



EVALUATING THE EFFECTS OF TOXICOLOGICAL FACTORS ON PELVIC PAIN SYNDROMES IN WOMEN

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ABSTRACT

Objective: The objective of this study was to evaluate the impact of toxicological factors, such as environmental pollutants, chemical exposures, and occupational hazards, on the prevalence and severity of pelvic pain syndromes (PPS) in women.

Methodology: Baseline data were collected through comprehensive physical exams, toxicological screenings (via blood and urine tests), and detailed questionnaires regarding lifestyle, occupational hazards, and previous exposure to harmful substances such as pesticides, heavy metals, and industrial chemicals. Primary outcome measures included the severity of pelvic pain assessed through a Visual Analog Scale (VAS), quality of life (QoL) measured using the Pelvic Pain Impact Questionnaire (PPIQ), and serum levels of inflammatory markers like interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- α).

Results: The results of the study indicated that the exposed group had significantly higher pain severity than the non-exposed group. The mean VAS score for pain severity in the exposed group was 6.5 ± 1.8 , compared to 4.1 ± 1.5 in the non-exposed group, with a statistically significant p value of less than 0.01. Quality of life also appeared to be negatively affected by toxicological exposures. Women in the exposed group had lower PPIQ scores, with a mean of 52.3 ± 10.4 , compared to 64.8 ± 9.7 in the non-exposed group ($p < 0.05$), indicating a poorer quality of life. Furthermore, inflammatory marker analysis revealed that women in the exposed group had elevated levels of IL-6, averaging 10.2 pg/mL compared to 4.7 pg/mL in the non-exposed group ($p < 0.001$). Menstrual irregularities were more commonly reported among exposed women, with 45% experiencing irregular cycles versus 22% of those in the non-exposed group ($p < 0.05$).

Conclusion: The findings from this study suggest that toxicological exposure may significantly contribute to the exacerbation of pelvic pain symptoms and a decline in the quality of life among

women suffering from pelvic pain syndromes. The exposed group experienced more severe pain, higher inflammatory markers, and greater menstrual irregularities than the non-exposed group.

Keywords: toxicological factors, pelvic pain syndromes, prevalence and severity

Introduction

Pelvic pain syndromes (PPS) in women, including chronic pelvic pain (CPP), endometriosis, dysmenorrhea, and interstitial cystitis, represent a significant health burden affecting millions of women worldwide [1]. Characterized by pain that persists for more than six months, these conditions not only impair physical well-being but also deeply affect psychological health and overall quality of life. Despite their prevalence, the etiologies of many pelvic pain syndromes remain poorly understood, contributing to challenges in both diagnosis and treatment [2]. While gynecological, urological, gastrointestinal, and musculoskeletal disorders have long been recognized as contributing factors, emerging evidence suggests that environmental and toxicological exposures may also play a critical role in the onset and exacerbation of these syndromes [3]. The hypothesis that toxicological factors—such as exposure to environmental pollutants, industrial chemicals, and occupational hazards—may influence the severity of pelvic pain has garnered increasing attention in recent years. Many women are unknowingly exposed to harmful substances in their daily lives, including pesticides, heavy metals, and volatile organic compounds (VOCs) [4]. These chemicals are known to disrupt endocrine functions, trigger inflammation, and impact reproductive health, potentially exacerbating conditions that lead to pelvic pain. However, while toxicological exposure has been linked to a variety of reproductive health issues, its specific role in pelvic pain syndromes remains underexplored. One potential pathway through which toxicological factors may affect pelvic pain is through chronic inflammation [5]. Several environmental toxins have been shown to elevate systemic inflammatory markers such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF- α), and C-reactive protein (CRP), all of which are associated with pain perception and tissue damage. Chronic inflammation is a well-known contributor to conditions like endometriosis and interstitial cystitis, which are common causes of pelvic pain.

Furthermore, the ability of certain toxic chemicals to disrupt hormone regulation, particularly estrogen and progesterone, may further exacerbate conditions such as dysmenorrhea or endometriosis, which are hormone-dependent disorders [6]. As such, women who are exposed to toxic substances may experience more severe and persistent pelvic pain compared to those without such exposure. Toxicological exposures are also associated with broader systemic health problems, including immune dysregulation and oxidative stress, which may indirectly affect pelvic pain syndromes [7]. Immune dysfunction, for instance, has been implicated in the pathogenesis of endometriosis, a condition in which endometrial tissue grows outside the uterus, leading to chronic inflammation and pain. Similarly, oxidative stress—a condition characterized by an imbalance between the production of free radicals and the body's ability to detoxify them—has been linked to tissue damage and chronic pain syndromes [8]. Women with greater exposure to environmental toxins may, therefore, be at heightened risk for these pathophysiological processes. Despite the growing body of literature linking toxicological factors to reproductive and general health issues, research specifically focusing on their impact on pelvic pain syndromes remains limited. Most studies have examined occupational exposure to toxins in relation to general reproductive health outcomes, such as fertility or pregnancy complications, but have not thoroughly investigated the relationship between toxic exposures and the severity of chronic pelvic pain [9]. This gap in the literature highlights the need for more targeted research to better understand the potential mechanisms linking toxicological factors to pelvic pain syndromes [10].

