

# Investigating the Effect of Second Trimester Fetal Anatomy Scan Soft Marker Findings on the Intolerance of Uncertainty

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## ABSTRACT

Prenatal diagnosis is essential for allowing for early detection of fetal anomalies. Soft markers, detected during fetal anomaly scans, are of uncertain significance. Most soft markers are transient; their detection can induce psychological distress. The relationship between soft markers, genetic conditions, and maternal psychological responses remains an area of investigation.

This cross-sectional study included 67 pregnant women with isolated fetal soft markers identified during routine second-trimester anomaly scans at a tertiary perinatal care center. Participants completed the Intolerance of Uncertainty Scale, Brief Symptom Inventory, and Coping Orientation to Problems Experienced Inventory. Sociodemographic and obstetric data were collected from medical records. Descriptive statistics were reported as mean  $\pm$  SD, median (interquartile range) and frequency (percentage).

The most frequently observed soft markers were echogenic intracardiac focus (40.3%) and echogenic bowel (32.8%). Higher intolerance of uncertainty scores were significantly associated with ventriculomegaly, thickened nuchal fold, and choroid plexus cyst. The presence of multiple soft markers did not result in higher intolerance of uncertainty scores. Religious coping was the most commonly used strategy, while substance use was the least employed. Anxiety and depression were the predominant, with moderate distress levels detected on the BSI.

The identification of soft markers may contribute to maternal psychological distress, with the severity of the response influenced by the specific ultrasonographic finding. The level of education and perceived economic status also play roles in shaping maternal risk perception. Enhanced prenatal counseling, incorporating clear risk communication strategies, may help mitigate anxiety and reduce intolerance of uncertainty.

**Keywords:** Soft marker, Intolerance of Uncertainty, Prenatal screening, Anxiety

## Introduction

Prenatal diagnosis is one of the main components of prenatal care. Therefore, management plans for current and future pregnancies can be structured accordingly (1, 2). The most common genetic anomalies that are detected with the help of prenatal diagnosis, are aneuploidies (1, 3). Soft markers are ultrasonographic findings with unknown importance and can be seen in totally normal fetuses as a variant. They are occasionally temporary and are not related with permanent sequelae (4, 5). Increased nuchal translucency, absence of nasal bone, hyperechogenic bowel, pyelectasis, shorted fetal long bones, hyperechogenic intracardiac focus, choroid plexus cysts are examples of ultrasonographic soft markers. Second trimester fetal anatomy scan is

recommended for all pregnant women after 18 gestational weeks (6, 7). Prenatal genetic counseling is beneficial if there are abnormal screening results or ultrasound findings.

Explanation of a common variant of normal as a possible cause of negative outcome (eg. a genetic disease), can be challenging from time to time and has negative impact on the expecting mother's mental status. Detection of soft markers during prenatal care can cause a wide spectrum of psychiatric issues, mainly anxiety (8). Regardless of the realization of the specific event, the potential possibility is unacceptable in women who have avoidance of uncertainty. The people with intolerance to uncertainty, respond in unpredictable ways of emotion, thought and behavior to uncertainty, thus an increase in their stress and anxiety level can be expected (9).

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Soft markers detected in the second trimester fetal anatomy scan may have different association levels with major anomalies or genetic conditions. In this research, we aim to investigate the impact of the type of ultrasonographic finding and its association with genetic disorders on uncertainty intolerance.

## Materials and Methods

This was a cross-sectional study of women who had appointment at a perinatal care center for second trimester fetal anatomy scan. Ultrasonographic soft marker positive patients were included in the study after being informed and a consent form obtained, asked to complete the Sociodemographic and Data form, Intolerance of Uncertainty Scale (10), Brief Symptom Inventory (11) and Coping Orientation to Problems Experienced Inventory (12) upon admission. A sociodemographic form consisted of eight questions regarding marital status, age, education level, perceived economic status, presence of any psychological illness, history of medication prescribed by a psychiatrist and whether the current pregnancy was planned or not. The exclusion criteria were a history of somatic and/or psychiatric disease and poor understanding of the study protocol. Maternal and obstetric data were obtained from electronic medical records. The patients who had findings other than soft markers were excluded, such as major structural anomalies.

