Analysis of morbidity and mortality in the Obstetrical Intensive Care Unit (O-ICU) April 2009 / December 2016

Zumiko Moriyama Estrada[●], María de Jesús Angeles Vázquez[■],
Rubén Castorena de Ávila[■], Hugo Mendieta Zerón[●■♦]

Abstract

Objectives: To determine the rate of admission to an Obstetrical Intensive Care Unit (O-ICU), maternal mortality rate and the main factors associated with it.

Methods: This was a retrospective study, analyzing all the admission to an O-ICU between January 1, 2009, and November 28, 2016. The registries were completed since the first day of recruitment until discharge or death.

Results: Among 2,145 patients admitted to the O-ICU during the study period, maternal mortality was of 4.6% (n = 100). The three main causes of hospitalization were hypertensive disorders (47.1%), bleeding disorders (18.9%) and infectious complications (5.4%). The Receiver Operating Characteristic (ROC) curve showed the patient's age was the variable with the largest area under the curve (0.569) in relation to mortality. Applying the linear regression model gave as a result that age, Mean Arterial Pressure (MAP), platelets at admission and haemoglobin are significant ($P \leq 0.001$) as predictive factors for mortality. The Weight Estimation test also showed significance for platelets count and MAP at admission.

Conclusion: From the analysis done, it showed that the patient's age, MAP and platelets at admission are the most important parameters to predict mortality.

Introduction

Obstetric morbidity and mortality have been a problem of great interest due to its social and economic impact during the past decades. Even more, the actual changes in obstetric practice because of the patients' age, and an increase of chronic comorbidities have increased the need of critical medical care because of pregnancy or delivery associated complications.

The admission of a pregnant woman into an Obstetric Intensive Care Unit (O-ICU) is a challenge for the health team. The mortality of such patients is variable, ranging from 0 to 40% depending mainly on the development of each country[1]. In this regard, the Maternal Mortality Rate (MMR) has been used as an important indicator of the health system's performance and is indirectly related to the population's sanitary conditions[2].

- Faculty of Medicine, Autonomous University of the State of Mexico, Toluca, México
- Maternal-Perinatal Hospital "Mónica Pretelini Sáenz" (HMPMPS), Toluca, México
- Asociación Científica Latina A.C. (ASCILA), Toluca, México
  Corresponding author: mezh_74@yahoo.com

According to the World's Health Organization (WHO), improving maternal health should be attained around the world, as established in the Sustainable Development Goals (SDG)[3]. Stated also by the WHO, obstetric mortality is defined as "the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes"[4]. Moreover, as settled in the SDG, it is a priority to decrease MMR to 70 per 100,000 live births, by 2030. Not withstanding, in developing countries such as Mexico, the MMR remains as one of the main health system challenges.

Unfortunately, the main causes of death among pregnant woman continue as preventable complications, which must be averted to achieve this goal. In this matter, the prevalence of maternal mortality has decreased significantly in the past decade in the State of Mexico, Mexico around 50%, as shown in the most recent inform[5]. Even so, the MMR is still very high, which enhances the necessity of determining the main causes, course and outcome of obstetric admissions in specialized maternal and perinatal centres.

The objective of this study was to determine an epidemiological profile and potential trends on the admissions into an O-ICU describing the main complications and factors associated to maternal mortality in a third level Hospital in a developing Country.

Methods

This was a retrospective descriptive study, performed at the "Mónica Pretelini Sáenz" Maternal-Perinatal Hospital (HMPMPS), Health Institute of the State of Mexico (ISEM), Toluca, Mexico, between January 1, 2009, and November 28, 2016.

Clinical data were collected by doctors in an Excel sheet designed for this survey. The registries were completed since the first day of recruitment until discharge or death.

Procedure

As a rule, candidate patients to be admitted to the O-ICU were considered based on the Priority model (Table 1). Data were collected on patient age; number of days at the hospital; existence of diseases prior to pregnancy; city and hospital of origin; parity; stage of pregnancy on admission; primary cause of hospitalization; clinical complications such as the need for antibiotics, mechanical ventilation, or haemodialysis; and maternal survival until discharge from the O-ICU or death. The primary cause of admission to the O-ICU was classified as direct or indirect obstetric, or non-obstetric. WHO criteria were used to classify maternal death.