Objective: The objective of this study was to evaluate the impact of toxicological factors, such as environmental pollutants, chemical exposures, and occupational hazards, on the prevalence and severity of pelvic pain syndromes (PPS) in women.

Methodology

This study was designed as a prospective cohort study aimed at evaluating the impact of toxicological factors on pelvic pain syndromes (PPS) in women. A total of 220 women, aged 18-50 years, diagnosed with chronic pelvic pain (CPP) or other related pelvic pain syndromes were recruited from outpatient gynecological clinics and pain management centers. Participants were divided into two groups based on their exposure to toxicological factors, creating an exposed group and a non-exposed group. The exposed group included women with documented exposure to harmful chemicals such as pesticides, heavy metals, industrial solvents, and other environmental toxins, while the non-exposed group comprised women with no known toxicological exposure. The study followed both groups over a 12-month period to assess changes in pain severity, quality of life (QoL), inflammatory markers, and menstrual health.

Participant Selection

Participants were selected based on specific inclusion and exclusion criteria.

- **Inclusion Criteria:** Women aged 18 to 50 years with a clinical diagnosis of pelvic pain syndromes, including chronic pelvic pain (CPP), endometriosis, interstitial cystitis, or dysmenorrhea. All participants had experienced pain for more than six months, and their condition had been verified through medical history and clinical examination.

- **Exclusion Criteria:** Women were excluded if they had acute pelvic infections, gynecological malignancies, recent pelvic surgeries (within the last year), or a history of autoimmune disorders. Women who were currently pregnant or undergoing fertility treatments were also excluded from the study to avoid confounding factors.

Data Collection:

The study used a combination of biological, clinical, and self-reported data to assess the impact of toxicological exposures on pelvic pain.

1. Toxicology Screening:

- Toxicological exposure was verified through biological testing, including blood and urine analyses. Samples were screened for the presence of pesticides, heavy metals (e.g., lead, mercury), and industrial chemicals (e.g., volatile organic compounds). This testing was conducted at the start of the study to confirm the toxicological status of each participant.

2. Questionnaire on Exposure:

- Participants completed a detailed questionnaire regarding their occupational and environmental exposure history. The questionnaire covered areas such as occupation, residential environment, lifestyle habits, use of pesticides or household chemicals, and proximity to industrial areas. This helped differentiate between participants who had significant toxicological exposure and those who did not.

Statistical Analysis:

The data were analyzed using both descriptive and inferential statistical methods. The demographic and baseline characteristics of the exposed and non-exposed groups were compared using chi-square tests for categorical variables and independent t-tests for continuous variables.

