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BIOCHEMICAL CHANGES IN AMNIOTIC FLUID AFTER MATERNAL COVID-19

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Abstract: The COVID-19 pandemic has profoundly affected maternal and fetal health, especially in pregnant women. This study examines specific and non-specific biochemical indicators in the amniotic fluid of pregnant women who contracted COVID-19. Despite increasing information, few studies examine the correlation between these markers and fetal development, especially regarding lung maturity and placental function. To address this disparity, we performed a biochemical examination of amniotic fluid obtained from 70 pregnant women categorized into three groups: those with healthy pregnancies and those with COVID-19 throughout the second and third trimesters. Metabolites including phosphatidylcholine, sphingomyelin, total protein, and alpha-amylase were quantified utilizing high-performance liquid chromatography and biochemical analyzers. The findings indicated markedly reduced levels of phosphatidylcholine, sphingomyelin, and protein markers in women with COVID-19 relative to the control group. These reductions signify fetal lung immaturity and possible impairments in placental and hepatic function. Increased alkaline phosphatase levels indicated potential cellular injury. These discoveries underscore the necessity for focused monitoring and interventions during pregnancies impacted by COVID-19 to reduce hazards to fetal development. This study highlights the significance of comprehending the biochemical milieu of amniotic fluid following COVID-19 and its ramifications for neonatal outcomes, facilitating enhanced maternal and fetal care measures in pandemic contexts.

Keywords: COVID-19, pregnancy, amniotic fluid, biochemical markers, phosphatidylcholine, sphingomyelin, fetal lung maturity, placental stress, neonatal outcomes.

Introduction

The COVID-19 pandemic has presented considerable hurdles to worldwide healthcare systems, with pregnant women recognized as a vulnerable population due to heightened risks of severe maternal and newborn outcomes. Recent research indicates that SARS-CoV-2 infection during pregnancy affects maternal health and alters fetal development, especially by modifying the biochemical composition of amniotic fluid. Amniotic fluid is crucial for fetal growth and development, as it contains critical biochemical indicators, including lipids, proteins, and enzymes, necessary for organ development and metabolic functions. Research indicates that COVID-19 in pregnancy correlates with preterm birth, low birth weight, and heightened neonatal critical care unit hospitalizations. Nonetheless, there is a paucity of study into the exact biochemical alterations in amniotic fluid induced by maternal COVID-19 and its ramifications for fetal health, particularly within the framework of emerging healthcare systems like that of Uzbekistan.

Comprehending these disruptions is essential for formulating appropriate prenatal care procedures and interventions. This study seeks to address this deficiency by examining specific biochemical markers (phosphatidylcholine, sphingomyelin) and non-specific markers (total protein, alpha-amylase, alkaline phosphatase) in the amniotic fluid of pregnant women impacted by COVID-19. This research aims to elucidate the biochemical alterations linked to maternal COVID-19 and their possible effects on fetal lung development, placental function, and overall newborn outcomes by comparing the findings with a control group of healthy pregnancies. The findings are anticipated to enhance healthcare policies for maternal and neonatal care, especially in regions such as our country.

Literature Review

The COVID-19 pandemic has significantly affected maternal and fetal health outcomes. Pregnant women with COVID-19 face a higher likelihood of preterm birth and intensive neonatal care compared to healthy pregnancies. Evidence suggests that COVID-19 compromises placental function and influences fetal development, including lung maturity.[1]

Biochemical markers in amniotic fluid, such as phosphatidylcholine, sphingomyelin, total protein, and alpha-amylase, play a vital role in fetal development. Phosphatidylcholine and sphingomyelin are crucial for lung surfactant production, while proteins and enzymes like alpha-amylase aid metabolic and organ development.[2] Research highlights a significant reduction in these markers among COVID-19-affected pregnancies, suggesting delayed fetal organ maturation.[3]

Elevated alkaline phosphatase levels in pregnancies with COVID-19 indicate potential placental or liver damage.[4] This aligns with studies reporting inflammatory responses in the placenta due to SARS-CoV-2 infection.[5] Reduced alpha-amylase levels further suggest disruptions in fetal carbohydrate metabolism.[6]

