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Finding solutions to ending preventable maternal mortality; early transfer of critically ill obstetric patients to intensive care unit is associated with improved maternal mortality

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Abstract
Background: Maternal mortality remains high in developing countries. According to sustainable development goals set by United nations (UN) a global target of 70/100,000 live births is to achieved by 2030. It is required that all countries accelerate their maternal welfare programs and identify barriers and facilitators in ending preventable maternal mortality (EPMM).
Methodology: The study was conducted in 18 bedded adult Medical/Surgical ICU of tertiary care teaching hospital. Retrospective data collection was done for all obstetric patients (pregnant or within 6 weeks postpartum) admitted from 01-December 2017 to 30-November 2018. Triggering events for ICU admissions were identified {seizures, respiratory failure, shock, acute kidney injury, postop care of emergency caesarean section/exploratory laparotomy and postop care of elective caesarean section with complicated medical disease}. Triggering event to ICU admission interval was noted. Unpaired t test / Mann Whitney U test / Chi- square test was used to compare the distributions between survivor and non survivors while binary logistic regression analysis used to identify the predictors of the non-survivors. A p value of <0.05 was considered statistically significant.
Results: A total of 339 patients were admitted in ICU during the study period, out of which there were 60 obstetric patients. There were 42 (70%) survivors and 18 (30%) non- survivors. Non-survivors had higher SOFA and APACHE II at the time of admission [(6.4 + 3.2 vs 9.8+3.2; p = 0.000) and (15.6 +6.0 vs 19.7+5.6; p=0.016) respectively]. In multivariate analysis only triggering event to ICU admission interval [AOR=1.93, 95% CI=1.18-3.18, P=0.009] and need of dialysis [AOR=6.86, 95% CI=1.74-27.11, p=0.006] were found significant and independent risk factors of mortality.
Conclusion: Our study shows that early transfer of critically ill obstetric patient to intensive care unit improves survival. Among the various types of delay in maternal care, delayed ICU admission requires attention of planners and policy makers targeting maternal mortality.

Keywords: Critically ill obstetric patients, maternal mortality, delay ICU transfer, obstetric transition

Introduction
Ending Preventable Maternal Mortality [EPMM] remains an unresolved issue for developing countries. World Health Organisation [WHO] in 2015, estimated that 830 women die every day due to preventable causes related to pregnancy and childbirth. Around 99% of these deaths took place in developing countries [1]. Post 2015, WHO set the new global target of Maternal Mortality Ratio [MMR] as 70/100,000 live births by 2030 [2].
Targeting to increase global equity in maternal mortality across the globe, supplementary national target includes that no country should have MMR >140 /100,000 live births (i.e. double the global average) by 2030.Therefore all countries should accelerate their efforts to reduce maternal mortality and improve maternal health. Along with this equity in maternal healthcare should be offered to all sub-populations within a country and across the globe, irrespective of financial and social status.
Maternal mortality is sensitive to timely intervention and early transfer of critically ill obstetric patient to intensive care unit [ICU] is an important component of care. Evidently, a randomised controlled trial [RCT] to evaluate the impact of early transfer to ICU vis-à-vis delayed transfer

holds practical and ethical implications. However observational data can be generated to guide programmers and policy makers to divert funds in appropriate direction. Current study was undertaken to evaluate the effect of early transfer of critically ill obstetric patients to ICU and its impact on maternal mortality and morbidity.

Methodology

Study setting and patient population

The present study is a retrospective observational study in an 18 bedded Adult Medical/ Surgical ICU at Department of Critical Care Medicine of a 4500 bedded tertiary care teaching hospital. Ethical clearance was obtained from institutional committee.

A research group (OBS-CRTICARE) was instituted comprising of specialists from different fields involved in maternal care. (Critical care medicine, Obstetrics and Gynaecology, Community medicine and Biostatistics). The group aimed to study outcome of critically ill obstetric patients and propose a strategy to optimise maternal care in our region.

Retrospective data of all obstetric patients (pregnant or within 6 weeks postpartum) admitted to our ICU from 01-December 2017 to 30-November 2018, was collected. All non-obstetric patients and patients who were more than 6 weeks postpartum were excluded from the study.

