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Research Article,

Correlation between the Symptoms of Major Depression during Pregnancy, Fetal Indicators and Delivery Complications

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Abstract:

Introduction: Studies have shown a high prevalence rate of the symptoms of major depression in the general population of women on Kosovo (43.18%), therefore research on the impact of depression during pregnancy on the intrauterine fetal development and complications during and after delivery in the population of women on Kosovo at reproductive age has scientific and professional rationale.
Objective: The purpose of the study is to research correlation of major depression symptoms during pregnancy with the indicators of intrauterine fetal development and complications during delivery.
Method: The research is prospective randomized and after fulfilling the selective criteria included three hundred pregnant women in the second trimester and at the beginning of the third trimester of pregnancy in the general population of women on Kosovo. Scale of the major depression symptoms was determined with the Hopkins Symptom Check List (HSCL-25). Statistical package for results analysis included software SPSS 12, ANOVA analyses, frequencies, Chi square test, and linear regression analysis.
Results: Significant correlation was proven between the symptoms of major depression during early and mid-pregnancy with: uterine contractions at the beginning of labor, perineal lacerations during delivery, tachycardia in the newborn baby, duration of newborn's stay in the neonatal intensive care unit, the woman's duration of hospital stay in the department before and after delivery, and the delayed start of breastfeeding. Findings proved that there is no significant correlation between the emotional state of pregnant women and the slowing down of the intrauterine fetal development.
Discussion: Based on the study results and the data from the literature, these clinical correlations are a result of interaction between the major depression during pregnancy with neuroendocrine trajectories of pregnancy, fetus and placental functions.
Conclusion: Major depression during early and mid-term pregnancy may have impact on specific clinical parameters of the childbirth and newborn baby. The obtained results suggest the need for systematic mental health support of the woman during pregnancy.

Keywords: depression, pregnancy, fetal indicators, delivery complications.

Introduction:

Epidemiological data from around the world show that depression is approximately twice as common in women as in men, and that its first episode most often occurs during the years when women may be pregnant. The peak prevalence of depression includes the generational age of 25-44 years (1), while about 10-15% of women suffer from depression during pregnancy or in the first year of childbirth.

Some studies have shown a high prevalence rate of symptoms of major depression (43.18%) in the general population of women on Kosovo (2, 3), therefore research on the impact of depression during pregnancy on the intrauterine development of the fetus and complications during and after childbirth in the general population of women on Kosovo of reproductive age has a particular scientific and professional rationale.

It is well known that post-pubertal women are twice as likely as men of the same age to experience major depression, with the prevalence of depression peaking in women's reproductive years (4); however, detection of depression during

pregnancy has not yet become routine in obstetric departments internationally. For this reason, depression during pregnancy remains very often unidentified and under-treated to the appropriate extent, causing negative consequences for the woman and the child.

Pregnancy, childbirth and the postpartum period include an intense series of hormonal developments, which create the possibility for special psychological conditions; however, in the absence of predispositions for psychological disorders or complications during pregnancy, most women adapt to these hormonal changes without obvious psycho-physiological difficulties. As pregnancy progresses and lifestyle changes, significant ambivalences arise as normal psychological responses to a radical life change. In general, most pregnant women manage to adapt to physical and psychological changes, and develop effective mechanisms or attitudes. Pregnancy is seen as a maturing event that brings about the consolidation of gender identity, and is an important determinant of the degree to which the pregnant woman constructs her autonomy and sexuality.

Depression is a mental state of depressed mood, which is initially manifested by one or more physical symptoms in different organ systems: lethargy, headache, pain in different parts of the body, difficulty in digesting food, subjective obstacles in the urogenital tract, breathing difficulties, and later is accompanied by disturbed sleep, loss of interest, increased excitability, irritability, sadness, loss of pleasure, poor concentration, guilt, and often suicidal thoughts. In terms of clinical weight, depressive symptoms extend across a wide spectrum, from minor depressive mood to major depression forms (DSM 5), whose symptoms are the subject of this study.

Clinical monitoring and assessment for anxiety and depression in the prenatal and postnatal period has been widely suggested but there are potentially problematic given issues such as: which instrument to use, which reference values to use to identify pregnant women at risk (4); and especially experts have questioned the validity of diagnosing depressive disorders using standard diagnostic criteria for mood disorders because they include typical physical symptoms that are also normal features of pregnancy such as fatigue, sleep disturbances, and appetite changes (5). These issues must be resolved before clinical monitoring and evaluation (screening) is widely recommended. However, it appears that if the above questions are answered, monitoring for depressive symptoms during pregnancy may be of significant clinical benefit to mothers and their infants (6, 7).

AIM

The aim of this study is to investigate the correlation of symptoms of major depression during the second trimester and the beginning of the third trimester of pregnancy, with indicators of fetal development and birth complications, including relevant clinical parameters of the woman and the newborn baby.

Hypotheses:

The hypotheses of this study are as follows:

1. Symptoms of major depression during early and mid-pregnancy are associated with delayed gestation and premature birth.
2. Symptoms of major depression during early and mid-pregnancy are associated with complications during childbirth.
3. Symptoms of major depression during the early and middle period of pregnancy are associated with disturbed clinical parameters of the newborn baby and with prolonged stay in the neonatal intensive care unit.
4. Symptoms of major depression during the early and middle period of pregnancy are associated with a prolonged stay of the mother in the department before and after delivery, as well as with a delayed start of breastfeeding.

Method and material:

The study is prospective, randomized. The study has included 366 pregnant women who visited the Gynecology – Obstetric Department of the University Clinical Center of Kosovo (UCCK) for routine morphological examination in the second or the beginning of the third trimester of pregnancy. The period of inclusion was February 1, 2009 to December 31, 2013. The selection of pregnant woman's was done randomly as they presented in the departments specialist ambulance for examination, on different working days during

the week. All pregnant women present on the relevant day were offered the opportunity to participate in the study.

The criteria for excluding pregnant women from the study were:

1) Inability to read and understand the questionnaire for any reason, and,

2) Failure to give written consent after prior information.

