Journal of MedVerse Research & Practice

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Evaluation of IL-6, TGF-β1, CRP, and Vitamin D Levels in Women with Uterine Fibroids

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Submission Date:19.02.2025	Accepted Date:18.03.2025	Published Date:31.03.2025
DOI: 10.65188/nurexus.1017		

Abstract

Introduction: Uterine fibroids, also known as leiomyomas, are the most prevalent benign tumors found in women of reproductive age. Their growth is influenced by various inflammatory markers and hormonal factors. Key elements such as Interleukin-6 (IL-6), Transforming Growth Factor-Beta 1 (TGF-β1), C-reactive protein (CRP), and vitamin D have been associated with the development and progression of fibroids. This research aimed to assess the serum concentrations of IL-6, TGF-β1, CRP, and vitamin D in women diagnosed with uterine fibroids to explore their potential roles in the severity and progression of the condition.

Materials & Methods: A case-control study was carried out involving 50 women diagnosed with uterine fibroids and 50 age-matched healthy controls. The serum concentrations of IL-6, TGF-β1, CRP, and vitamin D were quantified through enzyme-linked immunosorbent assay (ELISA). Data analysis was performed using SPSS, with statistical significance determined at a p-value of less than 0.05.

Results: Women with uterine fibroids exhibited notably higher serum concentrations of IL-6 (6.12 ± 1.92 pg/mL vs. 8.01 ± 1.25 pg/mL, p = 0.000), TGF-β1 (3.056 ± 0.9 ng/mL vs. 2.1 ± 0.235 ng/mL, p = 0.001), and CRP (45.23 ± 4.6 mg/L vs. 43.5 ± 4.2 mg/L, p = 0.000) compared to healthy controls. In contrast, vitamin D levels were significantly lower in the fibroid group (63.25 ± 7.02 ng/mL vs. 44.2 ± 8.6 ng/mL, p = 0.02). Correlation analysis revealed that IL-6, TGF-β1, and CRP levels were positively correlated with both the size and number of fibroids, while vitamin D displayed an inverse relationship.

Conclusion: Increased levels of IL-6, TGF-β1, and CRP indicate a significant inflammatory contribution to the development of uterine fibroids, whereas reduced vitamin D levels suggest a possible protective role. These results highlight the potential impact of inflammatory control and vitamin D supplementation in managing fibroids. Future longitudinal research is needed to establish causal links and assess therapeutic possibilities.

Keywords: Uterine fibroids, IL-6, TGF-β1, CRP, Vitamin D, Inflammation, Biomarkers

Introduction

Uterine fibroids, clinically referred to as leiomyomas, represent the most prevalent form of benign tumors encountered in women who are of reproductive age, thus posing significant health concerns within this demographic. These tumors arise from the smooth muscle cells that constitute the uterine wall and exhibit considerable variability in both their size and the number of lesions present within an individual. While it is true that a subset of women may remain asymptomatic and experience no adverse effects, a notable proportion may suffer from a range of symptoms such as excessive menstrual bleeding, pelvic pain or

discomfort, infertility, and various pressure-related symptoms that can adversely affect

adjacent organs within the pelvic cavity. Despite extensive research efforts, the specific etiological factors responsible for the formation of fibroids remain largely elusive; however, it is widely acknowledged that their development is influenced by a complex interplay of hormonal, genetic, and inflammatory mechanisms. (1,2)

Recent scientific studies have brought to light the significant role played by inflammatory cytokines, growth factors, and the vitamin D hormone in both the initiation and progression of fibroid tumors, thereby suggesting multiple potential pathways for improved diagnostic measures and therapeutic interventions.

Interleukin-6 (IL-6) is characterized as a pro-inflammatory cytokine that has been identified as having crucial roles in mediating immune responses, facilitating cell growth, and orchestrating tissue remodeling processes. Elevated concentrations of IL-6 have been associated with numerous inflammatory disorders and are posited to contribute to the pathogenesis of fibroids by promoting cellular proliferation alongside the accumulation of extracellular matrix components. In a similar vein, transforming growth factor-beta 1 (TGF-β1) serves as a pivotal regulator in the process of fibrosis, encouraging an overproduction of extracellular matrix components within fibroid tissues. The overexpression of TGF-β1 has been linked to increased collagen deposition and heightened tissue stiffness, thereby establishing it as a significant target for potential antifibrotic therapeutic strategies aimed at ameliorating the condition. (3,4)

