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Antenatal depression and anxiety during the COVID-19 pandemic: a cross-sectional study in pregnant women from routine health care contact in Greece

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Short title: Antenatal depression and anxiety during the COVID-19 pandemic in low-risk pregnant women in Greece.
Author contributions: Themistoklis Dagklis developed the original idea for the study, coordinated recruitment, interviewed patients, recorded patient data. Ioannis Tsakiridis designed, coordinated, implemented the project, evaluated the results. Apostolos Athanasiadis and Rebecca Pearson participated in the revision. Apostolos Mamopoulous supervised sample extraction and cooperated in results’ analysis. Georgios Papazisis participated in statistical analysis, evaluated the results and also supervised the manuscript development. All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Abstract

Objectives: The impact of the COVID-19 pandemic and the public health measures introduced to control it, on mental health, is largely unknown. Research conducted during past epidemics found that pregnant women are more vulnerable psychologically. The aim of this study was to investigate antenatal depressive and anxiety symptoms during this pandemic in Greece.

Methods: All women receiving routine antenatal care, during a three-month period, starting one week after the total lockdown in Greece, in a University department, were asked to fill in two questionnaires, the Edinburg Postnatal Depression Scale (EPDS) and the State-Trait Anxiety Inventory (STAI).
**Results:** Overall, 505 women (93.3% of the eligible population) agreed to participate. The prevalence of antenatal depression (EPDS score $\geq 13$) in the population of the study was 13.5%. Unplanned pregnancy (OR: 2.447; 95% CI: 1.235-4.846), smoking (OR: 2.268; 95% CI: 1.166-4.411) and antenatal anxiety (OR: 5.074; 95% CI: 2.898-8.883) increased the risk of antenatal depression during the COVID-19 pandemic. State (current)-anxiety affected 34.1% of the participants, whereas Trait (lifetime)-anxiety affected 15.8%. The State-anxiety score (median) was significantly higher than the Trait-anxiety (median) (41 vs 36; $p <0.001$), revealing an increase in the levels of anxiety in the pandemic, while there was also a positive linear correlation between the two scales ($\rho h o=0.592; p<0.001$).

**Conclusions:** The unprecedented situation of the COVID-19 pandemic has increased anxiety, but not depression levels of pregnant women in Greece. Population level interventions to address adverse effects on anxiety status in the initial phases of similar situations may be helpful in the future.

**Keywords:** COVID-19, depression, anxiety, EPDS, STAI, pregnancy
Introduction

The new coronavirus disease (COVID-19) was first detected in Greece on February 26, 2020. Then, on March 22, a total lockdown was enforced nationwide, as all citizens were asked to restrict themselves at home, a situation that lasted six weeks. As this was an unprecedented condition, the psychological impact could not be estimated, especially since at the beginning of the lockdown the exact duration was impossible to predict [1]. Previous studies on the effect of isolation on psychological wellbeing, reported a high prevalence of psychological symptoms of distress including depression, anxiety, irritability, insomnia, anger, fear, sadness, nervousness, guilt, post-traumatic stress symptoms and suicidality [2-5]. Moreover, based on the experience of previous epidemics (SARS and MERS), pregnant women may be prone to mental health disorders under such stressful conditions [6, 7].

Both antenatal depression and antenatal anxiety are common conditions, affecting approximately 15% [8] and 18% of women, respectively [9], according to data from Europe. A meta-analysis including 162120 women found a 6.3% incidence of coexisting antenatal anxiety and depressive symptoms [10]. The study of antenatal mental health is of major importance, since it has considerable negative consequences on perinatal outcomes; antenatal depression has been associated with adverse outcomes, including fetal growth restriction, preterm delivery and higher rate of neonatal intensive care unit admission [11]. In addition, many studies that investigated the relationship between antenatal anxiety and adverse perinatal and long-term outcomes, found a significant association with preterm delivery, low birthweight, small for gestational age neonates, smaller head circumference at birth, as well as child behavioral issues [12, 13].
The measures implemented to control the COVID-19 pandemic obviously intent to protect the lives of people in the short-term. However, to date, scarce data exist regarding their effects on the psychological status of pregnant women, which in turn may cause long-term adverse effects on perinatal outcomes. The aim of this study was to investigate the prevalence of depressive and anxiety symptoms and possible risk factors, during the COVID-19 pandemic, in pregnant women in Northern Greece.

Methods

*Study design, setting and participants*

This was a cross-sectional study conducted for 12 consecutive weeks, starting one week after the implementation of the total lockdown in Greece, in the Third Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki; this a tertiary center providing coverage to a population of more than two million people.

