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COVID-19 - Adverse Pregnancy Outcomes for the Mother

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Abstract It is known that pregnant women are more susceptible to coronaviruses of other generations (SARS-CoV, MERS-CoV), and the maternal mortality rates were higher than in the general population. The article deals with an analysis of four cases of maternal death in pregnant women with COVID-19.

Keywords COVID-19, Pregnancy, Complications, Maternal mortality

1. Introduction

The fourth year has passed since the start of the pandemic of coronavirus infection caused by a new virus - Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). Since the beginning of the pandemic 681,411,281 cases of coronavirus infection worldwide has been reported to date, and 6,811,207 (1%) people have died. Today, the medical community has learned not only how to manage this infection, but has already received a facility of specific prevention - vaccines. As a result, mortality from COVID-19 in 2022 decreased by 63% compared to 2020 [1].

The unique immune system and the peculiarities of the physiological changes during pregnancy make pregnant women vulnerable to any infections, especially to viral infections. COVID-19 is no exception in this sense. It has been established that pregnant women are as susceptible to coronavirus infection and subsequent development of severe pneumonia as the general population [2,5]. At the same time, a more severe course of a novel coronavirus infection in pregnant women was not determined. In addition, there is evidence that with COVID-19, the maternal mortality rate is significantly lower than with atypical pneumonia and the Middle East respiratory syndrome [4]. However, some researchers come to an opinion that the risk of severe coronavirus infection in pregnant women may be higher than in the general population. At the same time, risk factors in pregnant women are the same as in the general population [3].

One of the largest hospitals providing medical care to pregnant women, women in labor, postpartum women and their newborns in the Samarkand region of Uzbekistan was the Specialized Maternity Complex, where 812 women were hospitalized in 2021. According to the severity of coronavirus infection, the patients were distributed as follows: with a mild course of the disease were observed 231 (28.4%) women, with moderate severity - 502 (61.8%), with severe course - 75 (9.3%), with very severe - 4 (0.5%). 507 (62.4%) women were discharged pregnant, up to 22 weeks' gestation the pregnancy was terminated in 41 (5%) women, 264 (35.2%) women were delivered between 22 and 38 weeks' gestation. 128 women had spontaneous vaginal delivery, caesarean section was performed in 51.5% of cases. The main indications for caesarean section were: progression of respiratory failure (8 cases - 5.9%), placental abruption (4 cases - 2.9%), severe preeclampsia (13 cases - 9.6%), fetal asphyxia/ nonreassuring fetal status (19 observations - 14%). In the remaining 92 cases, which accounted 67.6%, caesarean section was performed due to the prior cesarean delivery.

By investigation of the problem of maternal mortality in women with COVID-19, it should be noted that, to date, there is still not enough data to draw specific conclusions and recommendations. Undoubtedly, two major factors were able to influence the maternal mortality rate during the pandemic: the first is the mutually aggravating influence of the pregnancy and acute COVID-19, which can be considered as an indirect cause of maternal mortality; the second is direct obstetric causes of death associated with a decrease in the quality of care due to the collapse of the healthcare system during a pandemic.

In this article, we provide an analysis of four cases of maternal death that occurred in the Specialized Maternity Complex in Samarkand.

2. Case No. 1

Patient D.S. Born in 1995, from Samarkand region, admitted on 14.10. 2020 y. Died – 18. 10. 2020 y. Presented with fever up to 39℃, cough, chest pain while coughing, bloody discharge from the genital tract, generalized weakness, malaise, sweating, muscle and body aches. Sick for 3 days.

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Anamnesis: Multipara – current pregnancy is II. In the second half of pregnancy, she was treated for ARI (acute respiratory infection) (at 30 weeks gestation).

Objective: General health condition is critical. Respiratory rate is 27 per minute. SpO_2 -80%. Pulse - 100 beats per minute (bpm), Blood pressure (BP) 90/60 mmHg. Temperature - 39.2℃.

Obstetrical status: Abdominal circumference (AC) -112 cm, height of the uterine fundus (HUF)-37 cm. Estimated fetal weight (EFW) - 4100±200. The fetal lie is transverse, the presenting part is not determined. Fetal heartbeat (FH) is 140 bpm, muffled, rhythmic.

Vaginal examination: The cervix is centered, softened, the vaginal portion of the cervix is 1 cm, the cervical canal is preserved, the external os passes the dome of the finger. Through the vaults, the presenting part is not determined.