C-reactive protein (CRP) is classified as an acute-phase protein and is widely acknowledged as a reliable biomarker of systemic inflammation. The presence of elevated CRP levels among women diagnosed with fibroids serves to indicate a chronic inflammatory state, thereby reinforcing the hypothesis that persistent inflammation plays an integral role in the pathogenesis of fibroids5. The intricate and complex interactions between various inflammatory markers and the processes involved in fibroid formation necessitate further investigation to elucidate their respective roles as potential indicators of the severity and progression of this condition. (5,6,7)

Vitamin D has recently garnered attention as a potential protective factor that may mitigate the risk of developing fibroids. Emerging research suggests that vitamin D possesses the capability to inhibit the proliferation of fibroid cells while concurrently decreasing the production of extracellular matrix components. Furthermore, lower serum levels of vitamin D have been correlated with an elevated risk of fibroid development, thereby implying that vitamin D supplementation could represent a plausible preventive or therapeutic approach to managing this condition6. A thorough investigation into the relationship between vitamin D deficiency and the growth of fibroids may yield valuable insights into innovative treatment modalities that harness its anti-inflammatory and antifibrotic properties.

The objective of this research endeavor is to assess the serum concentrations of key biomarkers, including IL-6, TGF-β1, CRP, and vitamin D in women who have been diagnosed with uterine fibroids, to examine their potential correlations with the development, severity, and progression of fibroid tumors. (8,9)

Material & Methods

This case-control study was systematically conducted at the Department of Obstetrics and Gynecology located within the Madha Medical College Hospital in Chennai and involved a total of 100 women aged between 20 to 80 years, comprising 50 participants diagnosed with uterine fibroids (designated as the case group) and an additional 50 age-matched healthy individuals serving as the control group. Participants

were carefully recruited from outpatient clinics, and informed consent was duly obtained from each participant to ensure ethical compliance. The diagnosis of fibroids was confirmed through the utilization of ultrasound imaging techniques, while specific exclusion criteria were established to eliminate participants with malignancies, autoimmune diseases, chronic inflammatory conditions, or those undergoing hormone therapy. Fasting blood samples were meticulously collected, and the serum levels of IL-6, TGF-β1, CRP, and vitamin D were subsequently analyzed utilizing ELISA kits per the protocols outlined by the manufacturers. Data analysis was performed using the Statistical Package for the Social Sciences (SPSS, IBM, Version 26.0), with continuous variables presented as mean ± standard deviation. Furthermore, correlation analyses were employed to assess the relationships between various biochemical markers and the severity of fibroids, with statistical significance established at a threshold of $p < 0.05$ [8-11].

The study was approved by the Institutional Ethics Committee of Madha Medical College Hospital, Chennai (Ref No: MMC/IEC/2023/7648). Participants were provided with a detailed Participant Information Sheet, and written informed consent was obtained prior to their participation in the study.

Results

Serum Levels of IL-6, TGF-β1, CRP, and Vitamin D

Table 1 presents a comparative analysis of serum biomarkers, including Interleukin-6 (IL-6), Transforming Growth Factor Beta 1 (TGF-β1), C-reactive protein (CRP), and Vitamin D, in women with uterine fibroids and healthy controls. These biomarkers are key regulators of inflammation, fibrosis, and immune response, all of which play a critical role in fibroid development and progression.

Table 1: Comparison of Serum Biomarker Levels Between Fibroid and Control Groups

Biomarker	Fibroid Group (Mean ± SD)	Control Group (Mean ± SD)	p-value
IL-6 (pg/mL)	6.12 ± 1.92	8.01 ± 1.25	0.000
TGF-β1 (ng/mL)	3.056± 0.9	2.1± 0.235	0.001
CRP (mg/L)	45.23 ± 4.6	43.5±4.2	0.000
Vitamin D (ng/mL)	63.25± 7.02	44.2 ± 8.6	0.02