Low-risk pregnancies were offered a minimum of three ultrasound scans during the pandemic, at 11-14, 20-24 and 30-34 gestational weeks, as part of their routine prenatal care. During the study period, these scans were offered routinely, despite the strict measures. All pregnant women that attended the antenatal clinic for a scheduled scan were eligible to participate in the study, provided they had graduated at least from the 6th grade of elementary school (lower educated women were excluded according to the Spielberger State Anxiety Index developer [14]). Further exclusion criteria were prior diagnosis of mental disorder, as well as pregnancies complicated by obstetric or medical comorbidities (identified as high-risk). The study population recruitment was conducted by two obstetric consultants (I.T. and T.D.). Sociodemographic characteristics, medical and obstetric history were recorded for each individual participant as part of the routine antenatal assessment.
Of note, this study is part of an ongoing research that focuses on the mental health of pregnant women. Preliminary data from the lockdown period have been published as a letter to the editor [15].

**Measures**

**Depression**

The most widely used questionnaire for depression screening, both in the antenatal and the postnatal period, is the Edinburg Postnatal Depression Scale (EPDS) [16, 17]. The EPDS is considered an accurate screening tool, for the prompt recognition of possible depression symptoms [18]. Each of the 10 selfanswered items that are included in the scale, receives a score between 0 and 3; hence the complete score ranges from 0 to 30 [19]. The EPDS has been validated for the pregnant population in Greece, with a high internal consistency; Cronbach’s alpha was estimated up to 0.90 [20]. A previous study conducted in Greece, in the postpartum period, found that the optimal cut-off was 9 for minor (sensitivity: 77%; specificity: 68%) and 13 for major depression (sensitivity: 88%; specificity: 86%) [18]. Since the EDPS cut-off point is higher during pregnancy, compared to the postnatal period [21], in the present study, a cut-off score $\geq 13$ was applied for the detection of symptoms of depression.

Of note, the EPDS questionnaire was administered from the second week of lockdown, as it was developed to assess depression symptoms of the past seven days. In addition, in cases with EPDS $\geq 13$ (probably depressed) a psychiatric consultation (by G.P.) was offered, while for women who scored positive in the suicide question of EPDS (#10), an urgent psychiatric referral was deemed necessary.
Anxiety

The anxiety status was assessed using the Spielberger State Anxiety Index - STAI (Form Y) [14], the most commonly used measure of antenatal anxiety [12], which had been validated in the population of Greece [22]. This is a 40-item, questionnaire which incorporates two types of anxiety: the first 20 items evaluate State anxiety (S-anxiety), which refers to current, transient, situational feelings and the next 20 items evaluate Trait anxiety (T-anxiety) which involves general, ongoing feelings. The S-anxiety scale assesses the intensity of the feelings: i) not at all; ii) somewhat; iii) moderately so; iv) very much so; the T-anxiety scale assesses the frequency of specific feelings: i) almost never; ii) sometimes; iii) often; iv) almost always. Each STAI statement is scored using a 4-point Likert type scale. Hence, scores for both the STAI sub-scales (State and Trait) range between 20 and 80. Both T- and S-anxiety values may be divided in five categories of severity: <36 (no anxiety), 36 to 45 (mild anxiety), 46 to 55 (moderate anxiety), 56 to 65 (high anxiety) and >65 (very high anxiety) [14]. In this study, we used the cut-off score of ≥46 (moderate anxiety cut-off) to divide women in two categories of severity (women identified with moderate anxiety were offered psychiatric consultation) [14].

As described by the developer of the test, the median S-anxiety score is expected to be equal to the mean T-anxiety score, when the S-anxiety part is completed in a normal condition, it is expected to be higher if completed during a stressful condition and lower if completed during a relaxed situation; the T-anxiety score, on the contrary, is not expected to be affected by stress [14]. Although the developer of the test did not include pregnant women, several studies have subsequently used this test in pregnancy [12]. Moreover, a validation study in pregnant women confirmed that the overall mean scores for S- and T-anxiety were not different in neutral conditions [23].
Other parameters

All women were categorized based on age (35 years was used as a cut-off), body mass index (BMI) (overweight cut-off 25kg/m²), parity (nulliparous/multiparous), planned pregnancy (yes or not), conception method (spontaneous/assisted reproductive technologies-ART), smoking status (yes or not), timing (during/after lockdown) and trimester of pregnancy (1<sup>st</sup>, 2<sup>nd</sup> or 3<sup>rd</sup>).

Statistical analysis

Following a precision approach, with an estimated prevalence of antenatal depression of 15%, we calculated that a minimum of 306 women was needed for sufficient precision, with 95% level of confidence and 4% margin of error.

