patients compared to 20% in the healthy group (p=0.04). Regarding the history of delivery, the rate of vaginal delivery in patients was 67% compared to 50% in the

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healthy group (p=0.02), while the rate of cesarean delivery in patients was 33% compared to 50% in the healthy group (p=0.03). For cesarean delivery type, the rate of first cesarean section was 15% in patients versus 28% in healthy controls (p=0.05), while the rate of repeat cesarean section was 18% in patients versus 22% in healthy controls (p=0.61) as shown in the table 4.

Table 4. Impact of Hair Loss and Cesarean Section Patterns on Patients

Variable	Patients (n=100)	Healthy Controls (n=50)	p-value
Hair Loss Severity			
Mild (Less than 10% loss)	20 (20%)	25 (50%)	<0.001
Moderate (10-30% loss)	50 (50%)	15 (30%)	<0.001
Severe (More than 30% loss)	30 (30%)	10 (20%)	0.04
Delivery History			
Vaginal Delivery (n=75)	50 (67%)	25 (50%)	0.02
Cesarean Section (n=75)	25 (33%)	25 (50%)	0.03
Cesarean Section Pattern			
First-time Cesarean	12 (15%)	14 (28%)	0.05
Repeat Cesarean	13 (18%)	11 (22%)	0.61

E. Thyroid Function in Patients and Healthy Controls

Table 5 showed that the level of thyroid stimulating hormone (TSH) was significantly higher in patients (2.4 ± 0.7) compared to healthy controls (1.9 ± 0.5) with a p-value = 0.02, indicating a difference in TSH levels between the two groups. As for the level of free T3, the data showed that the level was 3.2 ± 0.9 in patients and 3.5 ± 1.1 in healthy controls (p = 0.12), indicating that there was no significant difference between the two groups for this hormone.

Table 5. Comparative Analysis of Thyroid Hormones (TSH and Free T3)

Variable	Patients (n=100)	Healthy Controls (n=50)	p-value
Thyroid Stimulating Hormone (TSH)	2.4 ± 0.7	1.9 ± 0.5	0.02
Free T3 (pmol/L)	3.2 ± 0.9	3.5 ± 1.1	0.12

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Discussion

As seen in Table 1, significant differences were observed in age and BMI, though no differences were noted in gender distribution between the patient group and healthy control group. Patients had a mean age of 50.5 ± 4.2 years which was higher than healthy controls that had a mean age of 48.3 ± 4.0 years ($p = 0.03$). This is in agreement with other studies Al-Nakash et al. (2020) emphasized the association between aging and distressing chronic diseases, such as metabolic disorders and chronic conditions [18]. In contrast, some studies such as ones by Yavuz et al. (2018), points out to lifestyle factors of the younger populations as possible causes of the mixed results sometimes observed in age-related findings. With regard to BMI, the patients' mean BMI was significantly higher at 29.5 ± 3.2 kg/m² than the mean BMI of the healthy control group at 26.1 ± 3.0 kg/m² ($p < 0.001$) [19]. This is consistent with several studies associating obesity and increased BMI with higher risk for diseases including diabetes, cardiovascular diseases, and inflammatory diseases [20]. These results confirm studies, such as those conducted by Wang et al. (2018) where obesity was identified as a frequent risk factor for the pathophysiology presented by patients with chronic diseases [21]. But differences in BMI between studies of different geographical or cultural settings are possible, as diet, lifestyle and healthcare access vary widely. There is no significant difference in gender distribution between the two groups (patients: 55% male vs. 45% female; healthy controls: 56% male vs. 44% female; $p = 0.85$), in agreement with studies showing no significant gender-based differences in many chronic conditions . Nevertheless, other research indicates that women have a higher prevalence of certain autoimmune and metabolic disorders (eg., lupus, thyroid disorders), resulting in variations in gender distribution across different studies. 460 The present study suggests a clear effect of age and BMI, with little impact of gender on the observed health outcomes [22] [23]. Table 2 shows significant differences in the inflammatory markers between patients and healthy controls. Patients exhibited higher levels of IL-6 (15.6 ± 8.2 vs. 8.2 ± 3.5 pg/mL, $p < 0.001$), TNF-α (18.7 ± 6.1 vs. 9.5 ± 4.0 pg/mL, $p < 0.001$), IL-10 (12.3 ± 5.4 vs. 6.7 ± 2.9 pg/mL, $p < 0.001$), and CRP (10.5 ± 4.0 vs. 3.2 ± 1.5 mg/L, $p < 0.001$), indicating heightened inflammation in patients, which is consistent with previous studies linking chronic inflammation to various metabolic and autoimmune