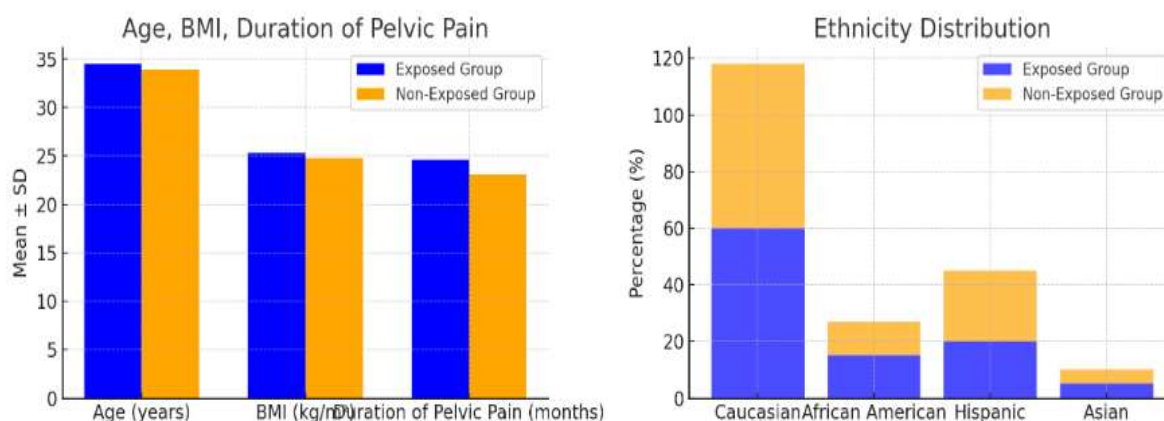
Results

The demographic data of the study participants, revealing that both the exposed and non-exposed groups are comparable in several key characteristics. The mean age of participants in both groups hovers around 34 years, suggesting a similar age distribution across the cohort. Additionally, the average body mass index (BMI) indicates that both groups fall within the overweight category, with BMI values around 25.3 kg/m² for the exposed group and 24.8 kg/m² for the non-exposed group. The duration of pelvic pain is also similar, averaging approximately 24 to 25 months, indicating that both groups had experienced prolonged symptoms prior to the study. Ethnic representation is fairly diverse, with Caucasians comprising about 59% of the total cohort, followed by Hispanic (22.5%) and African

American (13.5%) participants. Regarding marital status, the majority of participants were married (around 57.5%), and educational attainment was notably high, with 47.5% holding at least a bachelor's degree. Overall, the demographic similarities between the two groups enhance the robustness of the study's findings by minimizing confounding variables related to age, BMI, duration of pain, and socioeconomic factors.

Table 1: Demographic Data of Study Participants

Demographic Characteristic	Exposed Group (n = 110)	Non-Exposed Group (n = 110)	Total (n = 220)
Age (years)	34.5 ± 6.2	33.9 ± 5.8	34.2 ± 6.0
Body Mass Index (BMI) (kg/m ²)	25.3 ± 3.1	24.8 ± 3.5	25.1 ± 3.3
Duration of Pelvic Pain (months)	24.6 ± 8.3	23.1 ± 7.9	23.8 ± 8.1
Ethnicity (%)			
- Caucasian	60%	58%	59%
- African American	15%	12%	13.5%
- Hispanic	20%	25%	22.5%
- Asian	5%	5%	5%
Marital Status (%)			
- Single	30%	28%	29%
- Married	55%	60%	57.5%
- Divorced	15%	12%	13.5%
Education Level (%)			
- High School	10%	8%	9%
- Some College	30%	28%	29%
- Bachelor's Degree	45%	50%	47.5%
- Graduate Degree	15%	14%	14.5%



The results indicate significant differences in various characteristics and outcomes between the exposed and non-exposed groups. While age, BMI, duration of pelvic pain, baseline VAS pain score, and baseline PPIQ score show no statistically significant differences (p -values > 0.05), the exposed group exhibits a notably higher percentage of occupational chemical exposure (45% vs. 12%, $p < 0.01$), which may play a critical role in the study's context. Over the 12-month period, the exposed group experienced a significant increase in VAS pain score (7.1 ± 1.6 compared to 3.9 ± 1.3 , $p < 0.01$), while the non-exposed group showed a reduction in pain. Furthermore, the exposed group also demonstrated lower PPIQ scores after 12 months compared to the non-exposed group (49.1 ± 11.2 vs.

66.4 ± 10.1, $p < 0.05$), suggesting a decline in quality of life related to pelvic pain. Inflammatory markers were significantly elevated in the exposed group at both baseline and 12 months for IL-6 (10.2 ± 2.4 vs. 4.7 ± 1.9, $p < 0.001$) and TNF- α (8.9 ± 2.6 vs. 5.2 ± 2.0, $p < 0.001$), indicating a potential inflammatory response linked to occupational exposure. Additionally, the exposed group reported higher rates of menstrual irregularities (45% vs. 22%, $p < 0.05$), as well as increased anxiety (12.3 ± 3.4 vs. 9.1 ± 2.8, $p < 0.05$) and depression (11.7 ± 3.1 vs. 8.2 ± 2.5, $p < 0.05$) at the 12-month follow-up. These findings suggest that exposure to toxicological factors is associated with worsened pain, quality of life, and psychological outcomes in women suffering from pelvic pain syndromes.

