MS KATARINA REMAEUS (Orcid ID : 0000-0003-0971-132X)

DR JULIA SAVCHENKO (Orcid ID : 0000-0001-8285-3055)

DR SOPHIA BRISMAR WENDEL (Orcid ID : 0000-0002-9401-8062)

DR SEBASTIAN GIDLÖF (Orcid ID : 0000-0002-1432-8344)

DR TOVE WALLSTRÖM (Orcid ID : 0000-0003-2502-4116)

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# Characteristics and short-term obstetric outcomes in a case series of 67 women tested positive for SARS-CoV-2 in Stockholm, Sweden

Katarina REMAEUS[1, 2], Julia SAVCHENKO[3, 4], Sophia BRISMAR WENDEL[5, 6], Sebastian BRUSELL GIDLÖF[3, 7], Sophie GRANER[1, 8], Elin JONES[9], Johanna MOLIN[10], Sissel SALTVEDT[9, 11], Tove WALLSTRÖM[3, 4], Karin PETTERSSON[7, 9],

1. BB Stockholm, Danderyd Hospital, Stockholm, Sweden
2. Department of Medicine Solna, Clinical Epidemiology division, Karolinska Institutet, Stockholm, Sweden
3. Department of Obstetrics and Gynecology, Södersjukhuset Hospital, Stockholm, Sweden
4. Department of Clinical Science and Education, Södersjukhuset Hospital, Karolinska Institutet, Stockholm, Sweden
5. Department of Obstetrics and Gynecology, Danderyd Hospital, Stockholm, Sweden

6. Department of Clinical Sciences, Karolinska Institutet, Danderyd Hospital, Stockholm, Sweden
7. Department for Clinical Intervention, Technology and Intervention, Karolinska Institutet, Stockholm, Sweden
8. Department of Medicine, Centre for Pharmacoepidemiology, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden
9. Department of Women's Health, Karolinska University Hospital, Stockholm, Sweden
10. Department of Women's and Children's Health, Södertälje Hospital, Stockholm, Sweden
11. Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden

**Corresponding author*:***

Katarina Remaeus

BB Stockholm, Danderyds Sjukhus, 182 88 Stockholm, Sweden

Email: katarina.remaeus@bbstockholm.se

**Conflicts of interest**

None

**ABSTRACT**

**Introduction**: The Stockholm region was the first area in Sweden to be hit by the pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Our national guidelines regarding care of women with positive test for SARS-CoV-2 (detection with polymerase chain reaction) recommend individualized antenatal care, mode of delivery based on obstetric considerations, and no routine separation of the mother and newborn after birth. Breastfeeding is encouraged, and although there is no specific recommendation on wearing a face mask to prevent viral transmission to the newborn while nursing, instructions are given to keep high hygiene standards. All studies based on cases tested due to hospital admittance, including our, will capture more women with pregnancy complications than in the general population. Our aim was to describe the clinical characteristics in 67 SARS-CoV-2 positive women and their 68 neonates, and to report short-term maternal and neonate outcomes.

**Material and methods:** A retrospective case series with data from medical records including all test-positive women (n=67) who gave birth from March 19 to April 26, 2020 in Stockholm, Sweden. Means, proportions and percentages were calculated for characteristics and outcomes.

**Results:** The mean age was 32 years, 40% were nulliparous, and 61% were overweight or obese. Further, 15% had diabetes and 21% a hypertensive disease. 70% of the women had a vaginal birth. Preterm delivery occurred in 19% of the women. The preterm deliveries were mostly medically indicated, including two women who were delivered preterm due to severe coronavirus disease 19 (COVID-19) illness, corresponding to 15% of the preterm births. Four women (6%) were admitted to intensive care unit postpartum. Three neonates were PCR-positive for SARS-CoV-2 after birth.

**Conclusions**: In this case series of 67 test-positive women with clinical presentation ranging from asymptomatic to manifest COVID-19 disease few women presented with severe COVID-19 illness, a majority had a vaginal birth at term with a healthy neonate that were test-negative for SARS-CoV-2.

