

Prevalence of Fear of Childbirth among Nulliparous Women

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Objective: To assess the prevalence and factors associated with fear of childbirth (FOC) among nulliparous Thai women and to explore the relationship between FOC and postpartum depression (PPD).

Materials and Methods: A cross-sectional study was conducted at Thammasat University Hospital (TUH) among low-risk nulliparous women between March and August 2023. Sociodemographic data and obstetric history were gathered. FOC was assessed using the Wijma Delivery Expectancy/Experience Questionnaire-A (WDEQ-A) at between 32 and 37 weeks of gestation at the prenatal care clinic. The Edinburgh Postnatal Depression Scale (EPDS) was used to assess the risk of PPD within 72 hours after delivery at postpartum ward.

Results: The study included 271 participants, with 240 delivered at TUH. The average gestational age was 34.7 weeks. The prevalence of high-to-severe FOC and the risk of PPD were 19.5% and 46.7%, respectively. Lack of family support and no information about delivery were significantly associated with the levels of FOC. No family support was the only significant predictor of high-to-severe FOC (AOR 5.62, 95% CI 1.34 to 23.51). Factors that were significantly associated with the risk of PPD included health coverage, occupation, family income, and level of FOC. Additionally, pregnant women with high-to-severe FOC were 2.68 times more likely to develop PPD (AOR 2.68, 95% CI 1.29 to 5.56), while those with high income of more than 1,600 USD per month had a 67% lower risk of PPD (AOR 0.33, 95% CI 0.11 to 0.95).

Conclusion: The prevalence of high-to-severe FOC was 19.5%. Lack of family support and insufficient knowledge about delivery were associated with levels of FOC. FOC was a significant predictor of increased PPD risk. Screening for FOC during pregnancy should be performed to identify at-risk pregnant women and help prevent PPD. Moreover, providing knowledge and encouraging family involvement play a crucial role in reducing FOC.

Keywords: EPDS; Fear of childbirth; Nulliparity; Postpartum depression; WDEQ

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Pregnancy and childbirth alter women's anatomy, physiology, psychology, emotions, and social dynamics. These alterations could induce anxiety in pregnant women, leading to a condition known as fear of childbirth (FOC)⁽¹⁾. FOC may involve fear of the labor procedure itself, uncertainties regarding the timing of childbirth, apprehension of potential complications during and after childbirth, and concerns about the quality and readiness of healthcare facilities⁽²⁾. FOC can lead to negative outcomes for both mothers and fetus. Adverse neonatal outcomes

include preterm birth and low birth weight⁽³⁾. Unfavorable maternal outcomes include prolonged labor, increased use of assisted delivery devices⁽⁴⁾, and higher rates of cesarean delivery among nulliparous women⁽⁵⁾. Negative birth experiences may influence a mother's decision regarding future pregnancies, leading to reduced pregnancy rates⁽⁶⁾.

The worldwide prevalence of FOC has been continuously increasing, with severe FOC affecting between 14% and 19%⁽⁷⁾. In Thailand, only one study investigated FOC. It was found that the prevalence of high-to-severe FOC in low-risk pregnancies was 16.8% in both multiparous and nulliparous women⁽⁸⁾. A meta-analysis showed the prevalence of severe FOC was higher among nulliparous women, ranging from 14% to 20%, compared to 11% to 17% among multiparous women⁽⁷⁾. Previous studies had shown that various factors affecting FOC among pregnant women include marital status, educational level, income, family and social support, route of delivery, previous experience about childbirth, anxiety, and depression⁽⁸⁻¹⁵⁾.

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In addition to FOC, anxiety can develop at any time during pregnancy and may progress into postpartum depression (PPD) after childbirth⁽¹⁶⁾. A previous study in western country indicated that FOC was associated with an increased risk of PPD in low-risk pregnant women. PPD evidently resulted in detrimental outcomes, including preterm birth, infant illness, and impaired mother-infant bonding⁽¹⁷⁾. Therefore, the objective of the present study was to assess the prevalence of FOC, associated factors, and the association between FOC and PPD among nulliparous Thai women. The study would enable a better understanding of these implications that could lead to improvement of quality of life in pregnant women.

