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RESEARCH ARTICLE

Pulmonary oedema in the course of severe maternal outcome in South Africa: A cohort study combined with clinical audit

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Abstract

Objectives: To describe the incidence and outcomes of pulmonary oedema in women with severe maternal outcome during childbirth and identify possible modifiable factors through audit.

Methods: All women with severe maternal outcome (maternal deaths or near misses) who were referred to Tygerberg referral hospital from health facilities in Metro East district, South Africa, during 2014–2015 were included. Women with severe maternal outcome and pulmonary oedema during pregnancy or childbirth were evaluated using three types of critical incident audit: criterion-based case review by one consultant gynaecologist, monodisciplinary critical incident audit by a team of gynaecologists, multidisciplinary audit with expert review from anaesthesiologists and cardiologists.

Results: Of 32,161 pregnant women who gave birth in the study period, 399 (1.2%) women had severe maternal outcome and 72/399 (18.1%) had pulmonary oedema with a case fatality rate of 5.6% (4/72). Critical incident audit demonstrated that pre-eclampsia/HELLP-syndrome and chronic hypertension were the main conditions underlying pulmonary oedema (44/72, 61.1%). Administration of volumes of intravenous fluids in already sick women, undiagnosed underlying cardiac illness, administration of magnesium sulphate as part of pre-eclampsia management and oxytocin for augmentation of labour were identified as possible contributors to the pathophysiology of pulmonary oedema. Women-related factors (improved antenatal care attendance) and health care-related factors (earlier diagnosis and management) would potentially have improved maternal outcome.

Conclusions: Although pulmonary oedema in pregnancy is rare, among women with severe maternal outcome a considerable proportion had pulmonary oedema (18.1%). Audit identified options for prevention of pulmonary oedema and improved outcome. These included early detection and management of preeclampsia with close monitoring of fluid intake and cardiac evaluation in case of suspected pulmonary oedema. Therefore, a multidisciplinary clinical approach is recommended.

KEYWORDS
audit, high-risk pregnancy, obstetrics, pulmonary oedema, severe maternal outcome, South Africa

INTRODUCTION

Acute pulmonary oedema is an uncommon but life-threatening complication of pregnancy [1, 2]. It is most

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probably compounded by the physiological changes of pregnancy, such as increased hydrostatic pressure leading to elevated left ventricular end-diastolic pressure, decreased colloid osmotic pressure and/or increased capillary permeability [1, 3].

The scientific background to study pulmonary oedema in pregnant women is that in South Africa, the National Committee on Confidential Enquiries into Maternal Deaths (NCCEMD) reported in 2015 that the majority of all maternal deaths were related to pre-eclampsia with its associated complications of cerebral haemorrhage and pulmonary oedema [4]. Pulmonary oedema incidence in general populations of women during pregnancy or puerperium has been described for France as 0.05% during 2002–2010 [5], as 0.08% in the USA 1989–1999 [6] and as 1.5% in Brazil 2002–2005 [7]. Sibai et al. described 2.9% pulmonary oedema in a population of severe preeclampsia gathered during a nine-year period [8]. These reports are all retrospective evaluations. There are a few case series providing characteristics of the women with pulmonary oedema and their outcome. The study population sizes for this rare complication in various studies were: 53 from South Africa [9], 51 from USA [9], 50 from Brazil [10] and 15 from France. These studies were all retrospectively performed in tertiary hospitals with one exception: Pordeus sampled during one of the 4 years prospectively [10]. As the main underlying causes for the pulmonary oedema hypertensive disorders, cardiac disease and fluid overload have been reported. Women with pulmonary oedema have a higher risk of severe maternal outcome (SMO), maternal near misses (MNM) and maternal death.

Pulmonary oedema could therefore be seen as an indicator of MNM, although currently it would only fulfil the World Health Organization (WHO)-MNM criteria when associated with respiratory insufficiency. WHO defines MNM as 'a woman who nearly died but survived a complication that occurred during pregnancy, childbirth or within 42 days of termination of pregnancy' [11]. A common definition of pulmonary oedema, as proposed by Dennis et al. is 'sudden onset of breathlessness and accompanying symptoms including orthopnoea, agitation and cough, with clinical signs including tachycardia, tachypnoea, crackles and wheezes upon chest auscultation, cardiac gallop rhythm and murmurs and decreased oxygen saturation' [1].

