Pak. j. life soc. Sci. (2024), 22(1): 2211-2221 E-ISSN: 2221-7630;P-ISSN: 1727-4915

Pakistan Journal of Life and Social Sciences
www.pjlss.edu.pk

https://doi.org/10.57239/PJLSS-2024-22.1.00163

RESEARCH ARTICLE

Molecular Lipid Profile, Oxidative Stress and Histological Changes in Relation to the Placenta In Mothers With Gestational SARS-COV-2

Rafaah J. Al -Dahwi[1*], Denitza G. Kostadinova[2], Mariya A. Angelova[3], Galina D. Nikolova[4], Yanka D. Karamalakova[5]

[1, 2,3] Obstetrics and Gynaecology Clinic, UMHAT „Prof. St. Kirkovich, Stara Zagora, Bulgaria
[4,5] Chemistry and Biochemistry, Medical Faculty, Trakia University, Stara Zagora, Bulgaria

ARTICLE INFO

Received: May 28, 2024

Accepted: Jun 16, 2024

Keywords

SARS-CoV-2

Lipid Profile

Pregnancy

Oxidative Stress

Coronavirus disease 2019

***Corresponding Author:**

Rafa.dzhasim@trakia-uni.bg

ABSTRACT

The COVID-19 (Coronavirus disease 2019) outbreak has presented numerous threats to maternal and foetal health with gestational SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) infection concerning different maternal complications. The effect of this viral infection on maternal lipid profiles, oxidative stress in the placenta, and histopathological changes has not been well elucidated, hence the need for further research on it to establish useful data that could help clinicians manage pregnancies affected by this virus. This review aims to discuss the overall effects of gestational SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) infection regarding maternal lipid profiles, oxidative stress in the placenta tissue, and histopathologic alterations. Thus, based on the literature review, the aim is to understand the processes that contribute to these effects and find ways to treat negative outcomes of pregnancy caused by Coronavirus disease 2019. It testified the possible adverse effects of gestational Severe Acute Respiratory Syndrome Coronavirus 2 infection, including alteration in the mother's lipid profile, oxidative stress in the placenta and histopathological changes in the affected placenta. A systematic literature review was performed using electronic databases to select the relevant literature. In light of this, the review discusses how gestational Severe Acute Respiratory Syndrome Coronavirus 2 infection affects the lipid profile showing high total cholesterol and LDL (low-density lipoprotein) cholesterol in the maternal system. In addition, chorionic villi oxidative stress reduces the placental function and results in poor perinatal outcomes including preterm birth and foetal growth limitation. The pregnant coronavirus positive patient's placenta also revealed histopathological changes such as intervillous hematomas and chronic villitis which might suggest that nutrient and oxygen supply to the foetus are interfered with. SARS-CoV-2 infection has been linked with changes in maternal lipid profile, oxidative stress in the placenta and histopathological change that affect pregnancy outcomes. Tackling dyslipidaemia, placental inflammation and histopathological changes could reduce adverse maternal and foetal prognosis among this group. Further research is warranted to elucidate the underlying molecular mechanisms driving these phenomena and develop effective therapeutic strategies tailored to pregnant women with Coronavirus disease 2019.

INTRODUCTION

The emergence of vertical genus SARS-CoV-2 conception in pregnant females and the subsequent alterations in molecular lipid profiles present a twine that demands a grounded perspective of foetal and maternal health issues [1,3,4]. Such a sound link between the process of viral infection and metabolic events during pregnancy is a testimony of the validity of further investigation devoted to the elucidation of the complex molecular modes of these events. Have evidence that pregnant women considered subsequently a vulnerable populace due to this disease because of specific physiologic alterations and immunological accommodation with pregnancy [1]. Many studies have stated fundamental pathways through which SARS-CoV-2 enters the placenta-foetal pairs and appears to utilise ACE2 (angiotensin-converting enzyme 2) receptors for cell entry [4,1]. The viral proteins in placental tissue, especially the Covid 19 spike protein (CoV-2 SP), are suspected to cause vertical transmission and placental injury. Mreover, SARS-CoV-2 comes in a sequence of metabolic modifications mainly in lipid metabolism that harm pregnant women and foetuses [12].

The insulin resistance at the molecular and hormonal level and the carbohydrate metabolism are particularly unstable, thus threatening the blood sugar balance and the nutrition conveyance to the foetus. Similarly, adipokine regulation dysfunction and lipid profile manipulation compound the metabolic disorder's detrimental consequences for maternal bad health and childbirth defects [12]. The presence of this dysrhythmia is linked to energy metabolism disorders, insulin resistance and inflammatory response disorders in women which are detrimental to the health of the mother and the foetus [12]. Additionally, a several studies stated that adipokines can exert their function by interplaying with inflammatory cytokines, which might in turn aggravate the inflammatory cycle resulting in systemic complications such as respiratory distress syndrome and metabolic disorders in pregnant mothers who have gestational SARS-CoV-2 [2,12]. Furthermore, gestational SARS-CoV-2 infection weakens the adipokines balance [2]. The adipokines, leptin and adiponectin, are the most vital mediators of metabolic processes and inflammation. However, adipokine dysregulation is feasible within the scope of metabolic disorders and systemic inflammation relying on the positive diagnosis of COVID-19 [2,12]. Adding up the respiratory and inflammatory symptoms of COVID-19 in pregnant females facing high risks of respiratory distress syndrome and systemic complications, severe demand is placed on the appropriate surveillance and personalised therapeutic interventions [2]. Moreover, the lasting consequences of long-term viral sequelae reinforce the vital need for long-term research on the complex interaction between viraemic pathogenesis and metabolic homeostasis in foetal health and maternal well-being outcomes.

