Critically ill obstetric patients requiring mechanical ventilation in rural western India: A retrospective analysis

SMRUTI B. VAISHNAV, BHALENDU VAISHNAV, KAILAS N. DESAI, NITIN S. RAITHATHA, NEETA S. BOSE

ABSTRACT

Background. There is a dearth of studies on the clinical profile and therapeutic aspects of critically ill obstetric patients from rural areas, especially those requiring tertiary care support and ventilator therapy.

Methods. We retrospectively analysed the aetiological, clinical, interventional and outcome-related factors of obstetric patients requiring mechanical ventilation in western India. We analysed factors that influence seeking of antenatal care, pregnancy and its complications, severity assessment score, indications and initiation of mechanical ventilation, multiorgan failure and their correlation with maternal mortality.

Results. Of the 6708 obstetric admissions studied, 1112 were of critically ill (16.5%) patients and 200 (17%) of these required mechanical ventilation. Over three-fourths (77%) of patients were from rural areas, 83.5% were referred and 97% had inadequate antenatal care. Severe pregnancy-induced hypertension/eclampsia, massive haemorrhage and sepsis were the common obstetric complications. Pulmonary oedema (32.5%), acute respiratory distress syndrome (ARDS, 14%) and acute lung injury (22.5%) were the three most common indications for mechanical ventilation. In 26% of patients, mechanical ventilation was initiated early based on a worsening cardiorespiratory profile. A sequential organ failure assessment score of > 5 on admission and delay in treatment resulted in multi-organ failure and worsening outcome. The maternal mortality ratio was 32.5%, incidence of multi-organ dysfunction syndrome was 71%, and pregnancy loss was 43.5%. The odds ratio for maternal mortality in patients ventilated early was 0.39 as against 5 in those with ARDS.

Conclusions. Inadequate antenatal care, delayed referral practices, pregnancy-induced hypertension, obstetric haemorrhage and sepsis remain the major causes of complications in obstetric patients from rural areas. The common indications for mechanical ventilation were pulmonary oedema, ARDS and acute lung injury. Early initiation of mechanical ventilation upon detection of imminent

Pramukhswami Medical College, H.M. Patel Centre for Medical Care and Education, Karamsad 388325, Gujarat, India

SMRUTI B. VAISHNAV, KAILAS N. DESAI, NITIN S. RAITHATHA Department of Obstetrics and Gynaecology BHALENDU VAISHNAV Department of Medicine

NEETA S. BOSE Department of Anaesthesia

Correspondence to SMRUTI B. VAISHNAV; *smrutiv@charutarhealth.org*

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cardiorespiratory collapse was associated with reduced mortality.

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INTRODUCTION

Inadequate antenatal care, delayed referral, inadequate critical care support and pre-existing maternal anaemia account for a high maternal mortality in India. Pregnant women have a compensated cardiorespiratory reserve. Haemodynamic stress resulting from obstetric haemorrhage, complications of hypertension and medical disorders superimposed on pre-existing anaemia (present in 65%-75% of pregnant women in India)¹ lead to life-threatening decompensation of the cardiorespiratory system. This decompensation, although acute, has a better chance of recovery if treated diligently as compared to non-pregnant patients with chronic, irreversible illnesses. Haemodynamic support and assisted ventilation are the mainstay of early goal-directed intervention in these situations.² While patients requiring haemodynamic support and blood component therapy can be managed at secondary care centres, those requiring dialysis and assisted ventilation need support in intensive care units (ICUs) at tertiary care centres.

Pregnancy can be complicated by diverse pulmonary complications. The requirement of mechanical ventilation in obstetric patients varies from 12% to 55%.^{3,4} Our centre provides intensive care to a substantial number of critically ill obstetric patients who are referred from rural areas.

METHODS

This retrospective observational study, approved by our institutional human research ethics committee, was done in a 50bed medical–surgical ICU/high dependency unit (HDU), which is a part of a 550-bed, university affiliated, trust hospital and rural medical college in central Gujarat, India. Our hospital is the NABH (National Accreditation Board for Hospitals and Healthcare Providers) accredited medical college in Gujarat. It provides antenatal care to 1200 patients every year, of which 70% are high-risk pregnancies. In ICUs, the patients were looked after round the clock by a team consisting of an obstetrician, a neonatologist, an intensive care specialist and a physician. All pregnant women or those in the 42-days postpartum period requiring mechanical ventilation were included in the study that was done for a period of 6 years starting 1 January 2006.