Limited research exists on how biochemical marker reductions in amniotic fluid directly influence neonatal outcomes. This gap calls for a more comprehensive understanding of the metabolic pathways affected by COVID-19.[7]

The findings underscore the need for regular biochemical monitoring in pregnancies complicated by COVID-19. Early interventions could help mitigate risks and support fetal health.[8] Future research should also explore therapeutic strategies to enhance neonatal outcomes.[9]

Methodology

This study aimed to examine the specific and non-specific biochemical markers in the amniotic fluid of pregnant women who contracted COVID-19 during the second and third trimesters. The study was conducted in 2022 at the Republican Perinatal Center in Tashkent, Uzbekistan, involving 70 pregnant women categorized into three unique groups according to their COVID-19 exposure and gestational age. This methodology sought to guarantee a thorough and systematic examination of biochemical disturbances induced by maternal COVID-19, concentrating on fetal development and placental function. The study employed a cross-sectional design to analyze biochemical markers across three cohorts: (1) a control group

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of 10 healthy pregnant women without obstetric or somatic complications, (2) a group of 30 pregnant women who contracted COVID-19 in the second trimester, and (3) a group of 30 pregnant women who contracted COVID-19 in the third trimester. All subjects were granted informed consent, and ethical approval was secured from the appropriate institutional review board.

Amniotic fluid samples were obtained using transabdominal amniocentesis between 22 and 38 weeks of gestation in a sterile environment. The time of amniocentesis for the COVID-19 groups was meticulously coordinated with the participants' recovery from the virus. The samples underwent centrifugation at 2700 rpm for 5 minutes to isolate cellular debris, thereby concentrating the analysis on biochemical constituents.

High-performance liquid chromatography (HPLC) was utilized to quantify particular lipid indicators, such as phosphatidylcholine and sphingomyelin, essential for embryonic lung surfactant synthesis. The analysis utilized an Agilent Technologies Inc. 1100 series liquid chromatograph. This approach enabled accurate measurement of lipid contents in the amniotic fluid.

A biochemical analyzer (RT-1904C, Rayto, China) was employed for non-specific indicators, such as total protein, alpha-amylase, and alkaline phosphatase. The materials were examined utilizing colorimetric and kinetic techniques with test kits supplied by Cypress Diagnostics, Belgium. These markers were chosen to assess overall metabolic performance, nutrition transport, and possible stress responses in the placenta and liver.

Statistical analyses were conducted with SPSS software (version 26.0). Descriptive statistics were computed to summarize the data, encompassing means and standard deviations for biochemical markers among the three groups. One-way ANOVA and post-hoc Tukey testing were employed to assess group differences, with a significance threshold established at $p < 0.05$. This method confirmed the statistical significance of the variations in marker levels between the control and COVID-19-affected groups. Phosphatidylcholine and sphingomyelin were selected for their essential functions in the synthesis of lung surfactant, a vital marker of fetal lung maturity. Total protein levels were measured to determine nutrient transport efficiency, and alpha-amylase levels were included to examine carbohydrate metabolism. Increased alkaline phosphatase levels were deemed symptomatic of placental or hepatic distress, offering insight into possible inflammatory or structural damage resulting from COVID-19.

This work offers significant insights, however, it possesses limitations. The cross-sectional approach restricts the establishment of causal links, and the limited sample size may not encompass the complete range of outcomes. The study lacked long-term follow-up to evaluate neonatal outcomes, an essential area for further investigation.

Ethical guidelines were rigorously followed throughout the investigation. All participants were granted informed consent, and their confidentiality was preserved. The research adhered to the Declaration of Helsinki and local rules about human subject research in Uzbekistan.

This methodology offers a comprehensive framework for examining the biochemical effects of COVID-19 on pregnancy, enhancing the understanding of fetal development and placental function during the pandemic.