Laboratory studies

The laboratory tests registered in the Medical File from each patient were processed at the Clinical Laboratory of the HMPMP according to standardized procedures

recommended by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC).

Statistical analysis

Results were presented as mean ± standard error (SD) for continuous variables and in percentages for qualitative ones. Relationships between the quantitative measured variables (Hb, platelets and mean arterial pressure (MAP) on admission and Hb, platelets and albumin on delivery) were assessed using Pearson correlations. The Receiver Operating Characteristic (ROC) curve and the Cox regression test were used to determine a possible significance of mortality prediction with the clinical and Laboratory variables. Finally, the multinomial logistic regression was used to analyze the variable "dialysis" or "use of amines" as predictors of mortality. Significance was set at $P < 0.05$. All tests were performed with the SPSS version 23 statistical software program (IBM SPSS Statistics Armonk, NY: IBM Corp.).

Ethics

The study was approved by the Research Committee and the Ethics on Research Committee of the HMPMPS (code 2018-04-580). The process complied with the ethical principles of the Declaration of Helsinki (Fortaleza, Brazil), and written informed consent was waived as this was a retrospective study.

Results

Since the opening of the O-ICU on April 1, 2009, until December 31, 2016, 2,145 patients have been treated in critical condition. This mean an average of 268 patients per year attended at the O-ICU. Only 567 patients (26.4%) were from the city where this third level Hospital is located. During the period of the study, there were 73,625 births with an estimated 29.1 admissions to the O-ICU per 1000 deliveries. Most of the admissions (1,534 women, 71.5%) of the cohort study occurred during the postpartum period, and 22.3% were still pregnant. Four women (0.41%) were transferred to a National Health Institution (NHI).

Mean age of the attended women was of 27.4 years. Four hundred fifty-four (21.2%) were under 20 years, and 362 (16.9%) were over 35 years. From the full population, 1,358 (63.3%) women were referred from other hospitals or health units, 578 (26.9%) came directly from their homes and 209 (9.74%) from other services (Maternal-Fetal Medicine Service and Gynecology Service) of the same HMPMPS. Regarding the general cause of O-ICU admission, 1,010 (47.1%) were suffering from Hypertensive Diseases (HPDs), 405 (18.9%) of bleeding disorders and 115 (5.4%) of infectious complications (Table 2). Among the 1,010 women suffering from HPDs, the categories were preeclampsia/eclampsia: 640 (63.4%) and HELLP (haemolysis, elevated liver enzymes, low platelet count) syndrome: 370 (36.6%).

Table 1. Priority model classification

Priority level	Definition
High priority	Critical, unstable patients with potentially reversible conditions requiring intensive therapy (ventilatory support, vasoactive drugs), close and continuous observation. When reversibility and / or prognosis are uncertain, a limited therapeutic trial time can be given in the O-ICU. This category excludes patients with underlying chronic diseases and terminal patients.
I	a) Unstable patients requiring monitoring and / or treatment that can not be provided outside the ICU, b) Patients requiring mechanical ventilation and vasoactive drugs, c) Patients with shock, post-operative and Acute Renal Failure
II	a) Patients requiring intensive monitoring and may require immediate intervention, b) Patients with previous comorbid conditions who develop acute events.
III	a) Unstable patients, critically ill but who have reduced chances of recovery due to the underlying disease or the acute condition of the moment and can benefit from treatment in the ICU, b) They may receive intensive treatment to alleviate the acute complication, however, no extraordinary measures of support will be given as: cardiopulmonary resuscitation, endotracheal incubation, mechanical assisted ventilation, haemodialysis or high cost medication. Example of these: patients with cancer and superinfections.
IV	a) Patients who are generally not appropriate to admit to the ICU. Admission must be individualized under unusual and individualized circumstances under the supervision of the attending physician, intensivist or Chief of ICU, b) Little or no benefit from a low-risk intervention. "Too good to benefit from the ICU", c) Patients with terminal illness or imminent death. "Too sick to benefit from the ICU."
Low priority	a) This category includes patients at risk of requiring intensive therapy and patients with severe, irreversible and disabling medical conditions, b) Patients with chronic, irreversible or terminal illnesses who have suffered a catastrophic injury should be admitted only if there is opportunity for the patient to benefit from aggressive ICU management and if the patient and / or family members are prepared to accept the consequences of the necessary therapy.