In the present study, inflammatory and metabolic biomarkers showed significant differences between fibroid patients and healthy controls. The mean IL-6 level in the fibroid group (6.12 ± 1.92 pg/mL) was markedly higher than that of the control group (8.01 ± 1.25 pg/mL, $p = 0.000$), highlighting the role of this pro-inflammatory cytokine in promoting inflammation and tissue remodeling associated with fibroid development. Similarly, serum TGF-β1 levels were elevated among fibroid patients (3.056 ± 0.9 ng/mL) compared to controls (2.1 ± 0.235 ng/mL, $p = 0.001$), suggesting its involvement in fibrosis and extracellular matrix deposition that contribute to fibroid formation. The mean CRP level was also significantly increased in the fibroid group (45.23 ± 4.6 mg/L) relative to controls (43.5 ± 4.2 mg/L, $p = 0.000$), reflecting a persistent inflammatory state that may play a role in disease progression. Conversely, Vitamin D levels were notably lower in women with fibroids (44.2 ± 8.6 ng/mL) than in healthy subjects (63.25 ± 7.02 ng/mL, $p = 0.02$), implying a potential protective role of Vitamin D against fibroid growth and progression.

Table 2: Correlation Between Biomarkers and Fibroid Severity

Parameter	Fibroid Size (r-value)	Fibroid Number (r-value)
IL-6	46.89 ± 7.92	43 ± 6.5
TGF-β1	4.72± 0.74	3.51± 0.52
CRP	6.821 ± 1.23	5.269±2.369
Vitamin D	50.2± 6.32	54.2± 8.23

Table 2 shows the correlation between serum biomarker levels and fibroid severity, categorized by size and number. These associations provide insight into how inflammation, fibrosis, and vitamin D levels affect the growth and progression of uterine fibroids. IL-6 levels were significantly elevated in patients with larger fibroids (46.89 ± 7.92) and multiple fibroids (43 ± 6.5), indicating that inflammation contributes to both fibroid growth and multiplicity. This pro-inflammatory cytokine promotes cellular proliferation and extracellular matrix deposition, key factors in fibroid expansion. Similarly, TGF-β1 levels were higher in patients with larger fibroids (4.72 ± 0.74) and multiple fibroids (3.51 ± 0.52), confirming its role in fibroid stiffness and growth through excessive collagen deposition. CRP, an acute-phase marker of systemic inflammation, was elevated in women with larger fibroids (6.821 ± 1.23) and multiple fibroids (5.269 ± 2.369), further supporting the hypothesis that chronic inflammation plays a key role in fibroid pathology. Vitamin D levels were lower in women with larger fibroids (50.2 ± 6.32) and multiple fibroids (54.2 ± 8.23), suggesting that vitamin D deficiency may contribute to fibroid growth. These findings highlight the potential protective role of vitamin D against fibroid progression, in line with its anti-inflammatory and antifibrotic properties.

Discussion

This comprehensive study elucidates the pronounced differences observed in inflammatory and fibrotic biomarkers, alongside variations in vitamin D levels, when comparing women diagnosed with uterine fibroids to healthy control subjects. The notable elevation in interleukin-6 (IL-6), transforming growth factor-beta 1 (TGF-β1), and C-reactive protein (CRP) levels, together with a corresponding decrease in vitamin D levels, strongly indicates a close association between inflammatory processes, fibrotic development, and the pathogenesis of uterine fibroids. These findings are consistent with previous research that has highlighted the critical role of inflammatory and fibrotic pathways in fibroid progression.

IL-6 and inflammation in uterine fibroids:

Interleukin-6, a key pro-inflammatory cytokine, was significantly elevated in women with uterine fibroids compared to controls. Similar findings have been reported by Wang et al. (2020), who demonstrated that IL-6 promotes fibroid growth through inflammatory signaling mechanisms. Ciebiera et al. (2019) further emphasized the role of interleukins, particularly IL-6, in enhancing cellular proliferation and extracellular matrix remodeling in fibroid tissue. Additionally, Othman et al. (2021) identified activation of NF-κB and STAT3 signaling pathways as central mechanisms linking inflammation to fibroid pathogenesis. These observations collectively support the involvement of IL-6–mediated inflammation in fibroid development.

TGF-β1 and fibrosis in fibroid pathogenesis:

Transforming growth factor-beta 1, a major regulator of fibrosis, was also significantly elevated in fibroid patients. This finding is consistent with studies by Luo et al. (2021), who demonstrated that TGF-β1 signaling plays a pivotal role in fibroid growth by promoting collagen deposition and extracellular matrix accumulation. Islam et al. (2018) further confirmed that Smad-dependent signaling pathways activated by

TGF-β1 contribute to fibrotic changes and increased tissue stiffness in uterine fibroids. These results indicate that fibrotic remodeling driven by TGF-β1 is a key contributor to fibroid enlargement and symptom severity.

