



HELLP SYNDROME PREGNANCY COMPLICATED BY COVID-19 INFECTION- A CASE REPORT

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ABSTRACT

A 25-year old primigravida at 36 weeks of gestation was referred to us with a history of bilateral pedal edema of one month duration and history of tachypnea, dry cough, and yellowish discoloration of palms and soles of 4 days duration. She had raised blood pressure at admission and on evaluation a nasopharyngeal swab turned positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections. Her lab investigations were suggestive of HELLP syndrome, a severe form of pre-eclampsia. An emergency Caesarean section was performed at 36 weeks 1 day gestational age i/v/o HELLP syndrome, with a positive neonatal outcome. Post-surgery the patient made a rapid recovery with supportive management. There was no evidence of vertical transmission to neonate. Since COVID 19 infection exhibit lab parameters similar to pre-eclampsia and HELLP syndrome, it is not clear if HELLP syndrome can get exacerbated by concomitant COVID-19 infection in pregnant women or if the COVID 19 infection is acting independently as an etiology for pre-eclampsia and HELLP syndrome. Also how the termination of pregnancy can lead to an improvement of symptoms and patient prognosis in COVID 19 pregnancy is yet to be understood.

KEYWORDS

Covid-19, HELLP syndrome, concomitant infection, overlapping features.

INTRODUCTION

HELLP syndrome, a heterogeneous, multisystem obstetric complication, mimics a COVID-19 infection due to overlapping clinical and laboratory features such as headache, morbilliform rash, gastrointestinal symptoms, microangiopathic hemolytic anemia, elevated liver enzymes, and high d-dimer levels [1]. In these times of an ongoing COVID pandemic, these overlapping features pose a diagnostic dilemma to the obstetrician, necessitating differentiation between these two diagnoses to ensure optimum obstetric care. HELLP syndrome, described by Weinstein in 1982, carries a higher risk for maternal morbidity from acute renal failure, consumptive coagulopathy, acute respiratory distress syndrome, cerebral edema, hematoma ruptured liver, abruptio placentae, and hypovolemic shock. Symptoms may vary from a flu-like illness to gastrointestinal hemorrhage [2, 3].

In December 2019, COVID- 19, a beta coronavirus, emerged as a novel human pathogen for viral pneumonia [4]. The covid-19 infection causes a coagulopathy characterized by elevated D-dimer and fibrinogen degradation products (FDP) and macro and microvascular thrombi, suggesting hemostatic imbalances as contributory factors in its pathophysiology. A thrombosis induced by the innate immune system causes endothelial injury resulting in loss of thromboprotective mechanism, excess thrombin generation, and dysregulation of fibrinolysis and thrombolysis [5]. The critically ill patients with COVID-19 have acute respiratory distress syndrome and multiple organ failure in 20-30% of cases. Pregnancy itself is a hypercoagulable state, adding to further complexity.

We present the case of a primigravida with overlapping features of HELLP syndrome and a COVID-19 infection, posing as a diagnostic dilemma. In the presence of COVID-19 pneumonia, the features such as hypertension, albuminuria, hyperbilirubinemia, and thrombocytopenia helped us to clinch the diagnosis of a co-existing HELLP syndrome. The patient was resuscitated, delivered by a caesarean section, and showed remarkable recovery at discharge.

Case Presentation

A 25-year-old primigravida presented at 36 weeks of gestation with pitting, progressive bilateral pedal edema since one month. Dry cough, yellowish discoloration of eyes, palms, and soles since four days. She was diagnosed with a covid-19 infection on admission to the hospital. Her outpatient antenatal visits were infrequent, with no anomaly scan.

She had poor compliance to iron, calcium, and folic acid supplementation.

