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Impact of COVID-19 Lockdown on the Incidence of Common Pregnancy Complications—Is the Diagnosis of IUGR Generally Made Too Generously?

Maximilian Rauh [1,*], Silvia Suttner [1], Claudia Bartl [1], Marco Weigl [1], Sven Wellmann [2], Maurice Kappelmeyer [3], Börge Schmidt [4], Maria Emilia Solano [1,3] and Angela Köninger [1]

[1] Department of Obstetrics and Gynecology, Hospital St. Hedwig of the Order of St. John, University of Regensburg, Steinmetzstrasse 1-3, 93049 Regensburg, Germany

[2] Department of Neonatology, Hospital St. Hedwig of the Order of St. John, University of Regensburg, Steinmetzstrasse 1-3, 93049 Regensburg, Germany

[3] Laboratory of Translational Perinatology, University of Regensburg, Am Biopark 9, 93053 Regensburg, Germany

[4] Institute of Medical Informatics, Biometry and Epidemiology (IMIBE), University Hospital Essen, University of Duisburg-Essen, Zweigertstrasse 37, 45135 Essen, Germany

* Correspondence: maximilian.rauh@ukr.de

Abstract

Purpose**:** In 2020 a lockdown due to COVID-19 was ordered by the German government resulting in population-wide restrictions in daily behaviour. In this retrospective study, we questioned whether the lockdown had an impact on the incidence of relevant pregnancy complications. Methods**:** The incidence of relevant pregnancy complications was evaluated during all trimesters of pregnancy in a 6 month pre-pandemic period (April-September 2019) compared to the same period in the pandemic year 2020 including mothers and newborns who presented at the University Hospital St. Hedwig, Regensburg, Germany. Finally the incidence of preeclampsia and suspected IUGR (intrauterine growth retardation) as relevant obstetrical diseases was compared with a post-pandemic period (April-September 2023). Group comparisons were performed using Mann-Whitney-U-test, t-test, Fisher's exact test and Chi-Square-test. Results**:** 5137 newborn were included with 1709 born during the 6 month pre-pandemic, 1806 during the 6 month lockdown period and 1622 during the 6 month post-pandemic period. During the pandemic period, significantly less patients were hospitalized due to hyperemesis gravidarum (1.8% vs 0.9%, p=0.04). No differences were observed concerning the incidence of miscarriages before and after 14 weeks of gestation (WG), preterm deliveries (< 37 WG), gestational age at preterm birth and birth weight. Likewise, within preterm born babies no difference was observed in preeclampsia among the two periods. However, in the pandemic period, the frequency of preterm born babies with suspected IUGR was significantly lower than in the pre-pandemic period (1.5 % and 0.6 %, p=0.01). Regarding this point, we analyzed data of all newborns in the comparative post-pandemic period in 2023 (n=1622) resulting in a significantly increased IUGR incidence compared to the pandemic level and therefore returning to pre-pandemic level (1.5% and 1.4%, p=0.145). Conclusion**:** Lockdown associated changes in the health and social behavior of physicians and patients led to modest but partially significant variation in the incidence of pregnancy complications. Less preterm delivered babies due to antepartum diagnosed IUGR indicate that the diagnosis was made much more restrictively during the pandemic than before. After all COVID-19-specific restrictions on elective and outpatient services were passed, the incidence of antepartum suspected IUGR returned to its initial level. This suggests that the diagnosis of IUGR – a solely machine-dependent and not symptom based diagnosis- was partly exaggerated before and after the pandemic.

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Keywords: lockdown; COVID-19; pregnancy complications; intrauterine growth restriction (IUGR); fetal growth restriction (FGR); pre-pandemic; post-pandemic

Introduction

In December 2019 an outbreak of the coronavirus SARS-COV-2 (COVID-19) was registered in the Chinese city of Wuhan. Thereafter, the disease spread rapidly worldwide and became a pandemic.

