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Echocardiography with tissue Doppler imaging may help in bedside differential diagnosis of pulmonary oedema in pregnancy: case report

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Dear Editor,

The impact of diuretics on the foetus is controversial, and thus they are not preferred during pregnancy [1]. Excessive fluid retention during late pregnancy can lead to acute pulmonary oedema (APO), which increases the foeto-maternal morbidity and mortality [2, 3]. Reported incidence is about 0.08%, which can become 1.5% in pre-eclampsia [2–4]. Although most commonly reported during late pregnancy and early puerperium, the occurrence of APO during labour is very rare [2, 3].

Traditionally APO has been classified into cardiogenic and non-cardiogenic pulmonary oedema (CPO, NCPO) based on the cut-off value of pulmonary capillary wedge pressure (PCWP) of 18 mmHg [2, 3]. They differ both in pathophysiology and management. Their non-invasive differentiation was not possible until the introduction of echocardiography, which led to the estimation of left ventricular end-diastolic pressure and systolic function [2, 3]. Tissue Doppler imaging (TDI) was added later, which provides additional information to help in further differentiation of the diagnosis [5]. TDI is obtained using "on-line" pulsed-wave tissue Doppler to evaluate the peak longitudinal myocardial velocity. The ratio of E/e' measured by TDI was found to have some correlation with the left ventricular end-diastolic pressure (LVEDP) and PCWP [6]. An E/e' > 15 using septal e' or E/e' > 12 using lateral e' velocity is accepted as a surrogate marker of elevated LVEDP [7].

Adult respiratory distress syndrome (ARDS) was redefined in 2012 using Berlin criteria in an attempt to categorise the prognosis and thereby to direct the recommended therapeutic interventions [8]. Echocardiography was recommended to exclude any CPO if no recognized criteria of ARDS is identifiable. Notably, information on NCPO in special circumstances, such as pregnancy, was not included. However, use of the Berlin definition can be used to exclude any inflammatory NCPO. Thus, the combined use of Berlin criteria of ARDS and TDI echocardiography might improve the differentiation of pulmonary oedema [9].

Herein we describe a case of an otherwise uncomplicated pregnant female who developed a severe form of non-inflammatory NCPO (NI-NCPO) after having a caesarean section (CS), which was successfully diagnosed and managed using non-invasive means with this combined differential diagnostic approach. The patient gave written consent for publication of this case report in a medical journal.

A 22-year-old G1P0 woman was admitted with the complaint of having irregular labour contractions at 40 weeks of gestation. Her past medical history was unremarkable except she was mildly obese without having any hypertension or respiratory ailment. Her pregnancy was uneventful until 34 weeks, after which she started to gain weight rapidly (5 kg within the last 4 weeks) along with increasing dependent oedema. On examination, her baseline parameters were

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TABLE 1. Vital and laboratory parameters

Parameters	On admission	During clinical event
Body mass index	31	
Temperature (°C)	37.0	37.1
Blood pressure (mmHg)	125/76	115/72
Heart rate (beats min^{-1})	110	125
Respiratory rate (breaths min^{-1})	18	40
Oxygen saturation on room air (%)	96	95 (on facemask, FiO_2 0.4)
PaO_2 (kPa)		7.19
PaO_2/FiO_2		108
$PaCO_2$ (kPa)		3.59
White blood cells (reference range 4–11 G L^{-1})		10.45
CRP (reference: < 10 mg dL^{-1})		9.1
Procalcitonin (reference: < 0.15 ng mL^{-1})		0.1

PaO_2 – partial pressure of arterial oxygen tension, PaO_2/FiO_2 – ratio of PaO_2 and fraction of inspired oxygen concentration, $PaCO_2$ – partial pressure of arterial carbon dioxide tension, CRP – C-reactive protein

unremarkable barring bit tachycardia (Table 1). Her abdominal ultrasound showed moderate oligohydramnios. She was found to have hyponatraemia (123 mmol L^{-1}) without having any neurological manifestations. Her remaining laboratory parameters were unremarkable (Table 1). Because of the risk of having seizures associated with hyponatraemia and accompanying foeto-maternal complications, urgent delivery through CS was performed under spinal anaesthesia. A small for age foetus (2.35 kg) with a normal APGAR score and cord blood pH was delivered. Her intraoperative blood loss was 200 mL. Intraoperatively she received normal saline (1000 mL), etilefrine (10 mg), and oxytocin (5 IU as an intravenous bolus, followed by a continuous infusion of 0.07 IU kg^{-1} h^{-1}). Except for slight sinus tachycardia, all her intraoperative parameters remained stable throughout.

Postoperatively she received normal saline infusion (80 mL h^{-1}), tramadol (100 mg 3 times daily), and ondansetron (4 mg 3 times daily) as and when required. Her urine output reduced to 0.3 mL kg^{-1} h^{-1}, which responded to fluid bolus (250 mL of normal saline given over 30 minutes). She required oxygen by facemask because her peripheral oxygen saturation decreased to 95%. In the next hour, her respiratory condition deteriorated, and she became tachypnoeic with severe hypoxaemia (Table 1). Pulmonary rales were detected on chest auscultation. She was started on non-invasive ventilation (NIV) (CPAP: 10 cmH_2O and 60% oxygen). She was afebrile, and her infective markers were unremarkable. Her routine blood investigations and procalcitonin level were within normal limits. A contrast-enhanced computerized tomographic scan of the chest was performed, which ruled out any pulmonary embolism but revealed bilateral basal pulmonary oedema. An urgent bedside echocardiography was done to rule out any acute heart failure. Right and left ventricular size and function were seen to be within normal limits without having any valvular pathology. Right ventricular systolic pressure was found to be slightly elevated (40 mmHg) along with trivial tricuspid regurgitation, and inferior vena cava was seen not to be distended (2 cm diameter with 30% collapsibility). TDI revealed normal left ventricular diastolic function and pressure. She was neither fitting into the criteria of ARDS as per the Berlin definition, nor sepsis based on the Surviving Sepsis guidelines [8, 10]. By using this combined approach, we excluded the diagnosis of CPO and NCPO, and assumed the diagnosis of postpartum NI-NCPO [2]. A furosemide infusion (0.125 mg kg^{-1} h^{-1}) and NIV (bilevel positive airway pressure) were started. Her urine output, respiratory symptoms, and arterial blood gas parameters normalised over the next 6 hours. She had massive diuresis (6 L) over the next 24 hours. Thus, we successfully avoided impending tracheal intubation and invasive mechanical ventilation (IMV). Subsequently, her serum sodium normalised, and her remaining postpartum course remained uneventful. She was finally discharged from the hospital on the fourth day.

