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## Maternal stress in the fetal anomaly screening process: A prospective cohort study

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## Abstract

**Background:** Fetal health and pregnancy outcomes are significant contributors to increased prenatal stress. The effect of fetal anomaly screening on a mother's stress is controversial. The present study aimed to explore maternal stress throughout a multi-stage anomaly screening program among healthy pregnant women.

**Methods:** This prospective cohort study was conducted at the public health centers of Sirjan, Iran from March 2022 to January 2023 using the convenience sampling process. The population included 228 healthy pregnant women. Data were collected using a researcher-made checklist for demographic and obstetrics characteristics. Cohen's Perceived Stress Scale (PSS) was utilized to measure maternal stress at three distinct intervals, including before (Weeks 6-10 of pregnancy), during (Weeks 11-14 of pregnancy), and after fetal anomaly screening tests (Weeks 15-20 of pregnancy). Friedman test was used for measuring the association between maternal stress and fetal abnormality test results. Data were analyzed with Statistical Package for the Social Sciences (SPSS) software version 26 at a significance level of 0.05.

**Results:** The mothers with higher educational levels (p = 0.05,  $\beta = 1.74$ ), and having a live child experienced lower levels of initial stress (p = 0.016,  $\beta = 2.27$ ). Throughout the time, receiving a normal nuchal translucency (NT) result was associated with a significant decrease in perceived mother's stress (p < 0.0001), and abnormal NT ultrasound results (Reported in 3.8% of women) led to a rise in the downslope of stress in the third measurement; however, it was not significant.

**Conclusion**: The present study revealed that maternal stress decreased over time following normal results of fetal anomaly screening. Three factors were associated with lower maternal stress, including university education, having at least a living child, and a normal ultrasound result. Moreover, women at first pregnancy and/or with an abnormal ultrasound result experienced high-stress levels. The findings may be useful in guiding the formulation of health policies and the distribution of resources.

# Highlights

## What is current knowledge?

- The escalation of prenatal stress is attributed to factors such as fetal health and pregnancy-related changes and outcomes.
- Fetal anomaly screening tests are commonly employed to reduce the likelihood of delivering a baby with abnormalities.

### What is new here?

- The findings of this study indicate that the normal results of fetal anomaly screening tests decrease pregnant women's levels of stress.
- University education, having at least one living child, and a normal ultrasound finding are three elements connected with decreased maternal stress.

#### Introduction

A growing body of literature indicated that psychosocial, cultural and environmental stressors experienced during gestation can be detrimental to maternal and fetal health. Moreover, prenatal stress can influence the physiological, behavioral, and cognitive development of offspring (1-6). The prevalence of prenatal stress is 16.5-74% in various societies, ranging from 16.5 to 74% in Iran (7).

Pregnant women often experience significant levels of anxiety and stress due to the fear of developing fetal abnormalities (8, 9). Approximately one-quarter of miscarriages and 4% of stillbirths are attributed to trisomies. Trisomy 21 is most commonly non-lethal and hence has been the main focus of genetic screening programs. Amniocentesis is a prenatal test that can diagnose genetic disorders (Such as Down syndrome and spina bifida) and other health issues in a fetus (10).

Screening in the first trimester of pregnancy helps determine the risk of the fetus having certain birth defects (11). A nuchal translucency (NT) test is an optional ultrasound performed in the first trimester of pregnancy that serves as an effective screening tool for high-risk pregnancies and fetal abnormalities. An increase in NT (Accumulation of fluid in the back of the fetus's neck) implies a higher likelihood of fetal chromosomal disorders and diseases, such as cardiac issues and genetic syndromes is revealed (12). NT ultrasound, with its minimal complications, is the preferred approach for screening fetal anomalies during the

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first trimester of pregnancy (13). The possibility of Down and Turner syndromes can be established by measuring NT between the 11th and 14th week of gestation and evaluating the major risk factors (14,15). It has been revealed that even in fetuses with normal standard karyotype, increasing NT is associated with cardiac problems or anomalies, pathogenic or potentially pathogenic genetic variations identified through whole exome sequencing (16). Pregnant women are subjected to a significant degree of stress while awaiting the results of non-invasive anomaly screening tests.