Method of data collection

The intensive care unit records (Assessment file, investigation file, daily monitoring charts) of all obstetric patients (pregnant or within 6 weeks postpartum) admitted during the study period were collected. Following data was included for the study: Demographic and referral details, status at admission, SOFA and APACHE II score, event triggering ICU admission, triggering event to ICU admission interval, organ support needed (vasoactive drugs, renal replacement therapy, mechanical ventilation, etc) during ICU stay.

Definitions

Triggering event leading to ICU admission

Based on previous knowledge of obstetric patients being routinely admitted to our ICU, we defined the triggering event leading to ICU admission [Table 1].

Table 1: Triggering event for ICU admission

1	Seizures (refractory to standard therapy or associated with other organ failure),
2	Respiratory failure (requiring oxygen therapy, non-invasive ventilation or mechanical ventilation)
3	Shock (requiring vasopressor support)
4	Acute kidney injury (requiring renal replacement therapy)
5	Postoperative care of emergency caesarean section [CS]/ Exploratory laparotomy
6	Postoperative care of elective CS with complicated medical diseases

Triggering event to ICU admission interval

Triggering event to ICU admission interval was defined as the time interval in days between triggering event to ICU admission.

Statistical analysis: Normality of the continuous variable´s was tested and considered normally distributed when Z score of skewness was between ±3.29. Normally distributed continuous variables presented in mean± standard deviation (SD) and compared using unpaired samples t-test whereas non normal continuous variables were presented in median (inter-quartile range i.e. Q1-Q3) and compared using Mann Whitney U test. Categorical variables presented in frequency (%) and compared using Chi-square test. Univariate and multivariate binary logistic regression analysis was used to identify the predictors of the non-survivor. P value of <0.05 has been considered as statistically significant. Statistical package for social sciences, version -23 (SPSS -23, IBM, Chicago, USA).

Results

Out of 339 ICU admissions during the study period, 60 (17.7%) were obstetric patients (see figure 1; table 2). Mean (± standard deviation) SOFA and APACHE II at ICU admission were 7.4 ± 3.5 and 16.8± 6.1 respectively. Respiratory failure was the most common triggering event leading to ICU admission. All except one ICU admissions were postpartum/post-abortion. Infection (55%) was the most common complication in our study cohort followed by hypertensive disorder of pregnancy (35%) and obstetric haemorrhage (28%).

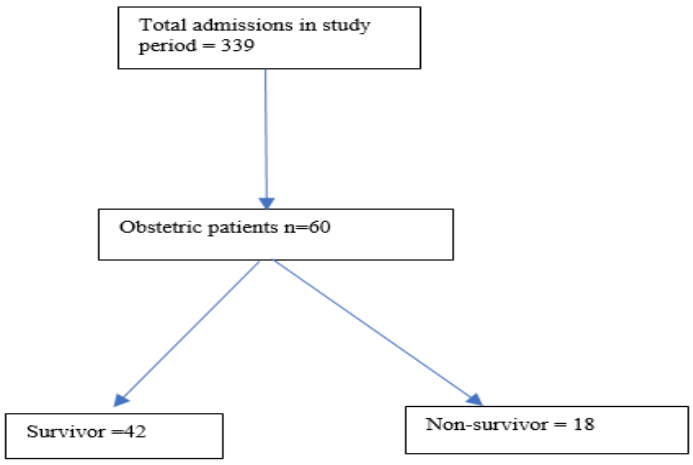

Fig 1: Patient Population

Table 2: Demography and clinical values of the study patients

S. No		Total Number of patients=60
1.	Age (Mean ± SD)	28.1 ± 5.7
2.	SOFA at admission to ICU (Mean ± SD)	7.4 ± 3.5
3.	APACHE II at admission to ICU (Mean ± SD)	16.8± 6.1

4.	Complications
	• Haemorrhage
	  ○ APH
	  ○ IPH
	  ○ PPH
		
		17 (28%)
		6 (10%)
		5 (8%)
		6 (10%)

