PREEKLAMPSİA : ANNE ÖLÜMLERİNİN ÖNLENMESİNE YÖNELİK BİR YÖNERGE

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Abstract

Pre-eclampsia is among the leading causes of maternal death in our country. The management of preeclampsia and the current strategies to prevent maternal deaths due to pre-eclampsia are presented.

Keywords: Pre-eclampsia, maternal death, eclampsia, magnesium sulphate, anti hypertensive agent

Özet

Preeklampsia, ülkemizde anne ölümlerinin başta gelen nedenlerinden biridir. Preeklampsia yönetimi ve anne ölümlerinin önlenmesine yönelik stratejiler sunulmaktadır.

Anahtar Kelimeler: Pre-eklampsia, anne ölümü, eklampsia, magnezyum sülfat, anti hipertansif ajan

The classical pattern of antenatal care, which involves visits at 16, 24, 28, 30, 32, 34 and 36 weeks and then weekly until delivery, was established in the first or even second trimester primarily aimed to detect preeclampsia. The reason for this strategy was to cope with the high maternal and infant mortality associated with pre-eclampsia that usually occurs after 20 weeks of gestation.

Over half a million women die each year from pregnancy related causes, 99% in developing or underdeveloped countries. In many underdeveloped countries, complications of pregnancy and childbirth are the leading cause of death amongst women of reproductive years. The Millennium Development Goals have placed maternal health at the core of the struggle against poverty and inequality, as a matter of human rights. Ten percent of women have high blood pressure during pregnancy, and preeclampsia complicates 2% to 8% of pregnancies (1). Pre-eclampsia, a dangerous condition for both the mother and the baby and of unknown cause, is a difficult and elusive condition, even for experienced clinicians. Pre-eclampsia is so called because it precedes eclampsia, which is characterized by grand mall convulsions, associated with signs of pre-eclampsia; however, even the terminology is inexact; eclampsia is not the only crisis of the condition, may occur without prodromal signs of pre-eclampsia and is by no means the inevitable end-stage of pre-eclampsia. The only consistent feature of pre-eclampsia is its inconsistency(2). Although the etiology of pre-eclampsia is not understood, the presence of a placenta is necessary and suficient to cause the disease and the removal of the placenta is the mainstay of the management. Until recently, it was impossible to explain the astounding variability of pre-eclampsia by a single underlying pathological process; certainly hypertension could not account for all these features; but the concept that the maternal endothelium is the target organ for the pre-eclampsia process has resolved this difficulty In short, the maternal preeclampsia syndrome can be explained if it is seen not as a sole hypertensive problem, but it is a disease with clinical features as the sum of the consequences of systemic maternal endothelial dysfunction (Table 1), arising from placental disease that evolves in two stages.

Table 1: Complications of pre-eclampsia:

Central nervous system	**Renal system**	**Respiratory system**
Eclamptic convulsions	Renal cortical necrosis	Laryngeal edema
Cerebral hemorrhage	Renal tubular necrosis	Pulmonary edema
Cerebral edema		
Cortical blindness		
Retinal edema		
Liver	**Coagulation system**	**Placenta**
Jaundice	DIC	Placental infarction
Hepatic infarction	Microangiopathic Hemolysis	Retroplacental bleding and placenta previa
HELLP Syndrome	HELLP Syndrome	
Hepatic rupture		

According of the Statistics of the Ministry of Health of Turkey, Population Institute of Hacettepe University and the Prime Ministry of Turkey together with the Government Planning Institute, the estimated number of deliveries in Turkey was 1.286,796 in 2008 and maternal mortality ratio was reported to be as 16 per 100 000 deliveries in 2010(3) , with an enormous decrease from 61 per 100.000 in 2003 (Figure 1a,b,c, Table 2). Obstetric deaths constitute %0.3 of hospital deaths (%0.7 of the female deaths). The predominant causes of maternal death has been reported to be thromboembolism, obstetrical hemorrhage, pre-eclampsia/eclampsia, and infection. Overall, 10% to 15% of direct maternal deaths are associated with preeclampsia and eclampsia. Where maternal mortality is high, most of deaths are attributable to eclampsia, rather than preeclampsia. Maternal mortality is high following preeclampsia, and even higher following eclampsia.

