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PRE-ECLAMPSIA PRESENTATION AND MANAGEMENT

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Abstract:

Background: *Pre-eclampsia a major source of global morbidity and mortality, it is a multisystem disorder which complicates 3%-8% of pregnancies in the western world. Overall, pre-eclampsia and eclampsia are directly associated with 10%-15% of maternal deaths. Genetical and immunological risks are hypothesized to be linked supported by some epidemiological findings. A previous maternal history of this disorder increases the risk of pre-eclampsia 2-fold to 5-fold higher in pregnant women. Depending on ethnicity, incidence rate of pre-eclampsia ranges from 1% to 3% in women who had multiple previous pregnancies and 3% - to 7% in healthy women who never had a pregnancy.*

Aim of work: *In this article, we highlight the pathophysiology, treatment and prognosis of pre-eclampsia disorders in pregnancy.*

Methodology: *We conducted this review using a comprehensive search of MEDLINE, PubMed, and EMBASE, January 1985, through February 2017. The following search terms were used: pre-eclampsia, pathophysiology of pre-eclampsia, clinical presentation of pre-eclampsia, management of pre-eclampsia.*

Conclusions: *Pre-eclampsia is considered a rare condition that appears during pregnancy with an unpredictable course that accompany with severe consequences for the mother and the fetus. Delivering the baby is the only cure to this condition. Likewise, recognizing delivery criteria in the event of pre-eclampsia is critical to ideal management. current research centers around the forecast of onset of pre-eclampsia or even severe pre-eclampsia in order to allow early management and enhance the morbidity and mortality related with this disease. specific instruments for secondary prevention should likewise be developed for recurrent pre-eclampsia.*

Key words: *pre-eclampsia, pregnancy disorders, hypertensive disorders of pregnancy.*

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INTRODUCTION:

Pre-eclampsia a major source of global morbidity and mortality, it is a multisystem disorder which complicates 3%-8% of pregnancies in the western world. Overall, pre-eclampsia and eclampsia are directly associated with 10%-15% of maternal deaths. Genetical and immunological risks are hypothesized to be linked supported by some epidemiological findings. A previous maternal history of this disorder increases the risk of pre-eclampsia 2-fold to 5-fold higher in pregnant women. Depending on ethnicity, incidence rate of pre-eclampsia ranges from 1% to 3% in women who had multiple previous pregnancies and 3% - to 7% in healthy women who never had a pregnancy [1].

Over the past years the criteria that help define pre-eclampsia have not changed. These are: onset at >20 weeks' gestational age of 24-hour proteinuria ≥30 mg/day or, if unavailable, a protein concentration ≥30 mg (≥1+ on dipstick) in a minimum of a two randomized samples of urine taken at least 4–6 hours however, these samples should not exceed 7 days apart, a diastolic blood pressure ≥90 mmHg or systolic blood pressure >140 mmHg as measured twice, using a sphygmomanometer, 4–6 hours and less than 7 days apart, and disappearance of all these abnormalities before the end of the 6th week postpartum. nevertheless, other presenting pregnancy-related hypertension in addition to clinical or laboratory abnormalities or intrauterine growth restriction must be added as a potential pre-eclampsia [2].

METHODOLOGY:

• Data Sources and Search terms

We conducted this review using a comprehensive search of MEDLINE, PubMed, and EMBASE, January 1985, through February 2017. The following search terms were used: pre-eclampsia, pathophysiology of pre-eclampsia, clinical presentation of pre-eclampsia, management of pre-eclampsia

• Data Extraction

Two reviewers have independently reviewed the studies, abstracted data, and disagreements were resolved by consensus. Studies were evaluated for quality and a review protocol was followed throughout.

The study was approved by the ethical board of King Abdulaziz University Hospital

Pathophysiology

While pregnant with the baby, the inner third of the myometrium is invaded by the villous cytotrophoblast, most of muscle fibers and endothelium of spiral arteries are lost. Some functional alterations are accompanied with these structural modifications, such as spiral arteries becoming low resistant vessels, and therefore becoming less sensitive, or rather insensitive, to vasoconstrictive substances.