Results

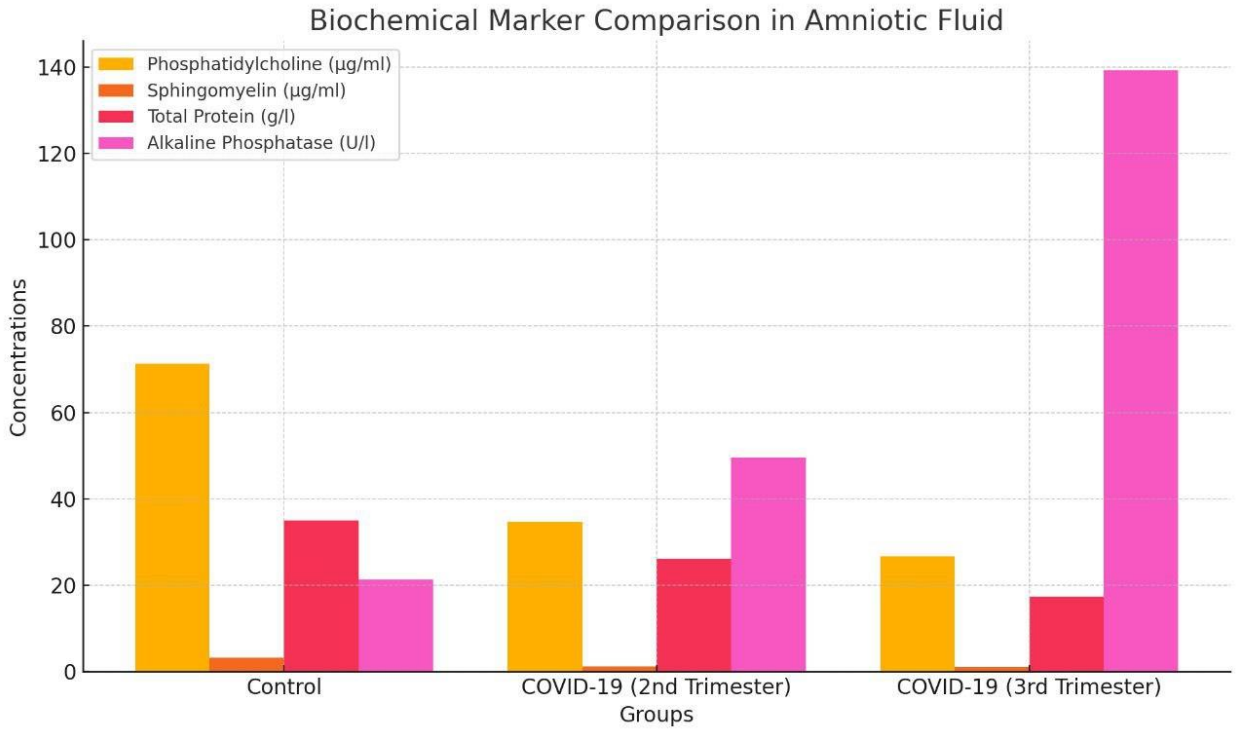
The biochemical examination of amniotic fluid in pregnant women demonstrated notable differences in specific and non-specific indicators between the control group and those impacted by COVID-19 over the second and third trimesters. These findings enhance comprehension of the disturbances inflicted by COVID-19 on embryonic development, particularly for pregnancies in Uzbekistan. The concentrations of phosphatidylcholine, an essential lipid in lung surfactant formation, were markedly diminished in the COVID-19-affected cohorts. In the control group, phosphatidylcholine concentrations were 71.30 ± 2.98

µg/ml, but in the second and third-trimester COVID-19 groups, they decreased to 34.68 ± 0.83 µg/ml and 26.74 ± 1.07 µg/ml, respectively. A comparable trend was noted in sphingomyelin concentrations, measuring 3.28 ± 0.08 µg/ml in the control group, but levels diminished to 1.17 ± 0.09 µg/ml and 0.98 ± 0.05 µg/ml in the second and third trimester COVID-19 cohorts, respectively. This decline signifies impaired lung development in fetuses of moms affected by COVID-19, thus heightening the risk of neonatal respiratory distress.

Non-specific indicators, including total protein, exhibited substantial decreases, indicating compromised nutrition delivery and metabolism. The control group had total protein levels of 35.08 ± 1.93 g/l, whereas the second and third-trimester COVID-19 groups displayed levels of 26.15 ± 2.18 g/l and 17.44 ± 0.83 g/l, respectively. Alpha-amylase levels, essential for carbohydrate metabolism, were similarly diminished, suggesting modified energy availability for the developing baby.