Among the causes of death, there are "three delays". Delay in deciding to seek care, delay in arriving at a place providing care, and delay in receiving care at the medical facility.

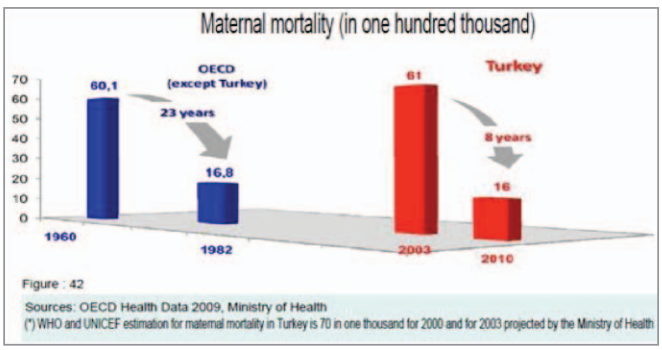

Figure 1-a: WHO and UNICEF estimation of maternal mortality for 2000 and 2003 and 2010 maternal mortality projected by Ministry of Health (4)

Figure 1-b: Maternal mortality between 1998 and 2010

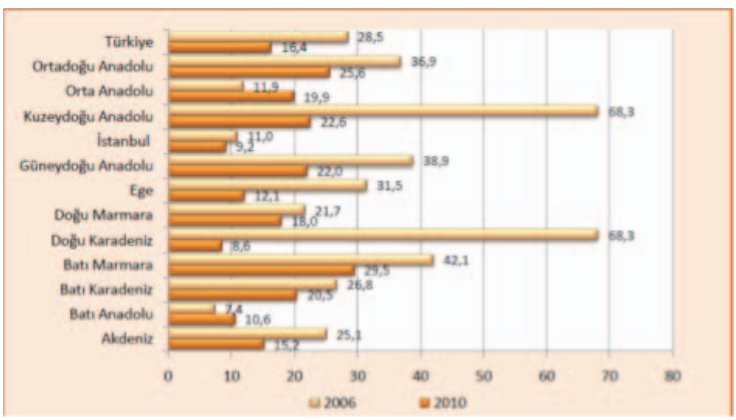

Figure 1-c: Maternal mortality according to georaphical localizations

Table 2: The numbers, maternal mortality ratio, live births, proportion of maternal deaths among deaths of females of reproductive age and life risk of maternal death in Turkey (5)

Year	Maternal deaths per 100 000 live births	Numbers	Live births (Thousands)	Proportion of maternal deaths among deaths of females of reproductive age	Lifetime risk of maternal death
2008	23 (15-36)	310	1347	1,8	1900
2005	29 (18-45)	390	1352	2	1400
2000	39 (25-61)	550	1401	2,4	940
1995	51 (32-79)	740	1457	3,1	630
1990	68 (43-110)	980	1446	3,9	420

More than %90 of the pregnant women has been reported to receive antenatal care and the average number of follow-ups per pregnant women according to the Health Statistics of Turkey by year 2010 are depicted in Figure 2, as 4.2 . The geographical localizations have been reported to affect the number of follow-ups. The average number of follow-ups per puerperant have been reported to be increased from 0,6 in 2000 to 1,5 by the year 2010 (4).