Materials and Methods

The present study was a cross-sectional study conducted at Thammasat University Hospital (TUH), Pathum Thani, Thailand, between March and August 2023. This research was approved by the Human Ethics Committee of Thammasat University (MTU-EC-OB-2-283/65) on February 17, 2023. The participants were Thai singleton nulliparous pregnant women aged at least 20 years old, had a gestational age between 32 and 37 weeks and attended prenatal care clinic at TUH. The participants were enrolled by simple random sampling. Participants with chronic illnesses prior to pregnancy, mental health disorders, fetal complications during pregnancy, fetal congenital anomalies, pregnancy-related complications, and participants who refused to participate in the present study were excluded.

Based on Phunyammalee et al.'s study, the prevalence of high to severe FOC was 16.8%⁽⁸⁾. The estimated sample size by Cochran's formula was at least 210 participants. The confidence level of the study was set at 95%. Thirty percent compensation for data loss was added. The sample size in the present study was 280 participants.

The participants were recruited at the prenatal care clinic without selection bias. The research team provided details and the aim of the study to the participants at the prenatal care clinic. Written informed consent was obtained after a thorough explanation in a private room. Participants were informed to complete a self-report questionnaire, which took approximately 10 minutes, privately during a prenatal visit. The questionnaire consisted of sociodemographic characteristics, obstetrics history, and the Thai version of the Wijma Delivery Expectancy/Experience Questionnaire-A (WDEQ-A)⁽⁸⁾. After delivery, the

participants were required to complete the Thai version of the Edinburgh Postnatal Depression Scale (EPDS) questionnaire⁽¹⁸⁾ within 72 hours to assess the risk of PPD. The questionnaire took around 10 minutes to complete, and no spouses or relatives were allowed in the postpartum ward.

Sociodemographic data, including age, occupation, educational level, average family income, family support, and planned pregnancy were collected. Obstetric data, including gestational age, history of abortion, infertility treatment for pregnancy, childbirth preference, and information received about childbirth were gathered.

The WDEQ-A was used to assess FOC. The questionnaire contained 33 items with six sections, including fear, negative appraisal, loneliness, lack of self-efficacy, lack of positive anticipation, and concerns for the child⁽¹⁹⁾. The items were categorized as positive and negative, and scores ranged from 0 for not at all to 5 for extremely on a Likert scale. FOC levels were classified as low for less than 38, moderate for 38 to 65, high for 66 to 84, and severe for 85 and above⁽¹⁹⁾. The Thai version of the questionnaire has been tested and validated⁽⁸⁾.

The EPDS was used to screen for PPD. The questionnaire consisted of 10 questions rating the severity of symptoms on a Likert scale from 0 to 3⁽²⁰⁾. A score of 8 or higher predicted individuals at high risk of PPD with a sensitivity of 77.0% and specificity of 56.3%. The Thai version of the EPDS has been tested and validated⁽²¹⁾.

After completing both questionnaires, data analysis was performed using IBM SPSS Statistics, version 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables were reported as frequency and percentage. For continuous variables, mean and standard deviation were reported.

Women were categorized into three groups, those with low, moderate, and high to severe FOC, according to WDEQ-A scores. In addition, they were also categorized into those with low- and high-risk for PPD according to EDPS scores. Various characteristics were compared between women with different FOC and PPD groups to evaluate possible risk factors. Chi-square test was used to compare categorical variables and Fisher's exact test was used when more than 20% of expected cell counts are less than 5. Student t-test was used to compare continuous variables between different PPD groups and analysis of variance (ANOVA) was used to compare continuous variables between different FOC groups after normality of the data was tested.

To determine independent associated factors for high to severe FOC and high-risk PPD, a logistic regression analysis was used. Various variables were entered into the analysis to eliminate the effect of potential confounders. The analysis was based on the assumptions that all observations were independent and there was no multicollinearity. Interactions between variables were also tested. Adjusted odds ratios and 95% confidence intervals were estimated and reported. A p-value of less than 0.05 was considered statistically significant.

Results

Of the 271 pregnant women in the present study, only 240 participants completed both questionnaires as shown in Figure 1. The mean age of the participants, gestational age at first questionnaire and at delivery were 29.5 years, 34.7 weeks, and 38.5 weeks, respectively. Three quarters (205 out of 271 participants) had intentionally planned their pregnancies. Almost all participants reported that they received family support and received information about delivery. One hundred forty-nine out of 271 participants preferred vaginal delivery as presented in Table 1.