In addition to NT measurement, other ultrasound parameters, such as the fetal nasal bone, tricuspid valve flow, and maternal serum markers, are also used for fetal anomaly screening process (17). First-trimester combined testing has yielded detection rates of 90% for Down syndrome, 97% for Edward syndrome, and 92% for Patau syndrome, accompanied by a false positive rate of 4%. This accuracy is realized through the amalgamation of various biomarkers, which include maternal free beta-human chorionic gonadotropin ( $\beta$ -hCG), pregnancy-associated plasma protein (PAPP-A), NT, and maternal age (18).

Considering the ability of non-invasive screening tests to detect fetal abnormalities in the first trimester, pregnant women often experience significant anxiety and stress before the tests and while waiting for the results. In the following steps, at-risk or high-risk mothers are subjected to invasive diagnostic tests (19).

As an invasive diagnostic test, amniocentesis is a prenatal test usually performed during the second or third trimester of pregnancy. It can diagnose certain chromosomal conditions (Such as Down syndrome) or genetic conditions (Such as cystic fibrosis) (20). In addition to being extremely expensive, invasive tests like chorionic villus sampling (CVS) and amniocentesis carry a risk of miscarriage (21). For this reason, some high-risk pregnant women refuse to undertake invasive diagnostic testing, and they experience high levels of tension and worry until the conclusion of their pregnancy (22). Although prenatal genetic screening tests help couples decide whether to proceed with a possible pregnancy, many pregnant women fear the procedure because they think it will hurt them. They are also worried about adverse effects and fetal harm during the sample procedure (23). As a result, they may experience substantial mental and emotional stress (22). Although it has gotten less attention, the psychological impact of prenatal anomaly screening methods is important. It is also worth pointing out that most studies conducted so far have looked at the association

between prenatal stress and outcomes like preterm delivery, birth weight, and other variables (24). Nevertheless, there have been few studies on the relationship between fetal anomaly screening and maternal stress.

The current study explored the background factors influencing maternal stress. Furthermore, the study compared the level of prenatal stress experienced by pregnant mothers with/without the results of fetal abnormalities prior to, during, and after the fetal anomaly tests. The results indicate those who require additional help in coping with stress and provide an answer to the question of whether screening for fetal anomalies reduces a mother's stress. Initially, the study identified the fundamental variables influencing maternal stress and then, the stress levels of women with and without fetal anomalies were compared before, during, and after the fetal anomaly screening tests.

### Methods

## Study design and participants

This prospective cohort study was conducted at the public health center of Sirjan, Iran, from March 2022 to January 2023 using the convenience sampling process to measure the mean score of perceived stress. Referring to analogous research (25), a sample size calculation was conducted with an alpha level ( $\alpha$ ) of 0.05, a power of 90%, and a precision of 2%. Accounting for a potential 30% decline in response rates, the study required a minimum of 228 participants.

To be eligible for inclusion in the study, participants had to be in their 6th-10th week of a singleton pregnancy, consent to undergo fetal anomaly screening tests, including serological and ultrasonographic tests, and have no complication with the current pregnancy (e.g., preeclampsia, spotting, an incomplete mole, an ovarian cyst or myoma), have no history of or current known mental illness, have no known medical anomalies, as well as have no current chorionic diseases (e.g., diabetes mellitus, hypertension, hypothyroidism, etc.). The study neither included mothers who had previous children with any type of congenital anomaly, nor those who had a positive history of diagnostic or screening fetal anomaly tests in the previous or current pregnancy.

Exclusion criteria were unwillingness to continue the study, refusal to carry out diagnostic tests following abnormal results from screening tests, the presence of any maternal disease or an unusual occurrence in a normal pregnancy course (High blood pressure, gestational diabetes, thyroid disorders, etc.), and finally detection of any unusual results in the course of pregnancy, including bleeding, spotting, early rupturing of the membranes, miscarriage, mole, ectopic pregnancy. After explaining research objectives and procedure, written informed consent was obtained from eligible participants.

## **Data collection**

The Perceived Stress Scale (PSS) developed by Cohen, Kamarck (26) was applied for data accumulation. Additionally, the individual would provide background details, including age, level of education, occupation, economic status, number of children, number of pregnancies, family history, and type of pregnancy (Wanted or unwanted pregnancy). For illiterate subjects, it would be completed by a midwife or a health expert.