However, maternal deaths due to pre-eclampsia/eclampsia are still on the second row of Confidential Enquiries into Maternal and Child Health (6) and maternal deaths due to pre-eclampsia/eclampsia have not been fallen. Pre-eclampsia /eclampsia as a cause of maternal death appears to be a clinical diagnosis rather than autopsy findings. Although most deaths associated with pre-eclampsia are clear-cut, there are cases where the differential diagnoses require a detailed autopsy assessment, if only for exclusion of other possibilities; so the importance of improving the the standards of the maternal autopsy together with reducing the numbers of locations where they are performed with specialist pathologists who performed careful histologic examination of kidneys, liver and uterine placental bed and taking them on as part of agreed job plans together become important.

Pre-eclampsia affects %2-5 of the pregnant population. A study from UK reported that in the era between 1997-2008, 117 women died due to pre-eclampsia/eclampsia (6). The numbers and the distribution of the deaths were not different. In comparison of the deaths in the consecutive trienniums, 1997-99, 2000-02, 2003-05, 2006-08, the number of deaths from pre-eclampsia/eclampsia has not fallen (Table 3).

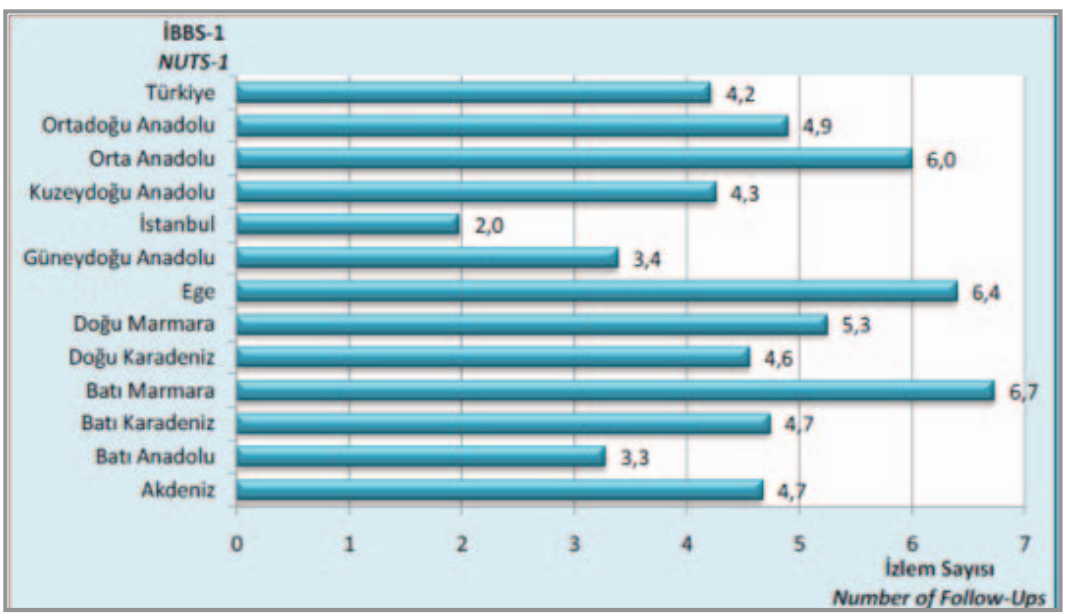

Figure 2 : Average Number of Follow-ups per Pregnant Women by Nomenclature of Territorial Units (NUTS-I) for Statistics and Provinces-1, 2010 Source: General Directorate of Primary Health Care Services Research and clinical definitions of pre-eclampsia are tabulated as folllows (7):

Table 3: Numbers and underlying cause of death due to eclampsia and pre-eclampsia, UK: 1991–2008 (CMACE, 2011) (6)

