Association between reproductive factors and fibromyalgia: a cross-sectional analysis of female health profiles

D. Kurtuluş[1], S. Dagci[2], K. Arkan[3], S. Akgol[3], B. Can[4]

[1]Department of Physical Therapy and Rehabilitation, SBU Ümraniye Research and Training Hospital, Istanbul; [2]Istanbul Provincial Health Directorate, Public Hospitals Services Presidency, 2nd Region, Istanbul; [3]Department of Obstetrics and Gynaecology, Division of Gynaecologic Oncology, Diyarbakır Gazi Yaşargil Research and Training Hospital, Diyarbakır; [4]Department of Obstetrics and Gynaecology, Division of Gynaecologic Oncology, Bower Hospital, Diyarbakır, Turkey.

Abstract

Objectives

Fibromyalgia (FM) is a chronic musculoskeletal pain syndrome predominantly affecting women, suggesting possible links with reproductive and hormonal factors. Although reproductive history has been associated with various long-term health conditions, its role in FM remains insufficiently explored. This study aimed to investigate the association between parity, age at first pregnancy, and the presence of fibromyalgia among women of reproductive age.

Methods

This cross-sectional observational study included 260 women aged 18-50 years with at least one prior live birth, recruited from Physical Medicine and Rehabilitation, Rheumatology, and Gynaecology Outpatient Clinics between March and December 2024. Demographic, clinical, and reproductive data were collected through structured interviews and medical records. FM diagnosis was based on the 2016 revised criteria of the American College of Rheumatology (ACR) using Widespread Pain Index (WPI) and Symptom Severity Scale (SSS) scores; the Global Symptom Score (GSS) was defined as their sum. Statistical analyses included independent-sample t-tests, chi-square tests, and multivariate logistic regression adjusting for age, body mass index, comorbidities, and educational level.

Results

FM was diagnosed in 104 participants (40%). Women with three or more live births had a significantly higher prevalence of FM compared with those with fewer births (p=0.006). In multivariate analysis, grand multiparity remained independently associated with FM (adjusted OR = 2.46, 95% CI = 1.28–4.72, p=0.006). No significant association was found between age at first pregnancy and FM (p>0.05). FM-diagnosed participants reported significantly higher WPI, SSS, and GSS scores (p=0.001 for all), with strong correlations between WPI and both GSS (r=0.782) and SSS (r=0.472).

Conclusions

Grand multiparity was independently associated with fibromyalgia, suggesting that cumulative hormonal and physiological stress from multiple pregnancies may contribute to chronic pain susceptibility. No association was found between age at first pregnancy and FM. Larger, longitudinal studies are warranted to clarify causal pathways between reproductive history and FM pathogenesis.

Key words

fibromyalgia, parity, reproductive history, age at first pregnancy, hormonal factors, chronic pain

Duygu Kurtuluş, MD
Selma Dagci, PhD
Kevser Arkan, MD
Sedat Akgol, MD
Behzat Can, MD

Please address correspondence to:
Duygu Kurtuluş
Department of Physical Therapy and Rehabilitation,
SBU Ümraniye Research and Training Hospital,
34750 Istanbul, Turkey.
E-mail: dygkurtulus@gmail.com

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Introduction

Fibromyalgia (FM) is a chronic, multifactorial disorder characterised by widespread musculoskeletal pain, fatigue, sleep disturbances, and cognitive impairment (1). It affects approximately 2%-8% of the global population, with a marked female predominance and an estimated female-to-male ratio of approximately 7:1 (2). Despite extensive research, the aetiology of FM is not fully elucidated. Current evidence points to a multifactorial pathogenesis involving genetic susceptibility, neuroendocrine dysregulation, immune dysfunction, and environmental triggers (1, 3, 4).

Growing evidence suggests that reproductive health factors, including pregnancy and hormonal fluctuations, may influence pain perception and the onset of FM symptoms. Pregnancy induces profound physiological changes, particularly in oestrogen and progesterone levels, which can modulate pain processing, immune responses, and central nervous system activity. Although hormonal changes during gestation have been reported to either alleviate or exacerbate FM symptoms, the mechanisms underlying these effects remain unclear (5-8).

