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# **DOCTORAL (PhD) THESIS**

**QUALITY OF LIFE AND OBSTETRIC CONSEQUENCES  
ASSOCIATED WITH SARS-COV-2 INFECTION**

**A B S T R A C T**

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# TABLE OF CONTENTS

List of published works .....	VI
List of abbreviations .....	VII
Figure index .....	IX
Table index .....	X
Acknowledgments .....	XI
INTRODUCTION.....	XIII
REVIEW OF LITERATURE .....	1
CHAPTER 1. COVID-19.....	1
1.1. Definition of the concept and current terminology.....	1
1.2. History .....	3
1.3. Epidemiology and clinical relevance .....	5
1.4. Taxonomy and structure of coronaviruses.....	12
1.4.1. Debate of the study subject.....	12
1.4.2. Sars-CoV-2 virus genome.....	13
1.4.3. The structure of the sars-cov-2 virus .....	15
1.4.4. Immunopathology of the infection.....	16
CHAPTER 2. EFFECTS OF PREGNANCY AND MATERNAL INFECTIONS ON THE NEWBORN AND THEIR QUALITY OF LIFE.....	18
2.1. General data.....	18
2.2. Hypothesis .....	19
2.3. Epidemiological data on maternal infections and pathoganes involved.....	20
2.4. Methods of transmission of infections during pregnancy .....	26
2.5. Immunological changes in pregnancy .....	28
2.6. Impact of hormonal changes, stress factors and microbioma on immunity in pregnancy.....	31
2.7. Complications of maternal infections.....	33
2.7.1. Prematurity .....	33
2.7.2. Chorioamnionitis .....	34
2.7.3. Newborn outcomes.....	35
2.8. Quality of life of pregnant women.....	37
PERSONAL CONTRIBUTION.....	38
STUDY 1: EXPLORING PREGNANCY OUTCOMES ASSOCIATED WITH SARS- COV-2 INFECTION.....	39
1.1. Objectives of the study .....	39
1.2. Motivation to carry out the study .....	39
1.3. Materials and methods .....	41
1.3.1. Study design.....	41

1.3.2. Eligibility criteria .....	42
1.3.3. Deontology and ethics .....	43
1.3.4. Statistical analysis .....	43
1.4. Results .....	44
1.4.1. Characteristics of the participants included in the study.....	44
1.4.2. Description of the study cohort .....	45
1.4.3. Regression analysis.....	47
1.5. Discussions .....	48
1.5.1. Review of literature .....	48
1.5.2. Study limitations.....	76
1.6. CONCLUSIONS .....	76
1.7. FINANCIAL SUPPORT.....	77
STUDY 2: COPING STRATEGIES AND HEALTH-RELATED QUALITY OF LIFE IN PREGNANT WOMEN WITH SARS-COV-2 INFECTION .....	78
2.1. Objectives of the study .....	78
2.2. Motivation to carry out the study .....	78
2.3. Materials and methods .....	80
2.3.1. Study design and participants .....	80
2.3.2. Study variables .....	80
2.3.3. Statistical analysis .....	82
2.3.4. Deontology and ethics .....	83
2.4. Results .....	83
2.4.1. Characteristics of the sample .....	83
2.4.2. Results of the COPE-60 questionnaire.....	85
2.4.3. Results of the HADS questionnaire .....	86
2.4.4. Results of the SF-12 questionnaire .....	87
2.4.5. Results of the CORE-OM questionnaire.....	88
2.4.6. QPP questionnaire results .....	89
2.5. Discussions .....	90
2.5.1. Debate of the study subject.....	90
2.5.2. Review of literature .....	92
2.6. Conclusions.....	109
2.7. Financial support .....	110
FINAL CONCLUSIONS AND ORIGINAL CONTRIBUTIONS.....	111
REFERENCES.....	112
ANNEXES.....	I

KEYWORDS: COVID-19, SARS-CoV-2 infection, quality of life, pregnancy outcomes

## INTRODUCTION

In this global context, Romania has had particular difficulties in controlling the spread of the virus and the effects of COVID-19 disease, ranging from medical infrastructure to demographic and social factors. Unlike other countries, due to the considerable diaspora, significant problems arose when a large number of people from regions severely affected by the pandemic returned to Romania, but the prompt implementation of control measures prevented the sudden increase in the number of COVID cases. -19, preventing an already overloaded health system from being overwhelmed in the early stages of the epidemic. The treatment of the COVID-19 problem in Romania demonstrates the critical importance of a first quick reaction that takes into account the social context of an epidemic. However, not all of Romania's problems are particular to our country, these findings may influence future public health initiatives globally.