## Instrument

### Perceived Stress Scale (PSS)

The PSS-14 is comprised of 14 items intended to measure how unpredictable, uncontrollable, and overloaded individuals find their life circumstances. It was developed by Cohen et al. (1983) (26). Each item is rated on a 5-point Likert scale, ranging from 0 = 'never' to 4 = 'very often'. Scores range from 0-56, with higher scores indicating greater perceived stress. Respondents' scores on the PSS-14 are intended to be compared to the larger sample. Scores are obtained by reverse scoring the positively stated items (items number 4, 5, 6, 7, 9, 10, and 13) and then summing the scores across all 14 items. A score of 0 to 18 indicates a low level of stress, 18 to 36 indicates moderate stress, and above 36 indicates a high level of stress. This questionnaire's validity was established through the use of a correlation coefficient of 0.63, a value that is statistically significant at p <0.05 level. Also, Bastani et al. applied PSS-14 in Iranian population and confirmed its reliability (Cronbach's alpha = 0.74) (27). Maroufizadeh et al. proved the validity of the Persian version of the 10-item PSS in adult asthmatic patients (28).

## Procedure

Initially, background variables were measured by a researcher-made questionnaire. Then, and all participants filled out the PSS-14 questionnaire at 6-10 weeks of pregnancy.

Maternal serum fetal anomaly screening (Free- $\beta$ -hCG and PAPP-A) and NT ultrasonography were required of all individuals at comprehensive health centers between weeks 11 and 14. Based on the likelihood that the fetus would have trisomy 13, 18, or 21 syndromes, the test was conducted using a maternal serum sample, and the findings showed low-risk, at-risk, or high-risk conditions. Additionally, NT ultrasound was conducted using the fetus's Crown-rump length (CRL) and the clear, bright space behind its neck as measurements. An abnormally high NT level was associated with a higher chance of trisomy 21 and fetal cardiac problems. Ultimately, the laboratory assessed the outcomes of maternal serum test and NT measurement to classify the mothers as belonging to either the low-risk or high-risk category.

After the first-trimester screening test (Weeks 11-14), a second stage of evaluation was carried out and the participants were divided into three groups:

low-risk, at-risk, or high-risk. When they had all been given their screening results, the subjects completed the PSS questionnaire. Without additional help, the low-risk group keeps their pregnancy going. It is recommended that the at-risk group get screening tests during the second trimester of pregnancy. The high-risk group was referred to a gynecologist or perinatologist for invasive diagnostic testing (Amniocentesis or CVS) to determine whether to terminate the pregnancy.

The last assessment of perceived stress was performed in the third stage of evaluation, in the 15-20 weeks of pregnancy, as follows: in the Low-risk group, the perceived stress was evaluated while completing standard pregnancy care at the health facility.

Following the results of screening tests (15-20 weeks), at-risk group participants were assigned to low-risk or high-risk groups, and the perceived stress in the groups (Low-risk or high-risk) was assessed. After obtaining the findings of invasive amniocentesis or CVS test, perceived stress was measured in the high-risk group. Finally, changes in pregnant mothers' perceived stress were assessed.

## Statistical methods

The Kolmogorov-Smirnov test was employed to analyze the normality of the stress score of expectant women in aggregate and in each demographic subgroup. In addition, the Freidman test and linear regression were used to compare the stress levels of background variables across two or more states. Friedman test was used for measuring the association between maternal stress and fetal abnormality test results. Data were analyzed with Statistical Package for the Social Sciences (SPSS) software version 26 at a significance level of 0.05.

### Results

In total, 228 women completed all three surveys (Response rate 79.21%). The results revealed that 86.4% (197) were 35 and younger, 88.6% (202) were housewives, and 26.3% (60) were in marriages with relatives. Also, 31.6% (72) had no children and 8.8% (20) had unwanted pregnancies (Table 1).

The findings demonstrated that education had a positive effect on the participants' initial stress levels, with university-graduated women reporting lower stress levels than those with a diploma degree or less (P=0.05,  $\beta$ =1.74). Also, there was a significant difference (P=0.016,  $\beta$ =2.27) between the group with previous live child and the group without. This implies those having at least one child were less stressed. Table 2 summarizes the variations for all subjects with/without typical NT ultrasound. The level of stress measured in all pregnant women indicated that the perceived stress on the first attempt was higher than on the second (P=0.0001) and the third times (p <0.0001).

Figure 1 depicts the trend of stress changes in all three groups (All participating pregnant women, pregnant women with abnormal NT ultrasound, and pregnant women with normal NT ultrasound).