The first case of COVID-19 in Germany was confirmed on the 27th of January 2020 [1]. In mid-March 2020, the German government ordered a national lockdown, including the closure of schools, non-essential shops and businesses and a ban on attending nursery homes and hospitals. Later on, curfews were imposed prohibiting physical contact with more than one person from outside one´s household. The healthcare systems confronted a challenging situation. To meet the needs of the emerging number of COVID-19 patients, restrictions were placed on elective and outpatient services.

As maternity care is an essential service, it was continuously offered to pregnant patients throughout the lockdown-phase. Adjustments were made where possible, including reducing the number of in-person visits, restricting accompanying visitors and schedule or even postpone maternal and fetal assessment appointments [2].

To date, there is no doubt that the SARS-COV-2 infection affects maternal and child health directly [3]. However, the indirect effects of the pandemic on the pregnancy outcomes, e.g. due to the national lockdown are less clear. Fear of seeking medical healthcare as well as reduced provision of routine antenatal visits have been suggested as a probable cause of adverse perinatal outcomes [4]. Several reports indicated that the rate of stillbirths and preterm births might have changed significantly during the lockdown and pandemic phase [5–17]. Likewise, the named changes in the maternity care services as well as maternal stress and anxiety during the lockdown may also affect the progress of pregnancy.

Hence, the goal of our present study was to investigate whether the strict lockdown at the beginning of the SARS-COV-2 pandemic in Germany influenced the incidence of selected pregnancy complications of high frequency in our tertiary maternity care hospital.

Material and methods

In this retrospective observational study selected common pregnancy complications of patients treated at the University Hospital St. Hedwig, Regensburg, Germany, were compared during 3 periods: from April 1, 2020, to September 30, 2020 (the time during the strict lockdown and shortly after, so called „lockdown“ or „pandemic” period), from April 1, 2019 to September 30, 2019 (so called „pre-pandemic period“) and from April 1, 2023 to September 30, 2023 (so called „post-pandemic period“).

Regarding early pregnancy, the number of hospitalized patients suffering from hyperemesis gravidarum and miscarriages before 14+0 weeks of gestation (WG) was analyzed. Hyperemesis gravidarum was defined as an excessive and persistent vomiting in the first trimester of pregnancy and objectified using the PUQE score [18]. Miscarriage before 14+0 weeks of gestation (WG) and after 14+0 WG were analyzed separatly. It should be noted that from 22+0 WG there may be an overlap between the catergories „late miscarriage“and „extremely premature birth“. Maximum care is provided for neonates born between 22+0 and 23+6 WG depending on several factors like e.g. estimated fetal weight or presence of a maternal infection. Parental decision on palliative or maximum neonatal care before 24+0 WG follow a discussion with an experienced neonatologist. Maximum care is usually provided for neonates born after 24+0 WG. Prematurity was defined as a gestational age between 22+0 and 36+6 WG [19].

In addition, we analyzed the incidence of preeclampsia and IUGR (intrauterine growth restriction) as common complications in pregnancy. Preeclampsia was defined as chronic or

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gestational hypertension with at least one new organ manifestation during pregnancy that could not be attributed to any other cause [20]. Patients with HELLP (hemolysis, elevated liver enzymes and reduced platelet count) syndrome were also included in this group [21].

Furthermore we used the DELPHI criteria to define IUGR and to differentiate from small for gestational age (SGA). IUGR is associated with a small fetal abdominal circumference and pathologies in the fetoplacental vascular resistance [22,23].

The sonographic examination was carried out using a high-resolution convex transducer (3.5mHz). Voluson S8, E8 and E10 ultrasound machines were used (GE Healthcare GmbH, 42655 Solingen). The examinations were carried out in accordance with everyday clinical practice by experienced sonographers. The fetal parameters were documented using the ViewPoint program (ViewPoint™, GE Healthcare GmbH, 42655 Solingen). Weight estimation is routinely performed using the Hadlock's estimation formula, which is based on measurements of biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femur length (FL):log10 G= 1.3596 - 0.00386 x AC x FL + 0.0064 x HC + 0.00061 BPD x AC + 0.0424 x AC + 0.174 x FL and is referred to as "Hadlock I" [24].