Abnormal placentation is the main cause in the complex pathophysiology of pre-eclampsia. Observation during pre-eclampsia shows defective spiral arteries invading cytotrophoblast cells. Some trials of late have determined that uterus getting invaded by cytotrophoblast is actually a unique differentiation pathway where fetal cells adopt certain attributes of the maternal endothelium they normally replace. This differentiation methodology is interrupted in pre-eclampsia. Nitric oxide a major contributor in the abnormality whom main function is to control vascular tone furthermore, embryo implantation can be prevented by inhibition of maternal synthesis of nitric oxide [3]. Oxidative stress and chronic placental ischemia can occur due to induced high sensitivity to vasoconstriction by increased uterine arterial resistance. Few fetal complications can happen due to this chronic placental ischemia this include intrauterine growth retardation and intrauterine death. In parallel, free radicals, oxidized lipids, cytokines, and serum soluble vascular endothelial growth factor release can be induced by oxidative stress. Dysfunction of the endothelium with vascular hyperpermeability, thrombophilia, and hypertension are the outcome of these abnormalities, in order to compensate for the lowered flow in the uterine arteries which is caused by vasoconstriction [4].

Major clinical signs observed in the mother such as, impairment of the hepatic endothelium contributing to onset of the HELLP (Hemolysis, Elevated Liver enzymes and Low Platelet count) syndrome, impairment of the cerebral endothelium inducing refractory neurological disorders, or even eclampsia are different examples of endothelial examples. Proteinuria pathophysiology includes, depletion of vascular endothelial growth factor in the podocytes making the endotheliosis more able to block the slit of diaphragms in the basement membrane, contributing to decreased glomerular filtration. In the end, microangiopathic hemolytic anemia, and vascular hyperpermeability accompanied with decreased serum albumin causing edema in the lower limbs or lungs are promoted by this endothelial dysfunction.

Abnormal placentation, is the primary mover of pre-eclampsia. Linkage of genetic and immunological

theories are common theories known. Various susceptible genes may contribute in pre-eclampsia appearing. These genes may interact in the hemostatic and cardiovascular systems, in addition to the inflammatory response. angiotensinogen on 1-q42–43 and eNOS on 7q36; other main important loci include 2p12, 2p25, 9p13, and 10q22 are of the few genes that were identified, and in candidate genes studies have given evidence of linkage to various genes [5].

Prevention of recognition of fetoplacental unit from maternal immune system is perceived as pre-eclampsia. Due to the over production of immune cells causing secretion of tumor necrosis factor alpha which in turn induces apoptosis of the extravillous cytotrophoblast [6]. In pre-eclampsia decreased levels of HLA-G and HLA-E also play a major role in the defective invasion of the spiral arteries. During normal pregnancies, natural killer cells secrete vascular endothelial growth factor and placental growth factor which in turn induce the interaction between these cells and the trophoblast. In women with pre-eclampsia, soluble fms-like tyrosine kinase 1 (sFlt-1), an antagonist of vascular endothelial growth factor and placental growth factor were found to be increased [7]. Accordingly, assays of sFlt-1, placental growth factor, endoglin, and vascular endothelial growth factor, all of which elevate 4–8 weeks prior to onset of the disease, may be helpful predictors of pre-eclampsia. Heme oxygenase 1 and its metabolite, carbon monoxide are shown to have a protective role in a recent data in pregnancy, which will be identified as a potential target in the treatment of pre-eclampsia [8].

Clinical Presentation

One of the clinical signs pregnant women present with is a new-onset hypertension when previously normal, with systolic and diastolic blood pressure readings of ≥140 and ≥90 mmHg, respectively, on two separate occasions that are at least 6 hours apart, along with proteinuria that appear after 20 weeks of gestation [9].