The prevalence of high-to-severe FOC was 19.5% (53 out of 271 participants), which was comparable to the low FOC group at 20.7% (56 out of 271 participants). As shown in Table 2, around half (26 out of 53) of the participants in the high-to-severe FOC group, had low family income. Only 12.5% (seven out of 56 participants) in the low FOC group was in high family income with 1,600 USD or more per month. Within the low family income group, or in the less than 800 USD per month group, 24% (26 out of 108) experienced high-to-severe FOC. Family support and information about delivery were identified as factors that significantly associated with FOC level ($p < 0.05$). Forty percent (eight out of 20) of the participants who lacked knowledge about childbirth had high-to-severe FOC, whereas only 17.9% (45 out of 251) of those who received information about delivery experienced a similar level of FOC, with statistical significance. Regarding the preferred delivery method, more than half (30 out of 53) of the participants with high-to-severe FOC opted for vaginal delivery, while only one-quarter (14 out of 53) chose cesarean delivery. After adjusting for other variables using logistic regression, participants with lack of family support were 5.62 times more likely to develop high to severe FOC.

The prevalence of high risk PPD was 46.7%

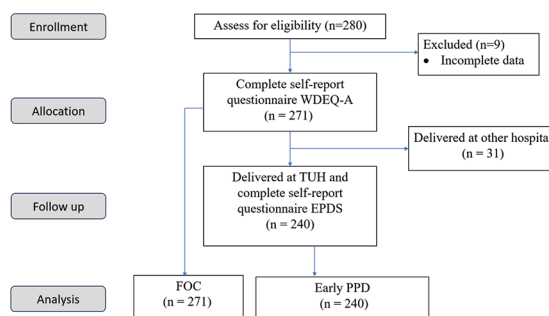


Figure 1. Flow chart of study.

WDEQ-A: Wijma Delivery Expectancy/Experience Questionnaire-A; TUH: Thammasat University Hospital; EPDS: Edinburgh Postnatal Depression Scale; FOC: fear of childbirth; PPD: postpartum depression

Table 1. Baseline characteristics of pregnant women

	n=271
Age (years); mean±SD	29.5±5.4
GA (weeks); mean±SD	34.7±2.0
History of abortion; n (%)	32 (11.8)
Health coverage; n (%)	
CSMBS	59 (21.8)
SSS	80 (29.5)
Cash	132 (48.7)
Occupation; n (%)	
Government officer	64 (23.6)
Employee	126 (46.5)
Personal business	41 (15.1)
Housewife	40 (14.8)
Education: Bachelor degree or higher; n (%)	173 (63.8)
Family income (USD/month); n (%)	
Low (<800)	108 (40.0)
Middle (800 to 1,600)	133 (49.0)
High (>1,600)	30 (11.0)
Single family; n (%)	152 (56.1)
Family support; n (%)	262 (96.7)
Planned pregnancy; n (%)	205 (75.6)
Infertility treatment; n (%)	11 (4.1)
Informed delivery*; n (%)	251 (92.6)
Preferred route; n (%)	
Vagina	149 (55.0)
Cesarean	78 (28.8)
Uncertain	44 (16.2)

SD=standard deviation; GA=gestational age; CSMBS=civil servant medical benefit scheme; SSS=social security scheme
1 USD=34.23 Baht, * Informed delivery: have been informed about delivery

(112 out of 240 participants). As seen in Table 3, PPD was significantly associated with health coverage, occupation, family income, and high to severe FOC. Approximately three-quarters (39 out

