ACUTE RENAL FAILURE INDUCED BY PREECLAMPSIA IN A PREGNANT WOMAN WITH COVID-19

Diana Secară^{1,2}, Daniela Cătălina Meca³, Ana Veronica Uzunov³, Aida Petca¹, Claudia Mehedințu^{1,4}, Răzvan Petca¹, Mihai Dumitrașcu^{1,2}, Francesca Frîncu^{1,4}, Monica Mihaela Cîrstoiu^{1,2}

¹Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

²Department of Obstetrics and Gynaecology, University Emergency Hospital Bucharest, Bucharest, Romania

³Doctoral School of "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania ⁴Department of Obstetrics and Gynaecology, Malaxa Clinical Hospital, Bucharest, Romania

CASE	Abstract
REPORT	
Doi: 10.33695/rojes.v3i1.38 Accepted: 15.05.2021	Pregnancy-related acute kidney injury, a pathology that develops secondary to obstetric complications, is associated with an increased risk of maternal mortality, especially in the post-partum period. The most common causes of acute renal failure include preeclampsia, puerperal sepsis, antepartum or postpartum hemorrhage, placental abruption or intrauterine fetal death. At the same time, COVID-19- induced nephropathy, translated into acute renal failure, further leads
	to increased maternal and fetal mortality, causing a higher incidence
Corresponding author:	of stillbirths, low fetal weight and premature birth.
Daniela Cătălina Meca	
daniella.meca@gmail.com	Keywords: pregnancy, acute renal failure, COVID-19, preeclampsia

Introduction

The incidence of acute renal injury during pregnancy is not precisely determined, given the lack of uniform diagnostic criteria, ranging from 1 in 50 to 1 to 20000 in different studies [1,2]. The early diagnosis of renal acute failure is hampered by the physiological reduction of serum creatinine during pregnancy, so the biological parameters may be within normal limits, although renal injury has occurred [3]. The renal disorder caused by preeclampsia is defined by the American College of Obstetricians and Gynecologists, as a serum creatinine level >1.1 mg/dl or an increase to 2 times baseline in the absence of renal disease [4]. Approximatively 1% of pregnant women with severe preeclampsia develop this condition [5].

Pregnancy related acute renal failure is classified as having prerenal, renal and postrenal etiologies and can develop at any time peripartum. The risk of developing acute renal injury is independent of age and clinical comorbidities and the gestational age is correlated with the underlying pathology [4,6].

The most frequent causes which lead to acute renal failure include preeclampsia, puerperal sepsis, postpartum or antepartum hemorrhage, placental abruption, or intrauterine fetal death [1]. Rarely, atypical hemolytic uremic syndrome or acute fatty liver of pregnancy can lead to renal failure [3,7].

Preeclampsia remains a leading cause of acute renal failure worldwide, with a

significant maternal morbidity and mortality. Although the pathogenesis of the glomerular disease is not precisely determined. considering the physiological renal changes which occur in pregnancy, the attention is addressed to the angiogenesis mechanism, with an altered expression of anti-angiogenic factors and glomerular endotheliosis. In many cases, the glomerular lesions disappear in 6 months postpartum, but it must be mentioned that severe, early-onset preeclampsia increases the risk of developing chronic renal disease [8].

The risk of caesarian delivery, uterine atony, placental abruption, disseminated intravascular coagulation is increased in pregnant women with acute renal failure. Also, this pathology is associated with stillbirths, low gestational age at delivery and low birth weight [9].

Considering that the etiology of acute renal failure can be multifactorial, the current epidemiological context brings in foreground the nephropathy induced by COVID-19, translated into acute renal failure, that affects around 3-9% of the patients [10]. In these cases, the exact subsequent pathogenesis is uncertain, but the role of angiotensinconverting enzyme 2 was reported [11,12].

The management of pregnancy related acute renal failure, although challenging, includes renal function supportive measures, referring to the etiologic treatment. The indications for dialysis are similar to the general population: hyperkalemia, metabolic acidosis, uremic symptoms, a glomerular rate under 20 ml/min/1.73m2 [13,14].

Case report

We present the case of a 34-years-old Caucasian patient who was admitted in the Department of Obstetrics and Gynecology of University Emergency Hospital in Bucharest transferred from Department of Obstetrics and Gynecology of County Hospital for preeclampsia complicating a 33-week pregnancy.

Regarding personal medical history, she had 2 abortions and two cesarean births, but none of them were complicated by hypertension causes. The patient had no known familial or personal pathologic history.