One of the existing problems not only in Romania, but also globally during the pandemic are the patients with chronic diseases and other special categories that require permanent follow-up, such as pregnant women. These categories received less personal care due to government restrictions on planned outpatient medical consultations and growing concern about SARS-CoV-2 virus exposure during private visits to the doctor or polyclinics. Thus, pregnant women are a vulnerable group of patients who need close medical care and regular follow-up, but whose access to these essential services has been limited. Given the decrease in hospitalizations and the association between delayed treatment and increased morbidity, it is reasonable to anticipate that future patients who delay hospitalization will have more severe illnesses than we usually encounter. We anticipate that pregnant women who are left behind for prenatal monitoring and treatment due to the limitations of the COVID-19 pandemic could have several pregnancy-related complications, including an increase in premature births and other major newborn morbidities. The body of pregnant women undergoes important immunological changes as a result of embryonic implantation, increasing the susceptibility and severity of infections. Simultaneously, acute or chronic infections significantly increase the incidence of premature birth, accounting for more than 50% of the etiology of prematurity. While maternal transmission of SARS-CoV-2 appears unlikely, there is an underlying risk of placental insufficiency due to prothrombotic propensity for SARS-CoV-2 infection.

Results from recent studies suggest that vertical uterine transmission of SARS-CoV-2 is feasible, although very unusual. COVID-19 infection is as dangerous for pregnant women as it is for non-pregnant women, increasing the risk of miscarriage or premature labor in some cases. While pregnant women have a lower risk of contracting COVID-19 than the general population, they may be more susceptible to a severe form of the disease if they suffer from respiratory failure. In addition to the negative physical effects, previous research has shown that epidemics have a widespread and harmful effect on people's mental health, resulting in the development of new psychiatric symptoms or worsening of pre-existing mental illness. As a public health emergency,

COVID-19 has caused considerable concern and psychological distress among pregnant women and their partners. Perinatal anxiety is a new complication of the pandemic, with possible serious consequences for the physical health of the mother and child. Thus, we can say that the COVID-19 pandemic has a direct and indirect negative effect on pregnant women as a result of SARS-CoV-2 virus infection, social isolation and other isolation measures used worldwide to prevent the spread of the virus.

Complications such as low birth weight, preterm birth, pregnancy-associated emetic syndrome, preeclampsia, lower APGAR scores, and prolonged hospital stay were all associated with anxiety and perinatal depression, as well as their effect on overall quality of life. The terms "quality of life" and "quality of care for pregnant women" are often used interchangeably to refer to a woman's health-related quality of life, as well as her perception of the quality of care received in a medical setting. Due to the high prevalence of COVID-19 and its harmful psychological effects on human life, as well as the lack of research on the psychological well-being of pregnant women during the COVID-19 pandemic, it is essential to assess the impact of COVID-19 on women's mental health. pregnancy, but also the effects that SARS-CoV-2 infection has on pregnancy.

It appears that hospital admissions decreased during the pandemic, with a decrease of over 50% in reported obstetric crises compared to the same calendar months in previous years. This phenomenon may be caused by the fear of pregnant women to go to the hospital, or by the impossibility of the medical system overcrowded by cases of COVID-19 to correctly diagnose obstetric emergencies. Considering the above, some of the premises of this study was the lack of attention to the care and delayed follow-up of pregnant women in Romania during the pandemic, as well as the widespread fear of contracting the virus through hospital visits among pregnant patients. The current study will look at pandemic pregnancies to determine whether single live birth results differ between mothers infected with SARS-CoV-2 and mothers who did not come into contact with the virus during pregnancy and whether COVID-19 is a risk factor. independently for unwanted results at birth.

In addition, pregnant women are more likely to worry than non-pregnant women, according to a previous study on the SARS epidemic. This includes concern about the infection, the transfer of the disease to the baby, the infection acquired after birth and the teratogenicity of microbes and drugs. They avoided hospitals and medical institutions for fear of contracting SARS-CoV-2, which led to a delay in prenatal treatment. Pregnant women who have tested positive for COVID-19 are advised to seek specialist assistance in diagnosing, managing and preventing complications for both mother and baby [95]. Complications at birth, such as low birth weight, premature birth, emetic syndrome during pregnancy, preeclampsia, low APGAR scores, and prolonged hospitalization were all related to anxiety and perinatal depression, as well as the impact on overall quality of life. The terms "quality of life" and "quality of care" are often used interchangeably to refer to both the quality of life related to a woman's health and her opinion on the quality of care received in the medical setting. Due to the high prevalence of COVID-19 and its harmful psychological effects on the lives of pregnant women, as well as the lack of research on the psychological well-being of pregnant women during the COVID-19 pandemic, it is essential to assess the impact of this disease on the mental health of pregnant women.

