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Prevention and Management of Pre-Eclampsia and Eclampsia in Tertiary Care Hospital of Islamabad

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Abstract:

Pre-eclampsia is a syndrome that is usually defined as the onset of hypertension and proteinuria after 20 weeks of gestation in previously normotensive, non-proteinuric pregnant women. If untreated, pre-eclampsia progresses to a major neurological complication known as eclampsia. The aim of this study was to analyze the management of pre-eclampsia and eclampsia and to explore the role of clinical pharmacists in the prevention of pre-eclampsia and eclampsia. A prospective study of 20 patients on the management of eclampsia and pre-eclampsia was carried out at the Mother and Child Health Hospital PIMS, Islamabad. Data analysis showed that 75% of women have pre-eclampsia and 25% of women have eclampsia. The primary treatments given to the patients consisted of intravenous infusions of magnesium sulfate, methyldopa, and nifedipine. Of these, 60% received magnesium sulfate and 90% received oral methyldopa and nifedipine. The increased workload of nurses and physicians due to the increase in the number of patients with pre-eclampsia and eclampsia requires clinical pharmacists to work side-by-side with nursing staff and physicians, resulting in reduced morbidity and mortality, and improved quality of life for mothers and infants.

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INTRODUCTION

Pre-eclampsia is a syndrome that is usually defined as the onset of hypertension and proteinuria after 20 weeks of gestation in previously normotensive non proteinuria pregnant women (Higgins and de Swiet, 2001). It is also known as "the disease of the first pregnancy". Although clinical manifestations are variable, most are associated with other complications, such as abnormal liver function, coagulation disorders, renal complications, and cerebral ischemia. It occurs in 5-8% of pregnant women and is responsible for maternal and fetal morbidity and mortality (de Swiet, 2000). If untreated, Pre-Eclampsia progresses to a major neurological complication known as eclampsia. It is defined as a seizure or any other sign of altered consciousness that occurs in the context of pre-eclampsia and cannot be attributed to a pre-existing neurological disorder. Compared with pre-eclampsia, eclampsia presents a greater risk to mother and baby and is characterized by persistent headaches, vision changes, and eclamptic grand mal seizure. Pre-eclampsia is characterized by the presence of hypertension and proteinuria.

Since hypertensive disorders other than eclampsia, such as gestational hypertension and chronic hypertension, also exist during pregnancy, the second most important feature that distinguishes pre-eclampsia from other hypertensive disorders is proteinuria. Globally, more than half a million women die each year from pregnancy-related causes, with 99% of these deaths occurring in developing countries (Karlsen *et al.,* 2011). In the UK, 1 in 50 of the women who have eclampsia die (Duley, 2009).

The incidence of eclampsia is also high in developing countries (1.6 per 1000 live births in Colombia and 12 in India) (López-Jaramillo *et al*., 2001). The major clinical features of pre-eclampsia are hypertension and proteinuria. First, it was defined as a rise in systolic blood pressure >30 mmHg or diastolic blood pressure >15 mmHg. Pre-eclampsia was later redefined in 2000 by the National Hypertension Education Program (NHBPEP) as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg after 20 weeks of gestation (Noris *et al.,* 2005). In nulliparous women, the factor that identifies and differentiates between pre-eclampsia and gestational hypertension is proteinuria, defined as ≥0.3 g of protein in a 24-hour urine sample (Noris *et al*., 2005).

Clinical and laboratory tests are used to access the severity of pre-eclampsia. Clinical manifestations of preeclampsia include hypertension, proteinuria, persistent severe headache, epigastric pain, visual disturbances, and vomiting; findings of hyperreflexia, tenderness, edema, thrombocytopenia, hemolytic anemia, ALT and AFTs cannot be ignored (Impey and Child, 2017). Complications of pre-eclampsia not only affect the central nervous system, but also disturb the renal system, leading to renal cortical and tubular necrosis, pulmonary and laryngeal edema, and maternal liver function and coagulation disturbances. Placental complications include placental infarction and abruption leading to intrauterine growth restriction, preterm birth, or death (Impey and Child, 2017). Investigation of mother and fetus to monitor and test for complications. If dipstick urinalysis shows proteinuria, infection is excluded by urine culture. A collected 24-hour urine protein concentration > 0.3 g/L confirms the diagnosis. It is possible that proteinuria may not be present early in the disease, so the proteinuria will be repeated (Impey and Child, 2017).