Reproductive characteristics such as age at first pregnancy and parity have been associated with long-term health outcomes, including metabolic, cardiovascular, and autoimmune disorders. However, their potential role in FM development remains insufficiently investigated (6-9). Most previous studies have focused on FM symptom changes during pregnancy or on adverse obstetric outcomes (*e.g.*, gestational diabetes, preterm birth, intrauterine growth restriction) among women already diagnosed with FM (5, 7, 9). In contrast, the long-term impact of reproductive history on subsequent FM risk is largely understudied.

This study aims to address this gap by investigating the association between age at first pregnancy, number of pregnancies, and FM diagnosis. We hypothesise that younger maternal age at first pregnancy and higher parity are associated with an increased risk of FM, potentially mediated by prolonged exposure to hormonal fluctuations and cumulative physiological stress. Our findings are expected to provide novel insights into sex-specific determinants of FM pathogenesis and to inform future epidemiological and mechanistic research on neuroendocrine vulnerability windows.

Materials and methods

This cross-sectional observational study investigated the association between parity, age at first pregnancy, and the diagnosis of fibromyalgia (FM) in women of reproductive age. Participants were recruited from gynaecology and primary care outpatient clinics of tertiary healthcare centres between March and December 2024. Data collection was performed through structured clinical interviews, review of medical records, and administration of validated symptom assessment questionnaires.

Women were eligible if they were aged 18-50 years, had at least one prior live birth, and had no history of FM or any other chronic pain condition prior to or during pregnancy. Exclusion criteria were pre-existing chronic pain syndromes (*e.g.*, myofascial pain syndrome, chronic fatigue syndrome), malignancy, autoimmune or significant neurological disorders, incomplete clinical documentation, or withdrawal before data collection completion.

Demographic and clinical variables included age, education level, body mass index (BMI), medication use, smoking status, and comorbidities (*e.g.*, migraine, thyroid disorder, diabetes, hypertension). Socioeconomic status was classified based on educational attainment and occupation. Reproductive variables of interest were age at first pregnancy and parity, analysed both continuously and categorically. Age at first pregnancy was grouped into four categories: ≤20 years, 21-25 years, 26-30 years, and ≥31 years. Parity was categorised as 1-2 live births or ≥3 live births (grand multiparity).

FM diagnosis was established using the 2016 revised American College of Rheumatology (ACR) criteria. The Widespread Pain Index (WPI) was calculated as the number of painful

body regions (range: 0-19), and the Symptom Severity Scale (SSS) score was obtained by summing fatigue, unrefreshed sleep, cognitive symptoms, and general somatic symptoms (range: 0-12). The Global Symptom Score (GSS) was defined as the sum of WPI and SSS scores (range: 0-31), providing a composite measure of overall symptom burden, as previously described in validation studies (10). All participants were evaluated to exclude alternative causes for symptoms.

To identify independent factors associated with fibromyalgia, binary logistic regression analysis was performed. Variables with $p<0.10$ in univariate analyses were included in a multivariate model using backward elimination. The final model adjusted for potential confounders, including age, BMI, comorbidities, and educational level.

The study protocol was approved by the Institutional Review Board of the University of Health Sciences, Umraniye Training and Research Hospital (approval number B.10.1.TKH.4.34.H.GP.0.01/87; date: 27.02.2024). Written informed consent was obtained from all participants. The research was conducted in accordance with the Declaration of Helsinki (2013 revision), with all data anonymised to ensure confidentiality.

Statistical analysis

All statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS), version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation (SD) for normally distributed data, or as median with minimum and maximum values for non-normally distributed data. Age at first pregnancy was categorised into four subgroups (≤20, 21-25, 26-30, ≥31 years), based on the distribution of maternal ages in our sample and on standard age groupings in reproductive epidemiology literature. These cut-offs reflect both common reproductive age patterns in our cohort and are consistent with established epidemiological references. Categorical variables were summarised as frequencies and percentages.

Table I. Demographic and clinical characteristics of participants.