## PURPOSE OF THE STUDY

The present paper aimed to identify relevant issues in the absence of previous research on pregnant women infected with SARS-CoV-2. This paper also wanted to provide topical and clinically relevant perspectives, by highlighting important parameters in assessing the consequences of COVID-19 infection in pregnant patients, but also assessing the risks to which newborns are exposed to these patients. In the same vein, we insisted on assessing the stress on demand exposed to pregnant women with SARS-CoV-2, and the methods they use to adapt to this burden.

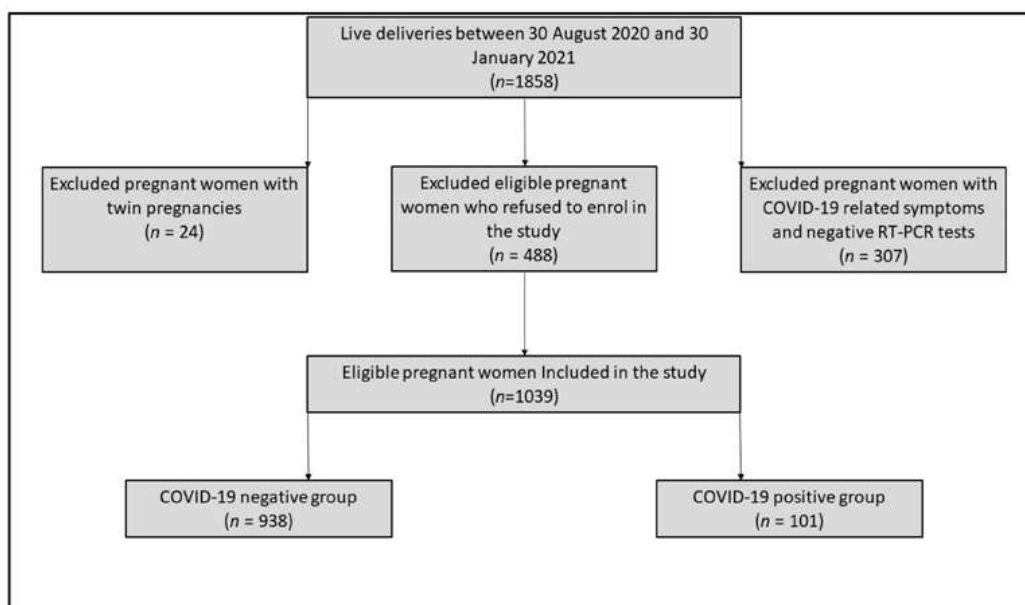
According to these aspects, the specific objectives of this paper can be systematized as follows:

1. Use of existing statistical methods to analyze the risk to which newborns are exposed to mothers infected with SARS-CoV-2 during pregnancy, as well as to assess pregnancy complications in the same pregnant women.
2. Assessment of adaptation to stress through complementary analysis questionnaires, which can determine the coping methods and the level of stress experienced by pregnant women infected with SARS-CoV-2, compared to pregnant women who have not gone through the disease, having the role of measuring their quality of life patients.

## STUDIUL 1: EXPLORING PREGNANCY OUTCOMES ASSOCIATED WITH SARS-COV-2 INFECTION

The current study aims to investigate the potential effects on obstetric outcomes after a positive SARS-CoV-2 infection. We aimed to analyze pregnancies that covered a longer period of pandemic and to determine whether live birth outcomes from mothers infected with SARS-CoV-2 differ from mothers who did not contact the virus during pregnancy and whether COVID-19 in itself is an independent risk factor for adverse birth outcomes.

The current research was conducted in Timisoara, Romania, at the Clinical Hospital of Obstetrics and Gynecology Dr. Dumitru Popescu, for a period of five months between August 30, 2020 and January 30, 2021. The following criteria applied to pregnant women accepted in our clinic: (a ) giving informed consent and accepting participation in research; (b) the birth of a single living child; and (c) testing positive for SARS-CoV-2 before or during hospitalization using the RT-PCR method. The research eliminated 307 pregnant women with COVID-19-associated symptoms who did not give birth and were tested negative for SARS-CoV-2 on at least two consecutive RT-PCR tests. In addition, 24 twin pregnancies were removed from the research, as were another 488 pregnant women who gave birth during the study period but refused to participate in the study. At the end of the study, 938 pregnant women who were tested negative for SARS-CoV-2 and 101 pregnant women who tested positive for SARS-CoV-2 infection met the inclusion criteria, as shown in Figure 1.