The patient investigated her pregnancy and there were no medical issues, until one week prior of her hospitalization. She started developing facial and peripheral edema and she presented to the emergency room of County Hospital where she was hospitalized. As the protocol in our country requests, a RT-PCR for COVID-19 was performed and it was negative. The blood samples indicated kidney injury with elevated value of creatinine -4.78mg/dl, urea - 92mg/dl, uric acid - 9.64 mg/dl, anemia and thrombocytopenia and normal liver blood tests. The arterial tension was more than 160/100 mmHg during hospitalization under the maximal antihypertensive therapy. Regarding the fetal growth and well-being an ultrasound was performed, and it was in normal parameters. Because of the maternal health status, corticosteroids were administrated to accelerate fetal lung maturation. After 48 hours of hospitalization, considering the worsening of maternal general condition, developing resistant hypertension under maximum specific dose therapy accompanied by oliguria and the exacerbation of edema, the medical team decided to transfer the patient to a multidisciplinary hospital.

When she was admitted in our department, she was retested for COVID-19 by RT-PCR and the result was negative. Tensional values were between 150-170/90-110mmHg under hypotensive treatment and laboratory findings showed azotemia with creatinine 4.47 mg/dl, potassium - 5.63 mmol/l, uric acid - 10.36 mg/dl, urea - 106.4 mg/dl with progressive increase. А transabdominal ultrasound was performed noticing an increased renal parenchymal echogenicity in both kidneys and fluid in

pleural and peritoneal cavities (Figure 1). Regarding the newborn evolution, it was within limit. After 24 hours, because of the multidisciplinary evaluation, including cardiological, nephrological, ophthalmological and obstetrical examinations was decided the need of an emergency Csection due to immediate concern for the health of the mother. She delivered a masculine fetus of 2.040 grams with an Apgar score - 6 at one minute and 8 at 5 minutes, with admission to the intensive care unit only for 5 days. The placenta was sent for histopathological examination. Post-operative evaluation was unpropitious with continuum increasing the creatinine values - the highest one 5.40 mg/dl and urea - 111 mg/dl under diuretic treatment. In the absence of uremic symptoms, it was decided not to institute dialysis. The arterial tension was stable with values between 120-140/60-90mmHg with progressive decrease with no treatment.



Figure 1 – Transabdominal ultrasound showing the hyperechogenic renal parenchyma noticed in both kidneys

The patient presented hypoalbuminemia - 2.8 g/dl - with the need of 9 Human Albumin vials. The day after surgery, the patient presented headache with scotoma, therefore a head MRI was performed under the suspicious posterior reversible encephalopathy of syndrome which was denied. Supplemental investigations were performed as tests for antiphospholipid syndrome, thrombophilia, immunophenotyping and lupus nephritis, but there were in normal parameters. Because the diagnosis was uncertain after 5 days, we decided to retest for SARS-CoV2 infection, and the result of the RT-PCR was positive. Therefore, a chest radiograph was performed, and the result presented no abnormalities. The newborn was also tested for SARS-CoV2 infection and it was negative. After 3 days of this moment on one hand, the patient started developing mild symptoms as rhinorrhea, dysphagia, headache, loss of taste and anosmia, but on the other hand kidney blood test revealed a progressive improvement. The patient needed no COVID-19 treatment, excepting the anticoagulant one. Meanwhile, the histopathologic result of the placenta described a retroplacental hematomas with a diameter of 5 cm.

After 14 days the patient was released with well-being health status, afebrile, primary surgically wound healing, with normal tensional values without medication and normal values of creatinine - 1.09 mg/dl and urea - 44mg/dl. The patient was released together with the newborn.

Discussion

As studies show, preeclampsia can cause serious complications as HELLP syndrome, disseminated intravascular coagulopathy and acute renal failure with a maternal mortality with 1.7% due to acute renal failure [15,16]. It is important to consider both obstetric and nonobstetric etiologies of acute renal failure in a pregnant woman. Nevertheless, the most common cause of acute kidney injury in pregnancy remains hypertensive disorders and more rarely causes like atypical hemolytic uremic syndrome or acute fatty liver of pregnancy can occur. The moment when this pathological status occurs can explain its causes, but it most commonly appears in the second trimester [3]. Our patient presented criteria for preeclampsia which subsequent was complicated with acute kidney failure.