Variable	FM diagnosed (n=104)	FM not diagnosed (n=156)	Total (n=260)	*p*
Age (mean ± SD)	42.1 ± 7.9	40.9 ± 7.4	41.4 ± 7.6	0.217
Education level				0.527
Primary	49 (47.1%)	65 (41.7%)	114 (43.8%)	
High school	34 (32.7%)	55 (35.3%)	89 (34.2%)	
University	20 (19.2%)	31 (19.9%)	51 (19.6%)	
Graduate	1 (1.0%)	1 (0.6%)	2 (0.8%)	
Comorbidities				0.352
None	48 (46.2%)	76 (48.7%)	124 (47.7%)	
Migraine	23 (22.1%)	31 (19.9%)	54 (20.8%)	
Thyroid disorder	16 (15.4%)	26 (16.7%)	42 (16.2%)	
Parity				**0.006**
Nulliparous (0)	4 (3.8%)	6 (3.8%)	10 (3.8%)	
Multiparous (1-2)	48 (46.2%)	90 (57.7%)	138 (53.1%)	
Grand multiparous (≥3)	52 (50.0%)	60 (38.5%)	112 (43.1%)	

Statistical analysis: differences between FM-diagnosed and non-FM groups were assessed using Independent Samples t-tests for continuous variables (age) and Chi-square (χ^2) tests for categorical variables. $p<0.05$ was considered significant
FM: fibromyalgia; SD: standard deviation.

The normality of the data was assessed using the Shapiro-Wilk test and visual inspection of histograms. For comparisons between two independent groups, independent samples t-test was applied for normally distributed variables, while the Mann-Whitney U test was used for non-normally distributed variables. Associations between categorical variables were evaluated using the Chi-square (χ^2) test.

To identify independent predictors of fibromyalgia diagnosis, binary logistic regression analysis was employed. Multivariate logistic regression models were constructed to adjust for potential confounding variables, including demographic, lifestyle, and clinical factors. Variables with a significance level of $p<0.10$ in univariate analyses were included in the multivariate models using a stepwise backward elimination approach.

All statistical tests were two-sided, and a p-value <0.05 was considered statistically significant. Results from regression analyses were reported as odds ratios (ORs) with 95% confidence intervals (CIs).

Results

A total of 260 women aged 18-50 years were included in the final analysis. The study evaluated the associations between age at first pregnancy, parity, and the diagnosis of fibromyalgia (FM), as well as the relationship between FM and selected demographic and clinical characteristics.

Comparison of demographic variables between participants with and without FM revealed no statistically significant differences in age (42.1±7.9 *vs.* 40.9±7.4 years, respectively; $p=0.217$), educational attainment, or comorbid conditions ($p>0.05$ for all). Educational status was similarly distributed across groups, with approximately 43.8% of the total sample having completed only primary education. Migraine (20.8%) and thyroid disorders (16.2%) were the most commonly reported comorbidities, with comparable frequencies between groups (Table I).

Regarding symptom severity, women diagnosed with FM had significantly higher scores in the Widespread Pain Index (WPI: 12.5±3.2 *vs.* 6.3±2.5), Symptom Severity Scale (SSS: 8.7±2.1 *vs.* 4.1±1.7), and Global Symptom Score (GSS: 7.9±1.8 *vs.* 3.8±1.5) compared to non-FM participants ($p=0.001$ for all comparisons). Strong positive correlations were observed between WPI and GSS r =0.782, $p<0.05$) and between WPI and SSS (r=0.472, $p<0.05$), supporting the internal consistency and construct validity of FM symptom domains (Table II).

Analysis of reproductive characteristics demonstrated a significant association between parity and FM diagnosis.

Table II. Comparison of symptom scores between FM and non-FM groups.

Variable	FM (n=104)	Non-FM (n=156)	*p*
WPI (mean ± SD)	12.5 ± 3.2	6.3 ± 2.5	0.001
SSS (mean ± SD)	8.7 ± 2.1	4.1 ± 1.7	0.001
GSS (mean ± SD)	7.9 ± 1.8	3.8 ± 1.5	0.001

Statistical analysis: differences between FM and non-FM groups were assessed using the Independent Samples t-test. $p<0.05$ was considered significant.
FM: fibromyalgia; SD: standard deviation; WPI: Widespread Pain Index; SSS: Symptom Severity Scale; GSS: Global Symptom Score.

Table III. Comparison of women with live births.

Parity (live births)	n	Mean age (years)	Mean WPI	Mean SSS	Mean GSS	FM prevalence (%)
1 live birth	17	40.7	8.8	5.1	10.6	58.8
2 live births	61	39.9	4.7	4.5	7.0	32.8

Differences between groups were not statistically significant ($p>0.05$).
Statistical analysis: differences in mean age, WPI, SSS and GSS were assessed using the Independent Samples t-test. Differences in FM prevalence (%) were assessed using the Chi-square (χ^2) test. $p<0.05$ was considered significant.