**Figure 1 - Flowchart of the study cohort**

Comparing the obstetric results for the examined patients, we found substantially more cases requiring emergency cesarean section in women infected with SARS-CoV-2 and significantly more PROM (11% in the positive group COVID-19 vs. 6% in the group COVID-19 negative; value  $p = 0.049$ ). Postpartum anemia was more prevalent after SARS-CoV-2 infection ( $p = 0.004$ ), and the newborns of these mothers had a substantially lower APGAR score than the control group, 18% compared to 11% in the other group (value  $p = 0.020$ ). Premature births occurred in 15% of COVID-19 cases, compared with only 8% of live births in COVID-19 negative women ( $p$  value  $<0.001$ ), as can be seen in Table 1.

**Table 1 – Obstetric features and complications**

	COVID-19 negative	COVID-19 positive	<i>p</i>
<b>Maternal outcomes</b>			
Anemia	263 (28%)	42 (42%)	0.004
Infection	413 (44%)	51 (51%)	0.214
Perineal laceration	366 (39%)	30 (30%)	0.066
<b>Neonatal outcomes</b>			
SARS-CoV-2 infection	-	2 (2%)	
Prematurity	75 (8%)	15 (15%)	$<0.001$
Intensive Care Unit admission	27 (3%)	6 (6%)	0.095
Malformations	19 (2%)	2 (2%)	0.975
Sepsis	56 (6%)	5 (5%)	0.678
Death	4 (0.5%)	1 (1%)	0.436
<b>Pregnancy outcomes</b>			
Hypertension	28 (3%)	6 (6%)	0.112
Preeclampsia	19 (2%)	2 (2%)	0.975
Gestational diabetes mellitus	66 (7%)	5 (5%)	0.429
PROM	55 (6%)	11 (11%)	0.049

Un model de regresie logistică multivariată (Tabelul 2) a fost construit utilizând variabilele "tipul nașterii", scorul APGAR, anemie postpartum, prematuritate și PROM, toate care anterior s-au dovedit a fi substanțial diferite între cele două grupuri de cercetare. Cu

excepția anemiei postpartum, niciunul dintre ceilalți factori nu a fost semnificativ statistic ca fiind corelat separat de infecția cu SARS-CoV-2. Mamele pozitive cu COVID-19 au avut un risc substanțial crescut de naștere prematură, fie cauzată iatrogen ca urmare a unor probleme conexe, fie spontan. În comparație cu mamele care nu au fost infectate cu COVID-19, cele cu o infecție confirmată au avut un raport de șanse ajustat (AOR) de 1,61 (interval de încredere 95% [CI] 1.19-2.04) pentru nașterea prematură; un AOR de 2,13 (95% CI 1,46-2,91) pentru un scor APGAR mai mic; un AOR de 1,24 (95% CI 1,09-1,45) pentru operație cezariană de urgență; și un AOR de 2,46 (95% CI) pentru PROM.

**Table 2 – Multivariate analysis of risk factors**

	COVID-19 negative	COVID-19 positive
<b>Premature birth</b>	75 (8%)	15 (15%)
OR (95% CI)	1.00	1.43 (1.08-1.79)
Adjusted OR (95% CI)	1.00	1.61 (1.19-2.04)
<b>APGAR &lt;9</b>	103 (11%)	18 (18%)
OR (95% CI)	1.00	1.93 (1.21-2.40)
Adjusted OR (95% CI)	1.00	2.13 (1.46-2.91)
<b>C-section</b>	159 (17%)	30 (30%)
OR (95% CI)	1.00	1.12 (1.04-1.37)
Adjusted OR (95% CI)	1.00	1.24 (1.09-1.45)
<b>PROM</b>	55 (6%)	11 (11%)
OR (95% CI)	1.00	2.28 (1.65-3.01)
Adjusted OR (95% CI)	1.00	2.46 (2.00-3.19)

### **Conclusions:**

1. This research shows that SARS-CoV-2 infection or diagnosis of COVID-19 during pregnancy in the third trimester is associated with an increased risk of preterm birth with indication for caesarean section.
2. This infection additionally causes a risk of premature rupture of membranes and results in lower APGAR scores in newborns from mothers with COVID-19.
3. COVID-19 was associated with a twice-increased risk of PROM and a 1.5-fold increased risk of preterm birth with an indication for an emergency cesarean section.