	• Infection	33 (55%)

	• Hypertensive disorder of pregnancy
	  ○ Eclampsia
	  ○ Severe Pre-eclampsia
		21(35%)
		11(18%)
		10 (17%)

	• Medical disorder
	  ○ Rheumatic heart disease
	  ○ Cardiomyopathy
	  ○ Anaemia
	  ○ Others (DM, CKD, CLD, COPD etc)
		
		8 (13%)
		10 (17%)
		22 (37%)
		8 (13%)

	• Accidental/Iatrogenic	2 (3%)
5.	Status at admission to Obstetric department • < 22 weeks • 22 to 34 weeks • 34 to 37 weeks • 37 to 42 weeks • Postpartum within 24 hrs • Postpartum 24 hrs to 1 week • Postpartum >1 week • Post-abortion	 3 (5%) 7 (12%) 15 (25%) 9 (15%) 3 (5%) 17 (28%) 4 (6%) 2 (3%)
6.	Status at admission to ICU • 37 to 42 weeks • Postpartum within 24 hrs • Postpartum 24 hrs to 1 week • Postpartum >1 week • Post-abortion • Post laparotomy for Ruptured Ectopic	 1 (1.6%) 23 (38%) 28 (47%) 5 (8%) 2 (3%) 1 (1.6%)
6.	Triggering event leading to ICU admission • Seizures (refractory to standard therapy or associated with other organ failure)	 9 (15%)
	• Respiratory failure (requiring oxygen therapy, non-invasive ventilation or mechanical ventilation),	24 (40%)
	• Shock (requiring vasopressor support)	4 (6.7%)
	• Acute kidney injury (requiring renal replacement therapy)	5 (8.3%)
	• Postop care of emergency CS/exploratory laparotomy	11 (18.3%)
	• Postop care of elective CS with complicated medical diseases.	7 (11.7%)
7.	Duration of ICU stay (Mean ± SD) Median (IQR 25-75)	 13.1 ± 12.2 9.5 (5 -16.75)
8.	Need for Vasopressor	44/60 (73.33%)
9.	Need for Mechanical ventilation	52/60 (86.7%)
10.	Need for Dialysis	16/60 (26.7%)

Survivor vs Non-survivor

There were 42 (70%) survivors and 18 (30%) non-survivors. Non-survivors had significantly higher SOFA and APACHE II at ICU admission as compared to survivors (6.4 ± 3.2 vs 9.8±3.2; p <0.001) and (15.6 +6.0 vs 19.7±5.6; p=0.016). Non-survivors required vasopressor support, mechanical ventilation and dialysis more frequently than survivors (see table 3). Triggering event to ICU admission interval (days) was significantly smaller in survivors as compared to non-survivors [Median (IQR): 0.87 (0.07- 1.5) vs. 2 (1-3.5); p=0.001]. Timely transfer to ICU was associated with decreased mortality (p<0.001).

In binary logistic regression analysis, (univariate analysis) variables i.e. SOFA, APACHE II score, triggering event to ICU admission interval (Days), duration of vasopressor, need of dialysis were found significant predictor of mortality without adjusting effect of other factors. Two variables (Need for vasopressor, Need for Mechanical ventilation) could not be included because 100% non-survivors needed mechanical and vasopressor.

In multivariate analysis only triggering event to ICU admission interval [AOR=1.93, 95% CI=1.18-3.18, P=0.009] and need of dialysis [AOR=6.86, 95% CI=1.74-27.11, p=0.006] were found significant and independent risk factors of mortality (see table 4).