METHOD AND MATERIAL

This research utilises a secondary qualitative research method for exposing the possible vertical transmission of SARS-CoV-2 through placental tissue and exploring its pathology sceneries. Subsequently, the secondary qualitative analysis consists of the purposefully structured involvement of prior research and information in order to generate new knowledge, merge the existing one, and make a full conclusion [26].

A representative step of literature collection was carried out to achieve the purpose that multiple academic databases, such as PubMed, Google Scholar, and Science Direct, were taken into account for searching. The keywords looked for were 'SARS-CoV-2 placental pathology' "vertical transmission COVID-19," "viral proteins in the placenta," and "COVID-19 pregnancy outcomes." The search was limited to the peer-reviewed research papers which were published in January 2020 and May 2024 to ensure the incorporation of the latest and the most relevant studies. The relevant publications were chosen based on the quality of their methods and data related to the topic [25,28]. With regard to the literature reviews, inclusion criteria specified SARS-COV-2 presence in placental tissues, viral protein detection and plausible mechanisms of the vertical transmission. Both prospective and retrospective studies and reviews with an important qualitative component on placental pathology

and outcomes of impregnation that have taken place in the conditions of COVID-19 were included. Proceeding with these studies entailed studies which were not all about the placental part of COVID-19 transmission, non-peer-reviewed articles, and studies with considerable methodological issues were not done.

The chosen articles were analysed by the Systematic Literature review method which is a method of analysis existing literatures or researches done by researchers [26]. The core concepts were grouped according to the presence and granularity of viral proteins in placenta tissues, the proof of viral transmission from the mother to the foetus, and the possible consequences of these pathologies on the health of the mother and the foetus. The research terms for this systematic literature review focused on and studied the characterisation of different proteins produced by the SARS-CoV-2 virus such as spike glycoproteins (CoV2 SP) and how these viral proteins are insufficiently involved in placental infection and damage. The overall approach towards this systematic literature review involved comparing and contrasting findings across studies to highlight common patterns and discrepancies. This approach enabled a comprehensive understanding of the current state of knowledge regarding the potential for SARS-CoV-2 vertical transmission through the placenta and its pathological consequences.

RESULTS

The changes in molecular lipid profile in patients with gestational SARS-CoV-2 Significance of COVID-19 diseases in lipid profile in placenta during pregnancy

During the pregnancy process, the maternal metabolism profile undergoes improved changes such as increased fat deposition in order to support the similar nutritional needs of the mother and foetus [10]. The lipid profile which consists of total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol and triglycerides is one of the key factors that determine normal placental function and the characteristics of the foetus. Transcript (mRNA) of coronavirus SARS-CoV-2 obtained during pregnancy showed to be a determinant in maternal lipid metabolism processes, the latter being a key factor in pregnancy resulting in either favourable or unfavourable outcomes.

The outcome of SARS-construing CoV-2 gestation pandemic on that mother's lipid profile

Research by Frankevich et al., 2023 determined that lipid metabolism had extensive changes in pregnant women with the infection of the SARS-CoV-2 when compared to the uninfected controls. Also, has been proven that there is an elevation in the total cholesterol and LDL cholesterol among infected individuals. In relation to this, it can be inferred that gestational SARS-CoV-2 infection possibly presents a dyslipidaemia formation that is likely to affect the course of placental function and the development of the foetus [7]. The relationship between maternal lipid profile and placental functioning in patients carrying SARS-CoV-2 infection during pregnancy is supported by the existence of a relationship between dyslipidemia and abnormal placental development (markers of placental dysfunction) [7,25]. This can lead to fetal growth retardation and placental insufficiency [7,25]. The fetal growth retardation or intrauterine growth restriction IUGR is seen more in cases of maternal dyslipidemia.