The IUS-12 is a validated self-report questionnaire designed to measure an individual's tendency to find uncertain situations distressing and to have difficulty functioning in the face of ambiguity. It consists of 12 items derived from the original 27-item Intolerance of Uncertainty Scale, covering two dimensions: prospective anxiety (anticipatory worry about future events) and inhibitory anxiety (avoidance or paralysis in uncertain contexts). Each item is rated on a 5-point Likert scale ranging from 1 ("not at all characteristic of me") to 5 ("entirely characteristic of me"), with total scores ranging from 12 to 60; higher scores indicate greater intolerance of uncertainty. The Turkish version of the IUS-12 has been shown to have good internal consistency and construct validity in nonclinical and clinical populations (10). In this study, the total score was used for analysis.

The BSI typically has a range from 60 to 240, with a higher score indicating greater distress. 117 is above the threshold for moderate distress, and it may indicate that the person is experiencing

noticeable psychological symptoms such as anxiety, depression, or other distressing feelings.

There are 60 items and 15 first-order factors (4 items each) in the multidimensional COPE Inventory assessment. The first-order components are predicated on prior study findings that identified elements that promote and inhibit adaptive coping, as well as theoretical presumptions regarding functional coping (13). These are the first-order factors: 1. Acceptance: embracing the circumstances; 2. Active coping: taking particular steps to address the circumstance; 3. Reactive reluctance to cope with stress is known as behavioral disengagement. 4. Denial: rejecting the situation's actuality; 5. Looking for emotional support: depending on other people's compassion and comprehension; 6. Humor: making jokes about the circumstances; 7. Seeking instrumental assistance: asking for knowledge or guidance from others; 8. Mental disengagement/self-distraction: engaging in activities that divert the individual's attention from disagreeable ideas associated with the issue; 9. Planning: coming up with a strategy for handling a difficult circumstance; 10. Positive reinterpretation: identifying the good aspects of a difficult circumstance; 11. Religion: turning to religious practices, including prayer, as a coping mechanism; 12. Exercise restraint by avoiding a reactionary reaction to stress; 13. Substance abuse: utilizing drugs to cope with an upsetting circumstance; 14. Suppression of competing activities: purposefully refraining from actions that don't assist the individual in resolving the issue; and 15. Venting: expressing unpleasant feelings.

**Statistics Analysis:** This study employed a single-center, observational, cross-sectional design to examine the relationship between second-trimester soft markers, intolerance of uncertainty, coping strategies, and psychological distress in pregnant women. Descriptive statistics were performed. Descriptive statistics were reported as mean $\pm$ SD, median (interquartile range) and n (percentage).

All analyses and figures were created using STATA software, version 18.0 Basic Edition (Copyright 1985-2021 StataCorp LLC).

Research involving human subjects complied with all relevant national regulations, institutional policies and is in accordance with the tenets of the Helsinki Declaration (as revised in 2013), and has been approved by the authors' Institutional Review Board (Zeynep Kamil Women and Children's Diseases Training and Research Hospital) (Decision number: 139/2022).

## Results

A total of 67 women who had fetal soft markers detected in routine ultrasound scan were included. Table 1 demonstrates clinical characteristics of the cohort.

The mean age of the population was found to be 29 and the majority of the women were graduated from college revealing that 2<sup>nd</sup> trimester anomaly scan is more available in the high education group. The perceived economic status was found to be average in the 2<sup>nd</sup> trimester anomaly scan, which is correlated with the education level.

The most common ultrasonographic soft marker was found to be echogenic intracardiac focus (40%) and the second was found to be echogenic bowel (32.8%). The patients who had three or more soft marker positivity were 3%.

Median scores of the cohort were 37 (Interquartile range 28-45) for IUS-12 scale, 144 (Interquartile range 126-158) for COPE scale and 59 (Interquartile range 31-117) for BSI. Table 2 shows detailed scores of the cohort with subscales.

COPE inventory score results showed that our study population was mostly driven to religious coping mechanisms and substance use was the least used coping method. This may be related with the study population including pregnant women only. Considering BSI, the two most common findings were depression and anxiety.

Figure 1 demonstrates median IUS-12 scores based on the type of soft marker, educational and economic status and the number of soft markers detected.

Higher scores for IUS-12 were found to be related with ventriculomegaly, thickened nuchal fold and choroid plexus cyst (>40 points). The education level under high school grade seems to increase the intolerance of uncertainty score. Interestingly, the presence of three or more soft markers does not lead to higher intolerance of uncertainty scores, despite their association with an increased risk of genetic anomalies. However, it is important to note that this finding is based on only two patients with this condition.