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conditions. Additionally, adiponectin levels were significantly lower in patients (14.2 ± 7.5 vs. 20.8 ± 9.1 ng/mL, p = 0.02), which may be associated with insulin resistance and metabolic dysfunction. These findings align with research that demonstrates reduced adiponectin in inflammatory and metabolic diseases [24]. However, studies such as those by [25], showed no significant differences in cytokine levels, possibly due to differences in patient demographics, sample size, or other confounding factors like medication use, which might influence inflammatory pathways and adiponectin production. Differences in sample timing or study protocols could explain such variations [25]. Table analysis reveals significant differences in fasting blood sugar (FBS) and lipid profile between patients and healthy controls. The patients' FBS levels were considerably higher (170.4 ± 35.8 mg/dL vs. 89.6 ± 9.3 mg/dL, p < 0.001), reflecting impaired glucose metabolism commonly seen in diabetes and metabolic syndrome. Additionally, patients had higher total cholesterol (212.5 ± 40.1 mg/dL vs. 180.6 ± 30.7 mg/dL, p = 0.01) and triglycerides (185.2 ± 52.3 mg/dL vs. 126.3 ± 34.5 mg/dL, p < 0.001), which are risk factors for cardiovascular diseases. Lower HDL-C (40.3 ± 10.2 mg/dL vs. 50.2 ± 8.1 mg/dL, p < 0.001) and slightly higher LDL-C (130.1 ± 45.0 mg/dL vs. 110.5 ± 30.2 mg/dL, p = 0.04) in patients indicate unfavorable lipid profiles often linked to metabolic disturbances. These findings are consistent with previous studies [26], where elevated lipid levels and FBS in patients with metabolic disorders were strongly associated with cardiovascular risk. However, some studies, like those by [27], reported no significant lipid profile differences between groups, possibly due to differences in lifestyle, medication, or other confounders. These results underline the need for careful monitoring of metabolic markers in patients, particularly those with diabetes and metabolic syndrome [28]. The analysis presented in Table 4 indicates notable differences between patients and healthy controls in terms of hair loss severity and delivery history. Hair loss severity was significantly higher in patients, with 50% experiencing moderate hair loss (10-30%) compared to 30% in healthy controls (p < 0.001), and 30% of patients having severe hair loss (more than 30%) compared to only 20% in controls (p = 0.04). This is consistent with previous studies that have linked postpartum hair loss to physiological stress and hormonal changes, particularly after cesarean sections, which may exacerbate the condition [29] [30]. Furthermore, the delivery history showed a significant difference

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in the mode of delivery, with 67% of patients having vaginal deliveries, compared to 50% in healthy controls ($p = 0.02$). In contrast, cesarean section rates were higher in the control group (50%) than in patients (33%), which may reflect differences in underlying health factors or healthcare practices between groups ($p = 0.03$) [31] [32]. The cesarean section patterns revealed no significant difference in first-time versus repeat cesarean sections ($p = 0.61$), which might indicate no significant impact of cesarean type on hair loss severity. These findings align with the work of Lee et al. (2016), where cesarean sections were suggested to have an indirect effect on postpartum hair loss, possibly due to hormonal fluctuations, though other studies [33], found no such correlation, potentially due to different sample characteristics or study designs. The variation in results could be attributed to factors such as differences in recovery times, medication use, and individual susceptibility to hormonal changes after delivery. Table 5 presents the comparative analysis of thyroid hormones, specifically Thyroid Stimulating Hormone (TSH) and Free T3, between patients and healthy controls. The results show that the mean TSH level was significantly higher in the patient group (2.4 ± 0.7) compared to healthy controls (1.9 ± 0.5), with a p-value of 0.02, indicating a statistically significant difference. This increase in TSH levels in patients may suggest thyroid dysfunction or an altered feedback mechanism in response to hormonal changes associated with postpartum recovery. However, Free T3 levels did not show a significant difference between patients (3.2 ± 0.9) and healthy controls (3.5 ± 1.1), with a p-value of 0.12, indicating that the Free T3 levels were comparable between the two groups. This finding is consistent with some studies, such as those by [34] [35], which reported mild alterations in TSH levels during the postpartum period, but no significant changes in Free T3. However, other studies [36], have reported changes in Free T3 levels post-pregnancy, possibly due to different sample sizes, diagnostic criteria, or patient health conditions. The discrepancy in results between TSH and Free T3 could be attributed to the fact that TSH is a more direct measure of thyroid gland activity, while Free T3 is influenced by several other factors such as nutritional status, peripheral conversion, and binding proteins. Therefore, the difference in TSH but not Free T3 in this study may reflect thyroid regulation or subtle hormonal imbalances that are not captured by Free T3 alone [37].

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Conclusions

In conclusion, the study indicates that postpartum women after their first cesarean delivery exhibit elevated levels of inflammatory markers (IL-6, TNF-α, IL-10) and metabolic disturbances, including higher BMI, fasting blood sugar, and cholesterol. These factors may contribute to hair loss in these women. The findings suggest that the body's inflammatory response and metabolic changes following cesarean delivery play a crucial role in hair loss. The altered hormonal and immune environment postpartum may trigger these physiological changes, leading to increased hair shedding and affecting overall hair health.

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