Table 2. General characteristics of the patients

Variable	Value
Age (years)[a]	27.4 (± 9.4)
Mean arterial pressure (mmHg)[a]	90.9 (± 11.2)
Primary admission cause	
Hypertensive disorders[b]	1,010 (47.08%)
Obstetric haemorrhage[b]	405 (18.88%)
Infectious disorders[b]	115 (5.36%)
Others[b]	615 (28.67%)
Length of stay at the ICU (days)[a]	5.6 (± 5.9)
	Median: 4, ICR: 3

Use of amines[b]	612 (28.53%)
Use of mechanical ventilation[b]	695 (32.40%)
Use of antibiotics[b]	2,079 (96.92%)
Use of renal replacement therapy[b]	140 (6.52%)
Blood therapy[b]	1,265 (58.97%)
Admissions from the same Hospital[b]	209 (9.74%)
Admissions from other Hospitals[b]	1,358 (63.3%)

a: mean (± SD), b: frequency (%), IQR: inter quartile range

Among the 615 patients admitted for indirect obstetric causes, 62 (10.1%) had heart disease and 56 (3.9%) acute pancreatitis. Table 3 shows other causes of seeking medical attention at the O-ICU.

Table 3. Other diseases

Thyrotoxic storm	Invasive mole with carcinomatosis
Guillain-Barré Syndrome	Diabetic ketoacidosis and hyperosmolar hyperglycaemic state
Ulcerative Colitis	Organophosphorus pesticides poisoning
Cardiomyopathy	Systemic Lupus Erythematosus
Pulmonary Oedema	Amytrophic Lateral Sclerosis
Liver Abscess	Haemorrhages and strokes
Pericarditis	Antiphospholipid syndrome
Leukaemias	Collapsed Lung
Liver cirrhosis	Acute fatty liver of pregnancy
Tamponade	Paralysis associated to hypokalemia
Snake bite	Myelodysplastic syndromes
Budd Chiari Syndrome	Neurocystic ercosis
Status epilepticus	Ovarian hyperstimulation syndrome
Brain tumours	Cancer (kidney, lung, stomach)
Leptospirosis	Meningitis and encephalitis
Cardiac Arrhythmia	Mendelson Syndrome
Haemangiomatosis	Traumatic brain injury
Haemo mediastinum	Haemolysis post transfusion
Phosphine poisoning	Suppurative Thrombophlebitis

In the follow-up period, 100 (4.6%) patients died. From these deaths, 63 were admitted with Priority IV. The percentage of mortality excluding patients who entered with Priority IV was 1.63%.

Among the 1,530 women admitted for direct obstetric causes, there were 64 (4.2%) deaths. By contrast, there were 36 (5.8%) deaths among the 615 women admitted for indirect obstetric causes. By using this approach, the mortality rate among the 1,010

women with hypertension complications was 2.9% (30 deaths). Similarly, from 115 women admitted because of an infectious complication, 23 (20%) died of septic shock. In addition, there were 13 (3.2%) deaths in the group who had a haemorrhagic disorder on admission (N = 405). In the present context, twenty-five women died from other causes, including atypical pneumonia (nine patients), massive pulmonary thromboembolism (four patients) and cardiopathy (six patients).

The length of hospitalization varied from a few hours (0 days) to 84 days (mean 5.6 ± 6.0 days; median 4 days). It was also noted that Mechanical Ventilatory Support (MVS) was used in more than one-third of patients (N = 695, 32.4%), with 68,998 hours of use and in one case; the Extracorporeal Membrane Oxygenation (ECMO) was implemented.

The Pearson test showed the next significant correlations: Hb on admission with platelets on admission ($r^2 = 0.065$, P = 0.003), Hb on delivery ($r^2 = 0.467$, P ≤ 0.001), albumin on delivery ($r^2 = 0.066$, P = 0.003) and MAP ($r^2 = 0.181$, P ≤ 0.001); platelets on admission with platelets on delivery ($r^2 = 0.563$, P ≤ 0.001), Hb on delivery ($r^2 = 0.106$, P ≤ 0.001); platelets on delivery with Hb on delivery ($r^2 = 0.093$, P ≤ 0.001) and albumin on delivery ($r^2 = 0.139$, P ≤ 0.001); Hb on delivery with platelets on delivery ($r^2 = 0.151$, P ≤ 0.001) and there were negative correlations between MAP with platelets on admission ($r^2 = -0.102$, P ≤ 0.001) and platelets on delivery ($r^2 = -0.058$, P = 0.008).