The research involved 366 pregnant women examined and treated at the Gynecological and Obstetrical Department of the UCCK including those that have finalized their pregnancy and childbirth in other public and private healthcare institutions in the country. All participants in the study had fully met the above-mentioned criteria and had complete official medical documentation on their pregnancy and the childbirth act. The study lasted until the moment when 300 selected women out of 366 who had completed the relevant Questionnaire in the second or third trimester of their pregnancy gave birth in the UCCK or in other healthcare institutions in the country. The clinical history of pregnancy, delivery and post-natal care was analyzed for each of these women. For the women who gave birth outside the UCCK (43 cases), telephone communication was previously established in order to obtain the appropriate data regarding the institution where access to the woman's clinical history was to be provided.

Among the many psychometric instruments for identifying the presence and measuring the degree of depression the Hopkins Symptom Measurement Questionnaire HSCL – 25 was used. This Questionnaire was selected as a well-known psychometric instrument for measuring depression on an international scale (8), which was also used in three researches on the state of mental health of the population of Kosovo in the post-war period (2, 3) in which case it showed high degree of validity and reliability.

Before the beginning of the ultrasound examination, the Hopkins questionnaire was offered to the pregnant women for completion after appropriate explanations regarding the study and the content of the questionnaire were given. The pregnant women who agreed to be interviewed signed the Informed Consent, and then they were asked to record their first and last name, date of birth, phone number, as well as to give their consent for the eventual phone call in the later period. The questionnaire was completed in the presence of the author of the study. Part of the interview was taking notes on: marital status, socio-economic status, smoking, alcohol consumption, the presence of psychiatric disorders and diseases (personal, family), and other non-communicable diseases. In this case, the notes on the previous abortions as well as the eventual treatment of sterility, which led to the current pregnancy, were also taken. In case any woman requested specific help or had suicidal thoughts, she was immediately referred for specialized psychiatric help.

The questionnaires were collected and saved by the author of the study. In the next phase of the study, the clinical histories of each of the women who completed the Questionnaire were examined. From the clinical histories are extracted data's related to relevant clinical parameters before, during and after the childbirth act: uterine contractions, dilatation of the cervix, premature birth, arterial hypertension including preeclampsia, oligohydramnion, vaginal hemorrhages of the third trimester (including placenta previa and placental dystocia), post-term pregnancy, episiotomy, use of vacuum or forceps, caesarean delivery (emergency or planned), postpartum hemorrhage. Also, the specific clinical parameters of the baby such as: fetal hypoxia, length, weight, heart rate, and hospitalization in the neonatal intensive care unit have been identified.

When completing the questionnaire, we keep in mind the possibility of random error during the self-reporting of pregnant women due to their educational level or specific emotional state, which may affect the analysis of the results. However, the possibility of error is minimized by conducting the interviews by the author of the study with necessary explanations.

Given the data from the literature and the specific nature of the study that aimed to illuminate the correlation between the emotional aspects of pregnancy and the outcomes of pregnancy and delivery, as distinctive factors of the study, from the Bishop Scale (9) for measuring the maturity of the cervix, I have identify the factor of dilatation of the cervix and the factor of the length of the cervix, respectively its effacement ("shortening"), represented by the percentage of the presence of the cervix at the beginning of the childbirth act, in the moment of admission in the department. Based

on data from the literature, these two factors from the Bishop Scale are the most relevant parameters that, after a detailed analyses, can shed light on the objectives of the study. For the purposes of this study, the lowest level of points necessary to rank the pregnant woman in the specified group (cut-off score) suitable for statistical correlation analysis was established:

According to the length of the cervix - the existence of the cervix expressed as a percentage during the examination at the beginning of the childbirth act (in the moment of admission at the department):

- 100% - 60%;
- 60% - 0%.

According to the dilatation of the cervix in "cm" at the beginning of the childbirth act (in the moment of admission at the department):

- 1-3 cm;
- 4-6 cm;
- 7-10 cm.

Statistical analyses

Data processing and statistical analysis was carried out using the computer program Microsoft Office Excel 2003 as well as the software of the statistical package SPSS 12. The values “p” were calculated using the ANOVA analysis, while the value $p < 0.05$ was considered statistically significant.

Frequencies and Chi square test were used for descriptive analysis; when there was a need to compare the percentages of the categories of one variable with the other variable, cross tables were used; however, in cases where the dependent variable was continuous and the average and standard deviation had to be determined, comparative averages were used.

For the final statistics of the evaluation of the significance ("p" values), and to prove the influence of one (dependent) variable on the other (independent) variable, the logistic correlation analysis was used; however, in cases where it was necessary to control the influence of any variable in addition to determining significance, linear regression analysis was used.

Results:

The results of this study are divided into three groups: 1) the results of socio-demographic parameters of pregnant women; 2) the results of the clinical parameters of the pregnant woman and the baby; and 3) the results of the correlation analysis between symptoms of the major depression and the results of the clinical parameters of the mother and the baby.

Summary results of socio-demographic parameters

- Three hundred pregnant women are included in this study, of which 21.6% were aged up to 24 years; 61.6% between 25 - 34 years old; and 16.6% aged 35-46.
- 36.6% were from villages, while 63.3% from cities, which is not a representative sample because according to the official population census of Kosovo, 61% of the population lives in rural areas, while 31% lives in urban areas. This difference can be explained by the fact that the majority of pregnant women from all over the country visits the University Gynecological and Obstetrical Department in the capital city of Pristina, which does not have a general hospital.
- According to the educational structure, only 3.3% had no education at all, 33.3% had primary education, 36.6% had secondary education, and 27.6% had university education.
- Regarding marital status, only 1% of pregnant women were unmarried.
- According to the self-assessment of pregnant women, 3% were in a poor economic condition, 50% had average economic conditions, while 47% lived in good economic conditions, which can be explained by the reasoning given for attending the clinic by pregnant women living all over the country.
- For 50.6% of pregnant women, it was their first pregnancy.
- As for the gestational age of the fetus at the time of the interview, 87.9% were pregnant within the second trimester (14-24 weeks), while 12.1% (36 women) were pregnant at 25-28 weeks of pregnancy.
- 16.3% of pregnant women in the sample consumed tobacco, while only 0.6% consumed alcohol.
- 9.6% of pregnant women presented that they had chronic non-communicable diseases in the past.

- Regarding psychiatric disorders and illnesses, personal or in the family, only 2% of pregnant women declared that they had a psychiatric illness in the past and only 7.6% that they had a psychiatric illness in the extended family, which is important when discussing results because it is a sample with a very low degree of prior contamination with psychiatric pathology.