Cause of Death	1997–99 n Rate 95% CI	2000–02 n Rate 95% CI	2003–05 n Rate 95% CI	2006–08 n Rate 95% CI
Cerebral				
Intracranial haemorrhage	7 0.33 0.16–0.69	9 0.45 0.23–0.87	9 0.43 0.22–0.82	9 0.39 0.20–0.75
Subarachnoid	0 0.00	0 0.00	0 0.00	0 0.00
Infarct	0 0.00	0 0.00	1 0.05 0.01–0.34	0 0.00
Oedema	0 0.00	0 0.00	0 0.00	0 0.00
Eclampsia	0 0.00	0 0.00	0 0.00	5 0.22 0.09–0.52
Subtotal	7 0.33 16–0.69	9 0.45 0.23–0.87	10 0.47 0.25–0.88	14 0.61 0.36–1.03
Pulmonary				
Adult Respiratory Distress Syndrome	2 0.09 0.02–0.38	1 0.05 0.01–0.36	0 0.00	0 0.00
Oedema	0 0.00	0 0.00	0 0.00	0 0.00
Subtotal	2 0.09 0.02–0.38	1 0.05 0.01–0.36	0 0.00	0 0.00
Hepatic				
Rupture	2 0.09 0.02–0.38	0 0.00	0 0.00	1 0.04 0.01–0.31
Failure/necrosis	0 0.00	0 0.00	1 0.05 0.01–0.34	2 0.09 0.02–0.35
Other	5 0.24 0.10–0.57	4 0.20 0.08–0.53	3 0.14 0.05–0.44	2 0.09 0.02–0.35
Subtotal	7 0.33 0.16–0.69	4 0.20 0.08–0.53	4 0.19 0.07–0.50	5 0.22 0.09–0.52
Overall Total	16 0.75 0.46–1.23	14 0.70 0.42–1.18	14 0.66 0.39–1.12	19 0.83 0.53–1.30
Acute Fatty Liver of Pregnancy	4 0.19 0.07–0.50	3 0.15 0.05–0.47	1 0.05 0.01–0.34	3 0.13 0.04–0.41

Eclampsia is a form of hypertensive evcephalopathy, an acute or subacute syndrome of diffuse cerebral dysfunction, not ascribable to uremia or hypertension, but commonly associated with both. Changes in the magnetic resonance imaging of the brain may be reversible or not. The symptoms include headaches, nausea, vomiting and cortical blindness. Convulsions commonly but not invariably occur. Blood pressure may be relatively low or normal. This is not, therefore a malignant form of hypertension which is characterized by gross papiledema and retinopathy, secondary to extreme hypertension, and are lesions which are rare in eclampsia. The pathophysiology is thought to be vasogenic edema secondary to loss of autoregulation combined with endothelial dysfunction. Autopsies on patients with hypertensive encephalopathy have demonstrated arteriolar fibrinoid necrosis with microinfarcts and failed to show brain edema; however, brain biopsy has shown edematous white matter with no evidence of vessel wall damage or infarction. Antepartum eclampsia occurs in approximately 75% of cases, with the remaining 25% of cases occurring postpartum (7,8) . Eclampsia rarely occurs before 20 weeks' gestation. Late postpartum eclampsia is defined as that beginning more than 48 hours postpartum but less than 4 weeks after delivery. Maternal mortality attributable to eclampsia depends on the management and has been reported to occur in 4.2% even in critical care units. The United Kingdom Obstetric Surveillance Study

has shown that the overall case fatality rate associated with eclampsia is low , but serious morbidity can occur (6) However, studies on maternal mortality have identified an unprecedented number of deaths associated with eclamptic seizures (6). This is a reminder that eclampsia is a serious complication that, where possible, should be avoided. However, a reduction in maternal mortality related with the use of magnesium sulphate could not be demonstrated.

The incidence of eclampsia has halved in the UK(8), presumably as a result of the widespread use of magnesium sulphate (Table 4) , following publication of the Magpie trial (9).

Magnesium sulphate use is associated with side effects: A quarter of women have side effects, primarily flushing. With clinical monitoring serious adverse effects are rare. Magnesium sulfate is the anticonvulsant of choice for treating eclampsia; more effective than diazepam, phenytoin, or lytic cocktail (10). Although it is a low cost effective treatment, magnesium sulfate is not available in all low and middle income countries; scaling up its use for eclampsia and severe preeclampsia may contribute to lowering the incidence of eclampsia and probably maternal mortality.