Data collection

Epidemiological, clinical, laboratory, intervention and outcomerelated data of critically ill obstetric patients requiring mechanical ventilation were collected. All consecutive patients were enrolled. Pregnancy-induced hypertension (PIH) was diagnosed according to the recommendations of the working group of the National High Blood Pressure Education Program (NHBPEP 2000).⁵ Acute respiratory distress syndrome (ARDS) was diagnosed according to the American-European Consensus Conference⁶ except we did not measure the pulmonary capillary wedge pressure (PCWP). Sepsis and septic shock were identified as per the definition of the American College of Chest Physicians and Society of Critical Care medicine.⁷ Organ dysfunction was evaluated using the sequential organ failure assessment (SOFA) score.8 Maternal mortality was considered as death occurring during pregnancy or within 6 weeks of delivery, as per the International Classification of Diseases (ICD) version 10. Perinatal death was defined as death before or within 6 weeks of birth. The obstetric status was defined as antepartum, postpartum and post-abortal. Severe anaemia was defined as haemoglobin ≤7 g/dl. Inadequate antenatal care was defined as <4 antenatal visits.9

Statistical analysis

The data were entered in Microsoft Excel and then transferred to SPSS (version 14) after applying data validation checks and rectifying any discrepancies. Descriptive statistics (mean, frequencies, %) were used to depict the sociodemographic characteristics and clinical profile of the study participants. Multivariate logistic regression (LR) models (with backward LR method) were developed to determine the individual contribution of independent variables in predicting maternal and foetal outcome. The change in Nagelkerke's R-square was used to determine the most important factors contributing to maternal outcome. Receiver operating characteristic (ROC) curve analysis explored the effect of SOFA at admission on maternal outcome.

RESULTS

Of the 6708 obstetric patients admitted during the study period, 1112 were critically ill (16.5%) and 200 needed mechanical ventilation (17.9% of all critically ill obstetric patients). The other critically ill patients (82.1%) were admitted to the HDU, intermediate care unit or ICU, and required treatment modalities other than ventilator support. These treatment modalities included vasopressor support, blood component therapy, dialysis, invasive monitoring and nasal oxygen therapy, and they were not included in the study.

The mean age of the patients was 25.6 years, 144 (77%) were from rural areas, 196 (98%) belonged to the poor socioeconomic class, and 194 (97%) did not have adequate antenatal care. One hundred and sixty-seven patients were referred (83.5%); 81 (40.5%) patients were primipara, 106 (53%) were multipara and 13 (6.5%) patients were grand multipara, 129 (64.5%) patients were antenatal and 71 (35.5%) were postpartum/post-abortal. The delivery was vaginal in 116 (58%) patients and by lower segment caesarean section in 58 (29%). Eight patients (4%) had a laparotomy, 7 (3.5%) aborted and 10 (5%) died undelivered. Severe anaemia was present in 68 of 200 patients (34%).

In patients on mechanical ventilation the commonest obstetric complication was severe PIH/eclampsia and the commonest medical complications was heart disease (Table I).

Of 200 patients requiring ventilator support, 181 (91%) were intubated while 19 patients (9%), all of them postpartum, were managed by non-invasive ventilation. The commonest indication for ventilator support was pulmonary oedema (Table II).

Obstetric conditions leading to ARDS included severe preeclampsia, complicated eclampsia, HELLP (haemolysis, elevated liver enzymes, low platelet) syndrome, major obstetric haemorrhage, massive blood transfusion and sepsis.

The mean duration of ventilation in ARDS, pulmonary oedema and cardiomyopathy survivors was 180, 41.3 and 28.3 hours, respectively. Sixty-five patients died and the maternal mortality rate was 32.5%. Multiorgan dysfunction syndrome (MODS) was present in 142 (71%) patients. Pregnancy wastage occurred in 87 patients (43.5%) due to intrauterine foetal death (IUFD), neonatal death (NND) and abortions. The maternal mortality was highest in patients with ARDS (Table II).

The cardiovascular system was most commonly involved (50%), followed by the respiratory system (42%). The rest of the organ systems were infrequently affected. There was a relationship between the number of failed organs and maternal mortality. It was lowest in patients with single-organ failure (16.1%) and highest in those with five-organ failure (66.7%). The average SOFA score on admission to ICU was 3.9 in survivors and 7.1 in non-survivors.