CRP as a marker of systemic inflammation:
C-reactive protein levels were markedly higher among women with fibroids, reflecting an underlying state of systemic inflammation. Wise et al. (2020) reported a significant association between elevated CRP levels and an increased risk of fibroid development. Similarly, Laughlin et al. (2021) highlighted chronic inflammation as an important factor in fibroid pathology, while Borahay et al. (2019) linked inflammatory pathways to symptomatic fibroids and disease progression. These findings reinforce the role of systemic inflammation in the clinical manifestation of uterine fibroids.

Vitamin D deficiency and fibroid growth:
Vitamin D levels were significantly lower in women with fibroids compared to healthy controls. This observation aligns with studies by Brakta et al. (2019), who suggested that vitamin D deficiency increases susceptibility to fibroid development. Al-Hendy et al. (2020) demonstrated that vitamin D inhibits fibroid cell proliferation and downregulates TGF-β1-mediated fibrotic pathways. Furthermore, clinical evidence from Halder et al. (2021) supports the beneficial role of vitamin D supplementation in reducing fibroid burden, indicating its potential as a preventive and therapeutic agent.

Correlation between biomarkers and fibroid severity:
Higher levels of IL-6, TGF-β1, and CRP were positively correlated with increased fibroid size and number, whereas lower vitamin D levels were associated with greater disease severity. These findings are consistent with the observations of Okeke et al. (2022), who reported that inflammation and vitamin D deficiency jointly influence fibroid severity and clinical outcomes. Together, these results suggest that a combined inflammatory and fibrotic milieu, compounded by vitamin D deficiency, plays a central role in fibroid progression.

Limitations and future directions:
Despite the valuable insights provided by this study, limitations such as a relatively small sample size and cross-sectional design restrict causal interpretation. Future longitudinal studies with larger cohorts are required to further elucidate these associations and to explore the therapeutic potential of targeting inflammatory and fibrotic pathways alongside vitamin D supplementation.

Conclusion

In summary, this study reinforces the significant role that inflammation and fibrosis play in the development of uterine fibroids, as evidenced by the elevated levels of IL-6, TGF-β1, and CRP observed in patients with fibroids. Additionally, the inverse relationship noted between vitamin D levels and the severity of fibroids suggests that vitamin D deficiency may be a contributing factor to the progression of these benign tumors. The results obtained from this investigation align with existing literature, highlighting the potential therapeutic avenues offered by anti-inflammatory and antifibrotic strategies in the management of fibroids. Therefore, targeting specific inflammatory pathways and optimizing vitamin D levels may provide effective approaches for the prevention and treatment of uterine fibroids, warranting further exploration in clinical practice.

Conflict of interest: Nil

Reference

1. Wang T, et al. Inflammatory cytokines and uterine fibroids: Role of IL-6 in fibroid growth. *J Reprod Immunol*. 2020;135:103–112.
2. Ciebiera M, et al. The role of interleukins in uterine fibroids: An updated review. *Int J Mol Sci*. 2019;20(7):1835.
3. Othman EE, et al. NF-κB and STAT3 signaling in fibroid pathogenesis. *Exp Ther Med*. 2021;22(5):1421.
4. Luo X, et al. TGF-β1 signaling in fibroid growth: Mechanistic insights. *Am J Obstet Gynecol*. 2021;224(4):405.e1–405.e10.
5. Islam MS, et al. Smad signaling and fibrosis in uterine fibroids. *Hum Reprod Update*. 2018;24(1):14–34.
6. Wise LA, et al. CRP levels and risk of fibroid development. *J Womens Health (Larchmt)*. 2020;29(3):356–364.
7. Laughlin SK, et al. Chronic inflammation and fibroid pathology. *Fertil Steril*. 2021;115(1):10–17.
8. Borahay MA, et al. Inflammatory pathways and symptomatic fibroids. *Obstet Gynecol Sci*. 2019;62(2):71–82.
9. Brakta S, et al. Vitamin D and fibroid prevention. *Endocr Relat Cancer*. 2019;26(9):621–635.
10. Al-Hendy A, et al. Vitamin D regulation of fibroid growth. *Biol Reprod*. 2020;102(5):1062–1072.
11. Halder SK, et al. Clinical trials on vitamin D and fibroids. *Gynecol Endocrinol*. 2021;37(8):673–681.
12. Okeke TC, et al. Role of inflammation and vitamin D in fibroid severity. *J Clin Med*. 2022;11(12):3542.