Robust and systematic audit of women who developed pulmonary oedema is highly recommended to learn lessons for maternity care, detect pulmonary oedema in an early stage and avoid future cases [12, 13]. Audit is commonly used to identify 'improvable care factors' at different levels in the health system [14]. WHO recommends audit of SMO, and there are various audit methodologies that could be applied [15]. An audit cycle has a higher chance of being effective if evaluation is implemented in the local setting, healthcare workers are involved in the audit process and when feedback is provided repeatedly within a safe learning environment. In addition, care adaptations should be audited in a repeated audit cycle [15, 16]. In our study set-up we apply three audit methods to optimise knowledge about the clinical management of pulmonary oedema in women with SMO: firstly a criterion-based audit on all women with pulmonary oedema within the group of women with SMO, secondly a critical incident in all women with SMO, and thirdly a criterion-based multidisciplinary audit in some women with pulmonary oedema. A combination of the three methods was applied since this combination was presumed to contribute to a deeper understanding of possible causes and contributing factors.

The present literature does not include studies that are large and robust enough to evaluate multifactorial causes of pulmonary oedema as a component of SMO. Therefore, the primary objective of this study was to describe prospectively the incidence and outcomes of pulmonary oedema in women with SMO in a specific region in South Africa and compare these with findings from Brazil, the US and with previous findings from the national level in South Africa. The secondary objective was to learn lessons for maternity care with regard to underlying causes and management of pulmonary oedema and to identify possible modifiable factors through audit.

METHODS

This cohort study used data from a prospectively obtained database on all women with SMO and pulmonary edema and without in the region. Study size was determined by the yield from Metro East region Western Cape province, South Africa during 2014 and 2015 [17]. The hospitals referring to the tertiary center were examined for potential missing women. [17] Women who were diagnosed by clinicians with pulmonary oedema in the selected group of women with SMO were eligible to participate.

In-depth information was collected as part of routine clinical practice for SMO, informed consent was therefore not obtained. For this study, we specifically analysed the women with SMO-associated pulmonary oedema with respiratory organ failure as defined by WHO-MNM criteria and compared these with women with SMO without pulmonary oedema. Depending on the severity of disease these women were admitted to the obstetric ward, obstetric critical care unit or the intensive care unit of the hospital.

Participants were women with SMO and pulmonary oedema, as defined by the clinician who saw the woman and recorded pulmonary oedema in the case file. Additional diagnostic methods applied in the South African setting were chest X-ray and transthoracic echocardiography for underlying cardiac causes.

Adherence to guidelines was audited. Management of pulmonary oedema in local, regional and international guidelines includes stabilising acute hypertension if present with appropriate medication, increase diuresis with furosemide, give morphine and/or oxygen to relieve symptoms and consider *continuous positive airway pressure* (CPAP) or mechanical ventilation in case of poor response [18–21].

Medical records were reviewed and audit was done in all women with SMO who had pulmonary oedema. To learn

lessons for clinical care, three types of audit were applied to collect in-depth information pertaining to clinical management from different perspectives.

(1) A criterion-based audit of the women with pulmonary oedema was performed by a consultant of the obstetric critical care unit (OCCU) [14, 22]. Medical records of women with SMO and pulmonary oedema were closely examined, with a focus on possible factors related to pulmonary oedema as described in the literature: pre-existing conditions (previous cardiovascular disease, obesity, hypertension), pregnancy-related conditions including pre-eclampsia, peripartum cardiomyopathy, fluid overload (fluid replacement therapy or blood transfusion), use of pharmacologic agents (corticosteroids, MgSO4, tocolytics, beta adrenergic drugs, oxytocin, misoprostol), endocrine disorders (pheochromocytoma, hyperthyroidism, chronic cardiac or pulmonary disease, sepsis), puerperal sepsis, preterm labour, pulmonary embolism and multiple pregnancy [1, 23–26].