Preliminary diagnosis: The main disease - Coronavirus infection, the virus is not identified (U07.2). Complications: Bilateral viral pneumonia caused by SARS-CoV-2. Concomitant condition: Pregnancy II, 40 weeks. Complete placenta previa (O44). Transverse fetal lie (032.2). Prior cesarean delivery (034.2).

Laboratory tests: *Complete blood count*: Hb-84 g/l, Erythrocytes - 2.8 g/l, Leucocytes - 11.04 g/l, Thrombocytes – 170 g/l, Segmented neutrophils - 70.5%, Stab neutrophils - 13%, Lymphocytes - 10.9%, Monocytes - 5.5%, Eosinophils - 0%, Erythrocyte sedimentation rate (ESR) - 34 mm/h. *Coagulation*: fibrinogen - 2.44 g/l, aPTT - 28 sec., Prothrombin index (PI) - 0.97 sec., INR 1.03, D-dimer 1066 ng/ml. *Biochemical testing*: urea 2.7 mmol/l, total protein - 53 g/l, creatinine 69 µmol/l, cholesterol 5.0 mmol/l, AST - 43 U/l, ALT - 76 U/l, C-reactive protein (CRP) - 24.7 mg /l, total bilirubin 19.5 µmol/l, procalcitonin - 2.23 ng/ml. *CT 4:* Lung tissue damage in the form of a combination of "Ground-glass opacity" and their consolidation of more than 75%. *Nasopharyngeal swab* - PCR RNA SARS CoV-2 – positive.

Final diagnosis: Main disease - Coronavirus infection, severe course, virus identified (U07.2). Complications: Bilateral viral pneumonia caused by SARS-CoV-2. Respiratory failure II degree. Concomitant condition: Pregnancy II, 40 weeks. Complete placenta previa (044). Transverse fetal lie (032.2). Prior cesarean delivery (034.2).

Recommended: ALV; paracetamol (infulgan) - 100.0 ml IV q.8.h.; The interval between doses is at least 4 hours. Dexamethasone 8 mg IV b.i.d.. Amoxicillin + Clavulanic acid 600 mg b.i.d. IV.

15.10. 2020: Operation. Laparotomy, caesarean section in the lower uterine segment. Blood loss – 900 ml. Male fetus, 3950/50 cm, Apgar score -2-3 points. Amniotic fluid meconium stained, 50 ml, foul-smelling. Placenta size: 22-26-30 cm, meconium stained, foul-smelling, umbilical cord -50 cm, meconium stained, macerated.

16.10.2020: On the second day - the general health condition is severe, the skin and visible mucous membranes are pale in color. Patient is on ALV, SpO_2 - 93%. In the lungs, breathing is conducted on both sides, respiratory rate 27 per 1 min. Heart sounds are muffled. The pulse is rhythmic, 112 bpm, BP - 100/70 mmHg. Body temperature - 37.2℃. The boundaries of the liver are enlarged by 3 cm, of the spleen - by 2 cm. Urination through an indwelling catheter, per day 640 ml.

Low-molecular-weight heparins was added to prescriptions - Clexane 0.6 ml b.i.d., subcutaneously; IV generation cephalosporins - cefepime 1.0 IV.

17.10.2020 Postoperation 2 days. Disseminated intravascular coagulation, hypocoagulation. Uterine hemorrhage. Conservative treatment measures did not work. *17.10.2020. Relaparatomy: total hysterectomy with appendages, drainage of the abdominal cavity, bilateral ligation of the internal iliac arteries.* The hemorrhage has been stopped.

18.10.2020 – 7.11.2020 - the general condition remains severe, despite the treatment measures taken. There is no spontaneous breathing.

18/10/2020 - with the progression of symptoms of respiratory failure, cardiac arrest occurred, resuscitation measures were not effective.

Final clinical diagnosis:

Main disease: COVID-19 U07.1

Complications: bilateral pneumonia, acute respiratory distress syndrome, respiratory failure

Concomitant: postpartum period, condition after caesarean section surgery (3 days), relaparotomy (2 days). DIC syndrome. Acute posthemorrhagic anemia

Pathological anatomical diagnosis

I Causes of death (main):

A) acute respiratory distress syndrome (1 day) - J80.X

B) bilateral pneumonia (8 days) - J18.1

C) COVID-19 - U07.1

II Other important conditions contributing to death:

Pregnancy II, 40 weeks. Complete placenta previa (044). Transverse fetal lie (032.2). Prior cesarean delivery (034.2). C-section. Relaparotomy, total hysterectomy with appendages, bilateral ligation of the internal iliac arteries.

