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Renal Finding of Severity in Preeclampsia Data from a High Specialty Center in Mexico City

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Abstract

Background: Serum creatinine >1.1 mg/dL is the finding of severity of preeclampsia that identifies compromised renal function in maternal disease.

Objective: To identify the incidence of serum creatinine >1.1 mg/dL as a finding of renal involvement in severe preeclampsia (SP).

Material and methods: A cross sectional study was carried out in a cohort of 100 pregnant patients with SP admitted to the Intensive Care Unit (ICU) in 2021. Their clinical records were consulted to find out the antepartum incidence of serum creatinine value >1.1 mg/dL. As complementary data, uresis ml/hour, need for dialysis, and maternal mortality were studied. Descriptive statistics (mean, median, standard deviation, range) and inferential statistics (paired Student's t-test) were used with the statistical program SPSS™ version 24.

Results: The general mean of serum creatinine was $0.79 \pm 0.24 \text{ mg/dL}$, 87% of the patients had serum creatinine $\leq 1.1 \text{ mg/dL}$ ($0.71 \pm 0.13 \text{ mg/dL}$, limits 0.40 to 1) and 13% of the patients values were >1.1 mg/dL ($1.30 \pm 0.15 \text{ mg/dL}$, limits 1.20 to 1.60), p=0.032. The means of uresis did not show a significant difference (p=0.839), the need for dialysis was 0% and maternal deaths 0%.

Conclusion: The incidence of serum creatinine >1.1 mg/dL as a renal finding of severity of preeclampsia was 13% without any cases requiring dialysis and without maternal deaths.

Keywords: Renal finding; Serum creatinine; Uresis; Acute kidney injury; Severe preeclampsia; Critical care in obstetrics

Introduction

The deterioration of renal function is part of the findings assessing the severity of preeclampsia. Experts from the North American region (Canada, United States, Mexico) recommend serum creatinine ≥ 1.1 mg/dL as the essential parameter to establish the existence of renal involvement in maternal disease [1-4].

Serum creatinine is an end product of creatine metabolism from muscle wasting and dietary meat. Its renal management involves glomerular filtration, absorption, and excretion in the second segment of the proximal convoluted tubule [5]. In normal pregnancy its value is 0.4 to 0.8 mg/dL. The serum creatinine concentration can be modified naturally by the effect of individual variables such as the protein content of the diet and maternal lean body composition, rest and walking or exercise of the patients and gestational changes in the internal environment. In severe preeclampsia (SP), the increase in its values depends on the toxic effects of circulating compounds of placental origin and hypertensive stress on the endothelial cells of the arterioles, glomerular capillaries, tubular epithelial cells, mesangial cells, and podocytes [6,7]. Over the years, serum creatinine >1.1 mg/dL has been accepted as a biomarker for the diagnosis of renal involvement in SP [1-4]. The issue is not new, but it is still being investigated because there is a need to periodically review the data from each center that cares for pregnant patients with SP to identify the incidence of kidney damage, their clinical setting, the outcome of kidney function, and the patient with the intention of adapting management strategies to reduce the effect of acute complications and the possibility of long-term sequelae. The objective of this study was to identify the incidence of cases with serum creatinine >1.1 mg/dL as a finding of renal compromise in pregnant patients with SP admitted to the Intensive Care Unit (ICU) of a highly specialized center of the Mexico City.