Table 1. The demographic characteristics of pregnant mothers and analysis of
maternal perceived stress in subgroups

Variables	Ν	%	Stress (6-10)			P-value**				
Variables IV /0 Mean (SD) Deta Beta IV and										
Age groups										
<u>≤ 35</u>	197	88.3	47.54 (6.54)	-	-	0.082				
> 35	> 35 26 11.7 45.19 (5.31) -2.35 (-4.99, 0.30)									
Education										
Diploma and less	132	57.9	46.55 (6.92)	-	-	0.050				
University degree	96	42.1	48.30 (5.73)	1.74	(-0.001, 3.49)					
Women job										
Housewife	202	88.6	47.40 (6.55)	-	-	0.500				
Employee	26	11.4	46.64 (6.69)	- 0.92	(-3.66, 1.81)	0.506				
Husband job										
Employee	106	46.5	47.25 (6.08)	-	-					
Self- employed	122	53.5	47.38 (6.99)	0.19	(-1.55, 1.92)	0.832				
			Familial ma	rriage						
Yes	60	26.3	48.18 (6.56)	-	-	0.000				
No	168	73.7	47.01 (6.54)	- 1.06	(-3.02, 0.91)	0.289				
			Husband di	sease						
Yes	6	2.6	47.40 (9.81)	-	-	0.897				
No	222	97.4	47.32 (6.49)	0.35	(-4.98, 5.68)					
			Income							
Low and medium	127	56.2	47.43 (6.54)	-	-	0.978				
Good	99	43.8	47.16 (6.64)	- 0.03	(-1.79, 1.74)					
Number of children										
No children	72	31.6	45.79 (5.18)	-	-	0.014				
One or more	156	68.4	48.06 (6.95)	2.27	(0.44, 4.11)	0.016				
Type of pregnancy										
Normal	208	91.2	47.51 (6.58)	-	-	0.094				
Unwanted or with medication	20	8.8	45.22 (5.98)	- 2.62	(-5.69, 0.45)					

\*Regression coefficient, \*\*p-value of linear regression model

Table 2. Stress changes trend in pregnant women at three stages before (6-10 weeks), during (11-14 weeks) and after (15-20 weeks) fetal anomaly screening

Channe based fotel enemoty severating results	Stress 6-10		Stress 11-14		Stress 15-20		P-value*
Groups based fetal anomaly screening results	Mean (SD)	Mean rank	Mean (SD)	Mean rank	Mean (SD)	Mean rank	r-value"
Total (N=213)	47.32 (6.55)	2.30	45.09 (5.49)	1.93	44.03 (5.10)	1.77	< 0.001
Abnormal (N=6)	48.33 (7.39)	2.42	43.50 (2.35)	1.67	45.00 (3.69)	1.92	0.223
Normal (N=207)	47.29 (6.54)	2.29	45.14 (5.55)	1.94	44.00 (5.13)	1.77	< 0.001

\* P-value of Friedman test

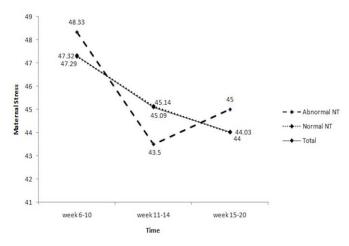


Figure 1. Level of perceived stress in pregnant women participating in the study.

As illustrated in Figure 1, the perceived stress of the pregnant women in the study was 47 in the initial phase, 45 in the second phase, and 44 in the third phase. There was an increase in stress before the screening test, but it was reduced following the tests. Besides, the initial measurement of perceived stress in pregnant women with abnormal NT ultrasound was 48, whereas dropped in the second and third levels.

#### Discussion

Our findings revealed that the mean perceived stress levels during weeks 6-10 were significantly higher than those observed in weeks 15-20. These are in agreement with other studies conducted on healthy singleton pregnant women that demonstrate a decrease in maternal stress over time (29,30). The researchers identified that the primary sources of stress during pregnancy stem from concerns about abortion, fetal development, prenatal results, and physical changes associated with pregnancy (31,32). By utilizing sonography to track fetal growth and surpass the high-risk abortion period in the first trimester, women can adapt to the changes of pregnancy more effectively, leading to a reduction in maternal stress over time.