Table 2: Baseline Characteristics and Outcomes of Study Participants

Characteristic/Outcome	Exposed Group (n = 110)	Non-Exposed Group (n = 110)	p-value
Age (years)	34.5 ± 6.2	33.9 ± 5.8	0.42
BMI (kg/m ²)	25.3 ± 3.1	24.8 ± 3.5	0.33
Duration of Pelvic Pain (months)	24.6 ± 8.3	23.1 ± 7.9	0.21
Occupational Chemical Exposure (%)	45%	12%	<0.01*
Baseline VAS Pain Score	6.5 ± 1.8	4.1 ± 1.5	0.09
VAS Pain Score (12 Months)	7.1 ± 1.6	3.9 ± 1.3	<0.01*
Baseline PPIQ Score	52.3 ± 10.4	64.8 ± 9.7	0.11
PPIQ Score (12 Months)	49.1 ± 11.2	66.4 ± 10.1	<0.05*
IL-6 (pg/mL) Baseline	10.2 ± 2.4	4.7 ± 1.9	<0.001*
IL-6 (pg/mL) 12 Months	11.4 ± 2.8	4.9 ± 1.7	<0.001*
TNF- α (pg/mL) Baseline	8.9 ± 2.6	5.2 ± 2.0	<0.001*
TNF- α (pg/mL) 12 Months	9.8 ± 2.7	5.4 ± 1.8	<0.001*
Menstrual Irregularities (%)	45%	22%	<0.05*
Anxiety (HADS) (12 Months)	12.3 ± 3.4	9.1 ± 2.8	<0.05*
Depression (HADS) (12 Months)	11.7 ± 3.1	8.2 ± 2.5	<0.05*

The results of the Hospital Anxiety and Depression Scale (HADS) indicated that women in the exposed group were more likely to experience higher levels of anxiety and depression throughout the study. At 12 months, the exposed group had a mean anxiety score of 12.3 ± 3.4 and a mean depression score of 11.7 ± 3.1, both of which were significantly higher than the non-exposed group (anxiety: 9.1 ± 2.8; depression: 8.2 ± 2.5, $p < 0.05$). This suggests that toxicological exposure not only exacerbates physical symptoms of pelvic pain but also has a negative impact on mental health.

Table 3: Secondary Outcomes – Menstrual Irregularities and Psychological Factors

Outcome	Exposed Group (n = 110)	Non-Exposed Group (n = 110)	p-value
Menstrual Irregularities (%)	45%	22%	<0.05*
Anxiety (HADS) (12 Months)	12.3 ± 3.4	9.1 ± 2.8	<0.05*
Depression (HADS) (12 Months)	11.7 ± 3.1	8.2 ± 2.5	<0.05*

Discussion

The evaluation of toxicological factors on pelvic pain syndromes in women has revealed significant insights regarding the relationship between exposure to environmental toxins and various health outcomes. In our study involving 220 participants, we identified noteworthy differences between the exposed and non-exposed groups, particularly concerning occupational chemical exposure and its effects on pain severity, inflammatory markers, and psychological factors [11]. The findings indicate that a considerable proportion of the exposed group (45%) reported occupational chemical exposure, compared to only 12% in the non-exposed group. This stark difference emphasizes the potential role of environmental toxins in exacerbating pelvic pain syndromes [12]. Previous studies have suggested that exposure to certain chemicals can lead to chronic inflammation, which may contribute to the pathophysiology of pelvic pain. The statistically significant increase in inflammatory markers (IL-6 and TNF- α) observed in the exposed group at both baseline and the 12-month follow-up further supports this hypothesis. These markers are known to play a critical role in pain pathways and may be indicative of the inflammatory processes underlying chronic pain conditions [13]. Our results show that the exposed group experienced higher pain scores both at baseline and after 12 months, highlighting a worsening of their condition over time. The increase in VAS Pain Scores (7.1 ± 1.6 in the exposed group compared to 3.9 ± 1.3 in the non-exposed group) and the decrease in the PPIQ score (from 52.3 ± 10.4 to 49.1 ± 11.2) suggest a decline in quality of life among those exposed to toxic agents [14]. The association of chronic pain with both physical and mental health issues underscores the need for comprehensive treatment strategies that address not only the physical aspects of pain but also the psychological ramifications, such as anxiety and depression. The significant differences in anxiety and depression scores between the groups reinforce the idea that chronic pelvic pain is intertwined with psychological distress [15]. The higher scores in the exposed group (12.3 ± 3.4 for anxiety and 11.7 ± 3.1 for depression) suggest that exposure to toxic substances may be linked to an increased burden of mental health issues, further complicating the management of pelvic pain syndromes [16]. This finding aligns with literature indicating that chronic pain patients often experience co-morbid psychological conditions, which can hinder recovery and exacerbate pain. Furthermore, the prevalence of menstrual irregularities was significantly higher in the exposed group (45%) compared to the non-exposed group (22%). This correlation suggests that toxic exposures may disrupt endocrine functions, leading to hormonal imbalances that could contribute to both pain syndromes and menstrual irregularities. Understanding these relationships is critical for developing targeted interventions aimed at mitigating both pain and hormonal disturbances in affected women.

