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 PROGNOSTIC SIGNIFICANCE OF IL-6 IN STILLBIRTH DURING COVID 19 PANDEMIC

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IL-6 პროგნოზული მნიშვნელობა ნაყოფის ანტენატალური სიკვდილის განვითარებაში
 COVID 19 პანდემიის პირობებში

თბილისის სახელმწიფო სამედიცინო უნივერსიტეტის პირველი საუნივერსიტეტო კლინიკა,
 თბილისი, საქართველო

რეზიუმე

იმუნოფერმენტული ანალიზით (IFA) შესწავლილი იქნა IL6 კოვიდინფიცირებულ ორსულთა სისხლის პლაზმაში ნაყოფის ანტენატალური სიკვდილის დროს.

ძირითად ჯგუფში გაერთიანდა 3 ორსული მკვდარი ნაყოფით, ხოლო საკონტროლო ჯგუფში - 25 ორსული იგივე ასაკობრივი მონაცემებითა და გესტაციის ვადით, ცოცხალი ნაყოფითა და ფიზიოლოგიურად მიმდინარე ორსულობით. ორივე ჯგუფში ლაბორატორიულად დადასტურებული COVID 19 პოლიმერაზული ჯაჭური რეაქციის მეთოდით (PCR), საშუალო სიმძიმის.

კვლევის შედეგებმა აჩვენა, რომ ანთებითი ციტოკინის IL6 კონცენტრაცია სისხლის პლაზმაში მნიშვნელოვნად მაღალია ორსულებში ნაყოფის ანტენატალური სიკვდილის დროს, ვიდრე ორსულებში ცოცხალი ნაყოფითა და ფიზიოლოგიურად მიმდინარე ორსულობით. კვლევის შედეგები ადასტურებს, რომ ციტოკინური პროფილის შემდგომი შესწავლა, განსაკუთრებით კი IL6 შესაძლოა გახდეს მნიშვნელოვანი პროგნოზული მარკერი ნაყოფის ანტენატალური სიკვდილის განვითარების დროს, განსაკუთრებით COVID 19 პანდემიის პირობებში.

INTRODUCTION. The worldwide incidence of coronavirus disease 2019 (COVID-19) infection is rapidly increasing, and after a year with this disease, we know that obstetric complications such as preterm delivery, IUGR, and stillbirths increase [5,6] but still we have limited information about influence of coronavirus disease on pregnancy and fetal well-being. On the other hand, it is well known that COVID causes hyper inflammation and cytokine storm as an immune response [3,6]. Accumulating evidence suggests that cytokine storm syndrome (CSS) an overactive immune response triggered by COVID 19, rather than the virus itself, is responsible for maternal and fetal complications [1].

In this article we represent our experience with 3 confirmed cases of covid-19 and antenatal fetal death presenting in the first University clinic of TSMU. This study aims to evaluate the immunological prognostic markers in pregnant women confirmed with COVID-19 and antenatal fetal death to provide the reference for clinical work. All 3 patients presented with symptoms of covid-19 disease, including cough, myalgias, fever, chest pain, and headache. All of them were admitted to the hospital in the obstetric/gynecology department. None requiring intensive care unit admission.

DESIGN: A prospective case-control study

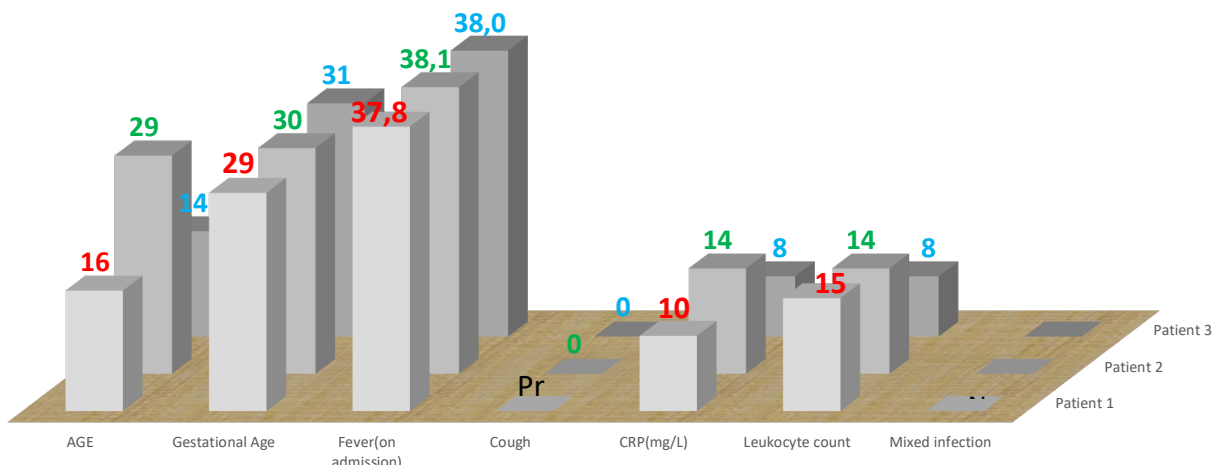
Case description: Represented below are 3 cases of COVID-19 during the pregnancy with antenatal fetal death. All patients were admitted to TSMU, the First University Clinic from 30.03.20 to 30.05.2021. All of the patients were stable on admission. They were in various gestational weeks so we had the opportunity to observe the effect of COVID-19 during the different phases of pregnancy.

Table 1. Clinical features of women with COVID 19 infection

	Patient 1	Patient 2	Patient 3
AGE	26	29	34
Gestational Age	29	30	31
Fever (on admission)	37,8	38,1	38,0
Cough	Present	-	-
CRP	10mg/L	14mg/L	8mg/L
Leukocyte count	15	18	10
Mixed infection	NO	No	No

Results: table 1 shows main clinical features of patients (n=3) and the patients in control group (n=25) the two groups were homogenous and no significant differences were noted in the clinical data.