High levels of triglycerides and changes in cholesterol levels in the mother's blood negatively affect the placenta to meet the nutrient and oxygen needs of the fetus. This contributes to low low weight of the new-borns [7,25]. Therefore, the lipid regulation is crucial for the normal foetal development during the SARS-CoV-2 infection. Dyslipidaemia in SARS-CoV-2-infected pregnancies was associated with placental insufficiency; a condition in which the placenta is unable to support the development of the foetus. The dyslipidaemia also resulted in increased placental inflammation, foetal oxidative stress as well as reduced placental function [7]. The shapes of placentae were grossly abnormal and numerous placental infarctions implying poor perfusion were noted, in these scenarios. Moreover,

the abnormal lipid profile of the mothers causes endothelial damage and alteration of the blood vessels in the placenta, making diseases such as preeclampsia and gestational diabetes worse. These conditions reduce the blood flow in the placenta and nutrients transfer, thereby enhancing the cycle of placental and foetal compromise [7]. Appreciation of the need to continuously check and control lipid status among pregnant ladies more so in this SARS-CoV-2 is very crucial in order to prevent any harmful effects on placental functions and development. In addition, abnormal maternal dyslipidaemia was related to an increased risk of adverse pregnancy outcomes, including early delivery and involvement of the foetus. These results highlight the need to evaluate lipid profile anomalies in the management of prenatal COVID-19 by utilising tailored treatments designed to prevent severe pregnancy outcomes.

Molecular mechanisms underlying lipid profile alterations

Despite a finding of some differences in lipid metabolism in pregnant women infected with SARS-CoV-2, the detailed molecular mechanism however remains unknown. SARS-CoV-2 infection can potentially activate both inflammatory responses and oxidative stress, thus possibly disturbing lipid metabolism pathways which could result in dyslipidaemia [27]. On the other side, the abnormal growth in hormone levels that can go with insulin resistance and secretion has been indicated to be an added reason that might consequently lead to dyslipidaemia in SARS-CoV-2-infected pregnant women [7]. The baseline hormonal levels in pregnant women change during pregnancy, and this change is worsened by infections including SARS-CoV-2. It has also been postulated that gestational SARS-CoV-2 infection affects hormonal changes that are critical to the development of dyslipidaemia, with the insulin hormone being critical. SARS-CoV-2-positive pregnant women have increased circulating levels of inflammatory cytokines and stress hormones, which produce direct or indirect inhibitory effects on insulin receptor signalling impairing insulin sensitivity [7].

Diabetes affects lipid metabolism in a way that increases the breakdown of lipids in the adipose tissue which leads to a subsequent release of free fatty acids in the circulation. These free fatty acids are transported to the liver which stimulates the production and secretion of very low-density lipoprotein cholesterol (VLDL) carriers that are dense in triglycerides. This process also contributes to the conclusion that SARS-CoV-2 infection results in raised lipid levels and other lipid disturbances in pregnant women [7].

In addition, the placenta, an organ that regulates hormones and fats, might also be impacted by these hormonal disorders. The hormones like human placental lactogen and cortisol secreted in higher amounts by the placenta can only add to the degree of insulin otherwise leading to dyslipidaemia which is a continuous cycle in most pregnancies [10]. They attenuate lipid metabolism disorder not only causes maternal adverse effects but also exerts a negative impact on placental function and foetal development thus warranting special emphasis on management of lipid profile in pregnant women.

The Changes in oxidative stress in the placenta in patients with gestational SARS-CoV-2

Concept of oxidative stress

Oxidative stress is considered to create variance while developing reactive oxygen components and antioxidant defences [13]. The imbalance can lead to harmful impacts like damage to the cells, proteins and DNA. Additionally, oxidative stress can be generated due to symptoms like fatigue, grey hair, decreased eyesight and headaches [23]. This type of condition in the human body can increase the potential of oxidative stress contributing to various diseases and stresses in the placenta. Apart from that, reactive oxygen species are capable of attacking lipids on the cell membrane which can increase cell damage during pregnancy [23]. This can lead to inflammation, apoptosis and the release of cellular debris into the maternal circulation. Hence, it can generate a high amount of damage to the

maternal body during pregnancy due to the occurrence of oxidative stress by damaging cells and inflammations.

Another study examined that the p53 protein is a tumour suppressor that regulates cell cycles and repairs DNA profile [12]. It is perceived as the guardian of the genome due to its capability of preserving genomic stability [12]. On the contrary, p53 acts as a protein within the transcription factor to control cell apoptosis, growth arrest and DNA repair in managing stress conditions [8]. The placenta in this situation produces a high amount of p53 protein during complicated pregnancy conditions. The high count of p53 can influence the transcription of elements and contribute to cell apoptosis and cycle arrest such as p21 [8]. Hence, it informs the role of p53 to generate the repairing of DNA under oxidative stress conditions during pregnancy and plays a major role in trophoblast apoptosis within the placenta [8].

Oxidative stress relation to the placenta or pregnancy

Oxidative stress (OS) is considered as the condition of imbalance between the free radicals and antioxidants present in the body which can cause placental imbalance like impaired angiogenesis [16]. This can be responsible for disrupting the blood vessels in the placenta which can cause insufficient blood flow and nutrient exchange. Additionally, OS contributes to the development of preeclampsia which is a critical condition due to damage to organs like kidneys and liver and higher blood pressure for pregnant women. Moreover, OS is a basic contributor to damaging the organs of pregnant women to induce maternal imbalance effectively.