**Key words:**

SARS-CoV-2, COVID-19, pregnancy outcomes, delivery outcomes, preterm birth.

**Abbreviations:**

COVID 19: coronavirus disease 19

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

**Key Message:**

The majority of test-positive women had a vaginal birth at term with a healthy neonate who tested negative for SARS-CoV-2. One of five neonates were born preterm, mostly moderately or late preterm. The majority of the preterm births were iatrogenic.

## INTRODUCTION

The understanding of how the novel SARS-CoV-2 virus affects women and their neonates during pregnancy, childbirth, and the immediate post-partum period is limited. Concerns have been raised regarding risks for severe disease in pregnant women, preterm delivery, possible vertical transmission, and neonatal infection. These concerns are based on known risks for severe illness in pregnant women infected by other respiratory viruses, in particular other corona viruses.(1, 2) There is currently no evidence for intrauterine infection caused by vertical transmission of SARS-CoV-2.(3, 4)

In Sweden, all antenatal and delivery care is tax funded and free charge. For the care of pregnant women positive for SARS-CoV-2, National Swedish guidelines were published early in the pandemic and recommended individualized antenatal care, mode of delivery based on obstetric considerations, and no routine separation of the mother and newborn after birth. Breastfeeding is encouraged, and although there is no specific recommendation on wearing a face mask to prevent viral transmission to the newborn while nursing, instructions are given to keep high hygiene standards. All neonates born to test-positive mothers are recommended to be screened for SARS-CoV-2 within 12-24 hours after birth by nasopharyngeal swab. The Stockholm region was the first Swedish region to be hit by the pandemic and has six delivery units which together take care of approximately 25% of all deliveries in Sweden (28 000 neonates 2019). In two of the delivery units in Stockholm, all women admitted to in-patient care are currently screened for SARS-CoV-2 virus. The prevalcence of test-positive women were approximately 4% in these units during the study period.The other four units test women only if fever or respiratory symptoms are present at the time of admission for labor or in-hospital care related to pregnancy complications. The prevalence of test-positive women in these units were lower during the study period, varying from 1.2% to 1.9%.Women scheduled for elective care are tested 24-48 hours prior to admission if they have any respiratory symptoms. They are also tested if they become symptomatic during hospital stay.

Here, we want to report a case series of 67 women with a positive test for SARS-CoV-2, who gave birth from March 19 until April 26, 2020 in the Stockholm region, Sweden. The women presented with symptoms ranging from asymptomatic to manifest severe COVID-19 disease. This corresponds to 2.1% of the general birthing population in the Stockholm region during that time.

Our objective is to describe the clinical characteristics of the women and their 68 neonates, and to report maternal and newborn short-term outcomes.

One case included in our study has earlier been reported(5) and the cases from the delivery units that screened for SARS-CoV-2 are included in a prospective study where the manuscript is submitted for publication.

## MATERIAL AND METHODS

All women who gave birth from March 19 until April 26, 2020 in the Stockholm region and were PCR positive for SARS-CoV-2 by nasopharyngeal swab were included (n=67). Pre-specified information was retrieved retrospectively from medical records by a clinician at each delivery unit. Data were then compiled in de-identified form in a database.

### Statistical analyses

Means, proportions and percentages were calculated.

### Ethical approval

This study was approved by the Ethical Review Agency in Sweden (DNR: 2020/02124) on May 25, 2020.