Women with three or more live births (grand multiparous) had a significantly higher prevalence of FM (50.0%) compared with those having one or two live births (46.2%) or none (3.8%) ($p=0.006$). No statistically significant association was observed between age at first delivery and FM status ($p>0.05$). These results suggest that higher parity may be associated with increased FM risk, possibly due to cumulative hormonal and physiological stress (Table I, parity section).

To further explore this relationship, a subgroup analysis was performed comparing women with one versus two live births. Although the differences did not reach statistical significance, women with one birth exhibited numerically higher mean WPI (8.8 *vs*. 4.7), SSS (5.1 *vs*. 4.5), GSS (10.6 *vs*. 7.0) scores, and FM prevalence (58.8% *vs*. 32.8%) than those with two births. These trends, although not statistically significant ($p>0.05$), indicate that the elevated FM risk is primarily associated with grand multiparity rather than lower parity levels (Table III).

In multivariate logistic regression analysis adjusting for age, body mass index, comorbidities, and educational level, grand multiparity remained significantly associated with fibromyalgia diagnosis (adjusted OR=2.46, 95% CI=1.28–4.72, $p=0.006$).

Taken together, these findings indicate that grand multiparity is independently associated with FM, while demographic variables such as age and education were not significantly related to FM diagnosis. Furthermore, the consistent elevations in WPI, SSS, and GSS among FM patients underscore the multidimensional and coherent nature of FM symptomatology.

Discussion

This study aimed to evaluate the association between age at first pregnancy, number of pregnancies (parity), and the presence of fibromyalgia (FM) among women of reproductive age. The findings revealed a significantly higher prevalence of FM in participants who had given birth to three or more children, suggesting a potential link between high parity and increased FM risk. However, no statistically significant relationship was observed between age at first pregnancy and FM diagnosis. Additionally, FM-diagnosed individuals had markedly elevated scores on the WPI, SSS, and GSS, which aligns with the clinical presentation of FM as outlined in the ACR criteria (10-12). This consistency reinforces the reliability of the diagnostic framework, as patients in our cohort exhibited symptom patterns highly concordant with established classification standards.

The observed relationship between high parity and FM may reflect the cumulative impact of repeated pregnancies on hormonal, immunological, and physiological systems. In particular, postpartum hormonal shifts may exacerbate central sensitization, a key mechanism in FM pathophysiology. Pregnancy induces substantial fluctuations in oestrogen and progesterone, which influence pain modulation within the central nervous system. Oestrogen is known to raise pain thresholds, whereas its sharp decline postpartum has been associated with heightened pain sensitivity. These biological changes may contribute to chronic pain vulnerability, especially in women with multiple pregnancies. Additionally, separate analyses comparing women with one versus two live births revealed no significant differences in FM prevalence or symptom severity. This finding suggests that the heightened FM risk is not driven by the distinction between one or two live births but is more clearly associated with grand multiparity (≥3 live births). Previous studies have similarly reported links between high parity and an elevated risk of autoimmune and chronic pain conditions. Grand multiparity has also been associated with prolonged exposure to pro-inflammatory states during and after pregnancy, which may contribute to persistent pain syndromes. Moreover, studies in rheumatology have suggested that hormonal imbalance following childbirth may predispose women to chronic pain disorders, including fibromyalgia and chronic fatigue syndrome (13-16).

The relatively high proportion of fibromyalgia cases (40%) observed in our study reflects the clinical recruitment setting rather than a population-based distribution. Participants were primarily enrolled from Physical Medicine and Rehabilitation and Rheumatology outpatient clinics, where fibromyalgia is more frequently diagnosed compared to general gynaecology or primary care populations. Therefore, this study was not designed to estimate population prevalence but to compare reproductive and clinical characteristics between women with fibromyalgia and pain-free controls within a clinical cohort.