Apart from that due to the high number of OS injuries, placental levels of vitamin D, vitamin E and Coenzyme-Q10 increase in the COVID-19 patients [16]. Also, it can be stated that the inclusion of COVID-19 is a major contributor to the imbalance in the vitamins levels and hampers its overall function. Hence, OS has impacted placental efficiency due to the reduction in the vitamins D, E and Coenzyme-Q10 concentrations. Additionally, the involvement of iron-related proteins such as divalent metal transporter 1 (DMT1), ferroportin-1 (*Fpn1)* and ferritin has been regulated in the placenta of COVID-19-infected individuals [16]. The alternation of these proteins can impact the iron availability for both the mother and the foetus to generate potential foetal anaemia. Hence, with the alterations of these iron-related proteins, the placental function can be hampered and lead to a condition of foetal anaemia. Furthermore, antioxidant defences, mitochondrial dynamics, and respiratory chain components exhibit reduced levels in the placenta due to the infection with COVID-19 [14,16]. Therefore, it informs that placental cells are highly susceptible to COVID-19 due to the low levels of antioxidant defences in the placenta to damage cellular functions. Additionally, lower values in the mitochondrial dynamics underscore the disruptions of COVID-19 in the mitochondrial distribution like shape, size and numbers [10,16]. It affects the entire cellular energy balance within the placenta. Furthermore, low functionality of the respiratory chain during COVID-19 shows impaired formation of the electron transport which hinders ATP (Adenosine Triphosphate) production to lower the energy formation [10,16]. Hence, lower functionality of antioxidant defences, mitochondrial dynamics and respiratory chain can increase cell damage by lowering the energy production in the cells of COVID-19-infected people.

Role of prostaglandins in pregnancy due to oxidative stress

Prostaglandin F2 alpha (PGF2α) is a type of prostaglandin involved in the physiological contraction of smooth muscle in the uterus. In relation to pregnancy, PGF2α is generated by the uterus, which has a crucial role in the initiation of labor by stimulating uterine contractions [22]. This is effective in regulating placental blood flow and developing placental expulsion after delivery. Thus, the involvement of PGF2α is significant for initiation of labor and efficient regulation of muscle flow. On the other hand, prostaglandins are considered to be lipid compounds that perform various functions such as regulation of inflammation, vascular tone and labor induction, during pregnancy [1].

However, COVID-19 induction creates a strong inflammatory response by releasing cytokines to stimulate the production of prostaglandins. Additionally, chronic inflammation causes impairment in placental function due to the reduction of nutrients and oxygen levels within the foetus [1]. So, this can lead to a reduction of the movement of blood and limits the normal growth of the placenta. Furthermore, abnormal prostaglandin activity due to oxidative stress inclusion leads to dysfunction in the labour patterns. So, this can generate consequences for the mother like induction or caesarean delivery. Hence, the overall impact of prostaglandin activity is highlighted which is impacted due to the COVID-19 infection reduces the blood flow and oxygen levels to the foetus and creates the potential for caesarean delivery.

COVID-19 relation to oxidative stress

A study examines that extreme acute respiratory syndrome coronavirus 2 (SARS Cov-2) induced COVID virus in 2019. This has led to infections for pregnant women by generating maternal and placental altercations. This has generated vascular defects like preeclampsia which represents high susceptibility towards SARS-CoV-2. Additionally, pregnant women attacked with SARS-CoV-2 represented extreme rates of premature birth and caesarean delivery with the placenta representing signs of vasculopathy [16]. So, COVID-19 is highly responsible for pregnant women causing preterm birth and caesarean delivery which disturbs the growth of the foetus. Different research, comented that oxidative balance regulates the placental psychology and can be disturbed due to the adverse impact of preeclampsia and gestational diabetes. This can generate higher risks with inflammation in the placenta and pregnancy jeopardies due to infection. Figure 1 below highlights the placenta samples from eight regions after being infected under SARS-CoV-2 in which four samples are collected from the maternal side while the other four have been adapted from the foetal side. From this study, it is found that samples from both sides have been homogenised to obtain a supernatant and used again in the downstream procedure [11]. Moreover, it helped to develop the recovery of COVID-19-infected patients by delivering vaccinations and assigning them to the control group to reduce the impact of the virus fully.

The placenta acts as an interface between the mother and the foetus which promotes vertical transmission after the mother gets infected with COVID-19 [11]. Another research indicates that placental dysfunction is one of the significant consequences of SARS-Cov-2 infection that can jeopardise the procedure of childbirth during the third trimester [24]. SARS-CoV-2 generates inflammation within the placenta which is defined as placentates to infect the foetal membranes and hamper the nutrient and gas exchange procedure [24]. Additionally, impaired placental function increases the threat of preterm labour resulting in complications for new-borns [24]. So, it can delay foetal formation and increase the risk of infection under SARS-CoV-2.