Summary results of clinical parameters of pregnant women

Table 1 – Descriptive data for presence of the symptoms of major depression

Scale of depression	Frequency	Percentage
Low (0 - 0.4)	30	10%
Average (0.5 – 1.75)	180	60%
High (>1.75)	90	30%

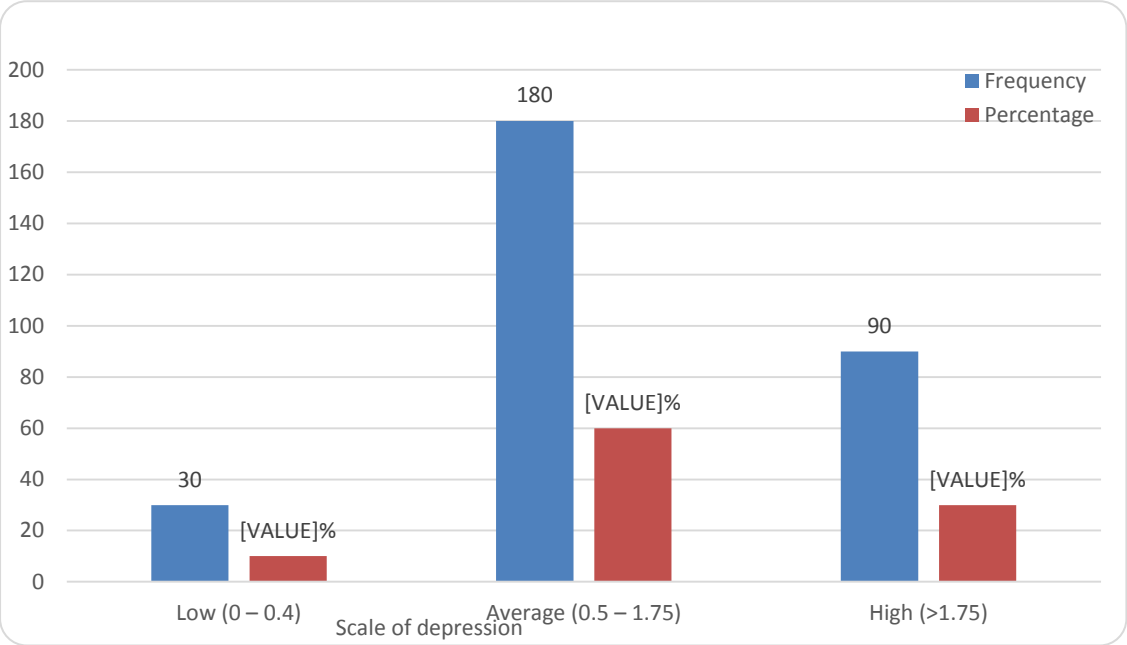

Figure 1 – Pregnant women according to the scale of symptoms of major depression

10% of pregnant women had a low level of symptoms of major depression in the second trimester and at the beginning of the third trimester of pregnancy; 60% were with medium degree, and 30% with high degree.

- According to the Guidelines of the Task Force of the European Association of Cardiologists and the European Association of Hypertension, pregnant women were divided into three groups in terms of blood pressure values at the beginning of the act of labor (at the time of admission to the clinic): 55.6% had optimal blood pressure (up to 120/80 mmHg); 39.3% with normal high blood pressure (up to 139/89 mmHg): and 5% were in the third group with high blood pressure (equal to or above 140/90 mmHg).
- In 41.6% of pregnant women, the cervix had begun to disappear (efface) and was present at the beginning of the childbirth act 60-0% (at the time of admission to the department), while in 58.4% it was present 100-60%.
- According to the degree of dilation of the cervix at the beginning of the childbirth act (upon admission to the clinic), the pregnant women were divided into three groups: 76.6%, with dilation of 1-4 cm;

16.3%, with 4-7 cm dilation 16.3%; and 6.6% with 7-10 cm dilation.

- At the beginning of the childbirth act (upon admission to the clinic), 26.3% of pregnant women had strong uterine contractions, 65.3% normotonic contractions and 6.6% weak (hypotonic) contractions.
- Regarding the time of stay in the department from admission to the end of delivery, 53% of pregnant women stayed less than 24 hours; 18.3% of 24 – 72 hours; whereas 28.6% of them stayed more than 72 hours.
- As for the mode of delivery, 35% of pregnant women were delivered by caesarean section, while 65% were delivered vaginally.
- In the group of women born vaginally, forceps was used in only 1% of cases.
- Delayed birth (post-term pregnancy) was found in 4.3% of cases.
- In 8.6% of pregnant women, oligohydramnion was detected before the membranes ruptured.
- Third trimester hemorrhages, including placenta previa and placental dystocia, were present in 4.7% of pregnant women.
- Slowed intrauterine development of the fetus was found in 7.1% of cases.
- Perineal lacerations including rupture of the anal sphincter (in one case) were found in 12.6% of pregnant women.
- Episiotomy was performed in 31% of cases.
- Premature birth according to WHO criteria – from 28th week to the 37th week, was evidenced in 14.6% of pregnant women included in the study.
- According to the hospital days of the pregnant woman in the department, 62.3% stayed for 0-2 days; 26% stayed for 3-6 days; while 6.6% stayed for 7-10 days.
- 82.6% of pregnant women started breastfeeding 0-2 days after birth; 8.6% between days 3 – 6; meanwhile, between days 7 and 10, 3.6% of pregnant women started breastfeeding.

Summary results of infant clinical parameters

- Newborns were grouped according to weight based on WHO criteria: 19.3% were of low weight (under 2499 grams); of 2500 - 4000 grams were 75%; while 5.6% of babies weighed more than 4000 grams.
- According to the tachycardia at birth, the newborn babies were divided into three groups where: 31% had a heart rate below 140/min, 64.6% between 140 – 160/min, while 2.6% were above 160/min.
- According to the values of the Apgar test that measures the physical condition of the newborn baby by evaluating with 2, 1, or 0: heart rate, respiratory activity, muscle tonus, response to stimulation, and skin color, babies are divided into three groups: 8% of newborn babies had very low Apgar score (0 – 2); with Apgar score up to average (3 – 6) were 12%; while with good Apgar score (7-10) were 80% of newborns.
- 85.3% of newborns stayed 0-2 days in the neonatal intensive care unit; 4.3% stayed for 3-6 days; while 5.3% stayed for 7-10 days.

