

What is the pathophysiology of eclampsia?

[Life](#)



Introduction

Section A: Case History

JB is a 38-year-old, gravida 4, para 0, Caucasian female who presented in hospital at 36 weeks plus 5 days gestation with sudden development of oedema in the face and upper and lower extremities along with a severe headache.

On examination her blood pressure (BP) was elevated at 171/107 mmHg. Her pulse 81 beats per minute (bpm), respiratory rate 15 breaths per minutes, and temperature was 36.4 °C. Her urine sample showed ++ 2 proteinuria. There was evidence of oedema in her face and upper and lower extremities and her lower deep tendon reflexes were brisk but without any clonus. JB denied any visual disturbances and epigastric pain. On palpitation of the abdomen, the symphysio-fundal height was 38cm. The fetal lie was longitudinal and the back appeared to be on the right. The presentation appeared to be cephalic and the head was 3/5 engaged.

Electronic fetal monitoring showed fetal heart rate at 135 bpm, with reassuring variability. There was no deceleration and acceleration was normal. It was also noted that contractions were absent.

Her antenatal care had been shared between the hospital and her general practitioner and was uneventful until she was admitted to hospital on this occasion.

On briefly reviewing JB's past medical history she has seasonal allergies as well as long standing asthma in which she uses salbutamol inhaler to relieve

her symptoms. JB also has a history of depression. In her family history her father suffers from hypertension as well as cirrhosis and her mother has a remarkable medical history of extensive medical conditions such as hypertension, angina, and transient ischemic accidents. Both her maternal grandparents had a history of type 2 diabetes.

With regards to her social history, JB works as a customer assistant and lives with her partner. JB has never smoked, and has not taken alcohol since finding out she was pregnant.

Her past obstetric history is remarkable for recurrent miscarriages. She had two miscarriages at 6-8 weeks and one ectopic pregnancy a year and a half ago which miscarried naturally at 10 weeks.

The initial investigations showed; a normal full blood count, liver enzymes and creatinine. However urate (0.37 mmol/l) and the protein: creatinine ratio (44 mg/mmol) levels were elevated. JB is demonstrating key cardinal symptoms of pre-eclampsia including hypertension, proteinuria, oedema, and increased reflexes. 1

A diagnosis of severe pre-eclamptic toxemia was made, JB was admitted and treatment was commenced with 10mg nifedipine.

With JB being admitted onto the ward, there was continuous monitoring of BP and fetal monitoring using cardiotocography (CTG). The next morning JB's BP stabilised to 128/74 mm Hg and she reported feeling better. With the BP stable and a reassuring CTG a decision to induce delivery was made and she was given Prostaglandin E2 (PGE2) over three days. However there was poor

response and the cervix remained obstinately unchanged and so it was decided the baby would need to be delivered via caesarean section.

Section B: Pathophysiology

Pre-eclampsia is part of a range of conditions known as the hypertensive disorders of pregnancy. 2 It is defined as a multisystem disorder characterised by the new onset of raised BP ($\geq 140/90$ mm Hg) and proteinuria (at least 1+ on dipstick or ≥ 0.3 g/24 hours) after 20 weeks of gestation. 3, 4, 5 Although the triggering event initiating the syndrome is unknown, a two stage model of pre-eclampsia has been proposed (figure 1). 1, 6, 7, 8, 9 The primary stage is asymptomatic, characterized by failure of placental vascular remodeling during the first trimester resulting in reduced placental perfusion leading to placental ischemia and release of placental products into the maternal circulation. 1, 6, 7 Consequently this initiates the second symptomatic stage, the maternal syndrome in which endothelial dysfunction precedes the clinical manifestations of the disease including characteristic hypertension, proteinuria, and glomerular endotheliosis. 1, 6, 7 There is also risk for developing the HELLP syndrome (haemolysis, elevated liver enzymes and low platelets), progression to eclampsia, and end-organ damage. 1, 6, 7

Stage 1

In normal pregnancy, following implantation, the surface trophoblast cells of the adhering blastocyst differentiate into an inner cellular layer, the cytotrophoblast, and an outer syncytiotrophoblast. 10, 11 The undifferentiated cytotrophoblasts found in the inner layer can develop into

hormonally active villous syncytiotrophoblasts, extravillous anchoring trophoblastic cell columns, and invasive intermediate trophoblasts. 10 The extravillous trophoblastic cells proliferate from the tips of anchoring chorionic villi to form the cytotrophoblast shell which line the uterine cavity. 10, 11 Cytotrophoblasts continue to migrate through the uterine endometrium until they reach the spiral arteries, by which time they have differentiated into an endothelial-like cell type. 10, 11 Endovascular trophoblast cells begin to remodel the spiral arteries by replacing the endothelium and smooth muscle cells resulting in the ‘destruction of medial elastic, muscular and neural tissue’. 10, 11, 12