Classification of PE can be whether mild or severe depending on the severity of the symptoms during presentation while onset can be divided to early onset (PE starting before 34 weeks of gestation) or late onset (after 34 weeks of gestation). When PE becomes severe, a great blood pressure increase in addition to a greater degree of proteinuria are noted. Symptoms that can accompany PE include oliguria (less than 500 mL of urine in 24 hours), cerebral or visual disturbances, and pulmonary oedema or cyanosis [10].

additionally, symptoms of PE can appear either insidious or fulminant since few women can be asymptomatic at start, even after the appearance of hypertension and proteinuria, while others can present symptoms of severe PE initially. In the end normal fetal growth can occur, although this condition can present as maternal disorder only, otherwise it may lead to intrauterine growth restriction or acute fetal distress [11].

Complications seen by obstetricians are commonly presented by hypertensive disorders of pregnancy, and they are all accompanied with greater rates of maternal and fetal mortality and morbidity. chronic hypertension, PE, PE superimposed on chronic hypertension, and gestational hypertension are all included in this category of disorders. When physicians are able to differentiate PE from other hypertensive disorders of pregnancy, diagnosis becomes easier although the etiology and pathology of these disorders vary [12].

In chronic hypertension, the increase in blood pressure may predate the pregnancy, be discovered before 20 weeks of gestation, or else be present 12 weeks post-delivery. This contrasts with PE, which is known by the existence of increased blood pressure and proteinuria after 20 weeks of gestation. Once cases become severe, an evolution into eclampsia can occur from PE which is a severe complication that is characterized by new-onset of epileptic seizures (generalized convulsions), due to angiospasms in the brain and brain edema, in a woman with PE. One significant cause of maternal death in eclampsia is the result of cerebral hemorrhage, where eclampsia usually happens in the second half of pregnancy [13].

new-onset proteinuria (or by an acute elevation in the protein level if proteinuria was already present), a sudden elevation in blood pressure (assuming proteinuria already exists), or the development of the HELLP (hemolysis, elevated liver enzyme, low platelet count) syndrome are characteristics of superimposed PE on chronic hypertension. In the end, factors which can distinguish gestational hypertension from PE is the presence of elevated blood pressure after 20 weeks of gestation, which normalizes within 12 weeks after delivery, together with the absence of proteinuria [10].

Management of pre-eclampsia

Preeclampsia management has not changed much, probably due to the fact of the poor understanding of condition and poor progress. early detection, prevention of preeclampsia, and treatment are the 3 categories of management. Women who are considered to be at high risk of preeclampsia (such as

those with chronic hypertension, coexisting renal disease, or antiphospholipid syndrome should be referred for evaluation before pregnancy to diagnose modifiable risk factors). Management may include stop of smoking, nutritional advice, adjusting medications to provide a better medical condition such as preexisting renal disease, and avoiding the potentially teratogenic agents such as warfarin and ACE inhibitors. Recording blood pressure, platelet function, renal function (plasma creatinine and urinary protein/creatinine ratios), and liver function is a must. pre-pregnancy evaluation and management can reduce risk of developing preeclampsia. High risk pregnant women should be given low-dose aspirin prior to 12 weeks gestation until 36 weeks gestation. for women with low-calcium diets, calcium supplementation (≥1 g/day) is associated with a significant reduction in the risk of preeclampsia [10].

There is no ideal antenatal program of care that has been demonstrated for women at high risk of preeclampsia. However, these women are often seen more frequently antenatally and management includes an early accurate dating scan, anomaly scan, regular (4 weekly to weekly depending on risk factors and gestation) blood pressure and urine checks, and 4 weekly growth assessments to monitor for fetal growth restriction if preeclampsia is detected. Nulliparity is one of the risk factors of preeclampsia, usually women have not preexisting comorbidities. therefore, regular antenatal check-ups are recommended to detect hypertension and proteinuria until better widespread predictive tests are accessible, which can be used to subdivide women into high- and low-risk groups. Depending on the individual hospital policy it is not yet clear whether mild preeclampsia is best managed in hospital or as an outpatient.