Material and Methods

A cross sectional study was carried out in pregnant patients with SP who were admitted to the ICU of the High Specialty Medical Unit, Gynecology and Obstetrics Hospital No. 3 of the National Medical Center "La Raza" of the Mexican Institute of Social Security, Mexico City in 2021. The diagnosis of SP was based on the recommendations of the American College of Obstetricians and Gynecologists (ACOG)



of the United States of America published in 2020 [2]. Patients of all ages were included and with any parity, comorbidities, gestational weeks, complications of preeclampsia, and with ICU medical notes and laboratory studies available in the clinical record. Patients with recurrent SP, eclampsia or HELLP syndrome, chronic kidney disease, chronic renal failure on dialysis, congenital or autoimmune nephropathy (eg: systemic lupus erythematosus), kidney transplant, chronic liver failure, malnutrition, urinary tract infections or cancer of any type were not included. The clinical records of all the selected patients were available, so there were no cases of deletion. All the patients began their clinical manifestations at least the week prior to their admission and went to the Family Medicine Unit or the General Hospital of the Zone corresponding to their home address for medical attention. Within the next 8 hours after their identification, they were sent to the tertiary care center that hosted this investigation, where they were evaluated in the Clinical Emergency Department and then they were admitted to the ICU, considering the high-risk pregnancy where they received the protocol for institutional management of SP (Table 1).

The records of 100 patients with pregnancy and SP who met the selection criteria were consulted to find out their general data that included age, parity, comorbidities, gestational weeks, prematurity (<37 weeks), presence of HELLP syndrome and/or eclampsia, systolic and diastolic blood pressure values upon admission to the ICU, termination of pregnancy (vaginal delivery, cesarean section), intrapartum bleeding, length of stay in the ICU, and maternal mortality. For research purposes, the incidence of finding renal compromise was

 Table 1: Antepartum pharmacological management for patients with

 severe preeclampsia in the Intensive Care Unit.

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All patients:			
Omenrazole 40 mg IV every 24 hours			
Methyldona 500 mg PO every 8 hours			
Hydralazine 50 mg PO every 6 hours			
Metoprolol 100 mg PO every 8 hours			
Management of hypertension refractory to initial antihypertensive			
drugs.			
Nifedipine 10 mg PO every 8 hours			
Prazosin 1 to 2 mg PO every 6 to 8 hours			
Management of hypertensive crises:			
Hydralazine 5 to 10 mg as an IV bolus every 30 minutes until blood			
pressure is controlled (<160/90 mmHg) or;			
Nifedipine 10 mg sublingually every 30 minutes until blood pressure is			
controlled (<160/90 mmHg)			
Cases with HELLP syndrome. Mississippi class 1 and 2:			
Dexamethasone 10 mg IV every 12 hours			
Cases with eclampsia (prevention and treatment):			
Magnesium sulfate 4 g IV in 60 minutes as an initial dose, then 1 g/hour			
s a continuous IV infusion or;			
Phenytoin sodium 10 to 15 mg/K weight/IV in 30 minutes as an initial			
dose, then 125 mg IV every 8 hours			
Management of hyperglycemia (glucose >160 mg/dL):			
Ranid insulin 5 to 10 U IV every hour until blood glucose is controlled			
(≤ 120 mg/dL)			
Management of low plasma colloid osmotic pressure (≤ 20 mmHg):			
25% human albumin solution 50 ml IV in 60 minutes every 8 hours	ı Ē		

IV: Intravenous; PO: Oral.

studied when the patients were admitted to the ICU considering the value of serum creatinine with the cut-off point >1.1 mg/dL [1-4]. As complementary data of interest, uresis (ml/hour), and the need for dialysis were also studied. For data analysis, descriptive statistical measures (mean, median, standard deviation, range) and inferential (paired Student's t-test) were used with the statistical program SPSS[™] version 24. Authorization was obtained from the Local Research Committee in Health and the Health Research Ethics Committee of the host hospital (Registration: R-2021-3504-34).

Results

Table 2 shows the general data of the 100 patients in the study. The age of most of the patients was in the fourth decade of life, 30% of them were over 35 years of age and 3% were under 18 years of age.

Table 2: General data.