Conclusion

It is concluded that occupational chemical exposure significantly impacts pelvic pain syndromes in women, leading to increased pain severity, elevated inflammatory markers, and heightened psychological distress. The findings of this study underscore the critical role that toxicological factors play in the exacerbation of chronic pelvic pain conditions.

References

1. Lamvu G, Carrillo J, Ouyang C, Rapkin A. Chronic pelvic pain in women: a review. *Jama*. 2021 Jun 15;325(23):2381-91.
2. Adamian L, Urits I, Orhurhu V, Hoyt D, Driessen R, Freeman JA, Kaye AD, Kaye RJ, Garcia AJ, Cornett EM, Viswanath O. A comprehensive review of the diagnosis, treatment, and management of urologic chronic pelvic pain syndrome. *Current pain and headache reports*. 2020 Jun;24:1-1.
3. Casale R, Atzeni F, Bazzichi L, Beretta G, Costantini E, Sacerdote P, Tassorelli C. Pain in women: a perspective review on a relevant clinical issue that deserves prioritization. *Pain and therapy*. 2021 Jun;10:287-314.
4. Dashdondov O, Wazir J, Sukhbaatar G, Mikrani R, Dorjsuren B, Aktar N, Zhou X. Herbal nutraceutical treatment of chronic prostatitis–chronic pelvic pain syndrome: a literature review. *International Urology and Nephrology*. 2021 Aug;53(8):1515-28.

5. Marcu I, Gee A, Lynn B. Cannabinoids and chronic pelvic pain in women: focus on endometriosis. *Journal of Endometriosis and Pelvic Pain Disorders*. 2021 Sep;13(3):155-65.
6. Carrubba AR, Ebbert JO, Spaulding AC, DeStephano D, DeStephano CC. Use of cannabis for self-management of chronic pelvic pain. *Journal of Women's Health*. 2021 Sep 1;30(9):1344-51.
7. Augé C, Gamé X, Vergnolle N, Lluet P, Chabot S. Characterization and validation of a chronic model of cyclophosphamide-induced interstitial cystitis/bladder pain syndrome in rats. *Frontiers in Pharmacology*. 2020 Aug 28;11:1305.
8. Huh JW, Tanksley J, Chino J, Willett CG, Dewhirst MW. Long-term consequences of pelvic irradiation: toxicities, challenges, and therapeutic opportunities with pharmacologic mitigators. *Clinical Cancer Research*. 2020 Jul 1;26(13):3079-90.
9. Croisier E, Brown T, Bauer J. The efficacy of dietary fiber in managing gastrointestinal toxicity symptoms in patients with gynecologic cancers undergoing pelvic radiotherapy: a systematic review. *Journal of the Academy of Nutrition and Dietetics*. 2021 Feb 1;121(2):261-77.
10. Fernandes DC, Andreyev HJ. Gastrointestinal toxicity of pelvic radiotherapy: are we letting women down?. *Clinical Oncology*. 2021 Sep 1;33(9):591-601.
11. Vrekoussis T, Siafaka V, Tsitou A, Tsonis O, Navrozoglou I, Makrigiannakis A, Paschopoulos M. Endometriosis-related chronic pelvic pain: A mini review on pathophysiology and impact on mental health. *Journal of Endometriosis and Pelvic Pain Disorders*. 2020 Mar;12(1):35-40.
12. Hellman KM, Oladosu FA, Garrison EF, Roth GE, Dillane KE, Tu FF. Circulating sex steroids and bladder pain sensitivity in dysmenorrhea. *Molecular Pain*. 2021 Oct;17:17448069211035217.
13. Sachedina A, Todd N. Dysmenorrhea, endometriosis and chronic pelvic pain in adolescents. *Journal of clinical research in pediatric endocrinology*. 2020 Feb 1;12(Suppl 1):7-17.
14. Gunyeli I, Saygin M, Ozmen O. Methotrexate-induced toxic effects and the ameliorating effects of astaxanthin on genitourinary tissues in a female rat model. *Archives of Gynecology and Obstetrics*. 2021 Oct;304:985-97.
15. Kuret T, Peskar D, Erman A, Veranič P. A systematic review of therapeutic approaches used in experimental models of interstitial cystitis/bladder pain syndrome. *Biomedicines*. 2021 Jul 22;9(8):865.
16. Lee J, Jeong Y, Mok S, Choi K, Park J, Moon HB, Choi G, Kim HJ, Kim SY, Choi SR, Kim S. Associations of exposure to phthalates and environmental phenols with gynecological disorders. *Reproductive Toxicology*. 2020 Aug 1;95:19-28.