According to the COVID-19 infection, its symptoms may vary from fever, cough, shortness of breath to acute respiratory problems and affection of other vital organs as kidney and liver [12,17,18]. Some studies show that the incidence of acute kidney injury in patients with COVID-19 is 15% with a mortality rate over 50% [19-21]. Also, researchers report albuminuria or proteinuria on admission in 44-63% of COVID-19 patients, elevated urea and creatinine in 13-27%, respectively 14-19% of cases with SARS-CoV2 infection [19, 22, 23]. COVID-19 during Preeclampsia and pregnancy share the same set of risk factors and similar pathological issues - specific vascular pathology [24]. A large, longitudinal, prospective, multinational observational study reports there is a strongly association between COVID-19 during pregnancy and preeclampsia and it seems that this association is independent of risk factors and preexisting conditions. Interesting is that the severity of SARS-CoV2 infections does not affect the association. Also, it shows that these conditions increase the risk factors for preterm birth, severe perinatal morbidity and mortality and adverse maternal outcomes [24]. Mendoza et al. have introduced the concept of "preeclampsia-like syndrome" associated with COVID-19, because it is clinically difficult to distinguish this syndrome from "true" preeclampsia [24,25]. The explication leads in that they both share characteristics of the

severe endothelial dysfunction seen in nonpregnant patients [24-26]. Studies show, on one hand that preeclampsia seems to be a high-risk factor for SARS-CoV2 infection, including its complications, but on the other hand there were not any evidence to support that COVID-19 is etiologically associated with preeclampsia [24]. As revealed previous, preeclampsia presents a high risk for placental abruption [3]. Pointing that preeclampsia and COVID-19 infection during pregnancy have almost the same histopathological substrate, it is clearly that the risk for obstetrical complications might be doubled. In our case the first manifestations were hypertension and acute kidney failure with no better improvement after delivery. It is interesting that the diagnose of COVID-19 disease was established after 5 days, because the patient previous had 2 negative tests. As studies show the newborn was delivered premature and a retroplacental hematoma was developing. It is important that the evolution both for mother and for the newborn was favorable. The explication for these complications may be due to the infection with SARS-CoV2 virus or preeclampsia. It is difficult to establish a delimitation between the two pathologies. Fortunately, neither the mother nor the newborn needed prolonged intensive care or COVID-19 treatment.

Conclusions

COVID-19 during pregnancy be can asymptomatic or can lead to severe complications including respiratory, renal or liver ones. The first manifestation of SARS-CoV2 infection can be similar to preeclampsia and they can affect the mother's or the newborn's prognostic. Due to the presented case and the studies that have been conducted, we support the need to use the "preeclampsialike syndrome" associated with COVID-19. Withal, when an acute kidney injury occurs during pregnancy an infection with SARS-CoV2 virus should be suspected. An increased attention should be given to women with preeclampsia in the actual pandemic context.

References

[1]J. Prakash, S.S. Niwas, A. Parekh, L.K. Pandey, L. Sharatchandra, P. Arora, A.K. Mahapatra "Acute kidney injury in late pregnancy in developing countries" Renal failure. Apr 1;32(3):309-13; 2010.

[2]A. Acharya "Management of acute kidney injury in pregnancy for the obstetrician"Obstetrics and Gynecology Clinics. 43(4), 747-765; 2016.

[3]J. Szczepanski, A. Griffin, S. Novotny, K. Wallace "Acute kidney injury in pregnancies complicated with preeclampsia or HELLP syndrome" Frontiers in medicine. 7, 22; 2020.

[4]ACOG Practice Bulletin No. 202: "Gestational hypertension and preeclampsia" Obstet Gynecol. 133: e1–25; 2019

[5] J. Prakash, V.C. Ganiger "Acute kidney injury in pregnancy-specific disorders" Indian journal of nephrology. 27(4): 258; 2017.

[6] D. Liu, W. He, Y. Li, M. Xiong, L. Wang, J. Huang, et al. "Epidemiology of acute kidney injury in hospitalized pregnant women in China" BMC Nephrol. 20:67; 2019.

[7]Q. Gao, X. Qu, X. Chen, J. Zhang, F. Liu, S. Tian et al. "Outcomes and risk factors of patients with acute fatty liver of pregnancy: a multicentre retrospective study" Singapore Med J. 59:425– 30;2018.

[8]A.M. Van der Graaf, T.J. Toering, M.M. Faas, A. Titia Lely "From preeclampsia to renal disease: a role of angiogenic factors and the renin– angiotensin aldosterone system?" Nephrology Dialysis Transplantation. 27(suppl_3), 51-57; 2012.

[9]Y. Liu, X. Ma, J. Zheng, X. Liu, T. Yan "Pregnancy outcomes in patients with acute kidney injury during pregnancy: a systematic review and meta-analysis" BMC Pregnancy Childbirth. 17:235; 2017.