## Discussion

Soft markers detected during the second-trimester fetal anomaly scan have been associated with heightened levels of anxiety and depression, with the degree of intolerance to uncertainty varying based on the specific pathology identified.

Psychological responses to such findings were linked to variations in patients' coping mechanisms, with strategies such as religious coping and positive reinterpretation being commonly employed to mitigate distress. Understanding these adaptive processes is essential for improving patient counseling and emotional support during prenatal care.

Uncertainty in pregnancy appeared to vary according to cognitive capacity, the familiarity to the specific finding, and the understanding of the perinatal risk concept (14). In our study, it is observed that the education level under high school is correlated with higher intolerance of uncertainty scores (Figure 1). The healthcare provider may focus on the ultrasonographic finding in their perspective, however the psychological impact on pregnant women ranged from minimal concern to depressive symptoms and was related to education level.

Uncertainty about the pregnancy and possible scenarios has been linked to effect on families from the first idea of child bare including the period that couples try to conceive (15). The psychological stress is heavier at the time when the time is important and there is risk of pregnancy loss (15). Understandably, after the antenatal care starts, intolerance of uncertainty, depending on the risk level of the pregnancy and the expecting mothers' familiarity to the concept, may be connected with higher distress levels.

Even the type of the prenatal screening method appeared to influence perceived risk and what is more, subtypes of techniques may also interfere; for example, expecting mothers who underwent a more expanded-panel test were more likely to report higher perceived risk (16). The IUS-12 is designed so that higher scores indicate a greater intolerance of uncertainty. With a median score of 37, it might be safe to say that our cohort experience a moderate level of distress when faced with uncertainty. In practical terms, this suggests that ambiguous or unpredictable situation such as having a fetal soft marker may be somewhat uncomfortable or stressful, but the intolerance is not at an extreme level. In this project we uncovered that different ultrasonographic findings at different levels of clinical and statistical importance, can have a wide spectrum of detrimental effects caused by uncertainty.

Ultrasonographic findings and genetic outcomes did not differ in terms of risk perception (17). However, in our research we found out that some ultrasonographic findings may increase the

**Table 1:** Sociodemographic and Clinical Characteristics of Women With Fetal Soft Markers

Age (years)	29 (19-40)
Parity	
Nulliparous	39 (58.2)
Parous	28 (41.8)
Number of prior children	1 (0-5)
Education	
Primary school	7 (10.5)
Secondary school	15 (22.4)
Highschool	17 (25.4)
College	27 (40.3)
Masters	1 (1.5)
Perceived economic status	
Low	2 (3)
Average	53 (79.1)
High	12 (17.9)
Unintended pregnancy	
No	46 (68.7)
Unintended pregnancy	21 (31.3)
Type of soft marker	
Echogenic intracardiac focus	27 (40.3)
Echogenic bowel	22 (32.8)
Urinary tract dilatation	14 (20.9)
Choroid plexus cyst	7 (10.4)
Nasal hypoplasia	6 (8.9)
Single umbilical artery	3 (4.5)
Aberrant right subclavian artery	3 (4.5)
Ventriculomegaly	2 (3)
Thickened nuchal fold	1 (1.5)
Shortened femur/humerus	1 (1.5)
Number of soft markers	
1	50 (74.6)
2	15 (22.4)
3 or more	2 (3)

\*Data represented as median (range) or n (percentage).

intolerance of uncertainty behavior. Ventriculomegaly, thickened nuchal fold and choroid plexus cyst were found to be most related with higher intolerance of uncertainty scores (Figure 1). We can argue that the greater its clinical importance, the more it seemed to relate to differences in risk perception and psychological stress. A study which was conducted in first trimester pregnant women undergoing nuchal translucency measurement, revealed that the women who were at real high risk were, half as the women who perceived themselves at high risk (18).