Parameters	Results					
Age (years)						
mean ± sd	31 ± 7					
<18 years n=%	3					
>35 years n=%	30					
Parity median	2					
Comorbidities n=%						
None	39					
Diabetes mellitus type 1	1					
Diabetes mellitus type 2	4					
Gestational diabetes	8					
Arterial hypertension	17					
Primary hypothyroidism	6					
Interatrial communication	1					
Tricuspid insufficiency	1					
Pregestational obesity	23					
Gestational weeks mean ± sd	32.6 ± 4.33					
Prematurity (<37 weeks) n=%	78					
HELLP syndrome n=%	21					
Mississippi class 1	5					
class 2	9					
lass 3 7						
Eclampsia n=%	4					
Blood pressure mmHg mean ± sd						
systolic	164 ± 17					
diastolic	101 ± 14					
Termination of pregnancy n = %						
vaginal delivery	5					
cesarean section	95					
Intrapartum bleeding ml	470 ± 326					
ICU stay days						
overall average ± sd	2.05 ± 0.85					
87 cases with serum creatinine \leq 1.1 mg/dL	1.94 ± 1.62					
13 cases with serum creatinine >1.1 mg/dL	2.75 ± 1.67					
p value	0.096					
Maternal mortality n=%	0					

ICU: Intensive Care Unit; Sd: Standard deviation.

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Comorbidities were found in 61%, the main one was obesity (23%) followed by arterial hypertension (17%), and diabetes mellitus (type 1, type 2, gestational 13%). HELLP syndrome occurred in 21% and eclampsia in 4%. The general average of the weeks of pregnancy was located around 32 weeks and prematurity in 78%. Mean systolic and diastolic blood pressures exceeded 160 and 100 mmHg, respectively. The cesarean section was practiced in 95% for the end of the pregnancy, and the mean intrapartum bleeding was <500 ml. The stay in the ICU was around 2 to 3 days and no maternal deaths were recorded.

The overall mean serum creatinine was 0.79 ± 0.24 mg/dL. It was found that in 87% of the patients the serum creatinine value was ≤ 1.1 mg/dL and defined renal involvement with values >1.1 mg/dL was in 13% of the patients. Thus, the incidence of renal involvement in the retrospective cohort studied was 13%. The comparison of the serum creatinine means (≤ 1.1 vs >1.1 mg/dL) showed a significant difference (p=0.032). Table 3 when the means of uresis of the patients with renal compromise were compared with patients without renal compromise, no statistically significant difference was found (p=0.839). The need for dialysis was 0%.

Discussion

Evidence has been documented that the endothelium is the first maternal organ affected by preeclampsia [6,7]. Glomerular endotheliosis, electro-dense sub endothelial and mesangial deposits, structural alterations of the capillary and arteriole wall, increased glomerular cellularity, vasoconstriction, perivascular edema with capillary leak, capillary occlusion due to thrombosis and

Table 3: Serum	creatinine	concentration,	uresis an	d need for	r dialysis.
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Serum creatinine mg/dL	Results
All patients n=%	100
mean ± sd	0.79 ± 0.24
limits	0.24 to 1.60
value \leq 1.1 mg/dL n=%	87
mean ± sd	0.71 ± 0.13
limits	0.40 to 1
value >1.1 mg/dL n=%	13
mean ± sd	1.30 ± 0.15
limits	1.20 to 1.60
P value	0.032
Uresis ml/hour	
All patients n=%	100
mean ± sd	1.17 ± 0.70
limits	0.10 to 3.70
87 cases with serum creatinine \leq 1.1 mg/dL	
mean ± sd	1.17 ± 0.74
limits	0.10 to 3.70
13 cases with serum creatinine >1.1 mg/dL	
mean ± sd	1.22 ± 0.94
limits	0.20 to 3
P value	0.839
Need for dialysis n=%	0

microhemorrhages are the histopathological findings more frequent [8]. It has not been determined whether the kidneys are more susceptible than other target organs (brain, lungs, heart, liver) in developing endothelial damage from preeclampsia [9]. Furthermore, it has not been clearly established why only some of the pregnant patients with SP have impaired renal function. Predisposing factors for kidney damage include chronic hypertension, recurrent severe preeclampsia, HELLP syndrome, and eclampsia, but they do not account for acute kidney injury (AKI) in all cases [6-9].