(2) A critical incident audit of all women with MNM including an assessment of possible 'improvable' factors in a monodisciplinary fashion, by two senior gynaecologists (experienced maternal death audit committee members), the principal researcher (AH) and a registrar (resident), monthly throughout the year in which data were collected. The principal researcher presented a summary of the histories of the women who met the WHO-MNM criteria who were managed in the previous month. The team reviewed the medical records with the laboratory and ultrasound findings and completed an audit form similar to the form used by the NCCEMD (Appendix A). The audit aimed to identify substandard factors at the women's, healthcare workers' and administrative levels. A summary of this audit meeting was presented during the monthly departmental meeting. During this meeting, participating consultants, registrars, medical officers, midwives, the principal nurse and students in the Obstetrics and Gynaecology Department were encouraged to identify additional lessons learned. Lastly, specific feedback was given to individual health care workers, including those from referring facilities.

(3) A criterion-based multidisciplinary session with an experienced gynaecologist of the OCCU, an experienced consultant anaesthetist with a special interest in cardiology and obstetrics, a consultant cardiologist and the principal investigator. A purposeful selection of seven women with MNM and pulmonary oedema was presented by the principal investigator, after reviewing the medical records of clinical situations and diagnoses in detail. For every woman, the echocardiographic findings were described and interpreted in relation to pulmonary oedema by the cardiologist. In clinical practice, performance of maternal echocardiography was limited to women with SMO suspected of underlying cardiac disease or pulmonary oedema. Suspicion arose when no clinical signs of improvement within a few days were observed after initial management with furosemide, antihypertensive drugs and CPAP.

Ethics approval

Ethical approval was obtained from the Health Research Ethics Committee (HREC), Faculty of Health Sciences, Stellenbosch University, on 03/10/2018 (Project ID: 1427, HREC Reference #: S18/02/023). Approval was also obtained from the Provincial Health Authority, the CEO of TBH and the heads of respective departments. A waiver of consent from participants was obtained from HREC, as the study was performed by auditing hospital records.

RESULTS

Incidence and outcomes

Among 32,161 pregnancies, 399 women with SMO were previously identified [17]. Of these 399 women, 72 (18.1%) were diagnosed with pulmonary oedema [18]. This implies that 72 out of 32,161 women (0.2%) had SMO-associated pulmonary oedema with respiratory organ failure as defined by the WHO-MNM criteria. Four women diagnosed with pulmonary oedema died, giving a case fatality rate of 5.6% (4/72) in this SMO group. In the other 327 women with SMO without pulmonary oedema, 16 women died (case fatality rate 4.9% [16/327]).

Women's baseline characteristics for the group with SMO with and without pulmonary oedema are shown in Table 1. Incidence of underlying hypertension or pre-eclampsia in the pulmonary oedema group was 44/72 (61.1%) versus 105/327 (32.1%) in the group without pulmonary oedema.

TABLE 1 Characteristics of the group of women with SMO with pulmonary oedema ($N = 72$) and for the other women with SMO without pulmonary oedema ($N = 327$).

	SMO with pulmonary oedema $n = 72$ Mean ± SD or N (%)	**SMO without pulmonary oedema $n = 327$ Mean ± SD or N (%)**
Age	26.42 ± 1.5	27 ± 6.6
Body mass index	29.42 ± 3.2	28.6 ± 7.7
Smoking	16/59 (27.1)	41/327 (12.5)
Primiparous	27/72 (37.5)	116/327 (35.5)
HIV-positive	18/72 (25)	70/327 (21.4)
CD4 < 200	4/18 (22.2)	12/51 (23.5)
Antiretroviral therapy	16/18 (88.9)	33/51 (64.7)
Caesarean section	40/72 (55.6)	178/327 (54.4)
Drug use (metamphetamine, cocaine)	4/72 (5.6)	7/327 (2.1)
Preterm labour (<gestational age 37)	48/72 (66.7)	188/289 (65.1)
Multiple gestation	4/72 (5.6)	13/292 (4.5)
Underlying Hypertension	44/72 (61.1)	105/327 (32.1)

TABLE 2 Criterion-based audit for women with SMO and pulmonary oedema $N = 72$ (Audit 1).