This case of maternal death from coronavirus infection can be considered as a mutually aggravating effect of complicated pregnancy and severe viral pneumonia, which required artificial lung ventilation, emergency caesarean section. These complications led to acute intravascular coagulation and the need for relaparotomy. Further efforts to combat multiple organ failure were ineffective. Was this patient's death preventable? It is impossible for us to give a simple answer. Hypothetically YES. However, there are many – if…

3. Case No. 2

Pregnant women N.U., born in 1994, 08/20/2020, was presented with fever, weakness, shortness of breath. Sick for 3 days. Confirmed case (PCR RNA SARS CoV-2 - nasopharyngeal swab - positive).

Anamnesis: Current pregnancy II. The first half of the pregnancy course was uneventful. In the second half of pregnancy, she was treated for ARI (30 weeks), on an outpatient basis.

Objective findings: the general health condition is severe, the body temperature is 39℃. Consciousness is clear, the skin and visible mucous membranes are pale pink in color, breathing is rapid, free through the nose, respiratory rate is 28 times per minute. SpO_2-82%. BP - 100/60 mmHg, Ps - 106 beats per minute. Urination by an indwelling catheter. The stool was during the day.

Obstetrical status: AC-101 cm, HUF-36 cm. EFW - 3600±200. The fetal lie is longitudinal, the presenting part – fetal head is floating above the pelvic inlet. FH is 140 bpm, muffled, rhythmic.

Vaginal examination: the cervix is centered, softened, vaginal portion is 1 cm long, the external os passes the dome of the finger, through the vaginal vaults the presenting part is determined – the fetal head.

Laboratory tests: *Complete blood count*: Hb-81 g/l, Erythrocytes - 2.2 g/l, Leucocytes - 4.8 g/l, Thrombocytes – 163 g/l, Segmented neutrophils – 76%, Stab neutrophils – 2%, Lymphocytes – 15%, Monocytes - 5%, Eosinophils - 1%, Erythrocyte sedimentation rate (ESR) – 20 mm/h. *Coagulation*: fibrinogen - 2.44 g/l, aPTT - 28 sec., Prothrombin index (PI) - 0.97 sec., INR 1.03, D-dimer 1128 ng/ml. *Biochemical testing*: urea 2.7 mmol/l, total protein - 53 g/l, creatinine 69 µmol/l, cholesterol 5.0 mmol/l, AST - 43 U/l, ALT - 76 U/l, C-reactive protein (CRP) - 24.7 mg /l, total bilirubin 19.5 µmol/l, procalcitonin - 2.23 ng/ml. *CT 3 of chest:* 60% damage of the lung tissue *Nasopharyngeal swab* - PCR RNA SARS CoV-2 – positive.

Diagnosis: COVID-19, severe course - U07.1. Bilateral pneumonia. Respiratory failure - II degree. Pregnancy II, 39 weeks, Delivery II.

Recommended: non-invasive respiratory support - CPAP; dexamethasone 8 mg IV b.i.d.; ascorbic acid 5% - 10.0 IV b.i.d.; Ultrapim 1.0 IV b.i.d.; Levodex 100.0 IV – once a day; thiotriazoline 4.0 IV b.i.d.; heparin 1.0 subcutaneously q.i.d.

21.08.2020. due to the lack of effect from the therapy and the severity of the patient's condition, labor was induced and term delivery occurred with a male fetus, the weight was 3100 grams; height 50 cm. Apgar score 5-6 points. Blood loss during delivery 150 ml. The postpartum period course was un eventful, the recommended therapy continued.

On the seventh day postpartum at 23:00, the general health condition sharply worsened and became severe, consciousness was clear, the skin and visible mucous membranes were pale-bluish, respiratory rate - 30 times per minute. SpO_2-80%. BP 60/40 mm Hg, Ps - rhythmic, 120 bpm. On auscultation murmur is noted at the apex of the aorta on the right. ECG shows signs of acute cor pulmonale.

With regard to pulmonary embolism, resuscitation was carried out, but without effect.

Clinical diagnosis: The main: COVID-19, severe course U07.1. Bilateral pneumonia. Respiratory failure II degree.

Complication: Pulmonary embolism.

Acute cardiovascular failure.

Concomitant: Postpartum period.