Qualitative variables are presented as absolute (n - %) frequencies, while quantitative ones as median (range: minimum-maximum). The variable “trimester of pregnancy” was dummy coded as a binary variable in order to estimate the independent effect of each category. The Kolmogorov-Smirnov test was used to assess normal distribution.

The Chi-square test was used in order to identify differences between categorical variables. The Spearman correlation coefficient was used to correlate the S- and T-anxiety scores, while the Wilcoxon test was employed to assess the differences in the median values of the two scales.

Univariate, followed by multivariate logistic regression models (using variables from the univariate model with p<0.20) were used to evaluate the independent risk factors for antenatal depression and anxiety. The dependent variables of interest were
the EPDS score with a cut-off score $\geq 13$ and the S-Anxiety score, with a cut-off score $\geq 46$. The odds ratios (ORs) and 95% confidence intervals (95% CI) were calculated and significance was assumed at 5%. All the analyses were performed with the software IBM SPSS v.25.0.

Ethics

The bioethics committee of the Aristotle University of Thessaloniki approved the protocol of the study (reference number: 5.172/28.2.2020). All women were informed in detail regarding the objective of the survey, no incentives were offered and a written informed consent was signed prior to participation.

Results

From a total of 541 women that attended their routine antenatal visits in our Department, in the study time frame (March-June 2020), 505 (93.3%) met the inclusion criteria and consented to participate. Obstetric and sociodemographic characteristics are presented in Table 1.

Regarding antenatal depression, the median EPDS score was 6 (range: 0-25); 13.5% (n=68) had a score $\geq 13$ and were identified as probably depressed; 5.3% (n=27) of women answered positive in the QUESTION #10 of the scale regarding suicide thoughts and were referred for urgent psychiatric evaluation. Table 2 summarizes the EPDS questionnaire and the relevant answers during the study period.

In the univariate analysis, the prevalence of antenatal depression was associated with S-anxiety; the presence of (at least moderate) anxiety increased the risk of depression five-fold ($p<0.001$; OR: 5.161; 95% CI: 2.982-8.933). In addition,
unplanned pregnancy, smoking and high BMI (at least overweight) were also correlated with depressive symptoms in the univariate model (p<0.05).

Based on the multivariate analysis, unplanned pregnancy (OR: 2.447; 95% CI: 1.235-4.846), smoking (OR: 2.268; 95% CI: 1.166-4.411) and anxiety during pregnancy (OR: 5.074; 95% CI: 2.898-8.883) were independent risk factors for antenatal depression. All the relevant analyses are presented in Table 3.

Regarding anxiety, a significant increase in the prevalence of anxiety in the pandemic was noted, as the S-anxiety score median was higher compared to the T-anxiety [41 (range: 20 to 72) versus 36 (range: 22 to 67) respectively; p<0.001]. Using the cut-off score of 46, (at least moderate) anxiety was reported in 34.1% (n=172) women (S-anxiety), while the lifetime anxiety, as measured by T-anxiety scale, affected 15.8% (n=80) of the study population, again showing a significant increase in anxiety symptoms (p<0.001). The correlation between S- and T-anxiety scores was moderate (rho=0.592; p<0.001). Significant differences between the S- and T-anxiety categories were identified (p<0.001) (Figure 1).

In the univariate analysis, none of the variables maternal age, lockdown, trimester of pregnancy, parity, method of conception, pre-pregnancy BMI and planned pregnancy was associated with antenatal anxiety. Smoking in pregnancy and depression (p<0.20) were included in the multivariate logistic regression. This confirmed that antenatal depression was associated with anxiety in pregnancy, as those women were five-times more likely to be depressed (p<0.001; OR: 5.038; 95% CI: 2.900-8.751) (Table 4).

Discussion
Main findings

The key findings of this study were that during the COVID-19 pandemic in Greece: i) about one out of eight pregnant women were identified as probably depressed, ii) antenatal anxiety, unplanned pregnancy and smoking were associated with depression, iii) pregnant women exhibited a significant increase in anxiety levels and, although it is considered as moderate anxiety, it affected about one out of three participants and iv) the 6-week total lockdown in Greece had no significant impact on the mental health of the pregnant women.