Summary results of Chi-Square analysis of the correlation between the degree of symptoms of major depression and the results of clinical parameters of pregnant women and infants

The Chi-Square analysis of frequencies did not result in a significant difference between most groups of results, but the investigation of interactions between some factors was accompanied by indicative results.

The difference with significant power was found between the groups of results, as follows:

1. The degree of symptoms of major depression and uterine contractions at the beginning of labor (p = .022);
2. The degree of symptoms of major depression and lacerations of the birth canal (p=.003);
3. The degree of symptoms of major depression and tachycardia in the newborn baby (p= .000);
4. The degree of symptoms of major depression and the stay (per day) of the newborn baby in the NIC unit (p= .021);
5. The degree of symptoms of major depression and the stay (per day) of the

pregnant woman in the department, (p=.039); and,

6. Degree of symptoms of major depression and initiation of breastfeeding (days after birth), (p= .013).

Results of the Chi-Square analysis of the significant correlation between the symptoms of major depression in pregnant women and the clinical parameters of the pregnant woman and the baby

Table 2 – The degree of symptoms of major depression and contractions of the uterus

The degree of symptoms of major depression	Uterine contractions				Number
	Missing (hypotonic)	Normal (normotonic)	Enforced (hypetonic)	Missing data	
0 – 0.4	3	19	6	2	30
0.5 – 1.75	15	108	54	3	180
>1.75	2	69	19	0	90
Total	20	196	79	5	300

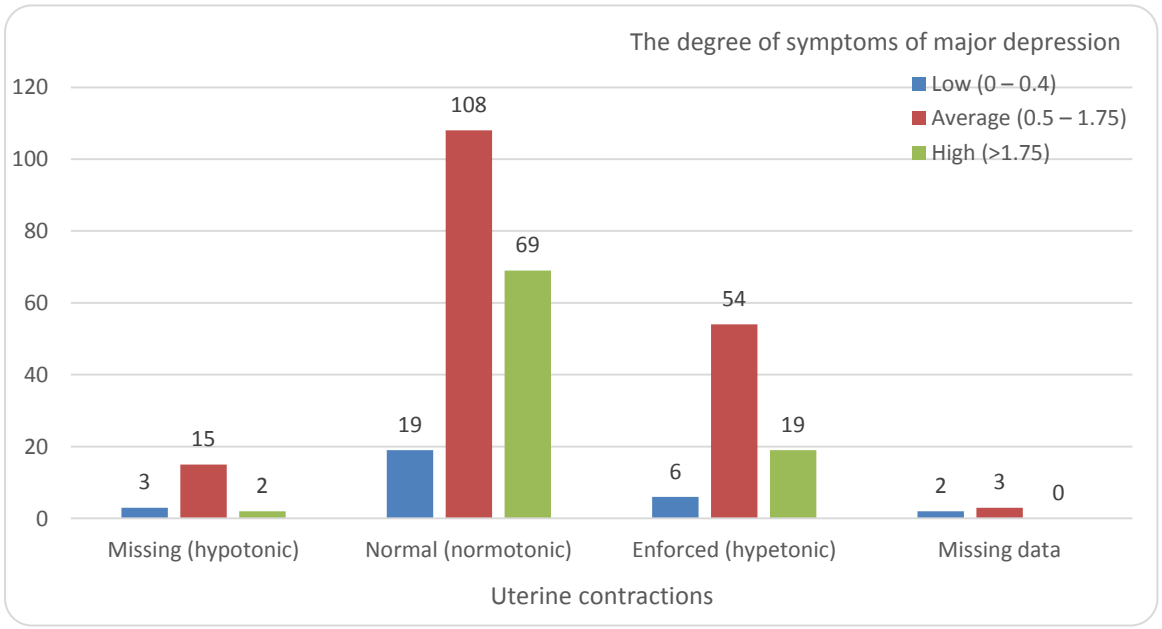

Figure 2. The degree of symptoms of major depression and contractions of the uterus

The Chi-Square analysis of the significance of the frequencies **does result in a significant difference between the groups χ^2 (6, *N* = 300) = 14.796, p= .022**

Table 3 – Symptoms of major depression during pregnancy and lacerations (tearing) of the perineum

The degree of symptoms of major depression	Perineal lacerations		Number
	Yes	No	
0 – 0.4	7	23	30
0.5 – 1.75	28	152	180
>1.75	3	87	90
Total	38	262	300

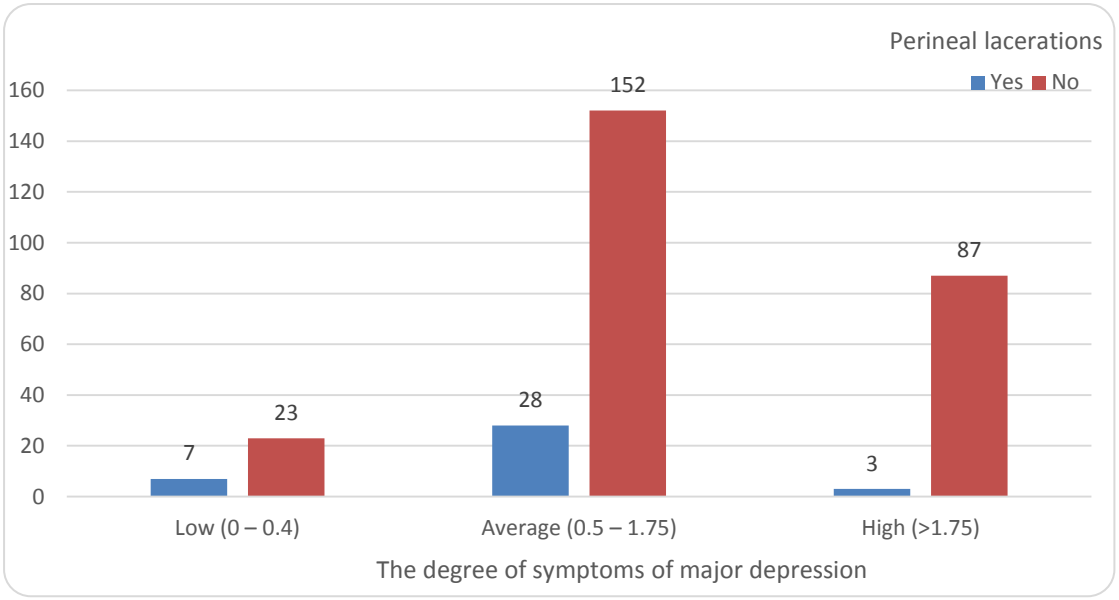

Figure 3. Symptoms of major depression during pregnancy and lacerations of the perineum