All pregnant women who were treated in the respective epoche due to the named diagnosis were included. For this purpose, ICD 10 codes were surveyed retrospectively. In addition, a comparison was made with the analogue documentation that had been carried out. Exclusion criteria such as age, BMI or ethnicity were not applied. All live births during the relevant period were included in the study - both singleton and multiple pregnancies.

All parameters and measured values were collected prospectively and finally drawn from the digital archive (SAP, Viewpoint)..

After initial analysis, a further subgroup analysis was added with regard to the incidence of IUGR and preeclampsia in a „post-pandemic“ period.

Group comparisons were made using Mann-Whitney-U test, t-test, Fisher’s exact test and Chi-square-test. The analysis was performed using R version 4.4.1. A p-value < 0.05 was considered statistically significant.

The study was approved by the ethics committee of the University of Regensburg (no. 24-4004-104).

Results

5137 newborn were included with 1709 born during the 6 month pre-pandemic period and 1806 n during the 6 month lockdown period and 1622 within the analysed 6 month post-pandemic period. Gestational age of the neonates was between 23+5WG and 36+6WG. We first evaluated if within the analysed pregnancy complications categories maternal age was different among the pre-pandemic and lockdown study populations. No differences between maternal age in all categories (Table 1) was observed, and therefore we did not adjust for this variable as a confounder.

During the pandemic period there was a significantly (p=0.04) lower frequency of admissions to the hospital due to hyperemesis compared to the pre-pandemic period: 0.9% (16/1711) vs. 1.8% (29/1641) (Table 2). Particularly at the beginning of the national mandated curfews (from April 1 until May 12, 2020) with a strict policy of limiting the contact to a maximum of one person outside the own household, there were no admissions to the hospital due to hyperemesis.

Compared to the pre-pandemic period, in the lockdown period there was a trend towards a reduced rate of miscarriages both before and after 14 WG, that did however not reach statistical significance. There were 2.6 % (43/1711) miscarriages with curettage (<14 WG) in the lockdown vs. 3.2 % (52/1641) in the pre-pandemic period (p=0.25), and 0.5 % (10/1711) miscarriages (≥14 WG) in the lockdown vs. 0.7 % (11/1641) in the pre-pandemic period (p=0.75) (Table 2). As shown in Table 1, maternal age differed significantly between subgroups of miscarriages between 14+0 and 23+6 WG, showing older women in the pre-pandemic period. This may be associated to the higher rate of known or visible fetal anomalies in the pre-pandemic (6 anomalies among 11 miscarriages) compared to the lockdown (3 anomalies among 9 miscarriages) period. Due to the fact that chromosomal

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analysis was not performed in all miscarriage cases and the small number of cases, we did not further discriminate our analysis between spontaneous labor of a viable fetus and intrauterine fetal demise.

The rate of preterm birth (<37+0 WG) showed no statistical difference between the two epoches. In the pre-pandemic period 13.1% (224/1709) of the children were born preterm, whereas in the lockdown period 12.0 % (217/1806) (p=0.33) (Table 2). Within the preterm birth group, we compared the birthweight and the gestational age between the children born within the two epoches. There was no difference between the gestational age at delivery. The median gestational age of the preterm born group in the pre-pandemic period was 244 days (IQR 231-251), and in the lockdown/pandemic period 246 days (IQR 231-253) (p=0.13). Similarly, there was no significant difference between the birthweight of preterms born alive: pre-pandemic the median birthweight was 2273 g (IQR 1803-2603), and during the lockdown period 2370 g (IQR 1885-2706) (p=0.11). An in depth comparison of the subsequent weight categories showed also no difference between the two periods (Table 3). Due to their low frequency, we included all babies with a birthweight ≤ 1000 g in one group. Among them, only 3 and 2 neonates with a weight ≤ 500 g were delivered in the pre-pandemic and pandemic study periods respectively.