Furthermore, placental dysfunction generates emergencies like foetal distress, placental abruption and severe preeclampsia to hinder the safety of both the mother and the baby during SARS-CoV-2. Hence, SARS-CoV-2 induces placental dysfunction to reduce foetal growth and increase preterm birth with severe preeclampsia [4]. On the other hand, another research has explained that the potential of mother-to-foetus transmission of SARS-CoV-2 is lower although the rates of stillbirths are double [5]. So, due to the virus blood circulation reduces through the placenta as the presence of fibrin protein causes bleeding to damage the blood tissues. This can generate thrombosis by forming blood clots and endothelial dysfunction to damage the inner blood vessels to affect childbirth. Hence, the involvement of SARS-CoV-2 impacts blood circulation by damaging the placental tissue due to oxidative stress and jeopardising childbirth procedures. An astounding research study indicates that SARS-CoV-2 goes into human cells by using ACE2 which is widely present in the placental syncytiotrophoblasts [9]. So, this can contribute effectively to transmitting the virus to the foetus and lead to placental inflammation. Furthermore, Figure 2 below shows the build-up of hypo-vascularity and stromal fibrosis in the placental tissue that is being generated due to SARS-CoV-2. Hypo-

vascularity considers the reduction in the density of blood levels in maternal and foetal health whereas stromal fibrosis is the excessive development of fibrous connective tissue within the stroma [9]. The combined impact of hypo-vascularity and stromal fibrosis on the placenta can reduce the delivery of oxygen and nutrients and delay foetal development. Hence, the presence of hypo-vascularity and stromal fibrosis increase hampers the blood density levels in the placenta to delay foetal formation effectively [4, 9].

Histological transformations in the placenta of patients under Gestational SARS-CoV-2

SARS-CoV-2 is perceived as a single positive-stranded ribonucleic acid (RNA) that belongs to the COVID-19 category. The transmission pathways from the infected women under COVID-19 and the foetus are generated due to tiny droplets, close contact with the virus carriers and breathing shortness. Histopathological observations of the placenta of mothers infected by COVID-19 have shown maternal and foetal outcomes [18]. This has basically focused on the microvascular changes due to the inflammatory response of SARS-CoV-2 on the tissue of the placenta. Even some researches have indicated that SARS-CoV-2 is a virus involved within the betacoronavirus genes [4, 19]. Additionally, other coronaviruses are involved in the MERS-CoV and SARS-CoV. Histopathological analysis has ensured that fibrin deposition, inflammatory infiltration and blood vessels are involved as macroscopic elements in detecting virus-like particles [19]. So, it has highlighted the ultrastructural aspects involved in the placentas for interpreting the impact of SARS-CoV-2.

Impact on different age groups and health conditions

Some researchers have examined that COVID-19 has shown significant consequences on women aged more than 34 with body mass index (BMI) levels of over 25 who face gestational diabetes and hypertension. So, the impact of COVID-19 is not the same for all the age groups of preferred women and worsens with an increase in age [18]. Hence, it informs about the histopathological changes of SARS-CoV-2 in pregnant women of various age groups and creates health implications [18] like diabetes and hypertension.

Maternal and foetal malperfusion

Another meta-analysis has explained that maternal Malperfusion and foetal blood vessels have generated immunohistochemical symptoms in relation to the histopathological changes [21]. This is significant in impacting pregnant women due to the infection severity of SARS-CoV-2 and the placental histopathology. Apart from that, the study has informed that ACE2 receptor expressions are low within the positive section of SARS-CoV-2-attacked pregnant mothers [21]. This has adopted histopathological analysis to retrieve the medical records that informed about the symptoms like mild fever, cough and alterations in taste due to COVID-19. So, it states the influence of coronavirus on pregnant women as they have shown symptoms like fever and cough can impair the blood vessels and reduce foetal growth effectively [21]. Hence, the histopathological changes can cause foetal malperfusion due to the infection of COVID-19 to hinder overall foetal development. On the other hand, SARS-CoV-2 caused kaleidoscopic conditions like intervillous hematomas and chronic villitis [2]. This is significant in understanding the pathohistological change within the placentas from coronavirus due to hematomas and chronic villitis. Figure 3 below informs about the areas of bleeding within the intervillous hematomas in which maternal blood flows to deliver nutrients and oxygen into the foetal villi. The formation of chronic villitis is considered as an inflammatory condition as per researcher to infect the placental development due to SARS-CoV-2 [2]. Hence, the combination of intervillous hematomas and chronic villitis indicates an overall impact on the placental histology due to the COVID-19 infection jeopardising foetal health. Placental intervillous hematomas (x20): intervillous hematomas in the placenta with Hematoxylin and Eosin (HE) staining; b) microvascular thrombosis (x100): microvascular thrombosis or blood clots in the blood vessel

areas with HE staining at 100X magnification. The arrows indicate the point of blood clots in the placenta to affect fetal development; c) decidual and villous inflammation (x30): area of inflammation within decidua and villi by using mitochondrial Anti-CD8 straining; d) decidual and villous inflammation (x80): similar results to C, gives a detailed view of inflammatory responses.