Table 4: Anticonvulsants (The Eclampsia Trial Collaborative Group)

Anticonvulsants

Give intravenous magnesium sulphate* if woman with severe hypertension or severe pre-eclampsia has or previously had eclamptic fit. **•Consider giving intravenous magnesium sulphate*** if birth planned within 24 hours in woman with severe pre-eclampsia. •Do not use diazepam, phenytoin or lytic cocktail as alternatives to magnesium sulphate* in women with eclampsia	**Features of severe preeclampsia** **Severe hypertension and proteinuria or** **Mild or moderate hypertension and** proteinuria with at least one of: - severe headache - problems with vision such as blurring or flashing - severe pain just below ribs or vomiting - papilloedema - signs of clonus (≥ 3 beats) - liver tenderness - HELLP syndrome - platelet count falls to < 100 x 10^9/liter - abnormal liver enzymes (ALT or AST rises to > 70 IU/liter).
Regimen for magnesium sulphate •Loading dose of 4 g given intravenously over 5 minutes, followed by infusion of 1g/hour for 24 hours. •Further dose of 2–4 g given over 5 minutes if recurrent seizures.	
Corticosteroids **For fetal lung maturation** **If birth likely within 7 days in** woman with pre-eclampsia: •give 2 doses betamethasone* 12 mg intramuscularly 24 hours apart between 24 and 34 weeks •consider giving 2 doses . betamethasone* 12 mg intramuscularly 24 hours apart at 35–36 weeks. **For HELLP syndrome** •Do not use dexamethasone or betamethasone.	**Fluid balance and volume expansion and mode of birth** **Fluid balance and volume expansion** In women with severe pre-eclampsia - Do not preload with intravenous fluids before establishing low-dose epidural analgesia and combined spinal epidural analgesia - Limit maintenance fluids to 80 ml/hour unless there are other ongoing fluid losses (for example, haemorrhage). - Do not use volume expansion unless hydralazine is antenatal antihypertensive **Caesarean section versus induction of labour** - Choose mode of birth according to clinical circumstances

Table 5: Management of severe hypertension

- Measure blood pressure continually
- Continue antenatal antihypertensive therapy
- If blood pressure controlled within target ranges, do not routinely limit duration of second stage of labour
- If blood pressure does not respond to initial treatment, advise operative birth
- Treat women admitted to critical care during pregnancy or after birth immediately with one of:
  - labetalol(oral or intravenous)
  - hydralazine(oral or intravenous)
  - nifedipine(oral)
- Monitor response to treatment to:
- Ensure blood pressure falls
- İdentify adverse effects for woman and the fetus
- Modify treatment according to response
- Consider using < 500 ml crystalloid fluid before or at the same time as first dose of hydralazine in the antenatal period
- Aim to keep the blood pressure< 150-80/100 mmHg (8)

In the developed world, pre-eclampsia is now a more important antecedent than eclampsia. Pre-eclampsia remain a prominent cause of death worldwide. Cerebral hemorrhage continues to be the predominant cause of death. The most pressing need, as before, is to treat hypertension (and especially systolic hypertension) quickly and effectively to prevent haemorrhagic stroke (Table 5).

Oral anti-hypertensives may also be used solely or in combinations. There are no placebo controlled trials of antihypertensive treatment in a critical care setting but the concensus is that lowering blood pressure in women with severe hypertension is necessary. The Guide line Development group (GDG) have recommended the commonly used antihypertensive regimens. There is no advantage of the route of delivery of antihypertensive therapy in trials, but the GDG agreed that the route of administration could be oral or intraveous for labetalol, oral for nifedipine and intravenous for hydralazine (Table 1). Labetalol is the only drug licensed for the treatment of hypertension in pregnancy.