The Chi-Square analysis of the significance of the frequencies **does result in a significant difference between the groups χ^2 (2, *N* = 300) = 11.531, p= .003**

Symptoms of major depression during pregnancy and tachycardia in the newborn baby

Table 4 – Symptoms of major depression during pregnancy and tachycardia in the newborn baby

The degree of symptoms of major depression	Heart rate				Number
	< 140/min	140 – 160/min	> 160/min	Missing data	
0 – 0.4	19	10	0	1	30
0.5 – 1.75	53	121	2	4	180
>1.75	21	63	6	0	90
Total	93	194	8	5	300

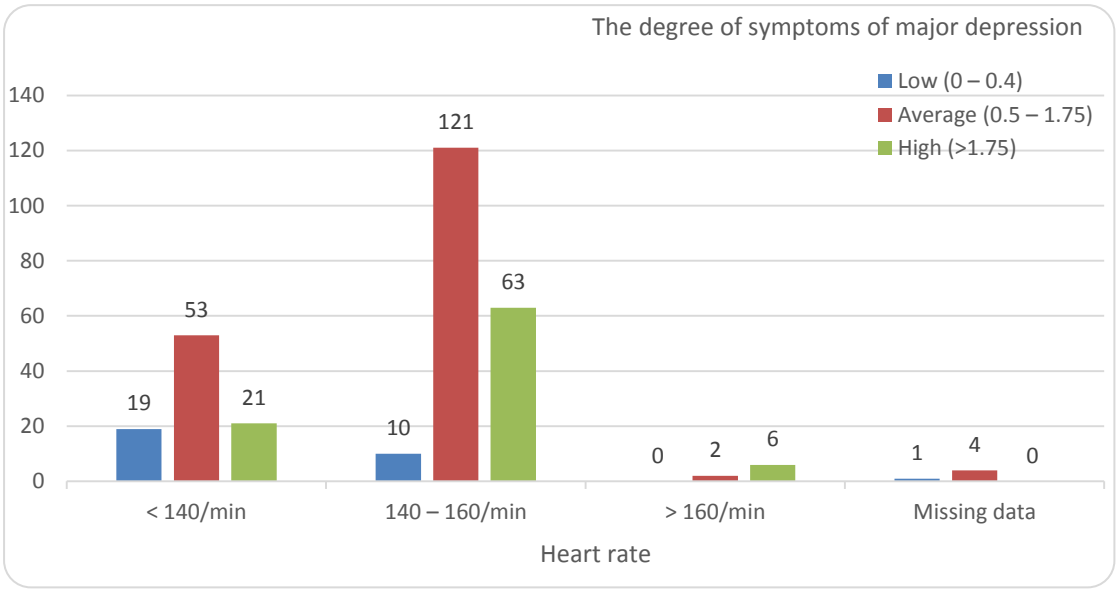

Figure 4. Symptoms of major depression during pregnancy and tachycardia in the newborn baby

The Chi-Square analysis of the significance of the frequencies **does result in a significant difference between the groups χ^2 (6, *N* = 300) = 27.263, p= .000**

Symptoms of major depression and days of stay of the newborn in the neonatal intensive care unit (NICU)

Table 5 – Symptoms of major depression and days of stay of the newborn in the NICU

The degree of symptoms of major depression	Days of stay in the NICU				Number
	0 - 2	3 - 6	7- 10	Missing data	
0 – 0.4	22	1	2	5	30
0.5 – 1.75	150	10	12	8	180
>1.75	84	2	2	2	90
Total	256	13	16	15	300

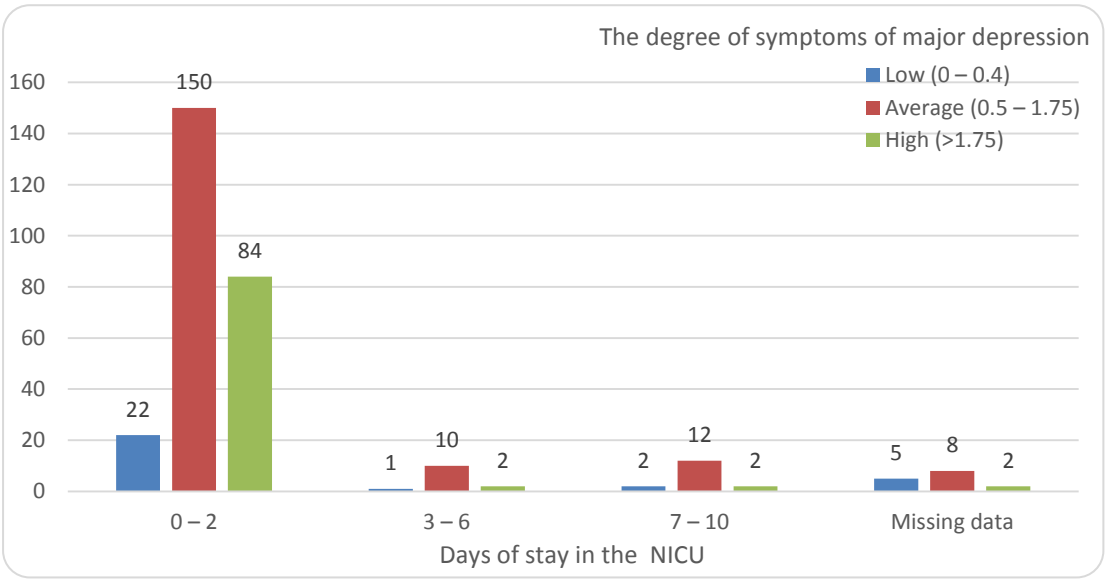

Figure 5. Symptoms of major depression and days of stay of the newborn in the NICU

