

EFFECT OF COVID-19 INFECTION ON PREGNANCY-INDUCED HYPERCOAGULABILITY

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COVID-19 ინფექციის გავლენა ორსულობით გამოწვეულ ჰიპერკოაგულაციაზე

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სტატიაში აღვწერთ საქართველოს სხვადასხვა რეგიონში კოვიდ 19-ით ინფიცირებული ორსული ქალების რამდენიმე კლინიკურ ქეისს. ინტენსიური დაკვირვებიდან გამომდინარე ირკვევა, რომ ყველა მათგანს აქვს მაღალი D-დიმერის დონე. მაქსიმალური D-დიმერის დონე იყო 6300 მკგ/ლ. ჩვენი ჰიპოთეზის თანახმად ეს და D-დიმერის სხვა მაჩვენებლები წარმოადგენენ ჰიპერკოაგულაციაზე ორსულობისა და კოვიდ 19-ის კომბინირებულ ეფექტს. სად გადის ზღვარი ორსულობითა და კოვიდ 19-ით გამოწვეულ ჰიპერკოაგულაციას შორის? უნდა დავიწყოთ თუ არა ანტიკოაგულაციური თერაპია კოვიდ 19-ით დაინფიცირებულ ორსულებში? ეს იმ კითხვების არასრული ჩამონათვალია, რომელიც გვინდა, აქტუალურად წარმოვადგინოთ საერთაშორისო სამედიცინო საზოგადოებაში. ჩვენ აქტიურად ვაგრძელებთ კვლევასა და დაკვირვებას ამ და სხვა კოვიდ 19-ით ინფიცირებულ ორსულ ქალებზე.

იმედი გვაქვს, რომ ჩვენი კვლევა კიდევ უფრო გაზრდის ინტერესს ორსულობისა და კოვიდ 19-ის კომბინირებულ ჰიპერკოაგულაციურ ეფექტზე როგორც ჩვენს, ქართველ, ასევე საერთაშორისო კოლეგებში და ეს კვლევა იქნება ამ თემაზე კიდევ უფრო ფართო-მასშტაბიანი და გლობალური პროექტების დაწყების ბიძგი.

Methods:

Retrospective analysis of 7 pregnant patients admitted to the TSMU First University Clinic and Chachava Clinic from 28.04.2020 to 10.12.2020

Introduction

COVID-19 is one of the most wide-spread pandemics in more than 100 years. At the time of writing this case report (Dec 19, 2020), there has already been a total of 75.5 million cases and 1.6 million deaths since the onset of the pandemic [3,6,7]. Although we have a good understanding of how various comorbidities affect the outcome of COVID-19 patients, we have less data about the clinical course of COVID-19 in pregnant patients [4,5]. One of the most significant aspect of pregnancy and concomitant COVID-19 is the risk of hypercoagulable complications in the patient [4,10]. Pregnant women are already at high risk of thrombotic conditions due to physiologic changes in pregnancy and COVID-19 has also been shown to exacerbate hypercoagulability [8,9]. Here we report the case series about 7 patients with

significant laboratory derangement possibly indicating worsening hypercoagulability. We believe that correlation between pregnancy and COVID-19 induced hypercoagulability will give rise to many further questions and the answers from the medical society will likely prevent many cases of life-threatening thrombotic complications in pregnant women across the world.

Case description

Represented below are 7 cases of COVID-19 during the pregnancy. All patients were admitted to TSMU, the First University Clinic or Chachava Clinic from 28.04.2020 to 13.12.2020 [1,2]. All of the patients were stable on admission. They were in various gestational weeks so we had the opportunity to observe the effect of COVID-19 during the different phases of pregnancy. We selected those patients who were from different parts of Georgia to eliminate sampling bias as much as possible. All of these pregnant women had normal white blood cell (WBC) count, LDH, AST and ALT levels. All of them had mild to moderate fever and only some of them complained of chest tightness, fatigue or cough. What drew our attention was that D-dimer was significantly elevated in some of our patients. According to UpToDate, the normal average value of D-dimer in pregnancy is <600 ug/L¹⁰. 5 out of 7 patients had more than 600 ug/L (view the table below). It is worth mentioning patient 7 who had a D-dimer value of 6300 ug/L. We were deeply concerned that these patients could develop deep venous thrombosis or pulmonary embolism [4], which is why we started all of them on anticoagulant therapy (specifically low-molecular-weight heparin). We regularly monitored their vital signs and fetal status and fortunately, all of them recovered from COVID-19 without any hypercoagulable sequelae. Patients were discharged home and they were counseled about the importance of regular obstetric follow-up and avoidance of sick contacts.

