

# **THE EFFECTS OF THE COEXISTENCE DESPITE IMMUNIZATION OF COVID-19 AND RUBELLA INFECTION IN PREGNANT FEMALES AND THEIR NEONATES**

## **ABSTRACT**

Pregnancy is a very crucial yet delicate phase of a mother's life. It is because of the several delicate and sensitive changes that take place in this phase that it is considered to be a crucial period where extreme care needs to be taken for the safe delivery of the fetus. Throughout pregnancy, there are several changes that need supervision and several parameters that need to be carefully evaluated to ensure that the neonate thrives in a healthy manner. The expecting mother has to receive several check-ups throughout her pregnancy to make sure that both she and the baby are doing fine and as expected according to the milestones of pregnancy. During this, a mother also receives some immunization and vaccination shots. These shots are given with the intention of preventing several infections that could affect a mother and her neonate in pregnancy. If these vaccination shots are not given within the specified time, then the mother may very much become predisposed to develop these infections that could have detrimental effects on both the mother and the baby. Therefore, it must be ensured that both the mother and the baby are in the optimal state of their health as a result of their continuous checkups and appointments with the doctor. This review will work to the occurrence of Rubella and the Coronavirus infection in expectant mothers who have already received immunization against the two pathogens. Although it is difficult for both conditions to co-exist, it is rarely seen and when it happens, it is important to explore the reasons as to what would have given rise to such a

situation. Therefore, this review will serve this purpose and help to see the reasons and the resultant effects of getting infected with these infections during pregnancy.

**Keywords:** rubella, COVID-19, pregnancy, pregnancy immunization, co-existence of infections, immunity.

## INTRODUCTION

Immunizing a pregnant woman serves as a vital shield, not only for her but also for her developing fetus and the subsequent newborn. It helps safeguard both the mother and her unborn child from infections that can have more severe consequences in this vulnerable population compared to the general public. (1)

This protective measure also plays a crucial role in diminishing morbidity and mortality among children under the age of five, making it one of the most cost-effective strategies to reduce the rates of early childhood illness and death.(2)

At the forefront of this effort is the GAIA project (Global Alignment of Immunization Safety Assessment in Pregnancy), a global initiative that applies worldwide. The primary mission of the GAIA project is to diligently monitor the safety of various vaccines administered during pregnancy, ensuring that expectant mothers and their unborn children receive the protection they need without unnecessary risks.(3)

During pregnancy, vaccination plays a crucial role in protecting both the mother and her newborn child from life-threatening infectious diseases. It involves a dual benefit: it bolsters the mother's active immunity against these diseases and imparts passive immunity to the neonate, offering protection from infections known for their high morbidity and mortality rates.(4)

Typically, the administration of live vaccines is avoided during pregnancy due to the potential risk of causing viremia or bacteremia in the developing fetus. In contrast, inactivated vaccines are generally considered safe and pose fewer concerns.

For expectant mothers, certain vaccines are considered safe and recommended. These include the tetanus toxoid (TT) vaccine, which guards against tetanus, as well as the combination vaccine for tetanus, diphtheria, and acellular pertussis (Tdap). In addition, the flu vaccine is recommended. Prior to conception, it is advisable to administer the measles, mumps, and rubella (MMR) vaccine, with a subsequent recommendation to postpone pregnancy for one month.(5)

As pregnancy progresses, all expectant mothers are encouraged to receive the TT and Tdap vaccines during the third trimester. The flu vaccine can be safely administered at any point during pregnancy, or even after the postpartum period, whatever seems applicable.

For women at an elevated risk of exposure to specific infectious diseases, additional vaccines may be recommended. These include vaccinations for hepatitis A and B, pneumococcal infections, meningococcal disease, yellow fever, Japanese encephalitis (JE), polio, typhoid, and cholera.

Certain vaccines are reserved for post-exposure prophylaxis (PEP), meaning they should be administered after a potential exposure to the relevant infection. These vaccines include those for smallpox, rabies, and anthrax.(6)

After childbirth, women should be offered the human papillomavirus (HPV) vaccine. If they have not received certain vaccines earlier, they should also be encouraged to get the MMR, Tdap, and flu vaccines immediately.