To ensure optimal care, general measures once severe preeclampsia has been diagnosed consist of admission and consideration for transfer to a high dependency care unit or delivery suite with multidisciplinary team input including obstetrics, anesthetics, hematology, and neonatology. Protocols should be agreed upon and implemented to make sure of the best care given. In the same manner, any decision for an intervention with medication should consider side effects profile, contraindication, and dosing considerations per local formulary guidelines. Steroids ought to be considered to decrease the risk of respiratory distress syndrome if delivery by cesarean section is arranged or if the embryo is preterm. baseline examinations must incorporate serum electrolytes (Na, K, urea, creatinine, and uric acid), liver function tests (observing specifically for increased transaminases), full blood count (checking for thrombocytopenia and hemolysis), clotting (particularly if liver function tests are abnormal), and group and save serum. To ensure a correct diagnosis of preeclampsia Urinary protein/creatinine ratio or 24-hour urine collection should be obtained to assess the degree of renal impairment along with serum urea and creatinine. All tests ought to be checked day by day, or more frequently if unusual and interpreted with reference to ordinary values in pregnancy. When severe eclampsia occur, blood pressure and pulse must be estimated at regular intervals (15 minutes) until settled – then half hourly. Risk of fluid overload can be reduced with maintenance of careful hourly fluid balances. When needed, an indwelling catheter must be inserted. vital signs ought to be estimated at normal intervals; respiratory rate estimated hourly and temperature estimated every 4 hours. Careful assessment should be done on fetal well-being with cardiotocography and growth scan, liquor assessment, and umbilical artery doppler [14].

The correct level at which antihypertensive treatment is started is vague however a blood pressure ≥160/110 mmHg ought to be viewed as a medical emergency because of the risk of stroke. The point of antihypertensive treatment is to lessen blood pressure to <160/105 mmHg (mean arterial pressure <125 mmHg). Blood pressure may drop all of a sudden on beginning of treatment; thus, dosage ought to be titrated gradually to abstain from affecting uteroplacental circulation, which may result in fetal distress. Antihypertensives which are given orally incorporate methyldopa, labetalol, and calcium antagonists, for example, nifedipine. For acute treatment of hypertensive crisis, intravenous drug might be required. Once more, protocols which are national and local must be followed and in place. A mixed alpha/beta adrenergic antagonist such as labetalol, is the first antihypertensive agent of choice. Two doses can be controlled orally. There should be a period of 30 minutes that elapses before giving a second oral dose. If oral treatment neglects to inspire a response or is inadequately endured, continue to give an intravenous bolus. Infusion of labetalol should be continued through syringe pump following the bolus dose if needed. Severe asthma is the principal contraindication for giving labetalol. The medication is cautioned in cardiac illness. a direct-acting smooth muscle relaxant such as hydralazine is the second antihypertensive medication of choice. Every 5 minutes a bolus infusion can be given with constant monitoring of blood pressure. A basal mixture can be followed. Confirmation of all doses must be done with updated formulary and pharmacy

locally. During management of severe preeclampsia continues fetal monitoring is appropriate [15].

To prevent eclampsia magnesium sulfate is the chosen drug. Drugs such as diazepam are not appropriate in the prevention of convulsions (eclampsia) and is an accepted fact, after 24 hours of delivery a loading dose of 4g of MgSO4 is given, followed by a maintenance infusion of 1g/hour. hourly assessment of urine output and respiratory rate, and reflexes checked every 4 hours, documented medical assessment should occur at 4 hourly intervals and all patients should have continuous pulse oximetry. Stopping or reducing magnesium treatment must happen if biceps reflex is absent or respiratory rate is below 12 per minute [14].