Clinical examination of a pre-eclamptic patient should include regular B.P measurement. Mother should be screened for edema, weight gain, cardiomyopathy and acute renal failure should be examined. A fetal ECG is necessary to ensure and assess fetal health (health) with examination of the placenta (Program NHBPE 2000).

Laboratory tests include: complete blood chart, clinical biochemistry, and LFTs tests to identify HELPP syndrome. Urea and creatinine assessment and screening for 24-hour proteinuria should be performed, PT and APTT are required to assess coagulation profile (Program NHBPE, 2000). Other examinations include Ultrasound scan to estimate fetal growth

with Doppler velocimetry of the umbilical, cerebral and uterine arteries.

Correct assessment of all pre-eclampsia and eclampsia major factors that need to be prevented. People with preeclampsia may lower their risk of high blood pressure if they rest at home for four hours a day, according to a pilot study but again data is sparse to show strong evidence that by taking more rest and exercise can reduce the risk of pre-eclampsia (Jørgensen *et al.,* 2006). Life style changes depend upon women's personal needs and preference.

Dietary supplements containing at least 1 gram of calcium per day reduce relative risk of pre-eclampsia but have no apparent effect on risk of stillbirth or death in infants before discharge (9 trials, 6763 babies; relative risk 1.04, 95% confidence interval 0.65 to 1.66) (Hofmeyr *et al*., 2018). No apparent effect of high energy intake or protein supplementation on the prevalence of preeclampsia was noted. There is also no evidence that low salt intake during pregnancy has any effect on the patient's condition. Antioxidants seem to reduce the risk of pre-eclampsia, primarily Vitamin C and E should be used in diet to improve health and minimize the risk factors of pre-eclampsia (Duley *et al*., 2006). This seems to be associated with an increase in preterm birth (3 trials, 585 women; relative risk 1.38, 1.04 to 1.82) with no proven efficacy. Hypertension is uncommon in the first half of pregnancy, but occurs in about 10% of pregnancies after 20 weeks. Secondary prevention of pre-eclampsia depends upon antihypertensive drugs. Most commonly used drugs are methyldopa, labetalol and calcium channel blockers (Abalos *et al*., 2018). In pre-eclampsia patient Antihypertensive drugs are given if B.P reaches 170/110 mmHg (Impey and Child, 2017). Oral nifidipine is used for initial control, methyldopa for maintenance in pre-eclampsia patients. Diuretics do lower blood pressure in non-pregnant women, but are no longer recommended for gestational hypertension. Atenolol is avoided due to fetal growth restriction. ACE inhibitors and Angiotensin receptor antagonists are contraindicated in pregnancy.

Eclampsia, considered a complication of severe pre-eclampsia, is usually defined as new onset of grand mal activity and/or unexplained coma during pregnancy or postpartum in a woman with signs or symptoms of pre-eclampsia (Mattar *et al*., 2000; Warrington, 2015). It typically occurs during or after the 20th week of gestation or in the postpartum period.

Most cases of eclampsia occur in the third trimester, with approximately 80% of eclamptic episodes occurring during or within the first 48 hours after delivery. Rare cases reported before 20 weeks gestation or 23 days postpartum (Douglas and Redman, 1994). Eclampsia is characterized by 1 or more seizures, each lasting 60-75 seconds. The patient's face may initially be deformed, the eyes may protrude, and the mouth may blister. Respiration ceases for the duration of the seizure (Nodler *et al*., 2009). Eclamptic seizures may be divided into 2 phases. Phase 1 lasts 15-20 and seconds begins with facial twitching (Chia and Huang, 2010). The body becomes rigid, leading to generalized muscular contractions. Phase 2 lasts about 60 seconds. It starts in the jaw, moves to the muscles of the face and eyelids, and then spreads throughout the body. The muscles begin alternating between contracting and relaxing in rapid sequence (Nodler *et al*., 2009). A coma or period of unconsciousness, lasting for a variable period, follows phase 2. After the coma, the patient may regain some consciousness and she may become aggressive and very agitated. However, the patient has no recollection of the seizure.