These physiological changes result in an increased vessel diameter leading to the creation of a low-resistance arteriolar system with the absence of maternal vasomotor control, and therefore allowing a notable increase in blood supply to the developing fetus. 7, 10

In pre-eclampsia this physiological dilatation does not occur adequately thus resulting in placental hypoperfusion and ischemia. 1, 8, 10 The ischemic placenta may lead to the production of cytokines and growth factors as well as simulate placental apoptosis or necrosis, resulting in release of humoral or particulate materials into maternal systemic circulation that promote generalised maternal vascular endothelium dysfunction, culminating in the clinical manifestations of pre-eclampsia. 1, 8, 10

The invasion of trophoblast cells is regulated by factors expressed by the decidual barrier. 7, 10 These factors include cell adhesion molecules, extracellular matrix, proteinases, growth factors and cytokines. 7, 10

Malfunctions in any these factors may lead to poor trophoblast invasion and subsequently pre-eclampsia. 7, 10 Immunological factors play a main factor in pre-eclampsia. 7, 10, 11 Abnormal placentation may be the result of maternal immune rejection of paternal antigens expressed by the fetus. Normally HLA-G, a class 1B MHC antigen, expressed by the extravillous trophoblasts protects from natural killer cell lysis. 11, 12, 13 Women who develop pre-eclampsia do not appear to express this HLA-G and therefore are not protected. 7, 10

Stage 2

The clinical manifestations of pre-eclampsia can be linked to the pathophysiological changes that occur including vasoconstriction, activation of coagulation cascade and reduced plasma volume. 14

Development of hypertension is a primary feature of pre-eclampsia. 1, 8, 14 During normal pregnancy, although through maternal physiological adaptations there is a 30-50 % increase in cardiac output, the decrease in peripheral vascular resistance results in decreased arterial BP. 14 However, women who develop pre-eclampsia experience widespread vasoconstriction, increased peripheral vascular resistance, and decreased cardiac output. 1, 13 Evidence shows there to be an exaggerated sensitivity of the vasculature of women with pre-eclampsia to all vasopressors hormones, best known is the increased responsiveness to angiotensin II. 1, 13 This increase in vascular reactivity is thought to be due to an alteration in the balance of prostaglandins as a result to the damage to vascular endothelial damage. 1 JB's BP when she presented was 171/107 mm Hg. This is a considerably

elevated and can be defined as severe pre-eclampsia ($\geq 160 / \geq 110$ mm Hg).
2, 3, 4

Although fluid retention and oedema occurs in patients with pre-eclampsia they are also a feature of normal pregnancy. Plasma volume increases by 50% in uncomplicated gestations and normal gravidas sometimes experience oedema. However in pre-eclampsia plasma volume is decreased by 15-20% and in these cases women experience rapid weight gain and generalised oedema as a result of an abnormal shift of extracellular fluid (ECF) from the vascular to the extravascular compartment hence maintaining a low plasma volume and an increased interstitial fluid volume. With excessive accumulation of interstitial ECF, the presence of peripheral oedema particularly in the face and hands is seen. JB haemoglobin was 130g/l, reflecting the relative haemoconcentration observed in pre-eclampsia as a result of the diminished intravascular volume.

Women with pre-eclampsia also have markedly decreased renal plasma flow (RPF) and glomerular filtration rate (GFR). The decline in RPF is attributed to vasoconstriction, whereas the fall in GFR is related both to the decline in RPF as well as to the morphological changes in the kidney. These characteristic pathological changes of pre-eclampsia are termed glomerular endotheliosis and comprise largely of evident swelling of the glomerular endothelial cells sufficient to occlude the capillary lumen, with some inclusions in the capillary basement membrane but with practically no change in renal podocytes. The morphologic lesion is accompanied by functional changes in renal hemodynamics which correlates

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best with the magnitude of hyperuricemia and proteinuria. 1, 5 Early to middle pregnancy serum uric acid usually falls well below 0.24 mmol/l, in patients with pre-eclampsia levels often rise > 0.27 mmol/l as seen in the case of JB (0.37 mmol/l). 14 A number of studies have correlated the rise in serum uric acid with the severity of pre-eclampsia and with the extent of glomerular injury. 5, 8 JB's PCR levels was also measured to estimate the extent of proteinuria. The result recorded 44 mg/mmol predicts significant proteinuria, the threshold being > 30mg/mmol. 16

Left untreated, pre-eclampsia can proceed to life threatening convulsions termed eclampsia. 17 Another specific complication that can arise from pre-eclampsia is the HELLP syndrome, which is illustrated by the sudden appearance of a microangiopathic haemolytic anaemia, elevation of liver enzymes and a rapidly falling platelet count. 17 In these cases rapid interruption of pregnancy is required to avoid hepatic or renal failure, sepsis, or even death. 1, 6, 7, 15, 17