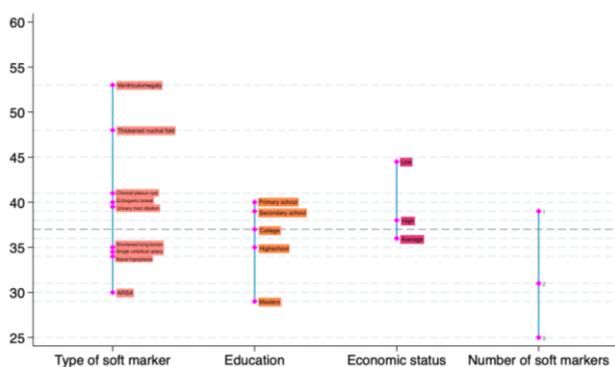
The overall COPE inventory score is in our cohort is 144, indicating a substantial use of various coping strategies. Notably, religious coping stands out with the highest score of 14, suggesting that reliance on spiritual or religious beliefs was common among those managing stress. This might be explained by the majority of our cohort consisting of Muslim women. Other adaptive, problem-focused strategies-such as positive reinterpretation and growth, active coping, instrumental social support, and planning-are also used frequently, each scoring around 12. In contrast, strategies that are generally considered

**Table 2:** IUS-12, COPE and BSI Scores of Women With Fetal Soft Markers

IUS-12	37 (28-45)
COPE	144 (126-158)
Positive reinterpretation and growth	12 (10-15)
Mental disengagement	10 (9-12)
Focus on and venting of emotions	11 (9-13)
Use of instrumental social support	12 (10-13)
Active coping	12 (10-13)
Denial	7 (5-8)
Religious coping	14 (12-16)
Humor	7 (5-9)
Behavioral disengagement	7 (4-9)
Restraint	9 (7-10)
Use of emotional social support	10 (7-12)
Substance use	4 (4-7)
Acceptance	9 (8-11)
Suppression of competing activities	11 (9-13)
Planning	12 (10-13)
BSI	59 (31-117)
Anxiety	24 (1-38)
Depression	20 (3-37)
Somatization	5 (2-19)
Hostility	5 (2-15)
Interpersonal sensitivity	5 (2-27)

Abbreviations: IUS 12, Intolerance of Uncertainty Scale; BSI, Brief Symptom Inventory and COPE, Coping Orientation to Problems Experienced Inventory

\*Data represented as median (IQR).



**Fig. 1.** Median IUS-12 scores based on type and number of soft markers, educational and perceived economic status

more avoidant or less adaptive, such as denial, humor, and behavioral disengagement, have lower scores of around 7, with substance use being the least common at a score of 4. Overall, these results suggest that individuals in this cohort tend to lean toward proactive and adaptive coping

methods rather than avoidant or potentially harmful strategies.

In this cohort of pregnant women, the overall psychological distress level—as measured by the Brief Symptom Inventory (11)—is moderate, with a global score of 59 (IQR 31–117). Anxiety emerges as the most prominent symptom, with a score of 24 (IQR 1–38), suggesting that feelings of nervousness or worry are relatively noticeable. Depressive symptoms are present as well, though to a slightly lesser extent, with a score of 20 (IQR 3–37). In contrast, symptoms related to somatization (physical expressions of distress), hostility, and interpersonal sensitivity are minimal, each registering a score of 5 (IQR 2–19, 2–15, and 2–27 respectively). Overall, these results indicate that while some anxiety and depressive symptoms exist within the cohort, other areas of psychological distress remain low.

This study is subject to certain limitations. The relatively small sample size ( $n = 67$ ) may limit statistical power and the precision of estimates.

The single-center design may introduce selection bias and limit the representativeness of the study population. Furthermore, the cross-sectional design precludes causal inference and restricts conclusions to associations observed at a single time point. These factors should be considered when interpreting the results and extrapolating them to other populations.

Soft markers of aneuploidy have had a shift in importance the last years because of the increasing availability of cell-free DNA, however a low-risk cfDNA result does not decrease the importance of the fetal anomaly scan (19) and thus these findings still need to be clarified, explained and managed. The consultation encounter should include a well description of the risk analysis to have better understanding of the concept and to avoid triggering intolerance of uncertainty, depression and anxiety.

In this single-center, cross-sectional study, the presence of specific second-trimester soft markers was linked to higher intolerance of uncertainty, with ventriculomegaly, thickened nuchal fold, and choroid plexus cyst showing the strongest relationships. Moderate levels of psychological distress were observed, with anxiety being the most prominent symptom, and adaptive coping strategies-particularly religious coping-were frequently reported. These findings highlight the importance of incorporating psychological assessment and tailored counseling into prenatal care for women with soft marker findings. While the study design precludes causal inference, the observed associations underscore the need for prospective, multicenter research to better understand these relationships and inform supportive interventions.

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