Observations and investigation that contributed to the diagnosis	
	***N* (%)**
Severe hypertension >160/110	50 (69.4)
Respiratory rate > 40	12 (16.7)
X-ray performed?	66 (91.6)
X-ray abnormal?	60 (83.3)
Blood gas abnormal (PaO2 < 10.2 with O2 40%/5.6 without O2)?	22 (28.9)
Cardiac ultrasound done	30 (41.7)
V/Q scan done	8 (11.1)
Was blood pressure > 160/110 when pulmonary oedema was diagnosed?	50 (69.4)
Respiratory support	
CPAP given?	62 (86.1)
PEEP more than 5 given?	50 (69.4)
Intubation?	30 (41.7)
Pharmacological agents that can effect PE	
Corticosteroids	21 (29.2)
Magnesium sulphate	54 (75)
Beta adrenergic tocolytic (salbutamol)	5 (6.9)
Oxytocin for induction/augmentation	32 (44.4)
Misoprostol for induction/augmentation	16 (22.2)
Fluid	
IV fluid >80 mL/h (80 mL/h is the recommended fluid restriction)	18 (25)
Blood transfusion	29 (40.2)
Diagnosis underlying pulmonary oedema	
Chronic hypertension	8 (11.1)
Pre-eclampsia/HELLP (Severe Early Onset Pre-eclampsia)	30 (40.3)
Eclampsia	6 (8.3)
Cardiac/dilated cardiomyopathy (peripartum)	5 (6.9)
Sepsis	3 (4.2)
Postpartum haemorrhage	3 (4.2)
Placental abruption	2 (2.8)
Lower respiratory tract infection	1 (1.4)
Additional diagnoses and involved organ systems	
Brain tumour	1 (1.4)
Pulmonary embolism	0
PRES Posterior Reversible, Encephalopathy Syndrome	0
Underlying pulmonary tuberculosis	2 (2.8)
Acute renal failure	15 (20.8)
Low albumin	18 (25.0)
ECG: left ventricle hypertrophy	14 (19.4)
Creatinine µmol/L (normal in pregnancy <77)	67.5
Albumin mg/L	25.11

Audit

The first audit assessing possible underlying factors showed chronic hypertension and early-onset pre-eclampsia before 34 weeks as an underlying factor in 44 of 72 (61.1%) women with pulmonary oedema (Table 2). A total of 62 women (86%) received CPAP as recommended management according to the local guideline of severe pulmonary oedema. Fluid restriction <80 mL/h, as recommended in the local protocol, was not applied in 18/72 (25.0%). Table 3 provides an overview of the different types of antihypertensives needed to manage hypertension in the women with SMO. As can be seen, most women started treatment with nifedipine (50%) but once diagnosed with pulmonary oedema, furosemide (77%) and enalapril (70%) were given most frequently. Multidrug treatment with different types of antihypertensives was needed to manage hypertension in the women with SMO and pulmonary oedema.

Maternal echocardiography was performed in 30 of the 72 (41.7%) women with SMO and pulmonary oedema. Cardiac involvement, mostly left-sided cardiac dysfunction, cardiomyopathy and pulmonary hypertension, as a possible cause of pulmonary oedema were confirmed with echocardiography in 19/30 (63.3%) (Table 4) and renal failure in 15/72 (20.8%) (Table 2).

The second audit, where improvable factors for all 399 women were assessed, showed women-related factors (attending antenatal care late or not at all) and healthcare workers-related factors (not recognising the diagnosis, incorrect management) as substandard care. These factors were assessed as probably having made a difference in outcome in 90 women (22.6%) (Table 5).

In the third audit, the multidisciplinary team of medical specialists agreed that there were lessons to be learned from six of the seven selected histories of women with SMO with pulmonary oedema. In three women too much fluid administration could be related to pulmonary oedema. In all seven consensus was reached with regard to the diagnosis as an explanation of respiratory insufficiency (Table 6).