A tonic-clonic seizure is followed by a period of hyperventilation. This compensates for the respiratory and lactic acidosis that occurs during the apnea phase (Banerjee *et al*., 2009). Seizure-induced complications can include tongue biting, head trauma, broken bones, and aspirations. The aim of this study was to analyze the cause of eclampsia and pre-eclampsia and the effectiveness of treatment given in Pakistan.

MATERIAL AND METHODS

A prospective (descriptive cross-sectional) study was carried out to study the management of eclampsia and pre-eclampsia in Pakistan Institute of Medical Sciences, Islamabad. The Pakistan Institute of Medical Sciences, Islamabad was selected for this study and patients from MCH were chosen as the study population. 20 patients were observed with pre-eclampsia and postpartum eclampsia and data was collected according to the patient's medical history, current situation and medication. Data on both pre-eclampsia and eclampsia patients and both pregnant and postpartum women with pre-eclampsia were collected during weekly visits to PIMS Hospital. Patients were observed and their files including the patient's medical history, laboratory tests, and all medications given were properly checked. Outpatient data was collected while patients were visiting MCH's OPD for routine checkups. The data was collected in two parts once a week, the first data collection session was September 2021-January 2022 and the second session was February 2022 to June 2022.

RESULTS

Data analysis shows that there were 75% females suffering from pre-eclampsia and 25% suffering from eclampsia (Table 1).

Table 1. Number of drugs for eclampsia and pre-eclampsia.

Disease condition	Number of cases
Pre-eclampsia	15
Eclampsia	5

Our results showed that 10% of patients were diagnosed with pre-eclampsia at age 15-20, while 15% were diagnosed at age 21-25, 30% at age 26-30, 40% at age 31-35, and 5% at age 36-40 years (Figure 1).

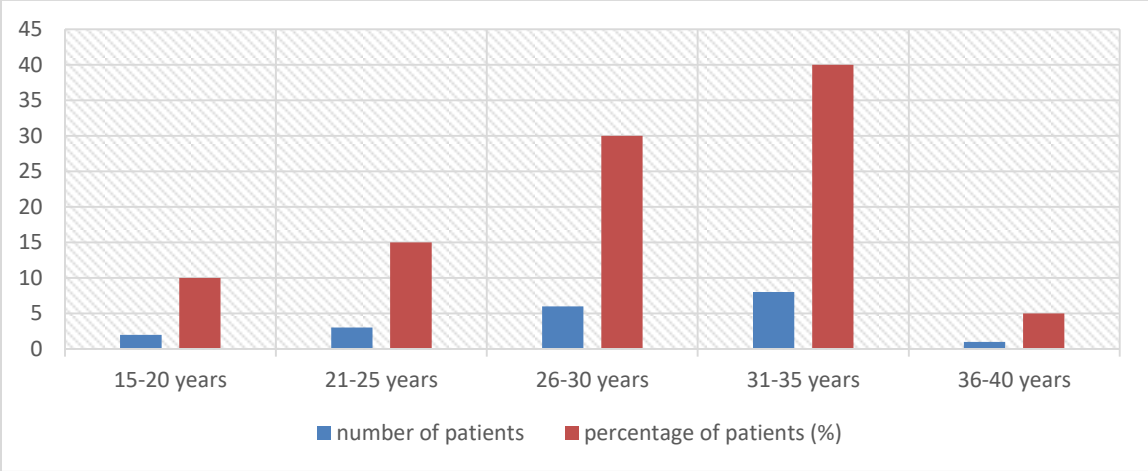

Fig. 1. Patients diagnosed as pre-eclamptic or eclamptic among different age groups.

Results of our data analysis showed the average number of pre-eclampsia medication drugs was 5, and the average number of eclampsia medication drugs was 6.6 (Table 2).

Table 2. Average number of drugs for eclampsia and pre-eclampsia.

Disease condition	Average number of drugs
Pre-eclampsia	5
Eclampsia	6.6

Number and percentage of patients with preeclampsia and eclampsia-related comorbidities are presented in table 3. 33% of patients were suffering from edema, 33% from pulmonary embolism, 17% with oligohydraminosis and 17% with gestational diabetes mellitus. Commonly prescribed brands were Aldomet, Adalat, Flagyl, Synto and Sulzone (Table 4).

Table 3. Number & Percentage of patients having co-morbidities associated with Pre-eclampsia and eclampsia.