Section C: Management

Treatment for hypertension in pregnancy raises a series of challenges to the healthcare team. 16 An in-depth knowledge of the adaptive physiological, psychological and social processes is required in order to choose the optimal management for the mother and her fetus. 16, 18

Incomplete understanding of the etiology in pre-eclampsia has hindered attempts at prevention. 12, 16 However effective and adequate prenatal care management of pre-eclampsia has led to the reduced mortality related to this disorder. 15 This includes early detection and referral of women at <https://assignbuster.com/what-is-the-pathophysiology-of-eclampsia/>

high risk, careful monitoring with prevention and treatment of complications, and a decision regarding timely delivery. 15 Delivery remains the definitive treatment for pre-eclampsia although the disease process may not resolve instantly. 8 After diagnosis, subsequent treatment will depend on the results of initial maternal and fetal assessment. 4 The main goal for management of pre-eclampsia is ultimately to protect the safety of the mother and prevent progression to eclampsia and then the delivery of a healthy newborn. 4 While delivery is always suitable for the mother, it might not be appropriate for a premature fetus. 4 Therefore the decision to deliver is influenced by gestational age, fetus status, and also severity of maternal condition at time of assessment. 4

JB management was given in accordance to guidelines from Royal College of Obstetricians and Gynaecologists. 5, 16 Based on JB diagnosis at 36. 5 weeks she was admitted to hospital with the decision to induce labour and allow a vaginal delivery.

Observations of vital signs including BP, heart rate, oxygen saturations, and respiratory rate were recorded every 15 minutes along with continuous CTG monitoring. 5, 15 A 10 mg dose of oral anti-hypertensive nifedipine was given to stabilize her BP before she could be induced. The sole need to treat is to prevent the hemorrhagic sequel of hypertension, in particular cerebral haemorrhage, rather than alter the progression of the disease process. 2 Antihypertensive drug therapy is advised for pregnant women with systolic BP of ≥ 160 or diastolic BP ≥ 110 mm Hg. 2, 5, 16 The goal of treatment is to lower systolic pressure to 130-150 mmHg and diastolic pressure to 80-100 mmHg. 5, 16 It is also important that BP is lowered gradually to prevent <https://assignbuster.com/what-is-the-pathophysiology-of-eclampsia/>

hypotension as placental perfusion can be adversely affected and compromise the fetus¹⁵. With a conservative management plan in place and JB stable, the BP was measured every four hours during the day. Full blood count, renal and liver function tests, were all carried out daily. 5, 16

There are many possible choices of antihypertensives that are appropriate in pregnancy. 8 Methyldopa and labetalol are first line antihypertensive drugs used in treatment of pre-eclampsia. 4, 5 Methyldopa is a centrally acting alpha₂ agonist that reduces sympathetic outflow activity. 15, 19 Although it has a long track safety record, due to the common drug side effects of depression, in the case of JB with a history of depression it was agreed an alternative should be used. 14, 15 The use of labetalol was also contraindicated in JB case as she is asthmatic. 5 Labetalol is a non selective beta blocker and a selective alpha blocker. 15, 20

As both of these were contraindicated in JB case, nifedipine was prescribed instead. Nifedipine is a type 2 calcium channel blocker which is usually used as a second line agent in cases where BP is noncompliant to treatment with methyldopa and beta blockers. 15, 19, 20 It acts by inhibiting the inward transfer of calcium ions from extracellular space and by the inhibition of uptake by smooth muscle cells. 15, 19, 20 Its primary effect is to cause smooth muscles relaxation. 15, 19, 20 Due to the ability to vasodilate the vasculature with full reversibility on discontinuing the drug, it has become a widely used antihypertensive. 15, 19, 20 With respect to use of drugs in pregnancy, nifedipine has been rated as a Category C drug. 20 This means that its teratogenic potential is uncertain, and so it is recommended that it is

used only where potential maternal benefit is seen to outweigh potential fetal effects. 20

Once the BP was stabilized, induction of labour commenced. It is recommended that women in presence of severe pre-eclampsia at or beyond 34 weeks' gestation to be induced to prevent the progression of the disease to eclampsia. 5 Induction of labour was stimulated via PGE₂, which contains dinoprostone. Its mechanisms of action are similar to the natural cervical ripening process. 21, 22 It is administered intravaginally to induce cervical ripening by directly softening the cervix, relaxing the cervical smooth muscle, and producing uterine contractions. 21, 22 There has been some debate of the use of dinoprostone in women with a history of asthma; however PGE₂ is a bronchodilator, thus not contraindicated to use, in JB case. 22