Histopathological changes in various organs and tissues

Inflammatory abnormalities have been detected with chronic intervillositis under the infection of COVID-19 engaged with maternal immunological conditions like lupus anticoagulant [2]. Hence, it gives knowledge of the impacts generated by COVID-19 which has an impact on the placental formation of pregnant women and reduces the immunological balance of the body. The study of another researcher states that psychological changes during pregnancy can make individuals more susceptible to generating severe illnesses such as alternations in the immune system, respiration system and coagulation systems [9]. It shows the vulnerability of pregnant women facing severe illness from the virus SARS-CoV-2 [9]. Furthermore, pregnancy generates complications in the interplay of tolerating the semi-allogeneic [15]. So, this can alter the immunity power to hinder the body's ability to control the virus of SARS-CoV-2.

DISCUSSION

Implications of gestational SARS-CoV-2 on maternal lipid profile

The research outcomes on the influence of gestational SARS-CoV-2 virus on maternal lipid profile, which in turn relate to the complex relationships between viral infection, lipid profile, and pregnancy outcomes. Total cholesterol elevation and low-density lipoprotein cholesterol, clearly discernible as the symptoms of dyslipidaemia, are observed to be the recurring pattern among pregnant women who had SARS-CoV-2 infection [7]. Lipid metabolism dysregulation arises from the inflammatory response and oxidative stress induced as a consequence of the viral infection as well as the hormonal alterations during the infection period [27]. It can be said that the candidates of lipid profile in a mother lead to placental function and child development which are significant. It is well known that dyslipidaemia has an adverse effect on both the vascularisation of the placenta, the transport of nutrients, and hormone production, which are regarded as the elements of detection of the pregnancy [10]. Thus, hyperlipidaemia considering SARS-CoV-2 in epigenesis, could be a determining factor to lead to placental insufficiency, foetal growth restriction, and other pregnancy problems during gestation.

Also, maternal conditions, such as preeclampsia and gestational diabetes, often come together with dyslipidaemia, which is one more difficulty for professionals who treat gestational SARS-CoV-2 infection [7]. Thus, routinely examining the maternal lipid profile of COVID-19-positive pregnant women is key to identifying those at higher risk of developing adverse obstetric outcomes and then initiating targeted intervention to improve maternal and foetal health.

Oxidative stress impact on the placenta with gestational SARS-CoV-2

The overall research outcome has found the role of the placenta is crucial during pregnancy. It transports nutrients and waste products within the mother and foetus. However, the dysfunction in the placenta creates inflammation that infects the foetal membrane and increases the potential of preterm birth [2]. This has increased the vulnerability of the mother and also the foetus due to the oxidative stress of pregnant women infected with COVID-19. Apart from that, ACE2 is highly present in the placental syncytiotrophoblasts which can increase placental inflammation more severely. Furthermore, the hypervascularity impact and stromal fibrosis is indicated for increasing the levels of blood density and delaying foetal development.

Histopathological impact on the placenta of patients with gestational SARS-CoV-2

The overall discussion has highlighted the implication of histopathological changes affecting the mother's body and foetus due to COVID-19. Hence, overall knowledge is effective in understanding the infection of SARS-CoV-2 along with placental tissue and vertical transmission of the pregnant woman's body. Another research found the impact of COVID-19 on people aged more than 34 and causing health implications like diabetes and hypertension [18]. This has informed about the changes due to the SARS-CoV-2 role on foetal development. Furthermore, conditions like intervillous hematomas and chronic villitis are highlighted which are crucial to delivering oxygen and nutrients to the foetus.

Limitations and future scope

This research has lacked the concepts about the molecular components and mechanisms of the lipid profile that are essential in pregnancy outcomes. Future studies will look to gain more information on the mentioned topics to bridge them effectively. Apart from that, this research has focused less on the specific treatment methods to control the effect of SARS-CoV-2 on expectant mothers. So, future studies will look to address those issues and find relevant information needed in the study. Furthermore, this study has not explained deeply on how the blood clots in the placenta during COVID-19 and how to mitigate those conditions fully. Hence, covering these areas will be the primary aim of future researchers to enhance the knowledge on this topic.

CONCLUSION

Conclusively, it can be said that pregnant women with SARS-CoV-2 infection are shown to demonstrate multiple changes in their maternal lipid profiles, including a rise in total cholesterol and LDL cholesterol levels. These developments can arise from the interplay of immune reactions and hormone changes involved during pregnancy. Dyslipidaemia, the condition that comes with SARS-CoV-2 infection creates a serious health threat to both the mother and the foetus and increases the risk of adverse outcomes in the pregnancy like placental insufficiency and foetal growth restriction. Appropriate surveillance of the triglyceride levels in pregnant women with SARS-CoV-2 virus is also very important so as to get the information of those that are at a higher risk and the necessary interventions can be implemented. Needing research to be done in such a way that will bring clarity to the underlying molecular components of the mechanisms as well as exploring strategies to counter the effects of dyslipidaemia on pregnancy outcome is advisable. The elucidation of these mechanisms will facilitate the generation of personalised steps directed toward effective pregnancies. In the long run, such an effect will improve maternal and neonatal health.