The Chi-Square analysis of the significance of the frequencies **does result in a significant difference between the groups χ^2 (6, *N* = 300) = 14.881, p= .021**

The degree of symptoms of major depression and the days of stay of the pregnant woman/mother in the department

Table 6 – The degree of symptoms of major depression and the days of stay of the pregnant woman/mother in the department

The degree of symptoms of major depression	Days of stay in the department				Number
	0 - 2	3 - 6	7- 10	Missing data	
0 – 0.4	19	4	2	5	30
0.5 – 1.75	114	45	13	8	180
>1.75	54	29	5	2	90
Total	187	78	20	15	300

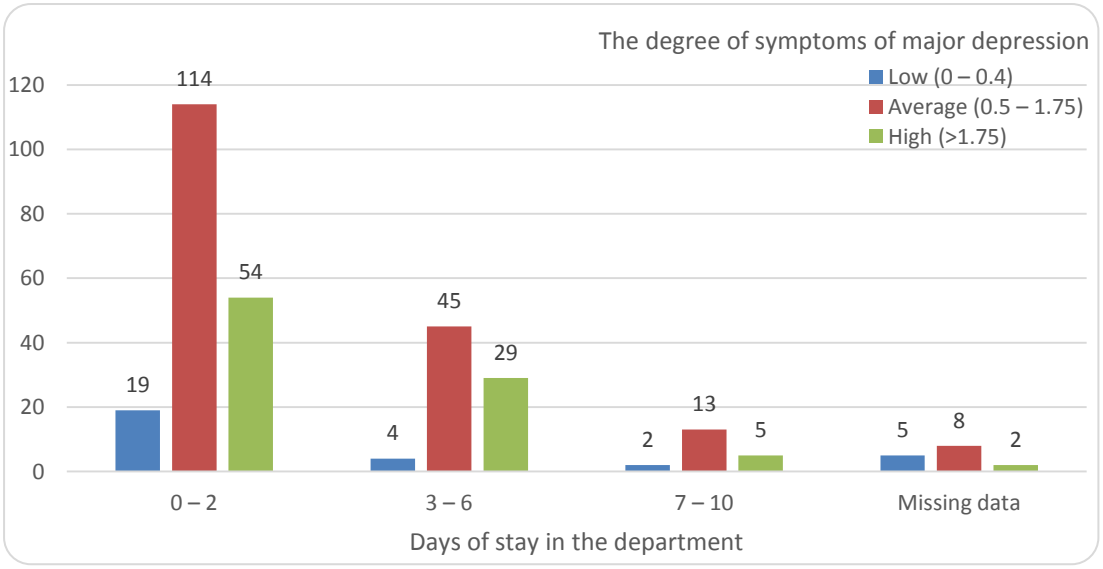

Figure 6. The degree of symptoms of major depression and the days of stay of the pregnant woman/mother in the department

The Chi-Square analysis of the significance of the frequencies **does result in a significant difference between the groups χ^2 (6, *N* = 300) = 13.290, p= .039**

Score of major depressive symptoms and initiation of breastfeeding (days after birth)

Table 7 – Score of major depressive symptoms and initiation of breastfeeding (days after birth)

The degree of symptoms of major depression	Initiation of breastfeeding (days after birth)				Number
	0 - 2	3 - 6	7- 10	Missing data	
0 – 0.4	22	2	1	5	30
0.5 – 1.75	145	17	10	8	180
>1.75	81	7	0	2	90
Total	248	26	11	15	300

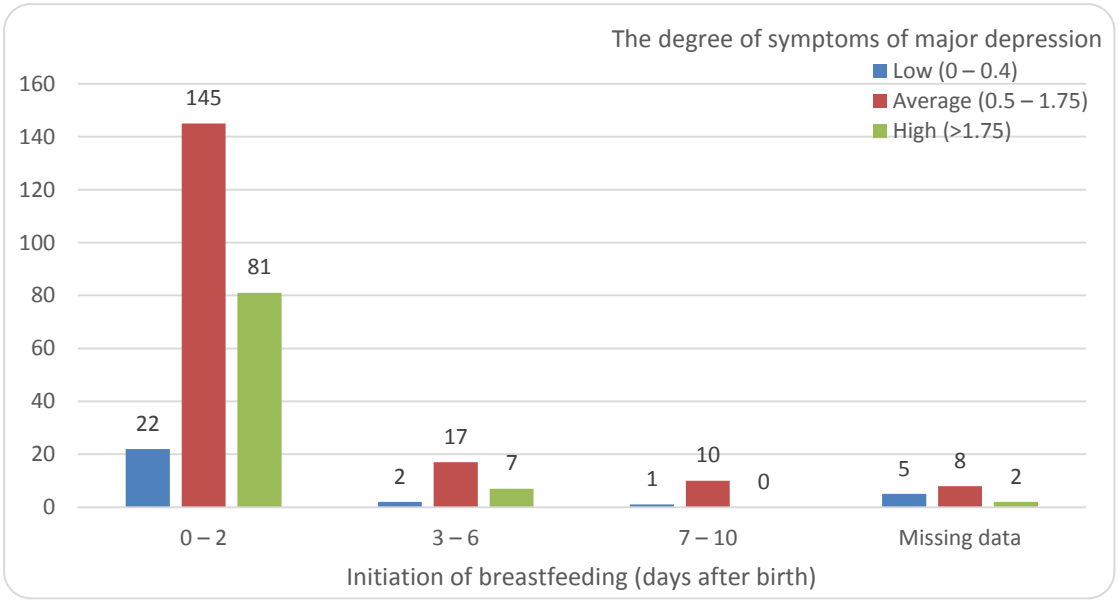

Figure 7. Score of major depressive symptoms and initiation of breastfeeding (days after birth)

The Chi-Square analysis of the significance of the frequencies **does result in a significant difference between the groups rupeve χ^2 (6, *N* = 300) = 16.072, p= .013**

Results from Linear Regression Analysis

Linear regression analysis was used to verify the correlation of the degree of symptoms of major depression during pregnancy and the following variables:

1. Contractions of the uterus – a significant correlation was observed between these two variables with values: F (1,298) = 5.071, p<0.025, and R2=.017. Uterine contractions are higher for 9.696, when the degree of major depressive symptoms during pregnancy is higher.
2. Lacerations of the perineum – a significant correlation was observed between these two variables with values: F (1,298) = 11.625, p<.001, and R2=.038. The rate of perineal lacerations is higher for 1.637, when the rate of major depressive symptoms during pregnancy is higher.
3. Tachycardia in the newborn baby – a significant correlation was observed between these two variables with values: F (1,298) = 61.675, p<0.000, and R2=.077. Tachycardia in the newborn baby is 2.212 more frequent in babies of mothers with symptoms of major depression during pregnancy.
4. Days spent by the newborn baby in the NIC unit – a significant correlation was observed between these variables with values: F (1,298) =7.359, p<.007, and R2=.024. The rate of stay of infants in the NIC unit (days of stay) is higher by 18,191 in women with symptoms of major depression during pregnancy.
5. Days spent by the pregnant woman that delivered in the department - a significant correlation was observed between these variables with values: F (1,298) =7.010, p<.009, and R2=.023. The rate of stay of pregnant women that delivered in the department (days of stay) is 18,120 higher among women with symptoms of major depression during pregnancy.
6. Beginning of breastfeeding (days after birth) – a significant correlation was observed between these two variables with values: F (1,298) =7.325, p<.007, and R2=.024. Delayed lactation is 18,172 more frequent in pregnant women with symptoms of major depression during pregnancy.

Discussion:

The findings of our study that the symptoms of major depression during pregnancy are in significant correlation with the start of the initial phase of the birth act through the "effacement" of the cervix and the increase of uterine contractions, prove the hypothesis of the study that psychological factors, in this case major depression, during early and mid-pregnancy can influence the course of pregnancy and obstetric outcomes through activation of the hypothalamic pituitary axis (HPA) from the center of emotional functions in the human brain (amygdala in the limbic system). This activation of the HPA axis in the first step occurs through the increased production of cortico-releasing hormone (CRH) in the hypothalamus of the pregnant woman and in the placenta, initiating a chain of reactions and complex biochemical mechanisms in the cervix and uterine myometrium, resulting in softening of the cervix and increasing uterine contractions.

Symptoms of major depression and uterine contractions

Until recently, little attention has been paid to the role of depression in the presentation of obstetric complications. Recent studies demonstrate increased interest in this issue, although the results are somewhat contradictory. The study proved that pregnant women with symptoms of major depression during the second trimester and the beginning of the third trimester of pregnancy have an increased risk of spontaneous premature onset of labor in the form of effacement of the cervix and hypertonic contractions of the uterus, although it is necessary to identify other factors that contribute to this process, so that this "threat" for premature birth ends with premature birth.

Törnblom et al. (10) in their study on the biochemical and physiological mechanisms of the dilatation of the cervix emphasized that the initial phase of the birth act includes the maturation of the cervix and the beginning of regular myometrial contractions in the uterus, which are necessary for vaginal delivery. The findings of this study provide evidence for a positive correlation between the degree of symptoms of major depression during pregnancy and hypertonic uterine contractions as essential components of the start of the initial phase of spontaneous labor (p = .022). The study by Dayan et al. (11) showed that when anxiety and

depression during pregnancy are combined with specific biomedical factors, they can cause the spontaneous and premature onset of labor. The authors have assumed the synergistic action of psychological and biomedical factors on placental CRH secretion. Also, the results of Soheila et al. (12) proved that there is a significant association between depression during pregnancy and premature onset of labor.

Significant association (or close to significance) was found in the study of Steer et al. (13) and Orr and Miller (14); no connection was found in the studies of Perkin et al. (15) and Copper et al. (16). Discrepancies in results between these studies can be explained by differences in their design: the populations were different, different measuring instruments were used to assess depression; there are differences in the coding of the obtained scores for depression in the logical models (results dichotomized, quartile, and continuous variables). The data on the association that was found between the symptoms of major depression and the spontaneous premature onset of labor in the form of increased hypertonic uterine contractions in pregnant women with an increased degree of symptoms of major depression during pregnancy are rare in the scientific literature. A meta-analysis of observational studies on the impact of depressive symptoms on neonatal and obstetric outcomes (17), like most similar studies, used self-report monitoring instruments to assess the intensity of depressive symptoms and then determined a reference value to illustrate significance. This meta-analysis reported a strong association between depressive symptoms during pregnancy and the risk of preterm birth and low birth weight, but did not prove the existence of a significant association with delayed intrauterine development.

Savitz et al. (18) suggested that it would be dangerous to derive specific risk factors for spontaneous onset of labor from findings on spontaneous preterm birth. As pointed out by Kramer et al. (19) the two complications must be clearly separated. First, spontaneous preterm birth is not always induced by the onset of labor, but it can also be the result of umbilical cord rupture during the onset of labor. Second, spontaneous premature onset of labor does not necessarily end in premature birth. From the review of the literature, it seems that premature onset of labor, when diagnosed prospectively (earlier), has a positive predictive value of 50 percent for premature birth, depending on the diagnostic criteria and the date of diagnosis (20, 21). Therefore, the risk factors for spontaneous premature onset of labor and those for spontaneous preterm birth may differ.

It is interesting to note that, while study found significant correlation between the degree of symptoms of major depression and hypertonic contractions of the uterus in the beginning of the act of childbirth, simultaneously, the effacement of the cervix and the hypertonic contractions of the uterus at the beginning of the act of childbirth have not resulted in a significant correlation with the dilatation of the cervix and in premature birth, which can be expected considering the data from the literature.

The results do not support the study's hypothesis that major depressive symptoms during pregnancy are associated with delayed gestation and preterm delivery. Also, there was no statistical significance in the correlation between symptoms of major depression ($p= .557$) with the weight of the baby at birth; although many studies have proven this connection. Also, surprisingly, the level of education, which indirectly reflects the social background and is known to have an impact on the presentation of preterm birth (22), was not found to have a significant association with the spontaneous onset of preterm labor in this study. However, this can be explained by the fact that the population of Kosovo does not have significant social heterogeneity, as well as by the fact that the pregnant women included in the study have early antenatal care, which can significantly improve pregnancy outcomes in women with social deprivation. (23).