A subgroup analysis of preterm delivered babies (224 in the pre-pandemic period, 217 in the lockdown period) was performed according to common pregnancy complications: Interestingly, preterm deliveries with suspected IUGR were decreased more than 50% in the lockdown period. Rate of preterm birth with suspected IUGR was 0.5 % (9/1806) during the lockdown vs. 1.5 % (23/1709) in the pre-pandemic period (p=0.01). The rate of preterm birth with preeclampsia was 1.5 % (27/1806) in the lockdown period vs. 1.3 % (24/1709) pre-pandemic (p=0.82) (Table 2).

Since the incidence of suspected IUGR cases in preterm deliveries changed significantly between the pre-pandemic and the pandemic period, we added a subgroup analysis of suspected preterm IUGR cases in 2023. In this post-pandemic period, the rate was 1.6% (26/1622) compared to 0.5% (9/1806) during the pandemic period (p=0.005). However, this reflects a return to the pre-pandemic incidence of suspected IUGR in preterms – there was no significant difference in the rate in 2019 (1.3%, 23/1709) and 2023 (1.6%, 26/1622) (p=0.54) (Table 4).

In contrast, incidence of preeclampsia within the preterm born cohort did not alter significantly during pre-pandemic, pandemic and post-pandemic period (Table 4).

The mode of delivery in the subgroup of preterm born IUGR fetuses did not change significantly between the pre-pandemic, lockdown and post-pandemic period (p=0.66): In the pre-pandemic period 87% (20/23) of the women had a cesarean section and 13% (3/23) gave birth vaginally. In the lockdown period the relation was 77.8% (7/9) versus 22.2% (2/9) and in the 6 month period in 2023 76.9% (20/26) versus 23.1% (6/26) regarding cesarean section versus vaginal birth (Table 5).

Birth weight for preterm infants with IUGR differed significantly between the analysed epoches (p=0.019). Comparing the prenatal diagnosis with the final postnatal diagnosis, pre-pandemic 78.2% (18/23) of the newborns classified as IUGR prenatally had a birth weight below the 10th percentile. In the lockdown period 100% (9/9) and in the 2023 period 53.8% (14/26) were born witha weight the 10th percentile (Table 5).

The indication for preterm delivery changed significantly between the pre-pandemic, lockdown and post-pandemic period (p=0.045). In the pre-pandemic epoche 60.8% (14/23) of the IUGR fetus were delivered due to suspected IUGR. In the remaining cases, IUGR was a suspected side diagnosis but nort the reason for delivery: 21.7% (5/23) were delivered because of preeclampsia and 17.5% (4/23) due to premature rupture of the membranes (PROM) or labour. In the lockdown, 66.7% (6/9) were delivered due to suspected IUGR, 22.2% (2/9) because of preeclampsia and 11.1% (1/9) because of premature labor. In the post-pandemic period 42.3% (11/26) were born because of suspected IUGR, 15.4% (4/26) due to preeclampsia, 38.5% (10/26) because of PROM or premature contractions and 3.8% (1/26) because of uterine rupture after previous cesarean section (Table 5).

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Discussion

In this study, the incidence of common pregnancy complications in a single center before, during and after the lockdown phase of the COVID-19 pandemic was compared. In general, the incidence of all analysed pregnancy complications showed a trend to decrease during the pandemic period compared to the pre-pandemic period. We found no difference between miscarriage rates, but there was a significant reduction of inpatient care due to hyperemesis. The rate of preterm born babies (<37 WG) did not differ as well. The same applies to gestational age and birthweight of preterm born babies. Numbers of early delivery with preeclampsia and preterm contractions or rupture of membranes did not differ between the studied periods. However, the overall incidence of preterm born babies with suspected IUGR was significantly lower during the pandemic period. Incidence of preterm birth with IUGR and preeclampsia was therefore analysed in a post-pandemic epoche. Interestingly the "post-pandemic" incidence of suspected IUGR returned to it's "pre-pandemic" level after all restrictions on elective and outpatient services were repealed.

The global pandemic of SARS-COV-2 has resulted in profound worldwide social and economic disruptions. Especially the healthcare systems are severely affected. Adversities in public health effects are not only caused by the SARS-COV-2 infection but to a great extend by the policies, which had to be taken to prevent uncontrollable spreading of the virus.