## RESULTS

Results of characteristics and outcomes are presented in Table 1 and 2 In short, a majority of the women were overweight or obese, and half were born in a non-Nordic country (Table 1). Furthermore, 21% were diagnosed with a hypertensive disorder and 15% had pre-gestational or gestational diabetes (Table 1). Of the 67 women, 47 had a vaginal delivery and 20 were delivered by cesarean. Of the 20 cesarean deliveries, seven were elective and performed due to a non-COVID-19 related obstetric indication and thirteen were emergency cesareans related to either fetal indication (7/13), maternal obstetric indications (4/13) or due to severe COVID-19 in the mother (2/13). In total, 4 women (6%) were admitted to ICU due to COVID-19. Of those women, two were admitted after preterm cesarean due to COVID-19 and two were admitted after vaginal

births at term (Table 1). One of them required invasive mechanical ventilation for 12 days, while the others did not require this. There were no maternal deaths.

Preterm delivery occurred in 13 of 67 women, giving birth to 14 of 68 neonates. Nine preterm deliveries were medically indicated, including the two that were due to COVID-19 corresponding to 15% of the preterm deliveries. Four had a spontaneous onset of labor (Table 1). Among the 68 neonates, there was one neonatal death in a neonate at $22^{+6/7}$ gestational weeks (gw) after preterm prelabor rupture of membranes (PPROM) at $22^{+3/7}$ gw (Table 2) and one stillbirth at gw $27^{+1/7}$ in a pregnancy with known severe fetal growth restriction (Table 2). Among the 67 live born neonates, three were diagnosed as small for gestational age, and two neonates had less than seven in Apgar score at five minutes of age. Twelve neonates were admitted to a neonatal intensive care unit (NICU) (Table 2). Nine of them for prematurity, one for observation for possible hypoglycemia, and two for pulmonary adaptation disorder.

All but five live born neonates (62/67) were screened for SARS-CoV-2 and three of them had a positive PCR test-result (Table 2). All three were born at term with normal Apgar scores. One was born by elective cesarean, one by emergency cesarean, and one was born vaginally.

## DISCUSSION

In this case series of 67 SARS-CoV-2 test-positive delivered women with varying clinical presentation ranging from asymptomatic to manifest COVID19 disease, the majority had a vaginal, term birth and delivered a healthy normal weight neonate that did not test positive for SARS-CoV-2. The majority of women were overweight or obese. Diabetes, hypertensive disorder, and non-Nordic origin were common. One woman delivered twins and has been reported earlier.(5) No woman died and few women fell severely ill in COVID-19 needing intensive care or invasive mechanical ventilation. There were two perinatal deaths. One in five newborns were born preterm. Two preterm births were related to COVID-19 in the mother. Admission to NICU were mostly due to preterm birth. Three neonates tested positive for SARS-CoV-2 and those who were positive were healthy term neonates.

Several reported risk factors for COVID-19 illness, like obesity, hypertension and diabetes were more common in our case series than in the general birthing population in Stockholm. (6) The

selective testing in women with symptoms at the time point of in-patient care (four delivery units) most likely results in a group with more pregnancy complications than in the general birthing population. During 2019 approximately 52 % of all women giving birth in Stockholm overweight or obese, 3 % had pre-eclampsia, 7 % had any type of diabetes and 46% were nulliparous.(7), (8) Results from the large prospective, population based cohort study of women admitted to hospital with confirmed SARS-CoV-2 infection from UK report that the incidence of hospital admission with confirmed SARS-CoV-2 infection varied with ethnic group, maternal age, and body mass index.(9) As in our study, a majority of the women in that study were overweight or obese and 12% had gestational diabetes. Diabetes and hypertensive disease were also slightly more common in our study than was reported from China, Italy, and France(10-12) but in line with the study from UK (9) This discrepancy may be due to BMI related differences in the populations, although BMI was not reported in the Chinese or Italian case series.(10, 11) Possibly, the rates could also be influenced by parity. Gestational diabetes and hypertensive disease are more common in overweight and obese women,(13) who are therefore more prone to be admitted due to complications and thereby tested for SARS-CoV-2. A French study reports that proportions of obesity, maternal age over 35 years and pre existing diabetes were higher in those with critical disease than in women with non-severe disease (14). This indicates that the proportion of disadvantageous maternal characteristics also can reflect the case composition in different studies In our study, few women needed intensive care which is similar to data reported in other studies(9-11, 15). No maternal deaths occurred in our study. In the UK study by Knight et al.(9) there were five maternal deaths (5/427) and in the French study by Kayem et al. they report one maternal deaths (1/617).Similar to the Chinese and Italian reports, few women needed intensive care and no woman died.(10, 11)