MGSO4 side effects consist of: paralysis, absence of reflexes, depression of respiratory drive, and arrhythmias. The restorative treatment for toxicity is 10 mL 10% calcium gluconate, which ought to be given gradually intravenously. around 97% of MgSO4 is cleared by the kidneys; thus, oliguria (<80 mL/24 hours) can prompt toxicity. During presence of oliguria, abnormal liver function tests, or more seizures, MgSO4 levels should be monitored, targeting for 2-4 mmol/L as a therapeutic range. Due to reduced plasma volume and increase risk of pulmonary edema, fluid management should be closely checked. exceeding 80 mL/hour (approximately 1 mL/kg/hour) should not be reached as a total input. One substance which is included as a part of total fluid input is oxytocin, and should be used at high concentrations when needed. Oliguria must not precipitate any singular intervention, save to encourage early labor [14].

Labor Is the only cure for preeclampsia, which should be done only when the mother has been on state of stability. The HYPITAT trial: is a multicenter, open-label randomized controlled trial, pregnant women selected in random with gestational hypertension or mild preeclampsia to induction of labor vs expectant monitoring post 36 weeks gestation. They exhibited that 117 (31%) pregnant women who had delivery induced suffered a poor maternal result compared with 166 (44%) checked expectantly (RR: 0.71, 95% CI: 0.59– 0.86, P<0.001). Therefore, they advocate induction of delivery past 37 weeks' growth [16].

In complications such as fetal distress, inability to control maternal blood pressure, eclampsia, worsening biochemistry, or worsening maternal symptoms delivery is recommended prior to this. It is only advisable to deliver with cesarean section when gestational age is <32 weeks. Vaginal delivery is considered when gestational age exceeds 34 weeks. Vaginal prostaglandin gives better chances of successful delivery. Throughout assessment and delivery, management with antihypertensive drugs should be maintained. 5 IU of intravenous oxytocin is considered in the management of the third stage, not ergometrine or oxytocin/ergometrine, which can cause a hypertensive crisis.

Women who had gestational hypertension should follow up after delivery to ensure full resolution of their hypertension. Women who had suffered from preeclampsia must be advised of future risk of developing increased risk of cardiovascular and renal disease later in life. discharge ought to be followed by regular participation with a general expert so blood pressure can be closely observed.

Women who have been diagnosed with severe preeclampsia are bound to encounter recurrence in their next pregnancy; nevertheless, the phenotype is ordinarily less severe, with symptoms around 2– 3 weeks later in gestation. Testing for antiphospholipid syndrome should be done when pregnant women suffer severe early onset preeclampsia, specifically if complicated with growth restriction or late fetal loss. It might be important to talk about the ramifications of these outcomes on future pregnancies. On a similar matter, women who have encountered severe preeclampsia complicated by stillbirth or abruption of placenta, might need to be tested for factor V Leiden, protein S, protein C, hyperhomocysteinuria, and antithrombin deficiency; nevertheless, the effect of these diseases on future pregnancies is not completely understood.

Pre-calculated counseling should to be offered for each one of those with essential hypertension, as certain antihypertensive drugs, for example, ACE inhibitors are teratogenic and may need to be changed pre-conceptually.

The NICE give out graphical presentations of guidelines to treatment of preeclampsia, which are appropriate for use as reference in clinical settings. Physicians ought to use forward-thinking rules from their ward in dynamic management [17].

CONCLUSION:

Pre-eclampsia is considered a rare condition that appears during pregnancy with an unpredictable course that accompany with severe consequences for the mother and the fetus. Delivering the baby is the

only cure to this condition. In any case, careful weighing of both maternal and fetal risk-benefit factors must be considered during induction of preterm delivery. Likewise, recognizing delivery criteria in the event of pre-eclampsia is critical to ideal management. current research centers around the forecast of onset of pre-eclampsia or even severe pre-eclampsia in order to allow early management and enhance the morbidity and mortality related with this disease. specific instruments for secondary prevention should likewise be developed for recurrent pre-eclampsia.

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