One in 20 (5%) women with severe pre-eclampsia or eclampsia was admitted to critical care. Over half of the admissions for acute kidney failure, one quarter of admissions for coagulopathy, one third of admissions for ventilation and cerebrovascular disorders occurred in women with hypertensive disorders. So the importance

Table 6 : Acute treatment of hypertension

	Onset of action (minute)	**Dose**
Hydralazine	10-20	5-10 mg intravenous every 20 minutes up to maximum dose of 30 mg
Labetalol	10-15	20 mg intravenous, then 40-80 mg every 10 minutes up to maximum dose of 300 mg or continuous infusion at 1-2 mg/minute
Nifedipine	5-10	10 mg peroral, repeated in 30 minutes (20mg peroral) x 2 doses; then 10-20 mg every 4-6 hour up to a maximum dose 240 mg/24 hour As continuous infusion at 3mg/h with increments of 0.5mg/h titrated according to blood pressure
Nicardipine		As continuous infusion at 3mg/hour with increments of 0.5mg/hour titrated according to blood pressure
Sodium nitroprusside	0.5-5	0.25-5 Ug/kg/IV infusion Risk of fetal cyanide poisoining with prolonged treatment

of the evaluation levels and the criteria for referral to Critical Care has become evident. Criteria for referral to critical care are tabulated as follows (Table 7).

Maternal morbidity and mortality related to preeclampsia are principally associated with eclampsia and HELLP syndrome. Criteria for the diagnosis of HELLP syndrome include at least two of the abnormalities listed below:

•Hemolysis

•Abnormal peripheral blood smear (burr cells, schistocytes)

•Elevated bilirubin ≥1.2 mg/dL

•Increased lactate dehydrogenase (LDH) of more than twice the upper limit of normal for the laboratory

•Elevated liver enzymes

•Elevated alanine aminotransferase (ALT) or aspartate aminotransferase AST ≥ twice the upper limit of normal for the laboratory

•Low platelet count (100000/mm³)

The complications and their occurence in the HELLP syndrome are summarized in (Table 8). The presence of complications are associated with an increase in maternal morbidity and/or mortality (11).

Acute fatty liver of pregnancy (AFLP) may be included in maternal deaths due to preeclampsia as this may be part of a spectrum of conditions related to pre-eclampsia (Table 3). The differential diagnosis of HELLP syndrome from thrombocytopenic purpurae (TTP)/hemolytic uremic syndrom /HUS) and acute fatty liver of pregnancy (AFLP) may be difficult (12). Though it is difficult to make the correct clinical diagnosis especially in complicated cases, clinical and laboratory findings in HELLP, TTP/HUS and AFLP are depicted in (Table 9).

Greater understanding of the pathophysiology of preeclampsia is the key to improving both fetal and maternal outcomes. In the present state of knowledge, women with severe disease should be referred to a critical care center with the experience and facilities to manage maternal complications. and provide intensive care for a preterm infant.

Recommendations having the possibility of reducing the risk of preeclampsia and maternal deaths due to pre-eclampsia are:

•Organization of the antenatal care: While in undeveloped countries, the main problems are access to medical services, the organization and range of available medical facilities,

•**Periodic training** and clinical skills of the medical and paramedical staff about pre-eclampsia-eclampsia

•**Pre-pregnancy counselling:** Women of childbearing age with pre-existing hypertensive disorders may require a change of medication, worsen or otherwise impact on a pregnancy should be informed of this at every opportunity

•**Defining the women at high risk for preeclampsia:** Women at high risk for preeclampsia are those with any of the following:

Table 7: Severe hypertension, severe pre-eclampsia and eclampsia in critical care

Level 1	Level 2	Level 3
- Pre-eclampsia with mild or moderate hypertension - Ongoing conservative antenatal management of severe preterm hypertension - Step–down treatment after the birth	- Severe pre-eclampsia with any of: - eclampsia - HELLP syndrome - haemorrhage - hyperkalaemia - severe oligouria - coagulation support - intravenous antihypertensive treatment - initial stabilization of severe hypertension - evidence of cardiac failure -abnormal neurology	- Severe pre-eclampsia and needing ventilaton

Table 8 : Complications reported in the HELLP Syndrome (7).