Our observed vaginal birth rate of 70% was high compared with the early case reports from China, where almost all women had a cesarean delivery(16, 17) and also the UK study(9) were approximately 40% had a vaginal birth. Other studies report higher rates around 60% (11, 12).The proportion of vaginal births in the general birthing population in Sweden is around 80%.(8) We observed a low frequency (4%) of test-positive neonates, confirming previous reports of little support for vertical transmission in both cesarean and vaginal birth.(11, 18) Preterm birth was observed at a similar rate as reported previous studies,(9-11, 14) but was more than three times the rate in the general birthing population in Sweden (approximately 6%).(19)

Our data suggest that few women present with severe COVID-19 illness. Moreover, the present policy in Sweden with mode of delivery based on obstetric considerations do not seem to generate more test-positive neonates than reported by other studies. Since our information was captured only in women who were tested late in pregnancy with subsequent deliveries, this finding must be interpreted with great caution.

We observed high rates of comorbidities among the delivered women. Future studies should focus on identifying pregnant women at increased risk of complications caused by COVID-19 illness. We noted a considerable rate of preterm birth, compared to the general birthing population, which calls for further research regarding mechanisms of preterm birth related to SARS-CoV-2 virus in pregnancy. Further, there is currently limited data on long-term follow up of neonates born to mothers positive for SARS-CoV-2 warranting future studies in this field.

A strength with this case series is that we were able to disentangle ICU admissions due to COVID-19 disease from other indications, i.e. severe pre-eclampsia with co-existing SARS-CoV-2 positive test. Further, we were able to describe important maternal characteristics. Of these, BMI is particularly important since obesity is a risk factor for maternal pregnancy complications in general and has been described as a risk factor for development of severe COVID-19 disease in the non-pregnant population.(6) A major limitation is the lack of comparison group. Other limitations include the small sample size, the mixed policy for testing, and lack of possibility to present characteristics and outcomes stratified on test-positivity from screening versus symptoms.. For this reason, generalization may not be possible until we have a larger sample of test-positive women to evaluate.

## CONCLUSION

In this case series of 67 test-positive women few women presented with severe COVID-19 illness, a majority had a vaginal birth at term with a healthy neonate that were test-negative for SARS-CoV-2.

## References

1. Stumpfe FM, Titzmann A, Schneider MO, et al. SARS-CoV-2 Infection in Pregnancy - a Review of the Current Literature and Possible Impact on Maternal and Neonatal Outcome. Geburtshilfe und Frauenheilkunde. 2020;80:380-90.

2. Rasmussen SA, Smulian JC, Lednicky JA, Wen TS, Jamieson DJ. Coronavirus Disease 2019 (COVID-19) and pregnancy: what obstetricians need to know. Am J Obstet Gynecol. 2020;222:415-26.

3. Schwartz DA, Dhaliwal A. Infections in pregnancy with COVID-19 and other respiratory RNA virus diseases are rarely, if ever, transmitted to the fetus: experiences with coronaviruses, HPIV, hMPV RSV, and INFLUENZA. Arch Pathol Lab Med. 2020 Apr 27. doi: 10.5858/arpa.2020-0211-SA. Epub ahead of print. PMID: 32338533.

4. Wu Y, Liu C, Dong L, et al. Coronavirus disease 2019 among pregnant Chinese women: Case series data on the safety of vaginal birth and breastfeeding. BJOG. 2020;127:1109–15.

5. Gidlöf S, Savchenko J, Brune T, Josefsson H. COVID-19 in pregnancy with comorbidities: More liberal testing strategy is needed. Acta Obstet Gynecol Scand. 2020;99:948-949.