Pathological anatomical diagnosis

I Causes of death (main):

A) pulmonary embolism (2 hours) - I26.9

B) bilateral pneumonia (7 days) - J18.1

C) COVID-19 - U07.1

II Concomitant: Postpartum period

A sudden complication - pulmonary embolism - led to the death of a young woman after delivery. We regard this case as unavoidable.

4. Case No. 3

Pregnant women N.U., born in 1987, 14.08.2021, was admitted with complaints of: fever, weakness, shortness of breath, pain in the lower abdomen. (PCR RNA SARS CoV-2 - nasopharyngeal swab - positive).

Anamnesis: Current pregnancy and delivery IV. In the second half of pregnancy, she was treated for the threatening preterm delivery (31 weeks), inpatient.

Objective: general health condition is severe, body temperature is 38.8℃. Consciousness is clear, respiratory rate is 26 times per minute. SpO_2-76%. Auscultation of the lungs revealed puerile vesicular breathing, coarse crackles in the lower sections on the both sides. BP 100/70 mm Hg, Ps106 bpm. Urination is independent. The stool was during the day. BMI- 34.

Obstetrical status: AC-96 cm, HUF-33 cm. EFW is 3100±200. The fetal lie is longitudinal, the presenting part of the head is "floating" above the pelvic inlet. FH is 130 bpm, muffled, rhythmic. There is no labor activity.

Laboratory tests: *Complete blood count*: Hb-84 g/l, Erythrocytes - 2.2 g/l, Leucocytes - 5.8 g/l, Thrombocytes – 183 g/l, Segmented neutrophils – 78%, Stab neutrophils – 2%, Lymphocytes – 16%, Monocytes - 7%, Eosinophils - 1%, ESR- 20 mm/h. Blood glucose level – 4,6 mmol/l. *Coagulation*: fibrinogen - 2.84 g/l, aPTT - 32 sec., Prothrombin index (PI) - 1.97 sec., INR 1.28, D-dimer 984 ng/ml. *Biochemical testing*: urea 2.9 mmol/l, total protein - 43 g/l, creatinine 84 µmol/l, cholesterol 7.0 mmol/l, AST - 53 U/l, ALT - 86 U/l, C-reactive protein (CRP) - 34.7 mg /l, total bilirubin 20.5 µmol/l, procalcitonin - 2.43 ng/ml. *CT 3 of chest:* 60% damage of the lung tissue.

Diagnosis at admission: COVID-19, severe course. U07.1 (PCR RNA SARS CoV-2 nasopharyngeal swab - positive). Bilateral pneumonia. Respiratory failure - II degree. Obesity II degree. Pregnancy IV, 38 weeks, Delivery III.

Recommended: non-invasive respiratory support - CPAP, paracetamol 500 mg b.i.d; dexamethasone 8 mg IV – b.i.d; ascorbic acid 5% -10.0 IV b.i.d; cefepime 1.0 IV b.i.d; ambroxol 30 mg t.i.d; heparin 2500 IU q.i.d, Clexane 0.6 q.d; Acetylcysteine 1 tab q.d, Vit D 5000 IU q.d.

On the second day after admission the patient presented severe pain in the lower abdomen, back pain, dizziness, bloody discharge from the genital tract.

Due to placental abruption an emergency laparotomy, caesarean section in the lower uterine segment under endotracheal anesthesia was performed. The postoperative period was uneventful, the recommended therapy continued, the condition improved.

On the third day at 19:00, the general state of health worsened sharply, the condition was severe, the skin and visible mucous membranes was pale-bluish, respiratory rate is 28 times per minute. SpO_2-73%. BP 90/50 mmHg, Ps rhythmic, 105 bpm. On auscultation murmur is noted at the apex of the aorta on the right. ECG shows signs of acute cor pulmonale.

Clinical (post-mortem) diagnosis: COVID-19, severe course. U07.1. COVID-19 associated pneumonia. Respiratory failure II degree. Postpartum period.

Complications: Pulmonary embolism. Acute cardiovascular failure.

Apparently, in this case, due to previous complications of pregnancy and obesity, there was initially a predisposition to thrombophilia, which developed in connection with the adjoining COVID-19, pneumonia, and delivery.

5. Case No. 4

Patient R.D. Born in 1999, she was admitted to the maternity complex on August 14, 2021 with complaints of fever up to 39℃, shortness of breath, pain in the lower abdomen and lower back. Sick for 5 days. PCR RNA SARS CoV-2 - nasopharyngeal swab - positive.