Table 2. Factors associated with the different levels of FOC

Characteristics	Level of FOC				Multiple logistic regression for high to severe FOC	
	Low (n=56)	Moderate (n=162)	High to severe (n=53)	p-value	AOR (95% CI)	p-value
Age (years); mean±SD	29.4±5.3	29.7±5.4	29.0±5.4	0.677	0.98 (0.91 to 1.05)	0.586
History of abortion; n (%)	5 (8.9)	18 (11.1)	9 (17.0)	0.552	1.83 (0.75 to 4.46)	0.186
Health coverage; n (%)				0.745		
CSMBS	13 (23.2)	37 (22.8)	9 (17.0)		Ref.	
SSS	19 (33.9)	46 (28.4)	15 (28.3)		1.76 (0.47 to 6.61)	0.402
Cash	24 (42.9)	79 (48.8)	29 (54.7)		2.04 (0.61 to 6.80)	0.244
Occupation; n (%)				0.909		
Housewife	10 (17.9)	23 (14.2)	7 (13.2)		Ref.	
Government officer	12 (21.4)	40 (24.7)	12 (22.6)		2.52 (0.64 to 9.98)	0.189
Employee	28 (50.0)	74 (45.7)	24 (45.3)		1.35 (0.49 to 3.72)	0.559
Own business	6 (10.7)	25 (15.4)	10 (18.9)		1.95 (0.61 to 6.23)	0.258
Educational level; n (%)				0.390		
Below bachelor	17 (30.4)	60 (37.0)	21 (39.6)		Ref.	
Bachelor or higher	39 (69.6)	102 (63.0)	32 (60.4)		1.39 (0.64 to 2.99)	0.406
Extended family; n (%)	23 (41.1)	76 (46.9)	20 (37.7)	0.450	0.59 (0.30 to 1.18)	0.135
Family income (USD/month); n (%)				0.627		
Low (<800)	21 (37.5)	61 (37.7)	26 (49.1)		Ref.	
Middle (800 to 1,600)	28 (50.0)	82 (50.6)	23 (43.4)		0.67 (0.32 to 1.44)	0.306
High (>1,600)	7 (12.5)	19 (11.7)	4 (7.5)		0.39 (0.10 to 1.45)	0.158
No family support; n (%)	2 (3.6)	2 (1.2)	5 (9.4)	0.015	5.62 (1.34 to 23.51)	0.018
Never informed delivery*; n (%)	5 (8.9)	7 (4.3)	8 (15.1)	0.030	2.50 (0.90 to 6.97)	0.080
Preferred route; n (%)				0.768		
Vagina	28 (50.0)	91 (56.2)	30 (56.6)		-	-
Cesarean	16 (28.6)	48 (29.6)	14 (26.4)		-	-
Planned pregnancy; n (%)	42 (75.0)	126 (77.8)	37 (69.8)	0.499	-	-

FOC=fear of childbirth; SD=standard deviation; AOR=adjusted odds ratio; CI=confidence interval; CSMBS=civil servant medical benefit schemes; SSS=social security schemes

1 USD=34.23 Baht; * Never informed delivery: never been informed about delivery

of 53) of the participants who used the civil servant medical benefit scheme (CSMBS) were categorized as low-risk for developing PPD. The majority of the participants in the high-income group, thus 70.4% (19 out of 27) were classified as having low-risk for PPD, while two-thirds (30 out of 45) of the participants with high-to-severe FOC were categorized into the high-risk for PPD group. After adjusting for other variables using logistic regression, high-to-severe FOC was a significant predictor for 2.68 times higher risk of developing PPD. High family income reduced the risk of developing PPD by 67%.

Discussion

FOC is commonly regarded as a normal phenomenon from the unexpected and unpleasant nature of labor, resulting in both positive and negative outcomes. The prevalence of high FOC in the present study was 18.8%, which was slightly higher than the previous study conducted in

Thailand that was 16.1%⁽⁸⁾. The prevalence of severe FOC was comparable at 0.7%⁽⁸⁾. The earlier study recruited of both nulliparous and multiparous women, whereas the present study focused solely on nulliparous women. A meta-analysis conducted in 2021⁽⁷⁾ revealed that studies from other countries exhibited higher prevalences of severe FOC than the present study in Thailand. Prevalence of severe FOC for Ireland, Netherland, Portugal, and Saudi Arabia were 7.4%⁽¹²⁾, 11%⁽¹³⁾, 11.2%⁽⁹⁾, and 6.7%⁽⁵⁾, respectively. The comparison of severe FOC among nulliparous women are summarized and presented in Table 4. These differences might be related to factors such as religion, ethnicity, cultural beliefs, socioeconomic status, income, and disparities in healthcare systems⁽¹²⁾.

Factors associated with FOC were family support and knowledge about childbirth in the present study. Existing research in European countries reported less social support from family to be related to the