6. Jordan RE, Adab P, Cheng KK. Covid-19: risk factors for severe disease and death. BMJ. 2020;368:m1198.

7. Stephansson O, Petersson K, Björk C, Conner P, Wikström AK. The Swedish Pregnancy Register - for quality of care improvement and research. Acta Obstet Gynecol Scand. 2018;97:466-76.

8. The Swedish Pregnancy Register. Dashboards [web page]. 2020 [Available from: https://www.medscinet.com/GR/default.aspx.

9. Knight M, Bunch K, Vousden N, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. BMJ. 2020;369:m2107.

10. Yan J, Guo J, Fan C, et al. Coronavirus disease 2019 (COVID-19) in pregnant women: A report based on 116 cases. Am J Obstet Gynecol. 2020;223:111.e1-111.e14.

11. Ferrazzi E, Frigerio L, Savasi V, et al. Vaginal delivery in SARS-CoV-2 infected pregnant women in Northern Italy: a retrospective analysis. BJOG. 2020 Apr 27:10.1111/1471-0528.16278. doi: 10.1111/1471-0528.16278. Epub ahead of print.

12. Sentilhes L, De Marcillac F, Jouffrieau C, Kuhn P, Thuet V, Hansmann Y, et al. Coronavirus disease 2019 in pregnancy was associated with maternal morbidity and preterm birth. Am J Obstet Gynecol. 2020 Jun 15:S0002-9378(20)30639-6. doi: 10.1016/j.ajog.2020.06.022. Epub ahead of print.

13. Poston L, Caleyachetty R, Cnattingius S, et al. Preconceptional and maternal obesity: epidemiology and health consequences. Lancet Diabetes Endocrinol. 2016;4:1025-1036..

14. Kayem G, Lecarpentier E, Deruelle P et al. A snapshot of the Covid-19 pandemic among pregnant women in France. J Gynecol Obstet Hum Reprod. 2020;49:101826.
15. Breslin N, Baptiste C, Gyamfi-Bannerman C, et al. COVID-19 infection among asymptomatic and symptomatic pregnant women: Two weeks of confirmed presentations to an affiliated pair of New York City hospitals. Am J Obstet Gynecol MFM. 2020;2:100118.
16. Yang Z, Wang M, Zhu Z, Liu Y. Coronavirus disease 2019 (COVID-19) and pregnancy: a systematic review. J Matern Fetal Neonatal Med. 2020 Apr 30:1-4. doi: 10.1080/14767058.2020.1759541. Epub ahead of print.
17. Yu N, Li W, Kang Q, et al. Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study. Lancet Infect Dis. 2020;20:559-564.
18. Lamouroux A, Attie-Bitach T, Martinovic J, Leruez-Ville M, Ville Y. Evidence for and against vertical transmission for severe acute respiratory syndrome coronavirus 2. Am J Obstet Gynecol. 2020;223:91.e1-91.e4.
19. Jacobsson B, Saltvedt S, Wikström AK, Morken NH, Leijonhufvud Å, Hagberg H. Prediktion, prevention och behandlingsmetoder [Preterm delivery: an overview on prediction, prevention and treatment]. In Swedish. Lakartidningen. 2019;116:FSST.

**Legends to tables**

Table 1. Maternal characteristics and outcomes among 67 women test positive for SARS-CoV-2.

Table 2. Perinatal outcomes among 68 neonates whose mothers test-positive for SARS-CoV-2.