## **STUDY 2: COPING STRATEGIES AND HEALTH-RELATED QUALITY OF LIFE IN PREGNANT WOMEN WITH SARS-COV-2 INFECTION**

The aim of this study was to examine and evaluate the psychological changes and coping mechanisms of pregnant women with COVID-19 disease, as well as the impact on health-related quality of life in pregnant women who were infected with SARS-CoV-2 during pregnancy. We hoped to obtain information about the physical and emotional health of pregnant women and to evaluate the quality of medical treatment during the COVID-19 pandemic, using the standardized questionnaires HADS, SF-12, COPE, CORE-OM and QPP.

The current study was cross-sectional in nature and we used a convenient sampling method to determine the optimal sample size, which was determined to be at least 377 people for a 95% confidence interval. Of the 412 women who agreed to participate in the

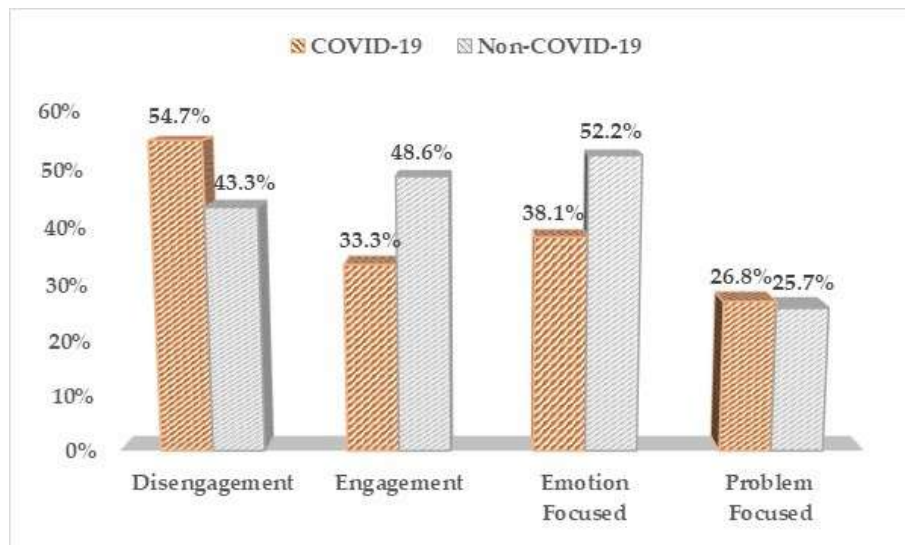


study and complete our questionnaires, 108 were excluded from the study due to lack of eligibility criteria or inadequate completion of the questionnaires, leaving 304 patients. This study included pregnant women who contracted SARS-CoV-2 (168 cases) and women who became pregnant during the epidemic but were not diagnosed with COVID-19 (136 cases). The questionnaires were completed between April and May 2021.

Our patients were classified by income as low, medium or high income, with a statistically significant difference in the proportions between groups ( $p$  value = 0.048). The largest difference was found between low-income pregnant women infected with SARS-CoV-2 and those who were not infected (22% versus 12%). Another grouping variable was employment status, with patients classified as employed, self-employed or unemployed, with a statistically significant difference in the proportions between the COVID-19 and non-COVID-19 groups ( $p$  value = 0.039). Pregnant women with SARS-CoV-2 infection lost their jobs at a rate of 20.9%, compared to only 11.8% in the other group. Finally, we found that 61.9% of patients in the COVID-19 group were from urban areas, compared to 72.8% of non-COVID-19 patients ( $p$  value = 0.045). The research groups did not vary substantially in terms of age, marital status, parity or level of education (Table 1).