Interpretation of the findings

The COVID-19 outbreak and the associated restricting measures created an unprecedented condition with unpredictable consequences on the mental health of the general population and also pregnant women [2]. Despite the beneficiary effect of slowing down the spread of the disease, previous research has shown that separation from friends and family, loss of freedom, sense of isolation, uncertainty over disease status and the future, boredom, in addition with financial consequences, may induce dramatic effects [24]. Moreover, the evidence regarding the effect of disasters on antenatal mental health and perinatal outcome is scarce. Higher levels of anxiety were identified in pregnant women immediately after disasters like hurricanes, the Chernobyl accident and the Three Mile Island accident, affecting some perinatal outcomes, while the intensity of the exposure was the main predictor of the mental health impact on pregnant women [25].

We found that the rate of antenatal depression was comparable to that reported in a Greek study conducted before the pandemic [26]. However, our results are in
contrast with similar studies from Canada and China, where it was reported that antenatal depression levels were increased during the pandemic and affected more than 30% of the women [27, 28]. This difference may be explained by the fact that strict measures were promptly enforced and appeared to be very effective in controlling the outbreak in Greece, as indicated by the lower number of overall COVID-19 patients and associated deaths. In addition, as we mentioned in the inclusion criteria, our study comprised of low-risk pregnancies only and this is in contrast with the other two studies, which included general pregnant populations (including high-risk pregnancies). Previous studies in high-risk pregnancies have shown that these women are more likely to be affected by depression [29-31].

Considering risk factors, the well-established association of antenatal depression with anxiety has been previously described and was confirmed in our study [10]. However, as already mentioned, despite the elevated levels of anxiety (S-anxiety), depression levels were not increased in our sample; this divergence of our study may reflect the unique stressor of this pandemic in Greece. Moreover, the pandemic is experienced by all and evokes a universal response and thus may impact depression, which is embedded in self-focus and self-blame, to a lesser extent compared to feelings of anxiety. Of note, the prevalence of antenatal depression was associated with unplanned pregnancy and smoking, which is in accordance with previously published data [32]. Additionally, the association between BMI and antenatal depression was not confirmed in our study; this is in contrast with data from a scoping review [32].

Regarding anxiety, our results confirmed that pregnant women exhibited a significant increase in the level of anxiety (S-anxiety), indicating the negative influence of the pandemic on maternal mental state. Additionally, we found a moderate correlation between the S- and T- anxiety scores; according to the manual of the STAI
questionnaire, lower correlations between S- and T-anxiety are expected in physical-danger situations [14]. This supports the validity of our results, since the pandemic is considered as a situation in which ‘subjects are exposed to or threatened with some form of physical danger’ [14]. A previous study in pregnant women showed that the Trait score mainly reflects general-anxiety levels which remain stable and are not affected by clinical risk level, while the State score more accurately reflects situation-specific anxiety [23].

In the report of our preliminary data, it was indicated that increased anxiety levels were more common among women in the third trimester of pregnancy [15]. However, this association was not confirmed in our final results. Of note, a systematic review including more than 200,000 women showed that the prevalence for self-reported anxiety symptoms gradually increased from the first to the third trimester (18.2%, 19.1% and 24.6%, respectively) [33].

Overall, the results of our study indicate that the 6-week total lockdown in Greece had no significant impact on the mental health of the pregnant women; this may be explained by the fact that the lockdown was enforced promptly, adequate supplies were available and a daily official announcement on the spread of the outbreak by the head of public health experts ensured that the population was offered a continuous reliable update of the situation and the ongoing need for maintaining the quarantine.

Strengths and limitations

An important strength of our study is the physical presence of the pregnant women attending their scheduled ultrasound appointments and the fact that we included 93.3% of the eligible population. This constitutes a significant advantage compared to
web-based studies that usually have a much lower response rate, which allows a potential bias.

However, there are certain limitations in the study. First, it involved a single institution, nevertheless, our unit covers a large population in northern Greece and our study is representative of the total low-risk pregnant population. Second, the T-anxiety score was used as a baseline value, in order to investigate an increase in anxiety levels, but this is a commonly adopted method [34]. Finally, antenatal mental health was assessed with self-reported measures, which are not diagnostic and the questionnaire-based type of the study may allow a recall bias.

Conclusions

It is clear that the unprecedented situation of the COVID-19 pandemic has adversely affected the level of anxiety in pregnant women in Greece, without, however, increasing the prevalence of antenatal depression. A possible explanation may be the prompt response of the government and the subsequent effective control of the spread of the pandemic in Greece. Our study suggests that mental health management strategies may be useful for pregnant women in similar circumstances, especially at the beginning of a crisis.
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Reference list


Legends

**Figure 1.** State and Trait categories according to specific scores in the study population. S- and T-anxiety scores were grouped as no anxiety (<36), mild anxiety (36-45), moderate anxiety (46-55), high anxiety (56-65) and very high anxiety (> 65)