[10]M. Mubarak, N. Nasri "COVID-19 nephropathy; an emerging condition caused by novel coronavirus infection" J. Nephropathol. 9(3):e21;2020.

[11]R. Tolouian, S. Z. Vahed, S. Ghiyasvand, A. Tolouian, M. Ardalan "COVID-19 interactions

with angiotensin-converting enzyme 2 (ACE2) and the kinin system; looking at a potential treatment" Journal of Renal Injury Prevention, 9(2), e19e19;2020.

[12]A.Taghizadieh, H. Mikaeili, M. Ahmadi, H. Valizadeh "Acute kidney injury in pregnant women following SARS-CoV-2 infection: a case report from Iran" Respir Med Case Rep. 30, 101090; 2020.

[13]N.K. Krane, M. Hamrahian "Pregnancy: Kidney diseases and hypertension" Am J Kidney Dis. 49:336–45; 2007.

[14]A.Acharya "Management of acute kidney injury in pregnancy for the obstetrician" Obstetrics and Gynecology Clinics, 43(4), 747-765;2016.

[15]S. Ngwenya "Severe preeclampsia and eclampsia: incidence, complications, and perinatal outcomes at a low-resource setting, Mpilo Central Hospital, Bulawayo, Zimbabwe" Int J Womens Health 17(9),353-357;2017.

[16]C. V. Ananth et al. "Serious maternal complications in relation to severe pre-eclampsia: a retrospective cohort study of the impact of hospital volume" BJOG: An International Journal of Obstetrics & Gynaecology 124(8),1246-1253;2017.

[17]A. Vabret, J. Dina, E. Brison, J. Brouard, F. Freymuth "Coronavirus humains (HCoV) Human coronaviruses" Pathol. Biol 57(2),149-160;2009.

[18]Y. Bai, L. Yao, T. Wei, F. Tian, D.Y. Jin, L. Chen, M. Wang "Presumed asymptomatic carrier transmission of COVID-19" JAMA 323(14),1406-1407;2020.

[19]A. Gulati, C. Pomeranz, Z. Qamar, S. Thomas, D. Frisch, G. George, R. Summer, J. DeSimone, B. Sundaram "A comprehensive review of manifestations of novel coronaviruses in the context of deadly COVID-19 global pandemic" Am J Med Sci. 360(1),5-34;2020.

[20]N. Chen, M. Zhou, X. Dong, J. Qu, F. Gong, Y. Han, Y. Qiu, J. Wang, Y. Liu, Y. Wei, J. Xia, T. Yu, X. Zhang, L.Zhang "Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study" Lancet 395(10223),507-513;2020.

[21] F. Zhou, T. Yu, R. Du, G. Fan, Y. Liu, Z. Liu, J. Xiang, Y. Wang, B. Song, X. Gu, L. Guan, Y. Wei, H. Li, X. Wu, J. Xu, S. Tu, Y. Zhang, H. Chen, B. Cao "Clinical course and risk factors for mortality of adult inpatients with COVID-19 in

Wuhan, China: a retrospective cohort study" Lancet 395(10229),1054-1062;2020.

[22]Z. Li, M. Wu, J. Yao, J. Guo, X. Liao, S. Song, J. Li, G. Duan, Y. Zhou, X. Wu, Z. Zhou, T. Wang, M. Hu, X. Chen, Y. Fu, C. Lei, H. Dong, C. Xu, Y. Hu, M. Han, Y. Zhou, H. Jia, X. Chen, J. Yan "Caution on kidney dysfunctions of COVID-19 patients" Europe PMC;2020.

[23]Y. Cheng "Kidney disease is associated with in-hospital death of patients with COVID-19" Kidney international 97(5),829-838;2020.

[24]A.T. Papageorghiou, P. Deruelle, R.B. Gunier, S. Rauch, P.K.García-May et. al "Preeclampsia and COVID-19: results from the INTERCOVID prospective longitudinal study" Am J Obstet Gynecol. 225(3),289-e1-289.e17; 2021. [25]M. Mendoza, I. Garcia-Ruiz, N. Maiz, C. Rodo, P. Garcia-Manau, B. Serrano, R.M. Lopez-Martinez, J. Balcells, N. Fernandez-Hidalgo, E. Carreras, A. Suy "Pre-eclampsia-like syndrome induced by severe COVID-19: a prospective observational study" BJOG 127(11), 1374-1380;2020.

[26]M. Dap, M. Olivier. "Proteinuria in Covid-19 pregnant women: Preeclampsia or severe infection?" European Journal of Obstetrics and Gynecology and Reproductive Biology 252, 612;2020.