Table 3: Comparison of demographic and clinical values between survivor /non-survivor

S. No	Variables	Survivor (n=42)	Non- Survivor (n=18)	P value
1.	#Age (Years)	28.2 ± 6.2	27.9 ± 4.6	0.880
2.	#SOFA at ICU admission	6.4 ± 3.2	9.8±3.2	<0.001
3.	#APACHE II at ICU admission	15.6 ±6.0	19.7±5.6	0.016
4.	$Duration of ICU stay (Days)	9.5 (6-16.25)	9.5 (2.5 – 23.7)	0.518
5	$ Triggering event to ICU admission interval (Days)	1 (0- 2)	2 (1-3.5)	0.001
6	$Duration of Mechanical ventilation	2 (1-5.25)	7 (2.5 – 16.75)	0.017
7	$Duration of vasopressor support	2.5 (0-5.25)	5.5 (2.5 -17.5)	0.006
8	Need for vasopressor	26 (61.9%)	18/18 (100%)	0.001
9	Need for Mechanical ventilation	34/42 (80.9%)	18/18 (100%)	0.046
10	Need for dialysis	6/42 (14.2%)	10/18 (55%)	0.002
Data presented in #Mean±SD / $Median (Inter-quartile range) / Proportion. Compared between survivors and non survivors using #Unpaired samples t test/ $Mann Whitney U test / Chi-square test. P<0.05 significant				

Table 4: Predictors of non-survivor

	Binary Logistic Regression Analysis					
	Univariate Analysis			Multivariate Analysis		
Variable´s	OR	95% CI	P value	AOR	95% CI	P Value
Triggering event to ICU admission interval (Days)	2.01	1.19-3.37	0.008	1.93	1.18-3.18	0.009
Need Dialysis (Yes)	7.5	2.11-26.69	0.002	6.86	1.74-27.11	0.006
Only significant variables in univariate analysis included in multivariate analysis. Outcome variable [Dead / Survive]. OR=Odds ratio, AOR =Adjusted odds ratio, p<0.05 significant						

Discussion

Our study highlights the importance of early transfer of critically ill obstetric patients to intensive care. ICU in government sector are always running short of beds due to high rate of patient admissions. Majority of patients are first wait-listed until a bed is available. The higher APACHE and SOFA at the time admission among non-survivors underline the fact that organ failure increases during waiting period leading to deterioration in parameters by the time patient reaches ICU.

Impact of delayed ICU admission

Cardoso *et al* evaluated the impact of delayed ICU admission in a prospective study involving 401 general critically ill patients. Delay in ICU admission varied from 2.3 hours to 67.2hrs in the study cohort. They reported a significant increase in mortality in patients with delay in ICU admission (p=0.002).[3] Delayed ICU admission and increased mortality has also been found in specific subgroups of patients like critically ill surgical patients, patients with acute respiratory failure and community acquired pneumonia [4-6].

'Delayed ICU transfer': Is it a Continuum of various delays in Obstetric care?

In 1990s, Thaddeus and Maine brought world's attention towards maternal deaths and its preventable causes [7, 8]. They emphasised that many of these patients die because of delay in receiving appropriate care. The "three delay" framework was introduced linking various causes responsible for maternal deaths. These include, phase I - delay in women/family seeking help, phase II- delay in reaching appropriate healthcare centre, phase III- delay in receiving appropriate treatment after reaching the healthcare facility.

We realised that delayed ICU transfer is a type of phase III delay which occurs either due to myriad reasons such as inability to identify the need for ICU transfer and/or delay in getting a bed in ICU due to a full unit. We sub-classified phase-III delay into 2 subtypes (delay in receiving definitive obstetric intervention and delay in receiving life support therapy) (see figure 2). Though scoring systems have been used to identify high risk obstetric patients in different cohorts i.e. critically ill, hospitalised and outpatients but most of them are complicated and difficult to apply bedside in a busy unit. Aoyama *et al* did a systematic review of meta-analysis including 38 studies to evaluate 12 various risk prediction models for maternal mortality [9]. The collaborative integrated pregnancy high dependency estimates of risk (CIPHER) (area under the receiver operating characteristic curve (AUC) 0.823 (0.811–0.835) and maternal severity index (discrimination: AUC 0.826 (0.802–0.851), studied in critically ill obstetric and hospitalised obstetric patients respectively had best discrimination power. Development of easily applicable bedside scores like qSOFA (quick SOFA) is warranted for early identification of critically ill obstetric patients. Basic critical care training of obstetric residents can help in early identification of potentially life-threatening event and intervention in such patients.