DISCUSSION

Pulmonary oedema is a rare complication during pregnancy and after childbirth with a relatively high mortality risk. Of note is that in women with SMO in this setting of Cape Town in the Metro East region, South Africa, pulmonary oedema was particularly common and it occurred in almost one in five women with SMO. In this study the severe pulmonary edema in a whole region is reported 0.2%, higher than reported in other studies with pulmonary oedema in a tertiary hospital in France (0.05%) and the US (0.08%) [5, 6], and lower than in an obstetric ICU in Brasil (1.5%) [7]. No other series of pulmonary oedema in women with MNM are available. The three main underlying factors identified that might contribute to the development of pulmonary edema, are in line with the literature.

Hypertensive disorders of pregnancy were found in two of three women from our study. This risk factor is confirmed in the retrospective case series reporting 18%, 62% and 83% hypertensive disease as underlying cause of the pulmonary oedema in respectively Western Cape Region in

TABLE 3 Medication to treat hypertension before and after diagnosis of the 72 women with SMO and pulmonary oedema.

Antihypertensives before pulmonary oedema *N*(%)		Antihypertensives to treat pulmonary oedema N(%)	
Nifedipine	42 (55.3)	Furosemide	59 (77.6)
Adalat XL	19 (25)	Enalapril	55 (73.4)
Methyldopa	16 (21.1)	Amlodipine	43 (56.6)
Labetolol /Trandate	12 (15.8)	Labetolol /Trandate	38 (50)
Enalapril	6 (7.9)	Tridil/nitroglycerin	25 (32.9)
Amlodipine	5 (6.6)	Hydrochlorthiazide	18 (23.7)
Dihydralazine	3 (3.9)	Nifedipine	18 (23.7)
Doxazosin	1 (1.3)	Doxazosin	16 (21.1)
Hydrochlorthiazide	1 (1.3)	Dihydralazine	14 (18.4)
Tridal	0	Carvedilol	11 (14.5)
		Adalat XL	8 (10.5)
		Methyldopa	4 (5.3
		Non hypertensive treatment for pulmonary oedema	
		Morphine	31 (40.8)
		Inotropes (adrenalin/dobutrex)	5 (9.2)

TABLE 4 Findings of Cardiac ultrasound examination ($n = 30$) reviewed by cardiologist in women with SMO and severe pulmonary oedema, as a possible cause for pulmonary oedema.

Echo conclusion	*N*
Severe left ventricular systolic dysfunction (LVEF<50%)	16
Severe diastolic dysfunction	10
Pulmonary Hypertension	7
Peripartum cardiomyompathy	6
Mitral stenosis	1
Pulmonary oedema with cardiac involvement in this group, diagnosed by cardiologist	19/30

US, Brasil and South Africa, and US. [6, 9, 10]. This indicates that strict management of hypertension and vigilance to induce labour in time are essential to prevent severe complications. NiIfidpine and methyldopa were the first-choice medications used to treat hypertension in pregnancy, in line with the South African protocol [27, 28]. For the treatment of hypertension in pulmonary edema polypharmacy was needed in most of the cases; furosemide, amlodipine and enalapril were most prescribed.

Fluid overload is the second factor of importance. This was confirmed by the case series in the US and France reporting 21.5% and 13.3% fluid overload as underlying cause [5, 6]. Administration of too much intravenous (IV) fluid and transfusion of blood products have been described as causal factors in many studies [29, 30]. In our study these factors could also have contributed to the development of pulmonary oedema, and therefore the volume of both intravenous fluid infused (recommended <80 mL/h) and the number of units of blood products transfused merit closer assessment.

Cardiac cause is the third underlying mechanism to develop pulmonary oedema and is confirmed in the various case series in South Africa (11%), Brazil (16%), USA (25.5%) and France (26.7%) [5, 6, 9, 10]. Left ventricular systolic- and diastolic dysfunction are main findings in pulmonary edema on cardiac ultrasound. [26, 31, 32]. A cardiac anomaly may appear for the first time during pregnancy, elicited by the increasing physiological demands and signs of early decompensation (tachycardia and tachypnoea). Findings on cardiac ultrasound may be helpful but are not always decisive. Still Dolley et al. emphasised that echocardiography led to a change in management in 27.3% of cases [5]. Sonographic evaluation of pulmonary interstitial oedema [33] or Magnetic Resonance Imaging to identify rare complications such as myocardial oedema have been reported to be of additional value but these investigations were not performed in our study [34, 35].