On multivariate logistic regression analysis, gestational age (29–37 weeks), obstetric haemorrhage, ARDS, acute lung injury, admission to initiation of ventilator time and SOFA score on admission were significantly associated with maternal mortality. There was no statistically significant difference in mortality of primipara and multipara patients. The predictive value of the model was good with 78.5% correct classification rate (Nagelkerke coefficient of determination 0.51) (gestational age: OR 4.49, 95% CI 1.63–12.34, p=0.004), obstetric haemorrhage (OR 15.56, 95% CI 2.96–81.84, p=0.001), ARDS (OR 65.43, 95% CI 10.25–417.58, p<0.0001), acute lung injury (OR 4.16, 95% CI 10.26–13.76, p=0.02), other therapeutic indications (OR 25.09, 95% CI 2.92–215.83, p=0.003), admission–ventilator time (OR 1.01, 95% CI 1.0–1.03, p=0.078), SOFA score (OR 1.29, 95% CI 1.11–1.50, p=0.001).

TABLE I. Medical and obstetric complications in the study group (n=200)

Complication	n (%)	Survived (%)	Died (%)
Obstetric			
Severe pregnancy-induced hypertension/eclampsia	88 (44)	61 (69.3)	27 (30.7)
Massive haemorrhage	45 (22.5)	26 (57.8)	19 (42.2)
Sepsis	14 (7)	7 (50)	7 (50)
Others	5 (2.5)	2 (40)	3 (60)
Medical			
Heart disease	29 (14.5)	22 (75.9)	7 (24.1)
Malaria	4 (2)	2 (50)	2 (50)
Jaundice	3 (1)	0	3 (100)
Pneumonia	4 (2)	0	4 (100)
Others	8 (4)	3 (37.5)	5 (62.5)

TABLE II. Indications for mechanical ventilation and outcomes

Indication	n (%)	Survived (<i>n</i> =135)	Died (%) (<i>n</i> =65)
Respiratory failure			
Pulmonary oedema	65 (32.5)	50	15 (23)
Acute respiratory distress syndrome	28 (14)	10	18 (64)
Acute lung injury	45 (22.5)	29	16 (35.6)
Elective intubation and ventilation	52 (26)	41	11 (21.2)
Cardiac arrest	6 (3)	4	2 (33)
Others: Pulmonary embolism	4 (2)	1	3 (75)

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TABLE III. Demographic and clinical characteristics and their relation to maternal mortality

Variable	Alive <i>n</i> (%)	Died <i>n</i> (%)	Total
Gestational age (weeks) and obstetr	ric diagnosis		
≤28	7 (50.0)	7 (50.0)	14
29–37	37 (58.7)	26 (41.3)	63
<u>≥</u> 38	80 (65.7)	43 (34.3)	123
Pregnancy-induced hypertension	61 (69.3)	27 (30.7)	88
Obstetric haemorrhage	26 (57.8)	19 (42.2)	45
Intrauterine foetal death	10 (50.0)	10 (50.0)	20
Pregnancy status			
Postnatal	45 (62.5)	27 (37.5)	72
Antenatal	77 (60.2)	51 (39.9)	128
Mode of delivery			
Vaginal	75 (64.7)	41 (34.4)	116
Abortion	4 (57.1)	3 (42.9)	7
Caesarean section	39 (67.2)	19 (32.8)	58
Undelivered	0 (0.0)	11 (100.0)	11
Laparotomy	4 (50.0)	4 (50.0)	8
Age (years)			
<20	17 (60.7)	11 (39.3)	28
21–25	59 (63.4)	34 (36.6)	93
26–30	36 (62.1)	22 (37.9)	58
31–35	8 (53.3)	7 (46.7)	15
>35	4 (66.7)	2 (33.3)	6

Similarly for foetal outcome, SOFA score on admission (OR 1.15, 95% CI 1.03–1.29, p=0.012) and mode of delivery (laparotomy) (OR 8.82, 95% CI 0.82–94.45, p=0.072) were statistically significantly associated with foetal mortality. The predictive value of the model was good with 73.6% correct classification rate (Nagelkerke coefficient of determination 0.381).

Nagelkerke R-square (adjusted) values which predict strength of contribution by different factors to maternal mortality were, for SOFA 0.33, admission–ventilation time 0.30, duration of ventilator 0.29, indication of ventilation 0.28, numbers of organ affected 0.20, obstetric diagnosis 0.19 and sepsis 0.19.

The ROC curve for SOFA versus maternal mortality indicates a sensitivity of 73.9%, specificity of 59.3%, cut-off point 5 and area under the curve 0.71 (Fig. 1).

DISCUSSION

Our study is one of the few studies from rural India that has analysed multiple aspects of a large number of obstetric patients requiring mechanical ventilation. The rural location of our institution and the unique setting enabled us to explore epidemiological factors contributing to critical illness in pregnant women with pulmonary complications such as locale, socioeconomic status and not availing antenatal care in patients being referred to a tertiary care set up from rural areas. It also gave us an opportunity to study the clinical profile of such patients, determinants of maternal outcome and identify clinical practices that were associated with improved outcomes in patients receiving mechanical ventilation.