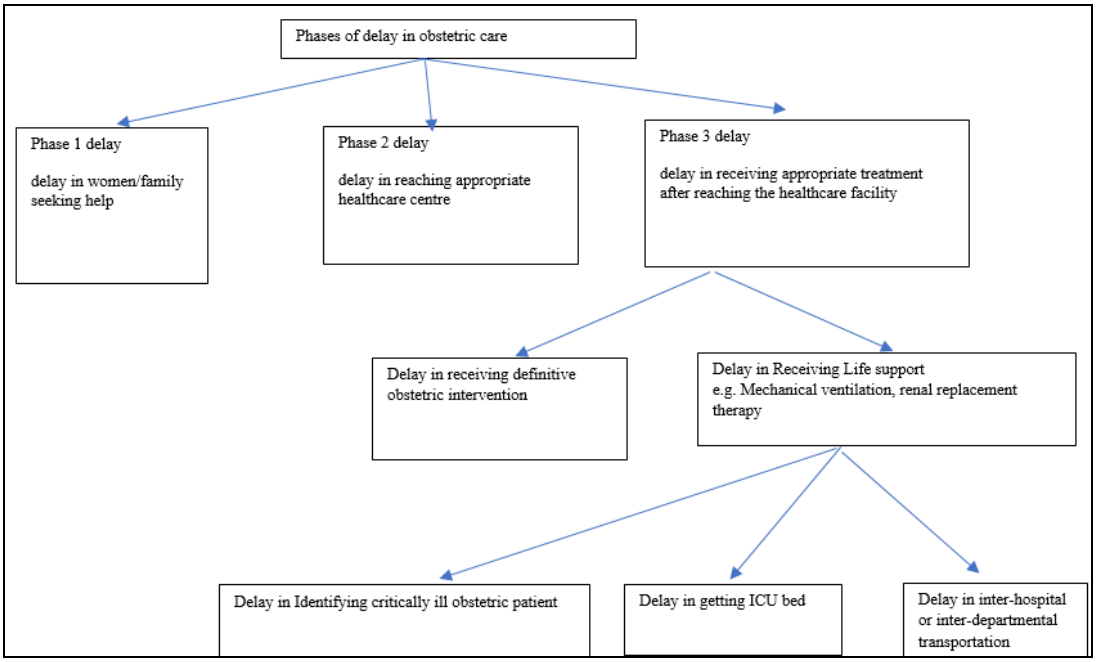

Fig 2: Figure showing three-delay framework

Strengths and Limitations

As the millennium development goals [MDG] have transitioned into sustainable development goals to be achieved by 2030, improvement along the continuum of care for women is needed [10]. With our study, we want to draw attention towards need for obstetric care transition from basic obstetric care to advance life support with evolving advancement in healthcare technology. There is urgent need for steps to increase awareness regarding early transfer of critically ill obstetric patients to ICU. Bedside easily applicable scoring systems are needed to help obstetrician and nursing staff identify potentially sick patients with increased risk of mortality. Our study is limited by its single centre and retrospective design.

Conclusion

Early ICU transfer of obstetric critically ill patients is associated with decreased maternal mortality. A structured and protocolised approach is needed to provide appropriate and timely life support to these potentially salvageable group of critically ill patients.

Abbreviations

EPMM: Ending Preventable Maternal Mortality
MMR: Maternal Mortality Ratio
APACHE: Acute Physiology and Chronic Health Evaluation
SOFA: Sequential Organ Failure Assessment
CIPHER: Collaborative integrated pregnancy high dependency estimates of risk

Ethics approval and consent for participation; was taken from institutional ethics committee.

Availability of data and materials: The datasets analysed during the current study are available from the corresponding author on reasonable request.

Consent for publication: Not applicable

Competing interests: The author declares that he has no competing interests.

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Author's contributions; A Ah and S S Si did data collection and manuscript preparation. P Mi did statistical analysis. A Az supervised the preparation of manuscript. N Mu, S Sa, A Pa, A Ag, Ay Ah and M Ag gave intellectual inputs.

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