Major depressive symptoms and birth canal lacerations

The study found a significant association between the degree of symptoms of major depression during pregnancy and birth canal lacerations ($p= .003$). During the review of the literature, no relevant and important studies on this issue were found. It is possible that the researchers' focus has been on other factors relevant to depression during pregnancy such as delayed intrauterine development, low birth weight, spontaneous premature onset of labor, and preterm birth. This suggests that the finding of significance in the relationship between symptoms of major depression during pregnancy and perineal

lacerations during childbirth in this study raises the need for further studies of the impact of the pregnant woman's depression on her abilities to cooperate with health personnel during labor, especially in terms of increasing the proper neuro-muscular relaxation of the birth canal.

Symptoms of major depression and tachycardia in the newborn babies

The study found a significant association between the degree of symptoms of major depression (p= .000) and tachycardia in newborn babies. The findings are in agreement with the longitudinal study of fetal ontogeny, by DiPietro et al. (24) who evaluated fetal variables in relation to pregnant women's reports of daily stress during weeks 20 to 36-38 of gestation. Fetuses of mothers who reported higher stress showed significantly lower heart rate variability than those of the low stress group, suggesting that exposure to maternal emotional distress may contribute to impaired parasympathetic control of the fetal heart (25). Similarly, fetuses of depressed mothers had a higher baseline heart rate, a delayed heart rate response to external stimuli, and a longer time to return to baseline after the stimulus compared to fetuses in the control group (26). A series of studies proved that fetuses of pregnant women who have experienced psychological distress (anxiety, depression) also show significantly different reactivity to maternal stress. Fetuses of depressed mothers showed significantly higher heart rate increases when the mother was presented with a laboratory-induced stressor (27). Similar increases have been found in the fetuses of pregnant women who had anxiety-depressive comorbidity (28, 29).

However, in the other study, DiPietro et al. (30) found increased heart rate variability (which was usually associated with slowed heart rates) and reduced movements during the arousal period compared to baseline. It is possible that these conflicting results between studies emphasize the role of chronic maternal mood on fetal responses to changes in the intrauterine environment.

A better understanding of the effects of maternal psychological state on fetal reactivity and adaptation requires more studies and protocols utilizing vibroacoustic stimulation and laboratory stressors (31).

Symptoms of major depression and the infant's stay in NICU

The study found a significant association between the degree of symptoms of major depression and the newborn's stay in the NICU (p= .021). In contrast, the meta-analysis by Grigoriadis et al. (32) that examined the relationship between symptoms of major depression during pregnancy and admission of the infant to the NICU did not find this correlation to be significant.

Symptoms of major depression and the days of stay of pregnant women in the department

The study proved the significant association of the degree of symptoms of major depression and the peripartum days of stay of the pregnant woman in the department, (p=.039). This finding is in agreement with the study of Lancaster et al. (33) in 867 pregnant women who proved that the presence of depressive symptoms during pregnancy is related to a longer peripartum stay. Palladino et al. (34) had similar findings regarding the influence of depressive symptoms during the prenatal period on worsened neonatal and obstetric outcomes, such as prolonged stay in the antenatal department.

Symptoms of major depression and the initiation of breastfeeding

The study found that there is a significant association between the degree of symptoms of major depression and the initiation of breastfeeding (p= .013). This result is similar to the result of Grigoriadis et al. (35) who found that the delay in the initiation of breastfeeding has a significant association with depressive symptoms during pregnancy. Even the study by Schetter et al. (36) found that depression during pregnancy has a direct impact on the mother's relationship with the baby in terms of breastfeeding.

Systematic review and meta-analysis of databases: MEDLINE, EMBASE, CINAHL and PsycINFO from their inception to June 2010, showed that maternal depression during pregnancy is associated with increased chance of preterm birth and reduced initiation of breastfeeding (35). Also, some individual observations and epidemiologic analytical studies suggest that depressive symptoms during the prenatal period may contribute to worsened neonatal and obstetric outcomes, such as decreased initiation of breastfeeding (37). In the context of these data from the literature, the results of the study prove

that major depression during pregnancy can be important factor for making the decision to breastfeed during pregnancy and the initiation of breastfeeding after birth, however, further research with high methodological quality is necessary in order to more accurately specify the relationship between prenatal emotional disorders and the intention during pregnancy to breastfeed, and their impact on the initiation of breastfeeding after birth, given the fact that in some studies the associations found were not significant (35).

Strengths and limitations of the study

The important advantage of this study is its prospective design, which enabled the detection of the symptoms of major depression early in pregnancy (on average, in the 19th week of pregnancy), a few months before the act of childbirth begins. Thus, the reporting of the symptoms of major depression was not influenced by the presence of complications during the childbirth act.

The limitations of the study include:

- Lack of repeated measurements of the symptoms of major depression during pregnancy, since this measurement in the study was done only once in the second trimester (88%) and at the beginning of the third trimester (12%); any subsequent change of these emotional states could change the significance of the correlations found. This may happen because the symptoms of major depression detected at the beginning or in the middle of pregnancy may go away until the end of pregnancy or the symptoms of major depression may be not present at the time of interview but may appear later during pregnancy.
- Potential error in determining the sample size due to the relatively low number of pregnant women participating in the study, although it is well known that the prospective design of the study reduces the impact of the low participation rate on the study results.
- Determining the degree of the symptoms of major depression during pregnancy is not part of the routine clinical examination procedure in the obstetric services of Kosovo.
- Validation and comparison with the results from the literature is difficult due to the use of different measurement instruments for the symptoms of major depression during pregnancy, and/or the use of different criteria for its diagnosis.

Conclusions and Recommendations:

This prospective randomized study included the socio-demographic and clinical factors of pregnant women and infants, putting them in statistical correlation with the clinical factor of symptoms of major depression during early and middle pregnancy (second trimester and beginning of the trimester third). The findings supported the study's hypotheses about the potential impact of major depressive symptoms during early and mid-pregnancy on specific obstetric complications during delivery, and on infant and maternal clinical parameters, including delayed initiation of breastfeeding. The results of the study did not support the hypothesis that symptoms of major depression during early and mid-pregnancy have a significant correlation with delayed fetal gestation and preterm delivery. Future research should confirm which are the complementary factors that condition the multiplication of the evident impact of major depressive symptoms during pregnancy on the act of delivery and childbirth in all its components.

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