Other factors such as capillary leak or renal failure may also be involved in the development of pulmonary oedema [36]. Frequently used medications possibly associated with the development of pulmonary oedema were MgSO4 and oxytocin [1]. Yet, these medications are also potentially life-saving as part of the management of pre-eclampsia and often used to induce labour and prevent post-partum haemorrhage. Close monitoring in already sick women is needed when these drugs are administered.

The three audits provided insights to adapt the protocols. The first criterion-based audit revealed that management to treat pulmonary oedema was in general performed according to the first steps of the local and international guidelines (furosemide, morphine, oxygen, CPAP) [1, 18–21]. The benefits of CPAP were recognised and since CPAP treatment is non-invasive, if available in low-middle income countries can be recommended as a life-saving treatment in pregnant women with pulmonary oedema [27, 28]. Moreover the large number of women needing blood transfusion (29/72, i.e. 40.2%) necessitated awareness that fluid overload can contribute to

TABLE 5 Critical incident audit of improvable care factors for pulmonary oedema and for SMO (Audit 2)[a].

Avoidable factors	SMO with pulmonary oedema, *n* = 72	SMO without pulmonary oedema, n = 327
Women-related (more factors per event possible)	*N* (%)	N (%)
No avoidable factor	35(48.6)	203 (62.1)
No antenatal care (ANC)	12 (16.7)	17 (5.2)
ANC initiated late in the pregnancy	9 (12.5)	35 (10.7)
Defaulted ANC	11(15.3)	32 (9.8)
Delay accessing medical care	4 (5.6)	2 (0.6)
Declined medication	2 (2.8)	17 (5.2)
Unsafe abortion	0	1 (0.3)
Missing	0	30 (9.2)
Administration-related (more factors per event possible)		
No avoidable factor	63 (87.5)	290 (88.7)
Transport problem home to health facility	1 (1.4)	2 (0.6)
Transport facility to facility (referral)	3 (4.2)	4 (1.2)
Delay initiating care	0	4 (1.2)
Delay initiating critical care	0	0
No ICU	1 (1.4)	2 (0.6)
Lack of blood products	0	0
Lack of appropriately trained staff: doctors	0	2 (0.6)
Lack of appropriate trained staff: nurses	0	0
Missing	3 (4.2)	32 (9.8)
Healthcare-worker related (more factors per event possible)		
No avoidable factor	51 (70.8)	240 (73.4)
Problem recognising diagnosis	5 (6.9)	20 (6.2)
Delay of referral	4 (5.6)	8 (2.5)
Managed at inappropriate level (antenatal)	2 (2.8)	10 (3.1)
Managed at inappropriate level (at time of event)	0	10 (2.5)
Incorrect management (incorrect diagnosis)	2 (2.8)	7 (2.1)
Incorrect management (correct diagnosis)	4 (5.6)	16 (4.9)
No/infrequent monitoring	1 (1.4)	6
Prolonged abnormal monitoring with no action taken	0	3 (0.9)
Missing	3 (4.2)	30 (9.2)
Impact on outcome		
No suboptimal care	32 (44.4)	179 (54.7)
Suboptimal care, different management would not have made a difference to outcome	17(23.6)	51 (15.6)
Suboptimal care, different management might have made a difference to outcome	18 (25)	59 (18)
Suboptimal care, different management would reasonably have made a difference to outcome	2 (2.8)	11 (3.4)
Missing	2 (2.8)	24 (7.4)

[a]more than one substandard care factors could be identified per woman.

pulmonary oedema. This contrasts with almost all studies from sub-Saharan African countries, where lack of packed red cells plays a major role in maternal mortality. In our study lack of blood for transfusion did not occur.