**Table 1 – Comorbidities at risk in COVID-19**

<b>Variable (Frequency)*</b>	<b>COVID-19 positive (<math>n = 168</math>)</b>	<b>COVID-19 negative (<math>n = 136</math>)</b>	<b>P</b>
<b>Age (mean<math>\pm</math>SD)</b>	31.4 $\pm$ 7.8	30.9 $\pm$ 6.4	0.693
<b>Civil status</b>			0.877
Married	153(91.0%)	127(93.3%)	
Single	4(2.3%)	3(2.2%)	
Divorced	7(4.1%)	4(2.9%)	
Widowed	4(2.3%)	2(1.4%)	
<b>Parity</b>			0.220
Primigravida	39(23.2%)	40(29.4%)	
Multiparity	129(76.8%)	96(70.5%)	
<b>Income</b>			0.048
Small	38(22.6%)	17(12.5%)	
Medium	86(51.2%)	72(52.9%)	
Large	44(26.2%)	47(34.5%)	
<b>Level of education</b>			0.548
$\leq 12$ years	42(25.0%)	30(22.1%)	
$> 12$ years	126(75.0%)	106(77.9%)	
<b>Occupation</b>			0.039
Employed	88(52.3%)	69(50.7%)	
Self-employed	45(26.8%)	51(37.5%)	
Unemployed	35(20.9%)	16(11.8%)	
<b>Place of residence</b>			0.045
Rural	64(38.1%)	37(27.2%)	
Urban	104(61.9%)	99(72.8%)	



**Figure 1 – Comparison between COVID-19 positive and COVID-19 negative pregnant women based on their high probability of using the coping mechanisms determined by the COPE-60 survey**

We found a substantial difference in coping methods depending on the presence or absence of SARS-CoV-2 infection using the COPE-60 questionnaire (Figure 1). According to the study, infected pregnant women were almost 55% more likely to adopt a stress management disengagement technique, compared with 43% of other pregnant women who had a pregnancy during the pandemic but were not infected ( $p = 0.048$ ). In addition, significant results were found in positive coping techniques, with almost 50% of patients in the non-COVID-19 group using an engagement coping strategy, compared with only one-third of women in the COVID-positive pregnancy group. -19 ( $p$  value = 0.007). Patients who tested positive for COVID-19 were more likely to use emotion-focused coping strategies at a rate of 38%, compared with 52% in the non-COVID-19 group ( $p$  value = 0.013).

### **Conclusions:**

1. COVID-19 treatment in pregnant women continues to be a challenge for obstetricians and surgeons.
2. It is essential that pregnant women receive holistic treatment during these periods.
3. Throughout this ongoing crisis, maternity hospitals must continue to meet the requirements necessary to meet the expected quality of medical care during the care of mothers, infants and their families.
4. Pregnant women and mothers have a higher risk of maternal, fetal and pregnancy complications, with studies highlighting the essential role of social connections throughout pregnancy.
5. Our research has revealed certain categories of pregnancy risks that are negatively influenced by COVID-19 stress and are more likely to engage in negative coping mechanisms, thus affecting their mental recovery and quality of life.

6. Unemployed pregnant women, especially those living in poverty in rural areas, appear to be at increased risk of SARS-CoV-2 infection during pregnancy, along with associated mental health complications, such as increased anxiety and depression or increased physical burden.
7. Finally, the quality of hospital care does not differ significantly between COVID-19 and non-COVID-19 maternity units, except for the lower technical competence of COVID-19 units, which can be attributed to the lack of experience in such scenarios; and constantly changing the rules governing patient care.
8. Unemployed pregnant women living in rural poverty had a higher incidence of SARS-CoV-2 infection during pregnancy. They experienced a higher level of worry, as well as increased physical pressure and fatigue. These results are not affected by the medical care, which remained consistent in all COVID-19 and non-COVID-19 maternity units in our country, except for the substantially lower technical competence ratings of the medical staff for the COVID-19 facilities.
9. As the effects of the pandemic become clear and new outbreaks appear, treatment should emphasize the additional physical burden on pregnant women who become infected with SARS-CoV-2, as well as psychological, emotional and mental health care.

## ORIGINAL CONTRIBUTIONS

The original contributions made by this paper can be summarized as follows:

1. The present studies are the only ones in Romania so far that have included a comprehensive population of pregnant women during pregnancy during the COVID-19 pandemic, in order to assess the obstetric outcomes and mental health of pregnant women who have gone through infection with SARS-CoV-2.
2. Alterations in the APGAR score have been identified when pregnant women became infected with SARS-CoV-2 during pregnancy. In addition, this infection during the third trimester of pregnancy significantly increases the risk of premature rupture of amniotic membranes and premature birth with indication for cesarean section.
3. Other important findings from our studies show that pregnant women are negatively affected by the stress of COVID-19 disease and are more likely to use negative coping mechanisms, thus affecting their mental recovery and quality of life. Categories of pregnant women who have a higher risk of SARS-CoV-2 infection and who are exposed to increased levels of anxiety and depression have been identified. However, it seems that the quality of hospital care does not differ significantly between COVID-19 and non-COVID-19 maternity units.

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