On admission to the hospital, she was afebrile, with a blood pressure of 150/100 millimeters of mercury, respiratory rate of 26 per minute, and oxygen saturation of 98% on room air. She was anemic, icteric, and had edema of the abdominal wall and feet. She was 36 weeks gestation with a live intrauterine pregnancy. Urine was clear on examination with albumin 2+. Her hematological investigations were as shown in Table 1. She was resuscitated with Packed Red Blood Cells, fresh frozen plasma, and platelet concentrate in the ratio of 1:1:1. Broad-spectrum injectable antibiotics were administered. Her chest radiograph showed an enlarged cardiac silhouette, pleural and pericardial effusions (Figure 1). An echocardiogram showed a normal ejection fraction (71%), and the presence of pericardial effusion was confirmed. The electrocardiogram was normal. An ultrasound of the abdomen showed mild ascites.

An emergency LSCS was performed because of increased blood pressure, a poor Bishop score, and features of HELLP syndrome. She gave birth to a term alive baby with a weight of 2.2 kilograms and an Apgar score of 8/10 and 10/10 at 1 and 5 min. Postoperative, she was managed in an intensive care unit. Low molecular weight heparin prophylaxis was initiated 12 hours later. Broad-spectrum antibiotics were continued. Her laboratory parameters improved post-operatively in the form of a declining trend in inflammatory markers and liver enzymes and improved coagulation profile and hemoglobin. She was discharged on the tenth postoperative day with a negative RT-PCR COVID-19 report. The baby was healthy at discharge. Written informed consent has been taken from the patient for publication purpose.

Table 1: Preoperative and post-operative investigations showing a declining trend in INR, APTT, Total bilirubin, AST, ALT, LDH, CRP, ESR, Urea, Uric acid at day 2 and day 10 following the caesarean section.

Investigations	Pre-operative	Post-operative	
		Day 2	Day 10
Haemoglobin(g/dl)	6.1	7.5	9.4
TLC/mm ³	15000	13000	9000
Platelet/mm ³	80,000	50,000	100000
INR	1.6	1.4	1
PT(sec)	14.3	45.9	15

APTT	38.1	39	37
Total Bilirubin (mg/dl)	11.25	8.2	2.2
AST (U/L)	179	82	26
ALT (U/L)	77	45	27
LDH (U/L)	1544	826	320
Total protein (g/dl)	5	4.9	5.5
D-dimer-(ml)	1	0.9	-
CRP (IU/lit)	36.96	23	11
ESR (mm/hr)	130	19	8
Urea (mg/dl)	24	44	14
Uric acid (mg/dl)	9.7	8	6.4
Na ⁺ (mmol/lit)	136	135	135
K ⁺ (mmol/lit)	3.9	4.0	4.0

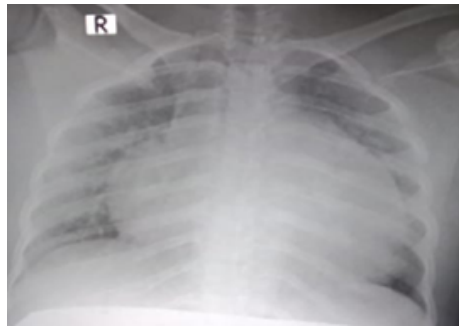


Figure 1: Chest radiograph AP view showing increased cardiothoracic ratio, straightening of left heart border, obliteration of right costophrenic angle and ground glass opacification of right lung field in middle and lower segments.

DISCUSSION

Here we have a case of a primigravida woman with simultaneous affections of HELLP syndrome and COVID-19 infection. Acute fatty liver of pregnancy (AFLP) is a disease entity based on liver histology originally derived from autopsy findings by Sheehan in 1940, while HELLP is a disease entity based on laboratory data. AFLP is associated with the enhancement of coagulation fibrinolysis, leading to consumptive coagulopathy [6]. Our patient did not fulfill the Swansea criteria for AFLP like nausea, vomiting, abdominal pain, polydipsia, polyuria, elevated bilirubin (>14mmol), leukocytosis (>11x 10⁹/L), ascites or bright liver on ultrasound, renal impairment (creatinine>150mmol) and, coagulopathy (prothrombin time >14sec) [6]. Hence, the first differential diagnosis considered was HELLP syndrome rather than AFLP. High blood pressure, jaundice, malaise, transaminitis, thrombocytopenia, albuminuria, raised levels of LDH, uric acid, serum creatinine were in favor of HELLP syndrome. Coagulopathy in COVID results from the concurrent activation of the coagulation and fibrinolytic cascade. Pregnancy is a physiologically hypercoagulable state, adding further complexity. Both HELLP syndrome and COVID-19 lead to microvascular angiopathy, endothelial damage, and multiorgan failure [5]. This patient had a severe form of HELLP syndrome. Raised inflammatory markers like ESR, CRP, D-dimer, and serum LDH suggested an ongoing inflammatory process due to COVID-19, further adding to the complexity of HELLP in COVID-19. Post-operatively, the inflammatory markers improved significantly, suggesting the improved outcome of mother and fetus after cesarean section [7].