Table 3. Factors associated with the risk of PPD

Characteristics	PPD			Multiple logistic regression	
	Low risk (n=128)	High risk (n=112)	p-value	AOR (95% CI)	p-value
Age (years); mean±SD	29.6±5.2	29.3±5.4	0.648	1.02 (0.97 to 1.09)	0.423
History of abortion; n (%)	15 (11.7)	16 (14.3)	0.560	1.35 (0.57 to 3.17)	0.492
Health coverage; n (%)			0.004		
CSMBS	39 (30.5)	14 (12.5)		Ref.	
SSS	35 (27.3)	38 (33.9)		1.67 (0.57 to 4.91)	0.355
Cash	54 (42.2)	60 (53.6)		1.71 (0.62 to 4.69)	0.299
Occupation; n (%)			0.005		
Housewife	20 (15.6)	18 (16.0)		Ref.	
Government officer	43 (33.6)	16 (14.3)		0.72 (0.23 to 2.24)	0.566
Employee	51 (39.8)	59 (52.7)		1.48 (0.66 to 3.32)	0.347
Personal business	14 (10.9)	19 (17.0)		1.60 (0.59 to 4.32)	0.358
Educational level; n (%)			0.091		
Below bachelor	37 (28.9)	45 (40.2)		Ref.	
Bachelor or higher	91 (71.1)	67 (59.8)		0.97 (0.51 to 1.86)	0.923
Extended family; n (%)	60 (46.9)	47 (42.0)	0.445	0.94 (0.53 to 1.67)	0.837
Family income (USD/month); n (%)			0.019		
Low (<800)	38 (29.7)	51 (45.5)		Ref.	
Middle (800 to 1,600)	71 (55.5)	53 (47.4)		0.60 (0.31 to 1.17)	0.133
High (>1,600)	19 (14.8)	8 (7.1)		0.33 (0.11 to 0.95)	0.039
No family support; n (%)	3 (2.3)	4 (3.6)	0.573	1.15 (0.22 to 6.04)	0.870
Planned pregnancy; n (%)	100 (78.1)	83 (74.1)	0.466	-	-
Preferred route; n (%)			0.693	-	-
Vagina	68 (53.1)	64 (57.1)		-	-
Cesarean	38 (29.7)	33 (29.5)		-	-
Never informed delivery*; n (%)	8 (6.2)	9 (8.0)	0.591	0.80 (0.27 to 2.42)	0.695
High to severe FOC; n (%)	15 (11.7)	30 (26.8)	<0.001	2.68 (1.29 to 5.56)	0.008

SD=standard deviation; AOR=adjusted odds ratio; CI=confidence interval; PPD=postpartum depression; CSMBS=civil servant medical benefit schemes; SSS=social security schemes; FOC=fear of childbirth

1 USD=34.23 Baht; * Never informed delivery: never been informed about delivery

Table 4. Comparison of the prevalence of severe FOC and associated factors

	O'Connell	Hendrix	do Souto	Elgzar	Present
Year	2019	2022	2022	2023	2024
Country	Ireland	Netherland	Portugal	Saudi Arabia	Thailand
Number of participants	298	364	462	342	271
Prevalence (nulliparity)	7.4%	11%	11.2%	6.7%	0.7%
Age (years)	32.2	30	31	24.58	29.5
GA (weeks)	18.42	27	-	32.53	34.7
Occupation	NS	-	NS	-	NS
Educational level	NS	NS	Significant	-	NS
Family income	-	-	-	-	NS
Family support	Significant	Significant	-	-	Significant
Planned pregnancy	-	NS	-	-	NS
Informed delivery*	-	Significant	NS	-	Significant
Preferred route	-	Significant	NS	Significant	NS

FOC=fear of childbirth; GA=gestational age; NS=not significant

* Informed delivery: informed about delivery

level of FOC^(13,15,22). A study from Sudan found no association between family support and FOC⁽²³⁾. The present study also found that lack of family support was a risk factor for FOC aligned with Hendrix's study⁽¹³⁾. In Thai culture, families often live together, including spouses and other family members. Even when not residing together, families maintain close communication, sharing emotional support and experiences, including childbirth experiences⁽²⁴⁾. This exchange of personal narratives helps alleviate fear, cultivates a positive outlook towards the impending delivery, and fosters a supportive environment for pregnant women. Such familial support reinforces women's confidence in childbirth as a natural and normal life event, contributing to their overall well-being and reducing FOC⁽²⁵⁾. This culture was reflected in the lower prevalence of severe FOC in Thailand.

Sheen & Slade's study in the year 2018 suggested that information regarding childbirth was associated with FOC⁽²⁶⁾. Gaining knowledge about childbirth can provide comfort to some women because it helps them to understand the rarity of certain complications and allows them to prepare for the birthing process⁽²⁶⁾. In Turkey, educating about childbirth, including coping with labor pain and preparation for labor pain was considered crucial and helped reduce FOC⁽²⁷⁾. The present study did find a significant association between inadequate information on childbirth and levels of FOC. In contrast, a study in Brazil found no significant association between knowledge about childbirth and FOC⁽¹⁰⁾. This difference came from the varied methods used to measure knowledge. The study in Brazil used a specific assessment tool, while the present study relied on subjective self-reporting.