Early reports showed a reduction of the incidence of preterm birth during the pandemic period. Some evidence suggested that the rate of stillbirths might have changed as well. Whilst some studies reported increased stillbirth rates [5–17], a link between prematurity, stillbirth and lockdown was not confirmed in a number of additional studies [25–28]. Hence, the adverse effects of the mandatory lockdown still remains a subject of debate.

The lockdown might have had an impact also on other pregnancy related problems and complications beyond preterm birth. There are only limited data on the direct and indirect effects of the SARS-COV-2 pandemic on first- and early second-trimester pregnancy complications and outcomes. One case-control study from Italy [29] comparing the rate of first trimester miscarriage between women who were infected or not with COVID-19 during pregnancy and found no significant difference between groups. A study performed in Turkey [30] showed a comparable incidence of miscarriages during the COVID-19 pandemic compared to the same epoche in 2019. However, the number of newly recorded pregnancies was lower during the study period in 2020 compared with the same pre-pandemic epoch in 2019. The authors assumed that reduced healthcare-seeking behaviour among pregnant women due to the pandemic or lockdown measures contributed this observation. This is in line with findings of our study. In our center, miscarriage rates before and after 14+0 WG did not differ between the compared epochs in 2019 (pre-pandemic) and 2020 (lockdown and pandemic period). However, we observed a significant reduction of admissions to the hospital due to hyperemesis in the 6 month study period 2020 compared to 2019. We hypothesize that for pregnant women the fear of harm to the child due to hyperemesis is not a main concern and therefore the threshold of seeking medical help for own wellbeing declined in the lockdown phase. Likewise, a decreased admission rate for complaints associated with pregnancy was reported by other studies [8,31,32]. We also suggest that the COVID-19-lockdown might have imposed behavioural and lifestyle modifications in the here studied population of pregnant women, for example with increased time for personal care and with family members, resulting in a lower number of hospitalized hyperemesis cases.

As mentioned above, early reports suggested that the pandemic period was marked by a reduction of preterm birth. Studies in Ireland [17], Denmark [9] and The Netherlands [5] reported a drop in premature babies, especially the ones with very low birthweight. Until now several reports focused on the impact of the corona-lockdown and pandemic period on preterm birth. A systematic review and meta-analysis [33] confirmed no overall changes in preterm births before 37 WG but their slight decrease in high-income countries during the pandemic. A recently published study of deliveries in Berlin, Germany, showed decreased numbers of preterm birth, especially within 28 and 35 WG but not before 28 WG. The authors also were able to demonstrate a lower rate of primary

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caesarean sections in pregnancies < 35 WG, indicating less iatrogenic preterm birth delivered by elective caesarean section [34]. Analysis of the Bavarian birth cohort and therefore including also our cohort, demonstrated decreased preterm birth rates in the first lockdown 2020 compared to the years 2010-2019 [25]. After adjusting for seasonal and long-term aspects, the significance of preterm birth decline was no more shown for the whole cohort but still for birth < 32 WG. Our study supports these results and highlights more details: The rate of preterm born infants in our study was also slightly lower in the pandemic compared to the pre-pandemic period (12% vs. 13% respectively) albeit statistical significance was not reached. However, we only analysed deliveries between April and September. As shown by Stumpfe et al. preterm birth rate trends to be lower during summer [25], therefore explaining some subtile differences between the whole Bavarian cohort and our population. The birthweight of the preterm born children did not differ either, as also shown in the whole Bavarian cohort [25]. However there was a decrease of preterm born babies delivered with IUGR in the pandemic compared to the pre-pandemic period.

This is unexpected since it could be demonstrated that SARS-CoV-2 infection during pregnancy is associated with a higher incidence of low placental weight and an increased birthweight/placental weight ratio regardless of which trimester the infection occurred. [35].

We hypothesize that the reduced access to prenatal services and the fear of seeking medical care caused a delayed diagnosis of intrauterine growth restriction resulting in less iatrogenic preterm birth with the diagnosis of IUGR. This hypothesis can be proven by the fact that the post-pandemic incidence of IUGR was similar to the pre-pandemic incidence in our study.