The abnormal outcome of maternal serum screening test or NT in the ultrasound suggested a high likelihood of fetal anomaly, thus requiring an invasive diagnostic test (Amniocentesis or CVS). The findings of the present research indicated that despite the use of these highly precise diagnostic tests, maternal stress did not decrease. Other investigations have evidenced the impact of fetal abnormalities diagnosis on the psychological well-being of mothers and the amount of perceived stress they endure (33,34).

The prevalence of fetal abnormalities in each nation has an extensive effect on the health of mothers. Previous studies have established a prevalence of 2.3% (35) and 2.6% in Iran (36). In the present study, six women received abnormal NT ultrasounds, which is consistent with other Iranian studies. Furthermore, this study aimed to explore the association between sociodemographic characteristics and maternal-reported stress. The results highlighted the important role of educational level and having at least one live child in decreasing basic maternal stress. Educational attainment plays a pivotal role in mental health (37). There is a growing amount of evidence exhibiting the positive influence of educational level on women's stress during pregnancy, delivery, and postpartum (38-40).

Low educational level as a principal social determinant may be a harbinger of a lower quality of life and a rise in maternal stress. Pregnant women of higher educational levels may be more likely to seek information about their concerns on scientific websites, discuss their fears with healthcare providers, understand the explanations provided, and grasp the accuracy of screening tests.

Although our study found no significant relationship between the number of children and maternal stress, having at least one previous live birth was associated with a decrease in pregnancy-specific stress. Previous studies demonstrated a substantial effect of the number of existing live births on stress during pregnancy (41-43). Based on previous experiences and challenges that resulted in a positive outcome, the mother's self-assurance was reinforced during the subsequent pregnancy. Although pregnancy is a novel experience for all mothers, previous pregnancies can alleviate the anxiety of facing unfamiliar and

unforeseen pregnancy difficulties. Though maternal stress has multiple sources, our research did not identify any additional factors that correlated with maternal stress levels. A larger sample size may have uncovered additional factors that could influence stress levels.

Overall, the mean perceived stress was 47 during weeks 6-10, with any score in above 36 considered a high amount of stress according to PSS. According to the PSS employed in other studies in Iran, the average stress score of healthy pregnant women was found to vary between 24 and 28 (44-46).

Zareipour et al. showed that 17.7% of pregnant women experienced high levels of stress (47). All of these articles showed a high level of maternal stress; however, the perceived stress score in our results was evidently higher than in previous studies (Approximately 47 compared to 24-28 in healthy women). The stress level in our study was even higher than perceived stress in mothers undergoing amniocentesis. It appears that confounding factors, such as the COVID-19 pandemic and the subsequent vaccination campaigns have led to this significant increase.

This study coincided with the outbreak of COVID-19 in Iran, and this unprecedented event might have affected maternal stress. Additionally, before our study began, a nationwide program for vaccinations was initiated against COVID-19 during pregnancy period, raising serious apprehensions about the potential for fetal mortality or morbidity in the wider population due to the use of the novel vaccine during pregnancy. Consistent with our results, other studies reported that pregnant women experienced a significant level of stress during the COVID-19 pandemic (48-50).

This study was conducted during a new wave of mass COVID infections and the introduction of a vaccination program for pregnant women, creating a challenging environment that resulted in serious mental and emotional problems. Designing a study under less stressful conditions with a higher sample size would provide more precise data.

#### Conclusion

The findings of this study demonstrated that pregnant women experience significant stress, especially those who are in the first pregnancy and those with unusual ultrasound results. In addition, women with a university degree and a normal ultrasound who had a second or subsequent pregnancy experienced significantly less stress than other women. For women with normal screening results, maternal stress levels decreased over time, while for those with abnormal NT sonography results, the stress level remained unchanged.

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#### Ethical statement

The ethical committee of Sirjan School of Medical Sciences approved this research (Ethics code: R.SIRUMS.REC.1400.018). Written informed consent was obtained from all participants. The participants' data were gathered and examined confidentiality, and the participants joined the study with full awareness and the liberty to withdraw from the research at any time.

## **Conflicts of interest**

The authors have no competing interests to declare.

## **Author contributions**

FA-A and BZ designed the study and carried out the necessary steps before starting the study. Coordination with health centers and data collection were done by MT and data analysis was done by MRB and M MA, F A-A, BZ, AI and S SM wrote the main manuscript text. All authors read and approved the final manuscript.

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