FOC was not associated with having a preferred mode of delivery in the present study. This was inconsistent with previous studies^(5,14). Demšar et al.'s and Elgzar et al.'s reports found that nulliparous women with high level of FOC tend to request cesarean delivery^(5,14). FOC may influence pregnant women to favor cesarean delivery as an intervention to prevent such fear. The lack of association between FOC and the preferred mode of delivery in the present study could be attributed to the low proportion of severe FOC, which was 0.7%. Compared to a Demšar et al.'s study examining mode of delivery, the prevalence of severe FOC was around 7%⁽¹⁴⁾.

The prevalence of self-reported PPD was 46.7% (112 out of 240 participants), which was higher than in previous studies, where the prevalence of PPD ranged from 3% to 38%⁽²⁸⁻³⁰⁾. This difference may be attributed to the cutoff point and timing of

PPD assessment, which resulted in the significantly high prevalence observed in the present study. The high prevalence observed in the early postpartum period can also be attributed to conditions such as maternal blues that can occur in the first few days after delivery⁽³¹⁾.

The present study indicated that family income was a risk factor for PPD. Consistent with previous studies, families with lower socioeconomic status and lower incomes had higher risk of PPD⁽³²⁻³⁵⁾. This association could be attributed to advantages associated with higher incomes, such as enhanced access to healthcare services and greater support systems. Early and effective support may play a crucial role in mitigating the symptoms of PPD⁽³²⁾. Occupation was not associated with PPD in the present study after adjusting the results for other variables. This finding aligns with a 2021 Italian study that there was no association between working status and PPD⁽³⁴⁾.

High-to-severe FOC emerged as a predictive factor for early PPD among nulliparous women, increasing the prevalence of PPD 2.68-fold. This finding is similar to that of a study conducted in Finland⁽¹⁷⁾. Screening for FOC levels facilitates early detection and intervention for mothers at risk of PPD. In addition, FOC screening enhances the quality of prenatal care, improves interpersonal relationships, and promotes the mother's ability to create a supportive environment for her infant. To accomplish this, further assessment and follow-up may be necessary, as PPD is usually diagnosed within four to six weeks of childbirth⁽²⁸⁾.

A strength of the present study was the use of the WDEQ-A and EPDS questionnaires. Both questionnaires were used worldwide. Moreover, the present study revealed a significant association between FOC and PPD. This finding held potential for application in the Thai context. The present study's limitations included its cross-sectional design, which revealed correlational relationships without establishing causation or identifying causative factors of FOC. In addition, the research focused exclusively on a specific population comprising uncomplicated, nulliparous, low risk pregnancies, which may limit its generalizability. Thus, diverse populations and multicenter approaches should be considered in future studies.

In conclusion, the prevalence of high-to-severe FOC was 19.5%. Factors associated with FOC were lack of family support and knowledge about delivery. No family support was the only predicted factor

for FOC. FOC was a significant predictor of PPD. Therefore, evaluation of FOC during the antepartum period is recommended for early detection and intervention to enhance the quality of both prenatal and postpartum care for both mother and infant.

What is already known about this topic?

Severe FOC affects women globally with a prevalence ranging between 14% and 17%. FOC is associated with adverse outcomes, such as preterm birth, low birth weight, prolonged labor, and increased rates of cesarean sections. This can influence decisions regarding future pregnancies. Nulliparous women have higher level of FOC than multiparous women. Multiple factors were associated with FOC including occupation, educational level, household income, family and social support, information about childbirth, planning of future pregnancy, and preferred delivery route.

What does this study add?

This study found the prevalence of high-to-severe FOC among nulliparous women at TUH was 19.5%, with severe FOC affecting 0.7% of the participants. Lack of family support and insufficient knowledge about childbirth were the most significant factors associated with levels of FOC. This study also demonstrated that high-to-severe FOC is a significant predictor of PPD in the specific cultural and healthcare context of Thailand.

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Data availability

The data that supports the findings of this study is available on request from the corresponding author. The data is not publicly available due to privacy or ethical restrictions.

Conflicts of interest

The authors declare no conflicts of interest relevant to this article.

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