For women whom there is a concern about the risk of eclampsia, it is recommended they receive magnesium sulphate as a prophylactic to protect against seizures, however in JB's case it was held off. The MAGPIE study demonstrates that the risk of eclampsia is more than halved in these women. 5, 8, 23 However, it is also worth noting that only 1-2 % of pre-eclamptic women in the UK had fitted in the absence of anticonvulsant treatment. Specific caution is needed when administering magnesium sulphate when nifedipine has previously been taken, as it increases plasma concentration and therefore the potency of the drug. When magnesium sulphate has been prescribed, it should be continued at least 24 hours post partum, as the risk of eclampsia does not resolve immediately after delivery. 5, 14, 15, 23

Most women with severe pre-eclampsia following delivery will need inpatient care for 4 days or more. 5 JB was discharged on the fourth day after careful review of her clinical signs. She was continued on her anti hypertensive treatment, and was to be reviewed as an outpatient. JB was also offered a postnatal follow up to discuss the events of the pregnancy as well as preconception counselling. 5

Section D: Psychological and Social Aspects

Epidemiology

Pre-eclampsia complicates about 2-8 % of pregnancies and may have serious effects on the mother and child, which makes it an important threat to public health in both developed and developing countries. 2, 23, 24 Worldwide maternal mortality and morbidity from pre-eclampsia and eclampsia remains high, it is estimated to be responsible for approximately 12 % of maternal deaths per year. 23 Pre-eclampsia is estimated to account for 67% of referrals to day-care assessment units, 20% of antenatal admission and 25% of obstetric admissions to intensive care units in the UK. 25

The cost of treating pre-eclampsia varies between ? 500-? 10000 including the sum of hospital stay, induction costs, mode of birth, and pre-admission costs. 16

Due to improvements in antenatal care in the UK, syndrome of eclampsia and development of HELLP syndrome is now rare. 16 Eclampsia is reported in 1 in 2000 pregnancies. 8, 15, 24 Also perinatal mortality rates are gradually improving, due to advances in antenatal care, early detection, improved anaesthesia, early delivery and expert neonatal paediatric care.

Factors associated with an increase risk of pre-eclampsia include nullparity, African-American ethnic background, multiple gestations, obesity, chronic hypertension, molar pregnancy, family history of pre-eclampsia and a previous history of pre-eclampsia. 4, 8

Psychosocial

Women developing pre-eclampsia are exposed to considerable amount of psychological and social stress. 26 These stress disturbances in turn may have a significant impact on the mother and baby during the important early months following delivery. 26, 27 Pre-eclampsia is a disease which develops without warning therefore as JB reported, she found herself having to deal with the unexpected and dramatic changes in fetal health risk as well as her own all of a sudden. The diagnosis of pre-eclampsia involves a degree of shock, fear and sometimes even disbelief particularly to those experiencing it well before term. Shock comes from the fact that they were being hospitalised and felt unprepared for delivery. 26, 27 JB was very nervous after being admitted to hospital as she and her baby were regularly monitored and the realisation of the serious consequences the disease possess. 27, 28

There was also a sense of frustration as well as disempowerment as JB felt she had no control over the situation, and it was no longer just a personal responsibility. These feelings were amplified through the lack of sufficient information given on the disease, not completely informed about her actual situation, and on the medical decisions being made. 26, 27

There was also an emotional burden of feeling responsible for developing pre-eclampsia and the guilt to the risks it may have propelled on her unborn child.

Other psychological stresses were requirement of bed rest, boredom and being separated from her partner during hospitalisation. 27

For those women who are diagnosed well before term, there is a greater risk of prematurity. 27 These women being unprepared for the experience of delivering a premature baby can be a major component of shock and fear experienced. When progression of disease leads to complications, an emergency caesarean section which is usually performed can be very traumatic experience and life can suddenly be thrown into chaos. 26, 27 These women usually have less early contact with their baby and are less likely to breast feed as they are recovering from surgery. 26, 27

For those who unfortunately lose their baby, they will be faced with the complex and traumatic events of grieving. This grieving process can be coupled to relationship problems as partners usually grieve differently. 27

Women with pre-eclampsia are at increased risk of recurrence with subsequent pregnancies; therefore it is important they are advised of this if they wish to conceive again. 27, 29

The experience of severe pre-eclampsia may be overwhelmingly stressful. There is little time to adjust to new realities. Women may blame themselves adding the burden of guilt to the acute emotional chaos that follows diagnosis.

Conclusion

In conclusion, pre-eclampsia remains a global problem and a clinical challenge. It is a significant cause of maternal and perinatal mortality and morbidity. As the triggering factors remain unknown, prevention of the disease becomes difficult. At present, the only treatment option for pre-eclampsia is delivery, but this is not always simple and usually involves a risk-benefit balance between health of mother and the maturity of the fetus.