Clinical features of women with COVID 19 infection

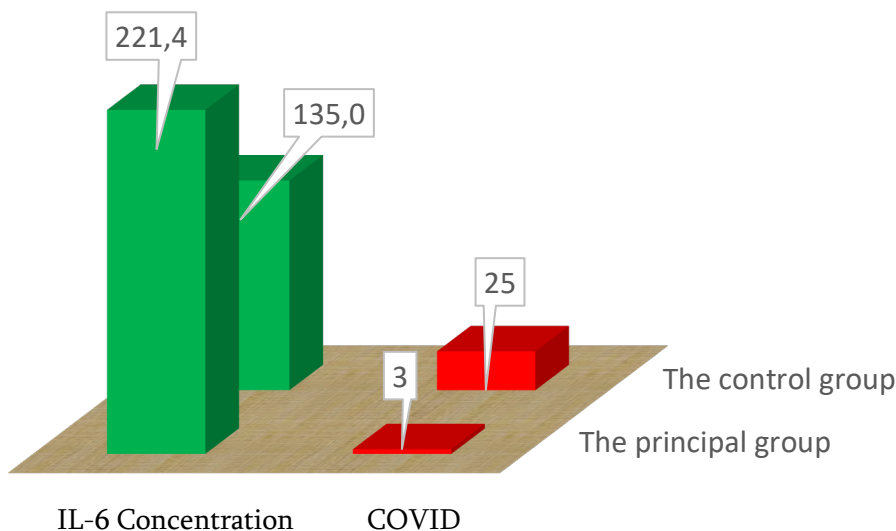


All the 3 pregnant women had a history of epidemiological exposure to COVID-19. The age of the pregnant women ranged from 20 to 35 years old. The gestational weeks of those patients ranged from 23 to 31 (in both main and control groups) weeks on admission. All patients had fever among three confirmed COVID-19 patients. Two patients had an occasional cough. All of them were diagnosed mild COVID-19, and none of them developed severe COVID-19 with severe respiratory distress. Data from laboratory tests showed that none of them had lymphopenia on admission. The patients had elevated concentrations of C-reactive protein (>10 mg/L). The concentrations of alanine aminotransferase (ALT) and aspartate aminotransferase (AST), lactate dehydrogenase were normal during hospitalization in our hospital. D-dimer in all patients were elevated. Additionally, we controlled IL-6 concentration in both groups, IL-6 level were high, but in patients with antenatal fetal death this immunological marker was significantly higher than in case of normal pregnancy, live fetus.

Table 2. IL-6 content in women with covid 19 and normal pregnancy and in women with covid 19 and Antenatal Fetal Death

Group	IL-6 concentration
The principal group	221,4+ ₋ 16,2
The control group	135 + ₋ 14,2

IL-6 content in women with covid 19 and normal pregnancy and women with covid 19 and stillbirth



Conclusion: COVID 19 infection seems to have a negative effect on the fetus, in mild/moderate symptoms in the acute phase of the infection although vertical transmission is not yet be proven [1,2]. This analysis reveals that coronavirus infections in pregnant women caused by SARS in these 3 cases COVID-19 did not lead to severe respiratory distress and maternal deaths, but may cause higher index of proinflammatory cytokines such as IL-6 which may serve as a prognostic marker for stillbirth, as well as assess the qualifying bit of infection progress, but further studies of larger number of patients are necessary to confirm the results reported in our article.

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НАТИА ПХАЛАДЗЕ, НИКОЛОЗ КИНТРАИЯ, НИНО ГОГОХИЯ, ХАТИЯ МИКАБЕРИДЗЕ
ПРОГНОСТИЧЕСКОЕ ЗНАЧЕНИЕ ИЛ-6 ПРИ МЕРТВОРОЖДЕНИИ В УСЛОВИЯХ ПАНДЕМИИ COVID-19

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РЕЗЮМЕ

В условиях пандемии COVID 19 методом иммуноферментного анализа (ИФА) была изучена плазма крови инфицированных пациентов для изучения возможности прогноза посредством значения ИЛ-6, при антенатальной гибели плода.

Основная группа представлена тремя инфицированными беременными с мёртвым плодом, в контрольную группу составили 25 беременных в том же возрастном и гестационном периоде с живым плодом и физиологическим течением беременности. В обеих группах COVID 19 лабораторно подтверждён методом (PCR) полимеразной цепной реакции.

Исследования показали, что содержание про воспалительных цитокинов ИЛ-6 у беременных с антенатальной смертью плода инфицированных COVID 19 значительно выше, чем у пациенток с нормальным течением беременности.

Полученные результаты подтверждают, что дальнейшее исследование цитокинового профиля, в особенности же ИЛ6, может стать важным маркером в прогнозировании антенатальной гибели плода, в условиях пандемии COVID 19.

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SUMMARY

The pro inflammatory cytokine IL-6 was studied by the method of immune-ferment analysis (IFA) in the blood serum in women with stillbirth during COVID infection. 3 patients suffering from this complication were examined (the principal group) and 25 patients - of adequate age groups and gestation periods but live fetuses in both groups presented SARS COV 2 infection which was confirmed with laboratory PCR (Polymerase Chain Reaction) test. The result of studies showed that the content of proinflammatory cytokine IL-6 in women with antenatal fetal death was significantly higher in the blood than in patients with normal progress of pregnancy. The obtained data prove that further studies of cytokine profile and especially of IL-6 may become an important method for the prognosis for stillbirth during SARS COV 2 pandemic period.

Keywords: Prognostic significance, IL-6, Stillbirth, COVID 19