## **RUBELLA INFECTION AND PREGNANCY**

Rubella, often referred to as German measles, is a viral infection that afflicts individuals of all ages. Its clinical manifestations typically entail a benign course, except for a critical caveat: during the early stages of pregnancy, exposure to the Rubella virus carries a significant risk of causing severe congenital anomalies in the unborn child. Specifically, if a pregnant woman contracts Rubella within the first four months of gestation, the potential for profound birth defects in her offspring looms large.(7)

Rubella infection presents as a viral illness typified by a characteristic maculopapular rash, lymphadenopathy, and fever. Its contagious nature is notably high, yet the vast majority of cases follow a mild and self-limiting course, sparing individuals from substantial long-term repercussions. However, the peril escalates when maternal infection occurs during the initial trimester of pregnancy, instigating a complex fetal malformation syndrome known as congenital rubella syndrome.(8)(9)

Prior to this milestone, Rubella was a pervasive affliction, primarily affecting young children. Yet, the United States managed to achieve Rubella elimination in 2004. Subsequently, the incidence dwindled to fewer than 10 reported cases per annum, predominantly originating from imported cases.

However, it is essential to underscore that Rubella remains a persistent health concern across various regions of the world, where many cases evade clinical recognition due to the nonspecific nature of the rash, often resembling other common ailments. In fact, up to half of all Rubella infections may manifest in a subclinical fashion, rendering them inconspicuous to the afflicted individual.(10)

Intriguingly, humans exclusively serve as the reservoir for Rubella infection, which primarily propagates through direct contact or via respiratory droplets containing nasopharyngeal secretions. Once inhaled, the Rubella virus embarks on a replication journey within the respiratory mucosa and cervical lymph nodes before disseminating throughout the body via systemic circulation. The contagious period spans roughly eight days before and eight days after the onset of the distinctive rash.(9)

Importantly, maternal Rubella infection during pregnancy can lead to a spectrum of adverse outcomes, including miscarriage, fetal demise, or the insidious onset of congenital rubella syndrome. Furthermore, a subset of infants affected by congenital Rubella can continue to excrete the virus in nasopharyngeal secretions and urine for an extended period, often exceeding a year. In a perplexing twist, the Rubella virus has been detected in lens aspirates from children afflicted with congenital cataracts, underscoring the virus's capacity to persist within affected individuals over an extended timeframe.(10)

Once inside a susceptible host, the virus enters and infects nasopharyngeal cells, subsequently spreading to the local lymphoid tissues of the upper respiratory tract. This stage is followed by a viremic phase, during which the virus disseminates via the bloodstream to various organs, typically occurring 5 to 7 days after initial exposure.

Contracting the Rubella virus during pregnancy can have devastating consequences. This virus has the potential to harm multiple organs and, when a vulnerable pregnant woman is exposed to it, particularly in the early stages of gestation, it can result in a range of congenital defects in the developing fetus. The impact of Congenital Rubella Syndrome (CRS) is substantial, not only on the affected families but also on governments in terms of economic burden and healthcare costs over the course of a person's lifetime.(11)

Around 85% of women who contract rubella during the first trimester of pregnancy unknowingly transmit the virus to their developing fetus. This unfortunate transmission can lead to a range of hallmark features in the child, including sensorineural deafness, congenital heart defects, learning difficulties, and various eye abnormalities such as cataracts, glaucoma, retinopathy, and microphthalmos. Additionally, bone defects, hepatosplenomegaly (enlarged liver and spleen), and miscarriages are not uncommon in such cases.(12)

Due to the high virulence of the rubella virus in the early stages of pregnancy, it is not recommended to administer the vaccine, which consists of a weakened live virus, during this critical time. Women who do receive the vaccine are advised to avoid conceiving for at least three months.