Obstetric care in rural and urban areas

A higher burden of critical illness observed in our study (16.5% patients of all obstetric admissions) is a reflection of patients not availing antenatal care (97% of patients were 'unbooked' cases) and adverse socioeconomic conditions compromising access to healthcare (98% of patients were poor). The higher incidence of

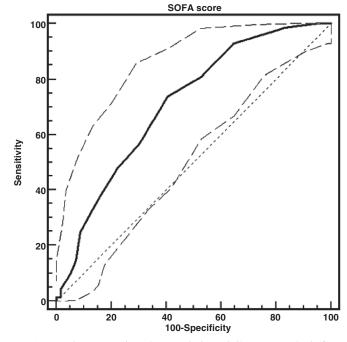


Fig 1. Receiver operating characteristic (ROC) curve analysis for sequential organ failure assessment (SOFA) score at admission

critical illness was inclusive of pulmonary and non-pulmonary complications. However, we analysed in detail only those patients who required mechanical ventilation. In comparison to our study, Bhadade *et al.*¹⁰ reported that the incidence of 'booked' patients in ICUs of Mumbai was 78%, and the mortality in booked patients was lower at 8.6% as against 61.6% in unbooked patients. Similarly, Vasquez *et al.*¹¹ reported more frequent antenatal care among survivors (33%) than non-survivors (6%). Igberase and Ebeigbe¹² also reported maternal mortality to be 10 times higher in unbooked patients in the Nigeria delta. The National Family Health Survey-3 (2005–06) indicates that 72% of maternal deaths can be prevented by effective antenatal care.

Referral status and admission rate in ICUs in rural India

The incidence of referred patients in our study was 83.5% (167/200). Obstetric patients are vulnerable for rapid clinical deterioration and any delay in availing critical care support worsens the clinical course and the outcome. Karnad *et al.*¹³ observed that a delay in initiating a corrective intervention increased the chances of MODS resulting in high mortality. In a study of 41 patients, Poornima *et al.*¹⁴ reported a 68.2% mortality in referred cases of ICU admissions of obstetric patients in costal India.

Home deliveries continue to be a factor for maternal mortality and its delayed detection and management. In a study by Patel *et* al.,¹⁵ the incidence of home deliveries in the same geographical area was reported to be 39.5%. Patients are referred to tertiary centres late, many arrive at referral centres after visiting more than one healthcare facility, and have high SOFA scores at admission. This delay in presentation is responsible for more severe illness on admission and higher ICU and HDU admission rates (16.5% in our study), in contrast to studies in metropolitan India where hospital deliveries are common. Karnad *et al.*¹³ have reported an ICU admission rate of <1% (548 per 100 000 deliveries) at General Hospital, Mumbai. The reported ICU admission rate in developed countries is 1%–2%.

Need for mechanical ventilation in obstetric patients

The incidence of mechanical ventilation in our study was 17.9%. Tang³ and Lepinsky⁴ have reported the same to be between 12% and 55% in various studies. In a study of 41 patients in Karnataka, it was reported to be 65%.¹⁴ A higher incidence of critical illness without a correspondingly high incidence of pulmonary complications in our study may be because the study population included patients admitted to the HDU as well as the ICU.

Clinical profile of ventilated obstetric patients

The obstetric conditions seen, indications for mechanical ventilation and medical complications observed by us were in partial conformity with other studies. Obstetric haemorrhage, severe pre-eclampsia and complicated eclampsia were important causes leading to a high maternal mortality. The indications for mechanical ventilation in our study included respiratory failure due to ARDS, acute lung injury, pulmonary oedema and neurogenic causes. Bhadade *et al.*¹⁰ reported a high incidence of infective conditions such as hepatitis E, H1N1 and malaria which we did not encounter. Tocolytic therapy-induced pulmonary oedema was also not seen by us. Poornima *et al.* reported acute respiratory failure 18%, haemodynamic causes 37%, impaired consciousness 15% and postoperative ventilation 5% as the main indications for mechanical ventilation.¹⁴

The incidence of pulmonary oedema in our study was 32%. This high rate was due to severe PIH, complicated eclampsia, massive obstetric haemorrhage and massive blood transfusion with coexistent anaemia (34%) and/or dilated cardiomyopathy (19%). Martin and Foley reported 1 in 1000 pregnancies to be complicated by pulmonary oedema.16 In a review of 63 000 pregnancies, Sciscione et al.¹⁷ reported pulmonary oedema to occur due to cardiac disease (25.5%), tocolytic use (25.5%), fluid overload (21.5%) and pre-eclampsia (18%). Pregnant women are predisposed to the development of pulmonary oedema, because of increased plasma volume (further increased in severe anaemia, hypoalbuminaemia and reduced colloid oncotic pressure, i.e. up to 14 mmHg, or 8 mmHg lower than their non-pregnant counterparts in case of severe pre-eclampsia). Excessive intravenous fluids, massive blood transfusion and the postpartum auto-transfusion effect can further increase the risk.