The second audit provided information about possible modifiable factors in SMO, especially as the women did not attend antenatal care and sometimes presented with severe pulmonary oedema at an unknown gestational age. Healthcare worker-related factors were failure to make the correct diagnosis or mismanagement. Additional studies employing qualitative methodologies could provide closer insight into these factors. The relatively low mortality index (ratio of deaths over maternal near misses) might indicate relatively high quality of care in the hospital. A focus on prevention might therefore be more beneficial than focusing on improving the quality of tertiary level clinical care. Additional studies employing qualitative methodologies could provide closer insight.

TABLE 6 Criterion-based audit of seven selected pregnant women with SMO and pulmonary oedema (Audit 3).

	Case description	Diagnosis right pulmonary oedema and…	Possible contributing factors	Cardiac involved echo results	Lessons learnt
D49	G5P4, 40 + 3 History: previous CS. Unbooked twin, obesity, pre-eclampsia shortness of breath, antenatally diagnosed pulmonary oedema Latent labour, metabolic acidosis. Caesarean under general anaesthesia, intubated to ICU. Creatinine 152 μmol/l Both babies alive	Late onset pre-eclampsia with cardiac and kidney failure	Twins Obesity	LV mildly dilated, EVF 45%, Cardiomyopathy/myocarditis	No antenatal care, early treatment could have prevented MNM Multidisciplinary approach might have had better outcome
J8	40 G2P1 HIV+ Severe early onset pre-eclampsia/HELLP, pulmonary oedema antenatal CS fetal distress intubated high spinal Baby alive	Severe early onset pre-eclampsia with cardiac diastolic dysfunction as contributing factor	HIV, volume overload preoperative with woman lying flat	borderline left ventricle hypertrophy, means LV relaxation, results in increased pressure in LA + pulmonary oedema. Diastolic dysfunction	Fluid monitoring and restriction
J30	24 G1 34wk HIV+, antiretroviral drugs+ cd4 261 Induction of labour Pre-existent hypertension /Acute severe hypertension Spontaneous birth Hypovolemic shock, Postpartum haemorrhage, retained products, evacuation Blood transfusion: 2 RBC, 2FFP pulmonary oedema, CPAP + furosemide Urinary tract infection Baby alive	Pre-eclampsia (early onset)	Tachycardia, Infection Fluid overload		Tachycardia before event as warning sign. Fluid restriction
K25	19 G1 39wk 177/110, protein 3+ (pre-eclampsia), MgSo4+, referral TBH Antenatal sudden shortness of breath, Acute respiratory failure, pulmonary oedema, intubation CS maternal condition, Baby alive	Pre-eclampsia (late onset)	–	no LV hypertrophy. decreased systolic function, high cardiac output and high BP, no diastolic dysfunction	uncontrolled blood pressure
H21	34 G1 24wk Chronic hypertension Pre-eclampsia/HELLP plt47, mgso4+, abruption with intra uterine fetal death during induction of labour, blood transfusion Pulmonary oedema direct postpartum on CPAP Baby Stillborn	Acute severe hypertension and severe early onset pre- eclampsia/HELLP and placental abruption	-Oxytocin (retains water) - Blood transfusion and fluid?	No echocardiography done, high chance of cardiac involvement	Monitoring fluid balance Cardiac ultrasound might have added information

(Continues)

TABLE 6 (Continued)

	Case description	Diagnosis right pulmonary oedema and…	Possible contributing factors	Cardiac involved echo results	Lessons learnt
C33	27 G2P1 35 + 2 Fetal anomaly (di George?) early onset preeclampsia Fetal tachycardia, CS: Good fetal condition Postpartum pulmonary oedema, needs ventilation/intubation and inotropic support (LV dysfunction), ICU DD/hospital acquired pneumonia? Baby alive	Chron hypertension (late onset) Infection? Discussion about diagnosis pneumonia. During CS inotropic support with adrenalin	Fetal anomaly Chronic hypertension	LV hypertrophy, thickened septum, shows diastolic dysfunction Cardiac function abnormal, due to chronic hypertension, reason for pulmonary oedema in pregnancy.	Possibly missed diagnosis of pneumonia instead of pulmonary oedema
E23	30 G3P2 39, obese BMI 57 Presents pulmonary oedema, earlier lower respiratory tract infection or diagnosed with 'asthma' (was this misdiagnosis cardiac failure in obesity?), and acute severe hypertension, now fever/cough CS, late onset pre-eclampsia, pulmonary oedema responding to furosemide/CPAP Echo normal, infection no signs Baby alive	Unsure diagnosis pulmonary oedema, DD/pulmonary embolism	BMI Late onset	Echocardiography done day 3, only mild LV hypertrophy	Possibly Missed diagnosis of pulmonary embolism instead of pulmonary oedema

Abbreviations: BMI: Body Mass Index; CS: Caesarean section; EVF, ejection fraction; LV: left ventricular.