However, retrospective evidence has indicated that the risk of the syndrome developing after vaccination in early pregnancy is relatively small. In a registry maintained by the US Centers for Disease Control and Prevention, which recorded cases of pregnant women who inadvertently received the vaccine between 1979 and 1989, no instances of the syndrome were found in the newborn infants of the 321 women who were enrolled.(13)

### **COVID-19 IN PREGNANCY**

Pregnant women who contract COVID-19 tend to exhibit a notable difference in symptoms when compared to their non-pregnant counterparts. Interestingly, nearly three-quarters of pregnant individuals with the virus remain asymptomatic, showing no signs of illness. (14)

For those who do experience symptoms, they are generally mild in nature, with the most common ones being a cough (reported by 41% of cases), fever (40%), shortness of breath (21%), and muscle pain (19%).(15)

The occurrence of severe COVID-19 disease during pregnancy primarily occurs in the later stages, typically during the late second or third trimester. The risk factors for severe illness align with those seen in non-pregnant individuals and include factors such as being overweight or obese, age greater than 35 and having pre-existing medical conditions.(16)

Furthermore, pregnant women from Black, Asian, and minority ethnic backgrounds have been observed to be at a heightened risk of COVID-19 complications both during and outside of pregnancy. This increased risk has been attributed to factors like health disparities, socioeconomic conditions, and a potential deficiency in vitamin D, which have been suggested as contributing factors to these disparities.

In the United Kingdom, a concerning statistic has emerged, revealing that 9% of all COVID-19 cases requiring admission to intensive care units (ICUs) involve pregnant women or those who have given birth within the past six weeks. (17)

This revelation stems from a comprehensive study conducted using the UK Obstetric Surveillance System. The study further explores that 5% of pregnant women hospitalized with COVID-19 have necessitated ICU care, with less than 1% requiring extracorporeal membrane oxygenation. Comparatively, pregnant women appear to face a higher likelihood of ICU admission and invasive ventilation when affected by COVID-19, with odds ratios of 1.62 and 1.88, respectively, compared to non-pregnant women of childbearing age who contract the virus.(18)

Notably, the proportion of women of childbearing age admitted to ICUs with COVID-19 who were either pregnant or within the first six weeks postpartum increased during the second wave of the pandemic. This suggests that the second wave and the emergence of the B.1.1.7 (alpha) variant had a more detrimental impact on pregnant women than the initial wave of the virus.

However, it is essential to consider that pregnant individuals are often admitted to ICUs at a lower threshold than their non-pregnant counterparts, and it is crucial to note that the overall maternal mortality rate remains relatively low, with 2.2 hospitalizations per 100,000 pregnancies.(19)

Symptomatic pregnant women with COVID-19 face an increased risk of pre-term birth when compared to women without the virus. This elevated risk is particularly pronounced for pregnancies that are less than 32 weeks gestation, with an adjusted odds ratio of 3.98, and those less than 37 weeks gestation, with an adjusted odds ratio of 1.87. (20)

It is important to mention that in nearly 80% of these cases, preterm births are conducted for medical reasons aimed at improving maternal oxygenation. This highlights the necessity for women experiencing severe SARS-CoV-2 infection to be managed in healthcare units with access to specialized neonatal care facilities.

### **COEXISTENCE OF COVID-19 AND RUBELLA INFECTION IN PREGNANT WOMEN**

Numerous studies across the globe have been conducted to investigate the relationship between measles, mumps, and rubella (MMR) antibodies and susceptibility to and severity of COVID-19 infections.

In a recent univariate analysis conducted by Cattaruzza et al. in 2022, a noteworthy finding emerged where antibodies were inversely associated with COVID-19 disease, although this relationship did not reach statistical significance.(21)

In the United States, a study by Mysore et al. in 2021 examined convalescent COVID-19 patients and identified a strong correlation between T cell responses to SARS-CoV-2 (both S and N proteins) and MMR antibodies. However, research conducted in Iran in 2021 suggested a unique interaction with measles vaccination. It appeared to stimulate cross-reactive B cells that

generated more measles-specific antibodies but had no discernible impact on mumps and rubella antibodies.

## **CONCLUSION**

Both Rubella and COVID-19 infections are of vital importance, especially when they occur in the context of pregnancy. Since pregnancy in itself is a crucial time of one's life, it is important to note that the presence of any infection, no matter how small or large, may have detrimental effects on the health of both the mother and the fetus.

Therefore, it is important to look into the causes and the factors of these infections and then consequently, work out the factors that help prevent it.

In the context of both Rubella and COVID-19, it was found that vaccination against the viruses could help put an end to the looming risk of these infections. In the majority of the cases, this might be even protective for the mothers to help prevent the occurrence of these viruses.

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