The ROC curve taking into account age, Hb on admission, platelets on admission and MAP to predict mortality, showed the patient's age as the variable with the largest area under the curve (0.569), followed by the MAP (0.423) (Figure 1).

Figure (1)
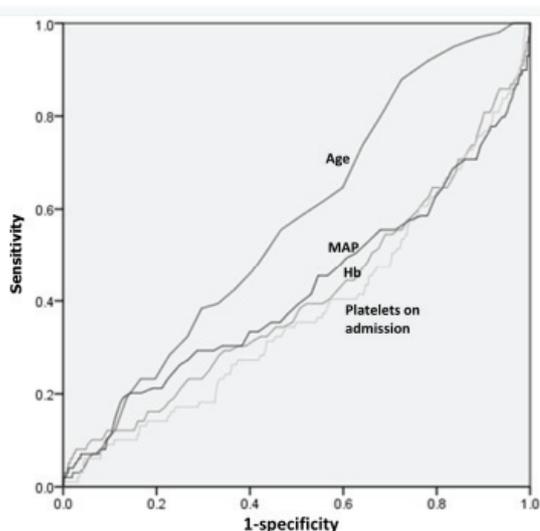
When constructing a model with the Cox regression, defining the "days of stay" as the variable time, the positive status was any case of mortality, and the covariates were age, Hb on admission, platelets on admission and MAP, a significant P value for platelets on admission and age (P = 0.010 and 0.026 respectively) was found. When doing this same model adding as strata the category of "dialysis treatment", the two covariates platelets on admission and age were significant (P = 0.039 and 0.029 respectively). Finally, when analyzing the variable "dialysis" or "use of amines" with multinomial logistic regression both were significant as predictors of mortality (P ≤ 0.001).

Discussion

The present study reports the finding of a tertiary obstetrical ICU; where over 70% of the patients were referred from a different hospital or healthcare facility. The incidence of 29.3 admissions per 1000 deliveries in this study was similar to the rate from a Brazilian study[2], being up to 16 times higher than the rate of developed countries[6].

This study further establishes a role for the main findings concerning the O-ICU admissions which contrasted with the results from other countries (Table 4). As expected, the incidence varies significantly between developed and developing countries, with rates reported from 1.3 up to 24 ICU admissions per 1000 deliveries. It can be seen that the rate of admission to therapy for each pregnancy was similar to that reported by Brazil[2], after making the adjustment excluding the patients referred from other medical units.

Table 4. Comparison among different countries

	Years of study	Admissions	Deliveries	Rate of Admission to an ICU	Deaths	Mortality rate (%)	Length of stay (days)	Age (years)
HMPMPS	7.75	2,145	73,625	29.1	100	4.6	5.6	27.4
Netherlands	2	847	358,874	2.36	29	3.5	2.9	
Hong Kong	10	50	37,505	1.3	3	6	2	31
Brazil	2	298	12,342	24.1	14	4.7	5	27.5
Argentina	2	242	30,052	8.1	5	2.0	2	31
India	3	765	61,615	1.24	119	15.5		
France	4	11,824	3,262,526	3.6	154	1.3	3	30.5
Sudan	1	99	5,400	18.3	22	22.2	3.8	
South Africa	5	138	14,478	9.5	48	35	8	28

HMPMPS: "Mónica Pretelini Sáenz" Maternal-Perinatal Hospital

It is clear from this study that the main cause of admission in this study was hypertensive disorders, followed by haemorrhagic complications; these outcomes are similar to those reported in Latin American countries, like Argentina and Brazil[2, 7]. By comparison, other studies report obstetric haemorrhage as the most common cause associated, like in Hong Kong and India[6, 8].

Despite the worldwide variation in the mortality rates, there is not a significant variation in the most common causes of admittance in the analysed studies, which includes hypertensive disorders and haemorrhage complications. Particularly, in the case of Mexico undesirable changes can be expected in the rates of admission and mortality after this survey due to financial reductions in the Health System that might compromise medical attention.

In the follow-up period of this study, the MMR was significantly lower than in other developing countries such as India and Sudan[8, 9] but higher than high-income countries such as the Netherlands and France[10, 11].