Although APO is mostly diagnosed clinically, the aetiology remains unclear. Utilising a bedside echocardiography combined with TDI permits instant estimation of cardiac function, which can help differentiation between CPO and NCPO, and thereby can guide the appropriate management, which can differ significantly [5, 6]. Without a proper diagnosis, specific treatment is frequently delayed, which potentially affects the foeto-maternal outcome [1, 2]. Incorrect treatment based on a misdiagnosis can sometimes be harmful. Thirty-four per cent of females were reported to develop APO in puerperium after having CS without having any heart disease [2]. In addition to excessive fluid retention during the third trimester, which triggers the APO, puerperium increases this vulnerability further due to the additional autotransfusion that occurs during delivery. Although no association has been found between the types of anaesthesia and APO, excessive fluid administration culminating in perioperative fluid balance > 2 L has been reported as a triggering factor [2, 3]. However, these studies could not predict that ensuing oliguria and associated fluid overload can lead to APO.

The pathophysiology of hypoosmolar and hyponatraemic NI-NCPO in pregnancy is poorly understood. Some researchers have found an association with intrauterine growth retardation (IUGR) [11]. Reduced foeto-placental perfusion has been proposed as a potential cause [2, 3]. Combined with reduced activity of placental vasopressinase, foetal vasopressin secretion may also increase to reduce the foeto-placental perfusion [12]. This

may upregulate the foetal aquaporin 2 receptors leading to oligohydramnios. Reduced placental vasopressinase activity leads to an increase in maternal vasopressin level, which upregulates the maternal aquaporin type-2 receptors resulting in maternal fluid retention. All these lead to hyponatraemic hypoosmolality culminating in NI-NCPO, mimicking inappropriate antidiuretic hormone secretion (SIADH) [13]. APO in NI-NCPO results from alveolar fluid leak due to reduced oncotic pressure resulting from hyponatraemia, despite having normal PCWP and no concurrent lung inflammation. Many of these pregnancies were complicated by pre-eclampsia [12].

Rather than the commonly known risk factors of ARDS, pregnancy-related factors might be the cause of pulmonary oedema (i.e. pre-eclampsia, tocolytic therapy, fluid retention, and hyponatraemia induced by increased vasopressin level) [2, 3]. Abnormal serum sodium level and osmolality usually normalise after delivery. Low levels of placental growth factor (PGLF) are found to be associated with oligohydramnios and IUGR in otherwise normotensive parturient, indicating that PGLF might be valuable in the diagnosis of foeto-placental unit hypoperfusion disorders [14]. However, the use of PLGF is still under investigation.

The occurrence of NI-NCPO in non-pre-eclamptic pregnant patients is rarely reported and recognised. Differentiation from CPO and ARDS is necessary because more aggressive management (i.e. tracheal intubation, IMV, organ support) is indicated in those cases, whereas NI-NCPO can be managed noninvasively. Given the rapid deterioration, any misdiagnosis at that point could have forced us to use such therapeutic options. In otherwise asymptomatic patients, fluid restriction and subsequent judicious use of diuretics should be adopted initially. But in non-responders with worsening hyponatraemia, urgent CS followed by respiratory support using NIV may be necessary, as in our case [2, 3]. If possible, oxytocin should be avoided, or at least the dose should be reduced. A pivotal risk reduction strategy including early antenatal recognition of high-risk women and targeted management aiming for judicious fluid balance using a multidisciplinary approach is the key to a successful outcome.

Our patient was normotensive and did not have any proteinuria. Thus, she did not fit into the criteria of hypertensive disorders of pregnancy [15]. However, she did have moderate oligohydramnios complicated with hyponatraemia. Parturient complicated with hypoosmolality caused by hyponatraemia may develop APO despite having normal PCWP [2, 3]. The fluid retention component of oxytocin might have contributed to the APO. Although our patient had oliguria, she did not have huge perioperative fluid administration nor a massive obvious fluid overload. Our patient did have IUGR, but she did not have any features of pre-eclampsia. In our case, no recognised causes of ARDS were found. Her hyponatraemia did normalise after delivery. We did not estimate PGLF. Echocardiography combined with TDI proved to be the key to the diagnosis and management. Using TDI-echocardiography, we rapidly excluded the diagnosis of CPO, while the absence of any major Berlin criteria led us to exclude ARDS as well.

Timely use of bedside echocardiography with TDI combined with Berlin definition of ARDS can help us to correctly differentiate a postpartum hypo-osmolar hyponatraemic non-inflammatory non-cardiogenic pulmonary oedema from other commonly occurring possibilities, and thereby can prevent unnecessary use of invasive, potentially harmful therapeutic options.

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