The third audit enabled the most detailed informative discussion of the diagnosis. Lessons include the need for increased attention for good-quality antenatal care, early recognition and treatment, fluid restriction and the need for a multidisciplinary approach. Early detection should include simply checking for tachycardia as well as more sophisticated methods such as cardiac ultrasound examination. Moreover, it is important to keep in mind a broad differential diagnosis that may include pneumonia as well as pulmonary embolism.

The strength of this prospective study is it being the largest cohort assessing pulmonary oedema in women with SMO. The cohort is representative of the Metro East region although most women were referred to TBH, some cases may inevitably have been missed as shown in our additional analysis in the referral hospitals over three months. [17]

Accurate data collection from medical records from one region in South Africa enabled performing various types of critical incident audit and thus eliciting more insight into the pathways to SMO. Consequently, it revealed that women attended antenatal care late, when already in advanced pregnancy. Focus on timely and frequent antenatal care attendance enabling earlier intervention may improve outcome and prevent SMO. A limitation is that we could not report about all women with pulmonary oedema in pregnancy, only about the most severely ill ones because of WHO MNM criteria, but in terms of mortality and morbidity that was valuable.

Moreover, involvement of midwives and nurses in the performance of audits was restricted, but they were present in weekly morbidity and mortality meetings, where audit findings were discussed. Audits might be more sustainable and effective when midwives, nurses and eventually also surviving women become involved rather than only medical specialists.

CONCLUSION

In conclusion, early detection and management of pre-eclampsia with close monitoring of fluid balance in sick women will reduce pulmonary oedema. Additional cardiac examination is needed when pulmonary oedema persists. The many contributing factors in pulmonary oedema require a multidisciplinary approach in a high-care setting. Regular audits help retain awareness of women-, health care- and administration-related factors for SMO and may help to learn lessons to improve clinical care and reduce SMO.

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DATA AVAILABILITY STATEMENT

Datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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APPENDIX 1: Form for the critical incident audit section g: avoidable factors (as used by the national committee for confidential enquiry into maternal deaths). More than 1 may be ticked

Patient-related factors					
1	**No avoidable factor**				
2	No antenatal care				
3	Initiated antenatal care late				
4	Defaulted antenatal care				
5	Delay in accessing medical help				
6	Declined medication/surgery/advice				
7	Unsafe abortion				
Administrative-related factors					
		MOU	**1**	**2**	**3**
8	No avoidable factor				
9	Transport problem: home to institution				
10	Transport problem: institution to institution				
11	Delay initiating care				
12	Delay initiating critical care				
13	Lack of health care facilities: ICU				
14	Lack of health care facilities: Blood products				
15	Lack of appropriately trained staff: Doctors				
16	Lack of appropriately trained staff: Nursing				
Health worker-related factors					
		MOU	**1**	**2**	**3**
17	No avoidable factor				
18	Problem with recognition/diagnosis				
19	Delay in referring patient				
20	Managed at inappropriate level (antenatal)				
21	Managed at inappropriate level (at time of event)				
22	Incorrect management (incorrect diagnosis)				
23	Incorrect management (correct diagnosis)				
24	Not monitored/infrequently monitored				
25	Prolonged abnormal monitoring with no action taken				

Impact of suboptimal care: could samm have been avoided? 1 = yes, 2 = no

26	No suboptimal care
27	Suboptimal care, different management would not have made a difference to outcome
28	Suboptimal care, different management might have made a difference to outcome
29	Suboptimal care, different management would reasonably have been expected to have made a difference to outcome

Note: Specific comment regarding avoidable factors.