Co morbidities	Pre-eclampsia patients	Eclampsia patients	Percentage of patients
Edema	2	0	12.5%
Pulmonary Embolism	2	1	18.75%
Oligohydramnios	1	0	6.25%
Gestational Diabetes Mellitus	1	0	6.25%

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Table 4. Number and percentage of drugs prescribed for Pre-eclampsia and Eclampsia.

Sr. No.	Generic Name	No. of patients using drugs	Percentage of patients using the drug (%)	No. of Pre-eclamptic patients using the drug	No. of Eclamptic patients using the drug
1	Inj. $MgSO_4$	12	60	9	3
2	Tab. Methyldopa	18	90	14	4
3	Tab. Nifidipine	18	90	14	4
4	Inj. Dexamethasone	8	40	6	1
5	Inf. Ringer Lactate	11	55	10	1
6	Inj. Mannitol	4	20	0	4
7	Inj. Furosemide	1	5	1	0
8	Inj. Cefoperazone + Sulbactam (Sulzone)	2	10	2	0
9	Inj. Labetalol	3	15	3	0
10	Inf. Oxytocin (Synto)	3	15	3	0
11	Inj. Ceftizoxime	1	5	0	1
12	Inf. Dextrose	1	5	0	1
13	Inj. Diazepam	3	15	0	3
14	Inf. Co-amoxiclav	1	5	0	1
15	Inj. hydrocortisone	1	5	0	1
16	Inj. Valproic acid	1	5	0	1
17	Tab. Paracetamol	4	20	4	0
18	Inj. Nalbuphine	1	5	1	0
19	Tab. Cefadrine	4	20	2	2
20	Tab. Metronidazole	6	30	4	2
21	Inj. Insulin	3	15	3	0

DISCUSSION

Our survey is quantitative type being conducted in MCH of Pakistan Institute of Medical Sciences, Islamabad (PIMS). The data collected includes the patient's demographic information, previous and current history of patients including gestational history, allergic history and socio-economic status. Due to the availability of proper medications and facilities, most of the patients were referred from primary or secondary care hospitals to tertiary care.

According to the results, more women were prone to pre-eclampsia i.e.; 75% patients were suffering from Pre-eclampsia and 25% patients were from Eclampsia. Among them, women above 30 years of age are more likely to have these disorders due to multiple pregnancies. Same type of study in Taiwan had observed that 58.9% patients suffered from pre-eclampsia. Maternal age >35 and twin pregnancy were significant risk factors for developing pre-eclampsia with worse complications in patients with placental abruption, acute renal failure, pulmonary edema, postpartum hemorrhage, pleural effusion, preterm labor, intrauterine growth retardation, stillbirth, neonatal mortality and low birth weight infants (Chen *et al*., 2000).

Different preexisting co-morbidities can exacerbate the complications of pre-eclampsia. Women with co-morbidities receive earlier intervention than women without co-morbidities, which may lead to fewer maternal complications but worse neonatal outcomes (Tanner *et al*., 2021).

Magnesium sulphate is the first-line drug treatment for seizures (eclampsia) and for recurrent seizures. Magnesium sulfate reduces maternal mortality compared with diazepam (Duley *et al*., 2010a). Use of $MgSO_4$ significantly reduces morbidity associated with pneumonia, mechanical ventilation, and intensive care unit admission compared with phenytoin (Duley *et al*., 2010b). Both intravenous and intramuscular routes of administration have been used effectively.

The major roles of clinical pharmacists in tertiary care hospitals includes dose adjustments (Cohen *et al*., 2009), processing of prescription to avoid possible drug interaction, monitoring of vitals and proper patient counseling but in PIMS majority of activities are performed by nursing staff in collaboration with physicians and Pharmacists but the proper clinical setup is lacking. However, the proper provision of all the medications under the supervision of hospital pharmacist was observed. Due to lack of clinical setup the patients were suffering regarding proper drug dose adjustments and proper consoling.

CONCLUSION

Due to increased number of pre-eclamptic and eclamptic patients, the workload on the nurses and physicians has increased so, that presents a problem for the proper management of the patients. This requires clinical pharmacists to work side-by-side with nursing staff and physicians in accordance with international standards, thereby reducing morbidity and mortality and improving patients' quality of life.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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