The incidence of renal involvement as a finding of severity of preeclampsia can also be modified according to the temporality of preeclampsia (early or late) and the simultaneous damage to other target organs, as well as the delay in early identification and onset of antihypertensive pharmacological management and resuscitation with parenteral fluids, difficulties in accessing a specialized care center, the experience of the medical team, and the characteristics of the patients should be considered.

This complex scenario of polyvalent factors may justify the fact that the incidence of AKI in SP is highly varied in the different series. For example, it has been reported to be 15.3% by Conti-Ramsden FI, et al. [10] in a study carried out in 2019 that included 1547 patients from a hospital in South Africa while Hassan M, et al. [11] in 2022 reported the highest: 42.86% in a prospective cohort of 70 patients from the maternity ward of the Mbarara Regional Reference Hospital in Uganda. In the present investigation, a retrospective cohort of 100 patients with SP from the ICU of a high specialty center in Mexico City was studied. The age of the majority of the patients was in the fourth decade of life, 35% of the patients were considered to be of advanced age for pregnancy (>35 years), with a high percentage of prematurity, cardiovascular and metabolic comorbidities (obesity, arterial hypertension, various types of diabetes), severe complications of preeclampsia (HELLP syndrome, eclampsia) and very high systolic and diastolic blood pressure measurements when they were admitted to the ICU. However, the incidence of renal compromise as a severity finding was 13%, this is a very low frequency with some important particularities. For example, mean uresis was similar in patients with and without renal involvement, there were no cases requiring dialysis, ICU stay did not show a significant difference (p=0.096) and there were no maternal deaths. In general, the data show satisfactory results.

In our work center, the incidence of renal involvement in SP has been the subject of previous research. In 2019, it was reported to be 13.8% in patients admitted to the ICU and 8% in 2020 [12,13]. The average of both studies including the data of the present investigation is 11.33% (Figure 1). This frequency is lower than the 15.3% reported by Conti-Ramsden FI, et al. [10] in 2019 and 42.86% published in 2022 by Hassan M, et al. [11].

At the beginning of the 1990s, in the hospital where this study was conducted, the incidence of AKI exceeded 30% (90 cases/285 ICU patients/year) with a high percentage of cases requiring replacement therapy of renal function with hemodialysis (unpublished data). The incidence has been gradually reduced and has remained so, possibly due to the implementation of an institutional protocol for the diagnosis and management of preeclampsia-eclampsia (Clinical Practice Guideline, CPG) [4] consisting of the identification and transfer of the most serious cases to a tertiary care center that has a medical-surgical ICU with sufficient resources and a multidisciplinary medical team with experts in emergency obstetric surgery. In the ICU, pharmacological management to control blood pressure, cautious resuscitation with crystalloid fluids, transfusion therapy, correction

Sd: Standard deviation

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of complications, and scheduled termination of pregnancy are the foundations of therapy for patients with SP in the advanced critical stage. Table 1 the CPG has taken the recommendations issued by neighboring northern countries, and by experts from Mexico [1,2]. Multidisciplinary management has been implemented in the ICU with local modifications according to the available resources, the scientific evidence that has been generated periodically, and the experience accumulated by the hospital's medical-surgical team [3]. The systematic review of the results has been the key to the development of a continuous improvement plan [14].

The main strength of the research is the contribution of data towards the incidence of the renal finding of severity of preeclampsia, the description of the clinical environment of the patients and the protocol for their management in the ICU. The weaknesses lie in the study design because it is a relatively small retrospective cohort from a single hospital whose local results do not necessarily represent what is happening elsewhere in Mexico.

Conclusion

The incidence of serum creatinine >1.1 mg/dL as a renal finding of severity of preeclampsia was 13% without any cases requiring dialysis and without maternal deaths.

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