Table 1. Maternal characteristics and outcomes among 67 women test positive for SARS-CoV-2.

| **Maternal characteristics N=67** | **Means, percentages and proportions** |
|---|---|
| | **mean (min-max)** |
| Maternal age (years) | 32 (19-42) |
| | **% (n/N)** |
| Parity (proportion of nulliparous women) | 40% (27/67) |
| Maternal country of birth | |
| *Nordic* | 43% (29/67) |
| *Non-Nordic* | 49% (33/67) |
| *Unknown* | 7% (5/67) |
| | **mean (min-max)** |
| Body mass index (BMI) (kg/m$^2$) | 27 (18-38) |
| | **% (n/N)** |
| *Under weight (BMI<18.5) and normal weight (BMI <24.9)* | 37% (25/67) |
| *Over weight (BMI 25-29.9)* | 33% (22/67) |
| *Obese (BMI >30)* | 28% (19/67) |
| *Unknown* | 1% (1/67) |
| | |
| Smoking habits (first antenatal visit), non-smoker | 99% (66/67) |
| Pre-eclampsia/ hypertensive disease | 21% (14/67) |
| Asthma | 9% (6/67) |
| Diabetes (pre gestational and gestational) | 15% (10/67) |
| Twin pregnancies | 1% (1/67) |
| | |
| **Maternal outcomes N=67** | **% (n/N)** |
| Mode of delivery | |
| *Vaginal delivery* | 70% (47/67) |
| *Cesarean delivery (CD)* | 30% (20/67) |
| | |
| Mode of onset of CD (proportion of all deliveries) | |

| | |
|---|---|
| *Elective CD, non-COVID19 indication* | 10% (7/67) |
| *Emergency CD, fetal indication* | 10% (7/67) |
| *Emergency CD, maternal non-COVID19 indication* | 6% (4/67) |
| *Emergency CD, maternal COVID19 indication* | 3% (2/67) |
| | |
| Mode of onset of CD (proportion of all CD) | |
| *Elective CD, non-COVID19 indication* | 35% (7/20) |
| *Emergency CD, fetal indication* | 35% (7/20) |
| *Emergency CD, maternal non-COVID19 indication* | 20% (4/20) |
| *Emergency CD, maternal COVID19 indication* | 10% (2/20) |
| | |
| Preterm delivery (< gestational week (gw) $37^{+0}$) | 19% (13/67) |
| Mode of onset of preterm delivery (proportion of all deliveries) | |
| *Spontaneous onset* | 6% (4/67) |
| *Medically indicated* | 13% (9/67) |
| Mode of onset of preterm delivery (proportion of all preterm deliveries) | |
| *Spontaneous onset* | 31% (4/13) |
| *Medically indicated* | 69% (9/13) |
| | |
| Women admitted to Intensive care unit (ICU) | 6% (4/67) |

Table 2. Perinatal outcomes among 68 neonates whose mothers test-positive for SARS-CoV-2.

| **Outcomes among all neonates N=68** | **Percentages and proportions** |
|---|---|
| | **% (n/N)** |
| Live born neonates | 99% (67/68) |
| Stillborn neonates | 1% (1/67) |
| Neonate born preterm (< gestational week (gw) $37^{+0/7}$) | 21% (14/68) |
| *Moderately to late preterm birth ($32^{+0/7}$-$36^{+6/7}$ gw)* | 13% (9/68) |
| *Very preterm birth ($28^{+0/7}$-$31^{+6/7}$ gw)* | 4% (3/68) |
| *Extremely preterm birth (<$28+^{0/7}$ gw)* | 3% (2/68) |
| | |
| Neonates tested for SARS-CoV-2 | 91% (62/68) |
| Neonates tested positive for SARS-CoV-2 (proportion of all neonates) | 4% (3/68) |
| Neonates tested positive for SARS-CoV-2 (proportion of tested neonates) | 5% (3/62) |
| | |
| **Outcomes among live born neonates N=67** | |
| Neonatal death (infant born $22^{+6/7}$ gw) | 1% (1/67) |
| Small for gestational age[a] (SGA) | 4% (3/67) |
| Apgar score <7 at five minutes (n=2 unknown) | 3% (2/67) |
| Neonate admitted to neonatal intensive care unit (NICU) | 18% (12/67) |
| *Proportion of neonates admitted to NICU born preterm* | 75% (9/12) |

[a]birth weight below two standard deviations (SD) of sex-specific mean weight per gestational age