IUGR is a risk factor for stillbirth. Several available reports showed an increased rate of stillbirth during the pandemic period [7,8,10,13,16]. Hence, a delayed diagnosis of IUGR might have contributed to a higher rate of stillbirth. However, the analysis of the Bavarian birth cohort, including also our cases, showed no increased still birth rates in the lockdown period [Stumpfe FM 2020]. Next to less iatrogenic preterm birth with IUGR diagnosis, another hypothesis to explain the decreased incidence of IUGR-babies is, that the lockdown and pandemic resulted in behavioural and lifestyle modifications, which could influence health and wellbeing as described by Philip et al. [17].

Ultimately, it must be considered that the diagnosis of IUGR before and after the pandemic was exaggerated in some cases. we strongly hypothesize that less frequent ultrasound examinations mainly result in less diagnosis of IUGR.

Preterm birth with preeclampsia showed subtle increased incidence during the pandemic period. There are reports that state that COVID-19 infection during pregnancy is strongly associated with preeclampsia [36]. However, in our study cohort neither the overall incidence of preeclampsia nor the rate of deliveries because of preeclampsia differed.

The strength of our study is the subgroup analysis of preterm birth indications in a total of more than 5000 newborns.

One limitation of our study is the retrospective design which was carried out at a single institution. The risks of the retrospective design include possible miscoding and lack of precision in the reported diagnoses of medical conditions. Furthermore we did not adjust for basic characteristics such as parity, obstetrical history (e.g. preterm birth history) which might be confounders for the analysis.

In addition, we didn't discuss the different variants of the coronavirus and their effects on pregnancy. In a retrospective study on pregnant women tested positive for SARSCoV-2 Favre et al were able to demonstrate that the delta period was associated with a higher risk of severe maternal adverse outcome and the Omicron period with a lower risk of severe adverse outcome compared to pre-Delta era. It was highly probable that most women were infected with the predominant variant of tha specific period respectively [37].

Furthermore we did not assess the percentage of confirmed COVID-19-positive mothers in this study as well as the total incidence of preeclampsia as well as IUGR (term and preterm) and we didn't discuss the influence of the corona vaccination, which has been possible in Germany since December 26, 2020 [38].

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Conclusion

This study evaluated the effect of the national lockdown on selected common pregnancy complications in a single maternity care center. We found no difference between the incidence of miscarriages before and during the lockdown period but there was a relevant reduction of hospitalized women who suffered from hyperemesis. We could not confirm the previously described association between lockdown and an overall reduction of preterm birth rates. However, the incidence e of preterm babies diagnosed with IUGR was significantly lower during the pandemic than in the pre-pandemic period. After the COVID-19-restrictions were passed, the incidence of suspected IUGR in preterms returned to its pre-pandemic level. In contrast to all other analysed pregnancy complications, IUGR diagnosis prenatally is a solely machine-depending and no clinical diagnosis. The results demonstrate how obviously physicians' diagnosis and their impact on clinical outcomes was influenced by the health policy restrictions. The results rise the question whether the diagnosis of IUGR results in iatrogenic preterm delivery too generously? Further studies that compare different medical access and care provision should focus on diagnoses that are solely made by a machine and not by any clinical symptoms.

Authors' contributions: CB, SS and MR: collection of data; MW and SW: help with literature research and proofreading; AK and MR: wrote the main manuscript; MS: proofreading and editing; MK and BS: statistical analysis

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Institutional Review Board Statement: Ethical review and approval were waived for this study due to the fact that it includes only the secondary analysis of existing data and does not involve identifiable private information, collection of biospecimens, or any risk to subjects as well as it did not affect their rights and welfare [39].

Informed Consent Statement: Patient consent was waived due to the fact that it includes only the secondary analysis of existing data.

Data Availability Statement: The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations:

COVID-19: Coronavirus disease 2019
IQR: Interquartile range
IUGR: Intrauterine growth retardation
SARS-COV-2: Severe acute respiratory syndrome coronavirus 2
SD: Standard deviation
WG:weeks of gestation

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