Acknowledgment

This research was funded by Project No 5/2023/ Trakia University and Ministry of Education and Science BG-RRP-2.004-0006" Development of research and innovation at Trakia University in service of health and sustainable well-being"

REFERENCE

1. Y. M. Almoghrabi, "Lipidomics of fetal membranes in labour and the initiation of parturition by fetal lung maturation markers", The University of Manchester (United Kingdom), 2021
2. L. Bertero, F. Borella, G. Botta, A. Carosso, S. Cosma, M. Bovetti, M. Carosso, G. Abbona, G. Collemi, M. Papotti, P. Cassoni, and C. Benedetto, "Placenta histopathology in SARS-CoV-2 infection: analysis of a consecutive series and comparison with control cohorts". Virchows Arch., vol. 479, no. 4, pp.715–728, 2021
3. N. Breslin, C. Baptiste, C. Gyamfi-Bannerman, R. Miller, R. Martinez, K. Bernstein, L. Ring, R. Landau, S. Purisch, A. M. Friedman, K. Fuchs, D. Sutton, M. Andrikopoulou, D. Rupley, J. J. Sheen, J. Aubey, N. Zork, L. Moroz, M. Mourad, and R. Wapner, "Coronavirus disease 2019

infection among asymptomatic and symptomatic pregnant women: two weeks of confirmed presentations to an affiliated pair of New York City hospitals. Am. J. Obstetrics & Gynecology Mfm", vol. *2*, no. 2, pp.100118, 2020.

4. K. J. Chang, K. M. Seow, and K. H. Chen, "Preeclampsia: Recent Advances in Predicting, Preventing, and Managing the Maternal and Foetal Life-Threatening Condition", Int. J. Env. Res. Pub. Health, vol. 20, no. 4, pp.2994, 2023.
5. H. Flynn, "*COVID-19 during pregnancy: Effects on the placenta and stillbirth risk*", 2022.
6. Di Gennaro Francesco, G. Guido, L. Frallonardo, V. S. Francesco, De Nola Rosalba, R.D. Gianluca, Elda De Vita, V. Totaro, M. Barbagallo, E.Nicastri, A. Vimercati, E. Cicinelli,G. Liuzzi., N.Veronese andA. Saracino, "Efficacy and safety of therapies for COVID-19 in pregnancy: a systematic review and meta-analysis", BMC Inf. Dis., vol. 23, no.1, 2023
7. N. Frankevich, A. Tokareva,V. Chagovets., N. Starodubtseva , N. Dolgushina , R. Shmakov, G. Sukhikh and V. Frankevich, "COVID-19 Infection during Pregnancy: Disruptions in Lipid Metabolism and Implications for Newborn Health". Int J. Mol. Sc., vol. 24, no.18, pp.13787–13787, 2023
8. G. Fu, J. Dai, Z. Li, F. Chen, L. Liu, L. Yi, Z. Teng, C. Quan, L. Zhang, T. Zhou, P. Donkersley, S. Song, and Y. Shi, "The role of STAT3/p53 and PI3K-Akt-mTOR signaling pathway on DEHP-induced reproductive toxicity in pubertal male rat". Toxic. Appl. Pharmacol., vol. 404, pp.115151–115151, 2020
9. R. Garg, R. Agarwal, D. Yadav, S. Singh, H. Kumar and R. Bhardwaj, "Histopathological Changes in Placenta of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Cov-2) Infection and Maternal and Perinatal Outcome in COVID-19", J. Obst. Gynecol. India, vol. 73, no. 1 (2023): 44-50, 2022.
10. M. Z. Jovandaric, M. Dokic, I. R.Babovic, S. Milicevic, J. Dotlic, B. Milosevic, M. Culjic, L. Andric, N. Dimic ,O. Mitrovic, A. Beleslin, J. Nikolic, Z. Jestrovic, and S. Babic, "The Significance of COVID-19 Diseases in Lipid Metabolism Pregnancy Women and Newborns." Int. J. Mol. Sci., vol. 23, no. 23, pp.15098–15098, 2022.
11. K. Macáková, P. Pšenková, N. Šupčíková, B. Vlková, P. Celec, and J. Záhumenský,"Effect of SARS-CoV-2 Infection and COVID-19 Vaccination on Oxidative Status of Human Placenta: A Preliminary Study, Antiox., vl. 12, no. 7, pp.1403–1403, 2023
12. Y. Kulaberoglu, A.Hergovich and V. Gómez, Chapter 15, "The role of p53/p21/p16 in DNA damage signaling and DNA repair", Sci. Dir., pp. 257-274, 2021
13. J. Luo, K. Mills, S. le Cessie, R. Noordam, and D. van Heemst, "Ageing, age-related diseases and oxidative stress: What to do next?", Ageing Res. Rev., vol. 57, pp.100982, 2020
14. C. Mandò, V. M. Savasi, G.M. Anelli, S. Corti, A. Serati, F. Lisso, C. Tasca, C. Novielli, and I. Cetin. "Mitochondrial and Oxidative Unbalance in Placentas from Mothers with SARS-CoV-2 Infection", Antiox., vol. 10, no. 10, pp.1517, 2021
15. B. R. Marie-Eve, D. Bouron-Dal Soglio, S. Dal Soglio, C. Couture, I. Boucoiran, Y. Nasr, K. Widdows, M. C. Sharps, D. El Demellawy, A. Ep Heazell, D. Menzies, And S. Girard. "Pandemic stress and SARS-CoV-2 infection are associated with pathological changes at the maternal-foetal interface", *Placenta*., vol. *115*, pp. 37-44, 2021
16. R. Marín, F. H. Pujol., D. Rojas and L. Sobrevia, "SARS- CoV-2 infection and oxidative stress in early-onset preeclampsia" *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease*, vol. 1868, no. 3, pp.166321, 2022
17. J. Moreno-Fernandez, J.J. Ochoa, C.De Paco Matallana, A. Caño, E. Martín-Alvarez, J. Sanchez-Romero, J. M . Toledano, M. Puche-Juarez, S. Prados, S. Ruiz-Duran, L. Diaz-Meca, M.P. Carrillo and J. Diaz-Castro,"COVID-19 during Gestation: Maternal Implications of Evoked Oxidative Stress and Iron Metabolism Impairment", Antiox., vol. 11, no. 2, pp. 184, 2022.