Conclusion

We report cases of COVID-19 infected pregnant patients from Georgia. Almost all of them had elevated D-dimer levels (the highest value - 6300 ug/L). We hypothesize that these values indicated the combined effect of pregnancy and COVID-19 on hypercoagulability [8]. Where can we draw the line of difference between pregnancy-induced and COVID-induced hypercoagulability? Should we start anticoagulant therapy earlier in COVID-infected pregnant patients compared to those without the infection? These are several questions that we wanted to raise amongst the health care professionals. We are actively continuing the research about this issue. We hope that our case series will be an object of interest and an impetus for even larger-scale research about the effects of COVID-19 on pregnancy-induced hypercoagulability.

Table 1. Different parameters on the day of patients' admission

Parameters	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Date of admission (dd/mm/yy)	28.04.20	15.05.20	20.08.20	18.10.20	10.12.20	12.12.20	13.12.20
Age (years)	36	26	28	33	35	30	25
Gestation age on admission (weeks)	8 0/7	15 3/7	22 5/7	34 2/7	36 6/7	25 6/7	26 3/7
Gravidity	3	4	2	4	3	4	3
Parity	2	3	1	3	2	3	2
Fever on admission	38.4 C	37.6 C	38.9 C	39.1 C	39.5 C	38.5 C	38.2 C
Place of residency	Tbilisi, Georgia	Bolnisi, Georgia	Kareli, Georgia	Kakheti, Georgia	Batumi, Georgia	Tbilisi, Georgia	Kutaisi, Georgia
Fever duration	10 days	7 days	12 days	14 days	9 days	7 days	11 days
Cough	Yes	No	Yes	No	Yes	Yes	No
Chest tightness	No	No	No	No	No	No	No
Fatigue	No	No	Yes	Yes	Yes	No	No
CRP (mg/L)	25	18	22	37	40	35	24
Lymphocyte count (%)	26	32	35	39	29	30	31
Lymphopenia	No	No	No	No	No	No	No
White Blood Cell count	5.2 x10 ⁹ /L	7.6 x10 ⁹ /L	8.5 x10 ⁹ /L	6.4 x10 ⁹ /L	10.4 x10 ⁹ /L	11 x 10 ⁹ /L	11.2 x10 ⁹ /L
AST (U/L)	22.5	15	16	19	13	24	18
ALT (U/L)	35	25	38	18	28	17	22
LDH (U/L)	170	200	120	155	136	159	170
D-dimer (ug/L)	359	600	650	1500	2000	2100	6300
Superimposed bacterial infection	No	No	No	No	No	No	No

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ВЛИЯНИЕ ИНФЕКЦИИ COVID-19 НА ГИПЕРКОАГУЛЯЦИЮ, ВЫЗВАННУЮ БЕРЕМЕННОСТЬЮ

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РЕЗЮМЕ

В этой статье мы описываем несколько клинических случаев заражения беременных женщин Covid 19 в разных регионах Грузии. Интенсивное наблюдение показывает, что все они имеют высокий уровень D-димера. Максимальный уровень D-димера составлял 6300 мкг / л. Согласно нашей гипотезе, это и другие показания D-димера представляют собой комбинированный эффект беременности и Covid 19 на гиперкоагуляцию. Где проходит грань между беременностью и гиперкоагуляцией Covid 19? Следует ли начинать антикоагулянтную терапию беременным женщинам, инфицированным Covid 19? Это неполный список вопросов, которые мы хотим задать международному медицинскому сообществу. Мы активно проводим исследования и мониторинг беременных женщин, инфицированных этим и другим Covid 19.

Мы надеемся, что наше исследование еще больше повысит интерес к комбинированному эффекту гиперкоагуляции беременности и Covid 19 как у наших грузинских, так и у зарубежных коллег, и это исследование послужит толчком для запуска еще более масштабных и глобальных проектов по этой теме.