In contrast, alkaline phosphatase levels exhibited a significant elevation in pregnancies impacted by COVID-19, attaining 49.57 ± 13.57 U/l in the second-trimester cohort and 139.21 ± 37.86 U/l in the third-trimester cohort, in comparison to 21.28 ± 3.002 U/l in the control group. This rise indicates stress responses in the placenta or liver, possibly resulting from inflammatory reactions to SARS-CoV-2 infection.

Diagram 1



The graphic presented visually contrasts the biochemical markers among the three groups: the control group, the second-trimester COVID-19 group, and the third-trimester COVID-19 group. It demonstrates the pronounced decreases in phosphatidylcholine, sphingomyelin, and total protein in the COVID-19 cohorts, alongside a notable elevation in alkaline phosphatase levels. These visual representations illustrate the metabolic disturbances and their consequences for prenatal health.

Discussion

These findings highlight the significant influence of COVID-19 on the biochemical composition of amniotic fluid and its consequences for fetal health. The noted decreases in phosphatidylcholine and sphingomyelin levels are significantly associated with delayed lung maturation, potentially leading to neonatal respiratory

issues. The reduction in total protein levels signifies disturbances in the transport and synthesis of essential nutrients required for fetal development, but the decrease in alpha-amylase levels suggests impaired carbohydrate metabolism, which may impact energy availability for the fetus.

The increased alkaline phosphatase levels seen in the COVID-19-affected groups underscore considerable strain on the placenta and liver, consistent with research linking SARS-CoV-2 infection to placental inflammation and injury. This marker may also signify potential abnormalities in the placental barrier, which can have enduring implications on embryonic development.

These findings are especially pertinent in Uzbekistan, where healthcare resources may be constrained. The findings underscore the necessity for improved prenatal care regimens, including regular biochemical assessment of amniotic fluid in pregnancies impacted by COVID-19. Policymakers and healthcare practitioners must prioritize the integration of advanced diagnostic techniques to identify and manage these hazards promptly.

This study offers helpful insights but also reveals considerable knowledge deficiencies. The long-term neonatal effects of biochemical marker alterations are uncertain, necessitating additional research to investigate the underlying molecular pathways. The significance of maternal immunization in enhancing biochemical profiles in amniotic fluid warrants further investigation, particularly in areas such as Uzbekistan with disparate vaccination rates.

Future research should employ a multidisciplinary methodology, integrating biochemical analysis, imaging technology, and longitudinal monitoring of newborn outcomes. This research could yield a more profound theoretical comprehension and pragmatic approaches for mitigating the effects of maternal COVID-19 on fetal development. Furthermore, the creation of a comprehensive database in Uzbekistan that records maternal and newborn outcomes associated with COVID-19 should improve clinical decision-making and inform policy development.

This work underscores the substantial alterations in biochemical markers in pregnancies impacted by COVID-19, highlighting the pressing necessity for tailored therapies. Enhancing maternal and newborn outcomes in Uzbekistan can be achieved through comprehensive research and the refinement of healthcare methods. These initiatives will enhance the global understanding of managing pregnancy issues during pandemics, establishing a basis for improved healthcare tactics in future crises.

Conclusion

This study reveals notable biochemical alterations in the amniotic fluid of pregnant women with COVID-19 during the second and third trimesters, characterized by substantial decreases in phosphatidylcholine, sphingomyelin, and total protein levels, as well as increased alkaline phosphatase levels. The data suggest delayed fetal lung maturity, modified glucose metabolism, and possible placental or hepatic stress, which may negatively impact newborn outcomes. The conclusions underscore the essential requirement for improved prenatal care protocols, encompassing routine biochemical monitoring and specific therapies to alleviate these risks. This research highlights the need for more studies to examine the long-term neonatal effects of these biochemical alterations, identify the molecular mechanisms behind these disruptions, and assess the impact of maternal immunization on pregnancy outcomes. These initiatives are crucial for enhancing maternal and fetal healthcare strategies in Uzbekistan and worldwide, so ensuring improved readiness for analogous healthcare difficulties in the future.

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