Although the similarities between COVID-19 and HELLP are evident (Table-2), it is essential to focus on some of the clinical criteria that can help the obstetrician differentiate between these two conditions. Up to 20% of patients with HELLP syndrome are hypertensive compared to COVID-19 patients, who are usually normotensive. Fever, raised total and differential leukocyte counts, dyspnea, and hypoxia point towards COVID-19. Raised D-dimer levels are an essential screening tool for COVID-19 infection, although its sensitivity in pregnancy is known to be low [5]. High D-dimer levels are also associated with a prolonged ICU stay. The International Society on Thrombosis and Hemostasis has suggested that a 3-4 fold elevation of D-dimer above the normal upper limit indicates hospitalization even in the absence of concerning symptoms [8]. Elevated D-dimer levels, thrombocytopenia, and low fibrinogen levels suggest poor prognostic indicators of mortality risk [8]. This patient had elevated D-dimer levels and thrombocytopenia, indicating a poor prognosis. Postoperative recovery of the patient was with a good outcome.

The simultaneous presence of both these diseases can have a synergistic or opportunistic effect. There is emerging evidence that pregnant women with covid-19 infection can develop pre-eclampsia-like syndrome [9]. Pre-eclampsia is characterized by a raised uterine artery pulsatility index, sFlt-1/PLGF ratio, and LDH levels more than 600, whereas in the pre-eclampsia-like syndrome of covid-19 infection, the uterine artery pulsatility index is normal, and LDH levels are less than 600 [9].

Table 2- Similarities between COVID-19 and HELLP syndrome

	HELLP syndrome	COVID-19
Clinical manifestations	Nausea, vomiting, diarrhea, malaise, abdominal pain, mid-epigastric pain, headache, jaundice, visual changes, ± elevated blood pressure	Diarrhea, malaise, headache, cough, fevers, tachypnea, hypoxia
Laboratory findings	Hemolysis, transaminitis, elevated LDH, elevated BUN/creatinine, thrombocytopenia, ± proteinuria	Hemolysis, transaminitis, elevated LDH, elevated BUN/creatinine, thrombocytopenia, elevated D-dimer
Complications	DIC, liver infarction, renal failure, pulmonary edema	Cardiopulmonary arrest, ARDS, septic shock, renal failure,
Treatment	Delivery	Investigational. currently in our institution the regimen is: azithromycin, Remdesivir

Radiographs or CT chest showing the ground-glass appearance, patchy or diffuse reticular-nodular opacities, and consolidation in bilateral basal and peripheral lung fields are diagnostic of COVID-19 pneumonia [10]. Whereas, upper lobe pulmonary venous diversion (Stag's antler sign) and increased cardiothoracic ratio point towards HELLP syndrome.

Neuraxial block, particularly spinal anesthesia, is the anesthesia of choice to carry out a cesarean section in moderate, non-progressive thrombocytopenia [11]. If general anesthesia is required, it is necessary to control the response to stress produced by intubation. Raised D-dimer levels, thrombocytopenia, and low fibrinogen indicate a poor prognosis with increased mortality risk. This patient had raised D-dimer levels and Covid-19 inflammatory markers along with transaminitis and hyperbilirubinemia. Both covid-19 and HELLP had a synergistic effect worsening the condition. A multidisciplinary approach and simultaneously treating both the conditions without missing the diagnosis of HELLP syndrome helped improve the patient's condition. The differential diagnosis of HELLP should be considered in women with covid-19 to avoid iatrogenic preterm delivery, delay in treatment, and complications of both undiagnosed and untreated HELLP and COVID-19.