ARDS

The incidence of and mortality due to ARDS in our study was 14% and 64%, respectively. Most deaths were due to associated MODS. Vasquez *et al.*¹¹ reported the same to be 19% and 33%, respectively. In a study done in Shanghai by the ARDS study group, mortality in ARDS up to 90 days was 68.5%-70.4%.¹⁸

Early mechanical ventilation: Our experience

Of our 200 patients, 52 with severe obstetric complications along with unstable cardiorespiratory status were ventilated before precipitation of cardiorespiratory collapse or full-fledged development of respiratory failure (early elective ventilation). In the remaining 148 patients (74%), mechanical ventilation was initiated in the presence of established respiratory failure. The mortality in patients ventilated early was 21% while among all patients it was 32.5%. In relation to the specific underlying condition the mortality was 23% in patients with pulmonary oedema, 64% in those with ARDS, 35.6% in those with acute lung injury and 75% in the pulmonary embolism group.

Obstetric complications in which early elective ventilation was initiated were haemorrhage requiring massive blood

transfusion, ruptured uterus, critically ill patients requiring surgery, those undergoing re-laparotomy and eclampsia with aspiration pneumonitis. When these patients developed haemodynamic instability in the form of tachycardia (pulse rate >140/minute), tachypnoea (respiratory rate >30 minute), hypotension (systolic blood pressure <90 mmHg), severe uncontrolled hypertension (>200/120 mmHg), evidence of cardiomyopathy on echocardiography, falling SpO₂ (<85%), a clinical decision to intubate them and initiate early invasive mechanical ventilation was taken without waiting for the standard criteria for invasive ventilation to be fulfilled.

The documentation of survival benefit of early ventilation is a unique finding of our study. There is growing evidence in critical care practice that early detection and rapid response to physiological deterioration can improve outcome in non-pregnant patients.^{19–21} However, no studies have documented early intervention to improve maternal outcome in obstetric patients.

Correlation between foeto-maternal outcome and coexisting maternal complications

In our study, a SOFA score on admission of >5 was associated with adverse outcomes. Perez et al.8 did real-time and sequential assessment of SOFA score as an important descriptor of MODS in obstetric patients and showed that increasing SOFA score after admission indicates worsening prognosis. There was a definite relationship between number of organs failed and maternal mortality. It was lowest in women with single-organ failure (16.1%) and highest in those with five or more organ failure (66.7%). In an unpublished study, we used logistic regression analysis to determine the contribution of individual maternal complications to maternal outcome. We found that ARDS/acute lung injury, acute renal failure and shock were independent factors contributing to maternal mortality in ventilated as well as non-ventilated obstetric patients. In the present study again we found a similar relation. The ventilator support was not the only factor that improved outcome. It was the result of a multi-pronged approach such as vasopressor support, invasive haemodynamic monitoring, dialysis and blood component therapy delivered by a dedicated team in a standardized, NABHaccredited tertiary care centre under strict infection control practices.

Thus, we found that (i) the incidence of critically ill rural obstetric patients referred to our tertiary care centre was high; (ii) inadequate antenatal care, late arrival to our centre, PIH and obstetric haemorrhage were common antecedent causes in patients requiring mechanical ventilation; (iii) ARDS, acute lung injury, acute pulmonary oedema, presence of multi-organ failure and a SOFA score of >5 at admission were important determinants of maternal outcome; (iv) maternal mortality was lowest in those with single-organ failure and highest in those five-organ failure; (v) early mechanical ventilation in critically ill obstetric patients based on detection of early warning signs was associated with improved maternal outcome; and (vi) maternal mortality in patients ventilated early was lower.

The practice of early initiation of mechanical ventilation in patients presenting to a well-equipped tertiary care centre along with improved sensitivity for prompt diagnosis of cardiorespiratory decompensation were associated with better outcome. The improved survival is the result of a multi-pronged therapeutic approach to critically ill pregnant women.

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