18. I. Pacu, G. George-Alexandru Roşu, Zampieri, A. Anca Rîcu, Matei, T. Ana-Maria Davițoiu, Vlădescu and I. Crîngu Antoniu,"SARS-CoV-2 Infection during Pregnancy and Histological Alterations in the Placenta", Diagn., vol. 12, no. 9, pp. 2258–2258, 2022
19. A. L. N. Parcial, N. G. Salomão, E. A. Portari, L.V. Arruda, J.J. de Carvalho, H. L. de Matos Guedes, T.C. Conde, M.E. Moreira, M.M. Batista, M.V. Paes, K. Rabelo and A Gomes-Silva" SARS-CoV-2 Is Persistent in Placenta and Causes Macroscopic, Histopathological, and Ultrastructural Changes", Viruses, vol. 14, no. 9, pp.1885, 2022
20. S. Park and I. Shimokawa." Influence of Adipokines on Metabolic Dysfunction and Aging" Biomed., vol. 12, no. 4, pp.873, 2024
21. L. Resta, A. Vimercati, G. Cazzato, M. Fanelli, S. V. Scarcella, G. Ingravallo, A. Colagrande, S. Sablone, M. Stolfa, F. Arezzo, T. Lettini and R. Rossi," SARS-CoV-2, Placental Histopathology, Gravity of Infection and Immunopathology: Is There an Association?", Viruses., vol. 14, no. 6, pp.1330–1330, 2022
22. L Riaposova, S. H. Kim, A. Hanyaloglu, L. Sykes, D.A. MacIntyre, P.R. Bennett and V. Terzidou," Prostaglandin F2α requires activation of calcium-dependent signalling to trigger inflammation in human myometrium," Frontiers in Endocrinol., vol.14, 2023
23. M. Tahir, M.Y.A. Rehman and R.N. Malik, "Heavy metal-associated oxidative stress and glutathione s-transferase polymorphisms among E-waste workers in Pakistan". Environm. Geochem. Health., vol. 43, no.11, pp.4441–4458, 2021
24. Y. Tang, N.R. Boggavarapu, A. Aronsson, K. Gemzell-Danielsson and P.G. Lalitkumar, "Global Transcriptomic Analysis of Placentas from Women with Gestational SARS-CoV-2 Infection during the Third Trimester of Pregnancy", Intern. J. Mol. Sci., vol. 25, no. 3, pp.1608, 2024
25. R. Vebrianto, M. Thahir, Z. Putriani, I. Mahartika, A. Ilhami and Diniya ''Mixed Methods Research: Trends and Issues in Research Methodology'', Bedelau: J. Educ. Learn., vol. 1, no. 2, pp.63–73, 2020
26. D. R. Verma, D. S. Verma and D.K. Abhishek, ''*Research Methodology*. *Google Books*.'' Booksclinic Publish., 2024
27. Y. P. Wong., T. Y. Khong and G. C. Tan,''The Effects of COVID-19 on Placenta and Pregnancy: What Do We Know So Far?'' Diagnost., vol. 11, no. 1, pp.94, 2021
28. O. Zawacki – Richter, ''Systematic Reviews in Educational Research, '' Wiesbaden: Springer Fachmedien Wiesbaden, 2020

.