CONCLUSION

HELLP syndrome and COVID 19 both lead to microvascular angiopathy and endothelial damage. The simultaneous presence of both these conditions can have a synergistic or opportunistic effect. Hence, a clinical index of suspicion for the presence of these coexisting conditions, a thorough laboratory evaluation, a multidisciplinary approach for perioperative management, and vigilant monitoring of the course of the patient in the hospital is paramount to achieve an optimum obstetric outcome.

REFERENCES

- Stone, J. H. (1998). HELLP Syndrome: Hemolysis, Elevated Liver Enzymes, and Low Platelets. *JAMA*, 280(6), 559. <https://doi.org/10.1001/jama.280.6.559>
- Sibai, B. M. (2004). Diagnosis, Controversies, and Management of the Syndrome of Hemolysis, Elevated Liver Enzymes, and Low Platelet Count. *Obstetrics & Gynecology*, 103(5, Part 1), 981-991. <https://doi.org/10.1097/01.aog.0000126245.35811.2a>
- Stella, C., Malik, K., & Sibai, B. (2008). HELLP Syndrome: An Atypical Presentation. *Obstetric Anesthesia Digest*, 28(4), 245-246. <https://doi.org/10.1097/01.aoa.0000337946.79394.85>
- Lake, M. A. (2020). What we know so far: COVID-19 current clinical knowledge and research. *Clinical Medicine*, 20(2), 124-127. <https://doi.org/10.7861/clinmed.2019-coron>
- Colling, M. E., & Kanthi, Y. (2020). COVID-19-associated coagulopathy: An exploration of mechanisms. *Vascular Medicine*, 25(5), 471-478. <https://doi.org/10.1177/1358863x20932640>
- Minakami, H., Morikawa, M., Yamada, T., Yamada, T., Akaishi, R., & Nishida, R. (2014). Differentiation of acute fatty liver of pregnancy from syndrome of hemolysis, elevated liver enzymes and low platelet counts. *Journal of Obstetrics and Gynaecology Research*, 40(3), 641-649. <https://doi.org/10.1111/jog.12282>

7. Ronnje, L., Länsberg, J. K., Vikhareva, O., Hansson, S. R., Herbst, A., & Zaigham, M. (2020). Complicated COVID-19 in pregnancy: a case report with severe liver and coagulation dysfunction promptly improved by delivery. *BMC Pregnancy and Childbirth*, 20(1). <https://doi.org/10.1186/s12884-020-03172-8>
8. Vlachodimitropoulou Koumoutsea, E., Vivanti, A. J., Shehata, N., Benachi, A., le Gouez, A., Desconclois, C., Whittle, W., Snelgrove, J., & Malinowski, A. K. (2020b). COVID-19 and acute coagulopathy in pregnancy. *Journal of Thrombosis and Haemostasis*, 18(7), 1648–1652. <https://doi.org/10.1111/jth.14856>
9. Mendoza, M., Garcia-Ruiz, I., Carreras, E., & Suy, A. (2020). Authors' reply re: Pre-eclampsia-like syndrome induced by severe COVID-19: a prospective observational study. *BJOG: An International Journal of Obstetrics & Gynaecology*, 128(3), 618. <https://doi.org/10.1111/1471-0528.16583>
10. Carotti, M., Salaffi, F., Sarzi-Puttini, P., Agostini, A., Borgheresi, A., Minorati, D., Galli, M., Marotto, D., & Giovagnoni, A. (2020). Chest CT features of coronavirus disease 2019 (COVID-19) pneumonia: key points for radiologists. *La Radiologia Medica*, 125(7), 636–646. <https://doi.org/10.1007/s11547-020-01237-4>
11. del-Rio-Vellosillo, M., & Garcia-Medina, J. J. (2015). Anesthetic considerations in HELLP syndrome. *Acta Anaesthesiologica Scandinavica*, 60(2), 144–157. <https://doi.org/10.1111/aas.12639>