The scarcity of robust epidemiological studies on this topic leaves significant gaps in our understanding of how reproductive history modulates chronic pain susceptibility. Although interest in the potential relationship between reproductive factors and FM has grown, the existing evidence on the association between parity and FM remains limited. Notably, there is a lack of studies that directly examine this relationship in the literature (11, 17, 18). The present study is among the first to specifically evaluate the association between parity and FM, marking a meaningful contribution to this underexplored area. The findings, particularly the observed association in women with high parity, underscore the potential role of reproductive history in the pathogenesis of FM (9, 19, 20). Previous inconsistencies in the literature may be attributed to methodological variations, such as differences in sample size, population characteristics, and diagnostic criteria, as well as the influence of unmeasured confounding factors including genetic predisposition, early life adversity, socioeconomic status, and chronic psychosocial stress. These variables can significantly affect both pain perception and susceptibility to central sensitization syndromes (21-24). In this context, the present study offers a novel perspective by highlighting reproductive history, especially grand multiparity, as a potentially important factor in FM aetiology.

In contrast, no significant association was found between age at first pregnancy and FM. Although early maternal age has been hypothesised to influence neuroendocrine regulation and pain sensitivity later in life, the evidence remains limited and inconsistent. Some researchers have suggested that early pregnancy may lead to altered lifetime oestrogen exposure, thereby modulating pain-related neural circuits (6, 9, 25, 26). However, our findings did not support this hypothesis, indicating that age at first birth may not independently contribute to FM risk. Further longitudinal studies are warranted to explore whether early or late childbearing exerts lasting effects on pain modulation and neurohormonal health.

Our findings partially differ from those of Tulay *et al*. (2016) (11), who reported that fibromyalgia did not significantly affect parity or breastfeeding duration in Turkish women. This discrepancy may be explained by differences in study design and population; Tulay *et al*. examined reproductive outcomes among women already diagnosed with FM, whereas the present study evaluated reproductive history as a potential factor associated with FM development.

The study also found strong positive correlations between WPI, SSS, and GSS scores among FM-diagnosed participants. These findings underscore the internal consistency and clinical utility of the ACR 2016 diagnostic criteria, where increases in widespread pain were paralleled by heightened symptom severity and overall symptom burden. This relationship supports the concept of FM as a multidimensional disorder with a consistent symptom profile across diagnostic instruments (10, 27, 28).

Interestingly, a weak yet statistically significant positive correlation was observed between participant age and symptom scores (SSS and GSS). While this suggests that symptom burden may slightly increase with age, the clinical significance of this finding remains uncertain. Age-related changes in pain processing, sleep quality, and comorbidity burden may partially account for this trend. Prior studies on the relationship between age and FM symptoms have yielded mixed results, and further investigation is needed to clarify whether age is a meaningful modifier of FM severity (29-32).

In summary, the present study provides evidence that grand multiparity may be associated with an increased risk of FM, potentially due to cumulative hormonal and physiological stress. Although no association was found between age at first pregnancy and FM, the role of reproductive factors in chronic pain disorders warrants further research. The findings also reinforce the validity of commonly used clinical measures in FM diagnosis and suggest that symptom burden may marginally increase with age.

Strengths and limitations

This study has several strengths worth noting. First, the cross-sectional design enabled a structured and simultaneous evaluation of reproductive factors and fibromyalgia (FM) status. Second, the relatively large sample size (n=260) provided adequate statistical power to detect meaningful associations and enhanced the reliability of the findings. Third, the use of the 2016 revised ACR diagnostic criteria ensured standardisation in FM case identification and strengthened the internal validity of the study.

Nonetheless, certain limitations should be acknowledged. The study was conducted at a single tertiary centre, which may limit the generalisability of the findings to broader populations. Additionally, psychosocial variables and hormonal profiles were not evaluated, although these factors are known to influence both reproductive health and chronic pain development. Furthermore, while the cross-sectional design allows for the identification of associations, it does not permit causal or predictive inferences regarding the temporal relationship between reproductive factors and FM onset. Future longitudinal studies are warranted to confirm whether the observed associations represent causal links or shared underlying mechanisms.

Conclusion

The findings of this study suggest that parity, particularly having three or more live births, is associated with an increased likelihood of fibromyalgia (FM) among women of reproductive age. Although no significant relationship was found between age at first pregnancy and FM, the results highlight the potential influence of reproductive history on chronic pain disorders.

These outcomes underscore the need for larger-scale, longitudinal studies to further clarify the role of reproductive factors in the pathogenesis of FM. From a clinical perspective, incorporating reproductive history into patient evaluations may help identify women at higher risk for FM, enabling earlier recognition and more individualised

management strategies. Overall, these findings emphasise the importance of considering reproductive history in future research on the aetiology and prevention of fibromyalgia.

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