Anamnesis: I pregnancy – current. In the second half of pregnancy, she was treated for iron deficiency anemia of moderate degree (26 weeks), inpatient.

Objective status: general health condition is severe, body temperature is 36.8℃. The consciousness is clear, the skin and visible mucous membranes are pale in color, the respiratory rate is 24 times per minute. SpO_2-86%. On auscultation in the lungs puerile vesicular breathing, coarse crackles in the lower parts of the lungs on both sides are revealed. BP - 120/70 mm Hg, Ps 105 bpm. The liver and spleen cannot be palpated. “Tapping” symptom is negative on both sides. Urination is independent. The discharge is bloody with clots.

Obstetrical status: AC-96 cm, HUF-33 cm. EFW is 3100±200. The fetal lie is longitudinal, the presenting part of the head is “floating” above the pelvic inlet. FH is 156 bpm, muffled. No labor activity.

Laboratory tests: *Complete blood count*: Hb-68 g/l, Erythrocytes – 1.6 g/l, Leucocytes - 4.8 g/l, Thrombocytes – 173 g/l, Segmented neutrophils – 78 %, Stab neutrophils – 3 %, Lymphocytes – 16%, Monocytes - 7%, Eosinophils - 1%, ESR- 35 mm/h. Blood glucose level – 5,6 mmol/l. *Coagulation*: fibrinogen - 3.84 g/l, aPTT - 37 sec., Prothrombin index (PI) - 2.32 sec., INR 1.48, D-dimer 1115 ng/ml. *Biochemical testing*: urea 2.619 mmol/l, total protein - 58 g/l, creatinine 94 µmol/l, cholesterol 6.0 mmol/l, AST - 53 U/l, ALT - 86 U/l, C-reactive protein (CRP) - 44.7 mg /l, total bilirubin 22.5 µmol/l, procalcitonin - 3.47 ng/ml. *CT 3 of chest:* 85% damage of the lung tissue.

Diagnosis: COVID-19, severe course (U07.1). Bilateral pneumonia. Respiratory failure II degree. Pregnancy I, 38 weeks. Placental abruption. (O.45).

Recommended: Laparotomy. Cesarean section in the lower uterine segment. Prescribed: Rheosorbilact 400.0 IV, drip; dexamethasone 8 mg IV b.i.d; ascorbic acid 5% -10.0 IV b.i.d; cefoperazone sulbactam 1.0 IV – b.i.d; ambroxol 30 mg t.i.d; Clexane 0.6 q.d. 4 hours postoperation; Acetylcysteine 1 tab q.d, Vit D 5000 IU q.d.

Performed: laparotomy, caesarean section in the lower uterine segment under endotracheal anesthesia. The live, female fetus was extracted, weight 2900, height 50 cm. Apgar score 5-7 points. Blood loss 950 ml. Prolonged ALV.

The postoperation period was uneventful, the recommended therapy continued.

On the second day at 20:00, general health condition suddenly worsened, body temperature 39.6℃, chills, general health condition severe, soporous consciousness, skin and visible mucous membranes pale, respiratory rate - 30 times per minute. On ALV SpO_2-83%. BP 80/50 mmHg, Ps - 105 bpm. Anuria. The discharge is bloody - moderate. Septic shock was diagnosed. Resuscitation was carried out for 2 hours, without effect.

Post-mortem clinical diagnosis:

Primary: COVID-19, severe course (U07.1.)

Complication: Bilateral pneumonia. Cytokine storm - septic shock.

Concomitant: Postpartum period, condition after caesarean section (2 days).

Unfortunately, this clinical case demonstrates the impossibility of saving the life of patients with the development of septic shock associated with coronavirus infection in general medical practice.

6. Conclusions

Thus, pregnancy itself may be a risk factor for severe COVID-19 and associated risks of maternal death. An aggravating factor in our observations was obesity, multiparity and multigravidity. However, it should be noted that one of the four dead women was primiparous. Her pregnancy proceeded on the background of chronic anemia, she presented to the doctor late - on the fifth day from the moment of worsening of her general condition. On the background of severe coronavirus infection and pneumonia, placental abruption developed, which led to emergency caesarean section. The progression of pneumonia, surgery and blood loss became trigger factors for the development of septic shock. In conclusion, it should be noted that the impact on the health of the mother and fetus, on the course and complications of pregnancy of a novel coronavirus infection will still be studied for a long time. More research will be needed to explore the impact of COVID-19 not only on maternal health, but also on the health of future generations.

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