Globally, maternal mortality has declined significantly since 1990. While better access to emergency obstetrical care is partially responsible, women's empowerment might also be a contributing factor. Notwithstanding, over the last two decades, the MMR in the United States has doubled from 7.4/100,000 live births in 1986 to 14.5/100,000 today. As a response to this trend, that country has added the obstetric critical care simulation training[12]. The feasibility to introduce such training in other countries depends on the financial resources, which may be compromised by economic disparities[13].

An analysis in Slovak Republic reduces the MMR points due to decrease in the caesarean section rate and episiotomy[14]. In the case of our institution, it is not probable to reach a significant reduction in cesarean sections in a short term of time as the patients belong to the group of risk pregnancies. Furthermore, a delay in the decision to perform a cesarean section in cases of prolonged vaginal deliveries could be detrimental for the maternal evolution[15].

In relation to vital support, a total of 32.4% patients required MVS during their stay in the O-ICU, which was comparable to the rates from 20% to 30% reported by other groups[2, 10]. Of particular concern, the use of ECMO during pregnancy may be indicated in very select cases and should be delivered in centres with dedicated specialized units[16]. Unfortunately, our experience with only one patient restricts us to issue an enriching opinion.

Overall, the most common cause of pregnancy-related Acute Kidney Injury (AKI) in the O-ICU was eclampsia/HELLP syndrome (79/140, 56.4%), followed by chronic kidney disease exacerbation (24/140, 17.1%). As such, 112 (80%) women were discharged with improvement, 24 (17.1%) died and four (2.9%) were transferred to an NHI in Mexico City. Adding to the above-mentioned information, in the studied population, the requirement of dialysis was similar to rate reported by a Brazilian study (8%)[2] but considerably higher than in the Netherlands (1.9%)[10]. We suggest, therefore, that improving the quality of prenatal attention during pregnancy, paired with adequate management might help to reduce maternal morbidity and mortality related to AKI and this happens by making a correct evaluation of kidney function[17]. Much attention has to be focused on the fact that in the O-ICU, 76.64% of all deaths were patients referred from other hospital units with a fatal outcome independent of the established treatment; and the main causes of mortality were septic shock, followed by hypertensive complications and hypovolemic shock. As has been published previously, a threshold time of 12-h with sepsis before getting specialized medical attention, shows a good predictive value for maternal death and could be considered for evaluating the severity of complicated obstetrical patients[18].

Because infections, chronic hypertension, coagulopathies, and underlying prothrombotic conditions increase the risk of pregnancy-associated stroke (PAS) risk in women with preeclampsia, these women may warrant closer monitoring[19]. A very important aspect that cannot be omitted is the possible underdiagnosis of rare conditions or diseases that are not considered the first cause of hospitalization such as Peripartum cardiomyopathy (PPCM)[20].

According to the Pearson test, the negative correlation between platelets and MAP is to some extent expected if we think about the association between the main complications of pregnancy responsible for the highest mortality in the world, preeclampsia/eclampsia and HELLP syndrome that would precisely explain a decrease in platelets with cases of hypertension.

On the other hand, several early warning scores have been developed and proposed as a potential tool to reduce maternal morbidity and mortality, based on the identification of predetermined abnormal values in the vital signs or laboratory parameters, to generate a rapid and effective medical response[21, 22].

In Colombia, a country with similar characteristics to Mexico, Paternina-Caicedo *et al*[23] evaluated through the area under the ROC curve (AUC) an Obstetric Early Warning Score in 702 obstetric admissions to critical care. The AUC of the score in conditions directly related to pregnancy and postpartum was 0.87 (95% confidence interval, 0.79-0.95), while in indirectly related conditions the AUC was 0.77 (95% confidence interval, 0.58-0.96). While further work is required to define in detail the suitable variables for the construction of early warning scores in obstetrics, these scores may be a highly useful approach in the early identification of women at an increased risk of dying.

We cannot forget to mention that the socioeconomic level and type of health institution might be a limitation to extrapolate our results to richer countries and even to other health systems with more resources that also take care of wealthier people that live nearer to hospitals, than the poorest.

From the analysis done, it can be concluded that the most consistent variables for a bad prognosis in the O-ICU are age, MAP, platelet and haemoglobin at admission; so special attention must be paid to finding the causes that compromise their normal levels in pregnant and postpartum women, and they may be the crucial elements to adjust the forecast scales for pregnant women. Proper management of O-ICU patients requires intensive and multidisciplinary cooperation.

Acknowledgements

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