Complications	%
Eclampsia	4-9
Abruptio placenta	9-20
DIC	5-56
Acute renal failure	7-36
Severe ascites	4-11
Cerebral edema	1-8
Creatinine	+
Pulmonary edema	3-10
Wound hematoma/infection	7-14
Subcapsular liver hematoma	between 0.9- and<2
Liver rupture	about 1.8
Hepatic infarction	combined with anti-phospholipid syndrome
Retinal detachment	1
Cerebral hemorrhage	1.5-40
Maternal death	1-25

Moderate risk

•First pregnancy

•Age ≥ 40 years

•Pregnancy interval > 10 years

•BMI ≥ 35 kg/m² at first visit

•Family history of pre-eclampsia

•Multiple pregnancy

High risk

•Hypertensive disease during previous pregnancy

•Chronic kidney disease

•Autoimmune disease such as systemic lupus erythematosis or antiphospholipid syndrome

•Type 1 or type 2 diabetes

•Chronic hypertension (9)

•Estimate patient specific risks for pregnancy complications: Endothelial dysfunction appears to be caused by increased circulating levels of anti-endothelial factors produced in excess by the oxidatively stressed placentae, namely the soluble vascular endothelial growth factor receptor 1, and soluble endoglin. There is also reduced availability of the angiogenic factor placental growth factor. Together these factors synergize on their effect on the endometrium. These factors provide links between the pre-eclampsia placenta and the maternal disorder. Estimation early, intermedia, and late pre-eclampsia may shift prenatal care from a series of routine visits to a more individualised patient and disease-specific approach both in terms of the schedule and content of such visits. Effective early identification of the high risk group could potentially improve the outcome by directing high risk

Table 9: Clinical and laboratory findings in HELLP, thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS) and acute fatty liver of pregnancy (AFLP)

	HELLP	TTP/HUS	AFLP
Ammonia	Normal	Normal	Elevated
Anemia	+	Severe	Normal
Antithrombin III	+	Normal	Decreased
AST	Elevated	Normal	Elevated
Biluribin	Elevated mostly indirect	Elevated	Elevated, mostly direct
Creatinine	+	Significantly elevated	Significantly elevated
Fibrinogen	Normal	Normal	Decreased in all cases Glucose
	Normal	Normal	Decreased
Hypertension	Present	+	+
LDH	Elevated	Significantly elevated	Elevated
Proteinuria	Present	+	+
Thrombocytopenia	Present	Severe	+

patients for pre-eclampsia to specialist clinics for close surveillance (13-25)

•**Advise women at high risk of pre-eclampsia to take 75 mg of aspirin daily from 12 weeks until the birth of the baby. If previous: severe eclampsia, pre-eclampsia needing birth before 34 weeks, pre-eclampsia with baby's birth weight < 10th centile, intrauterine death, placental abruption** (26). Although the evidence for the use of low-dose aspirin to reduce the risk of pre-eclampsia in women at high risk is clear, the benefits for those at moderate risk are more difficult to establish and research is required for this group (9). A problem with the available evidence is the difficulty in quantifying benefit for individual moderate risk factors and determining what interactions exist between them. Although low-dose aspirin appears a safe drug to use in pregnancy there needs to be clearer evidence of benefit within the moderate-risk group of women.

•**Predict early, intermedia and late preeclampsia from maternal factors, biophysical and biochemical markers at 11-13 weeks**, including maternal characteristics and history, uterine artery pulsatility index, mean arterial pressure and serum pregnancy-associated plasma protein-A, maternal serum or plasma concentration of placental growth factor, placental protein-13, inhibin-A, activin-A, soluble endoglin, pentraxin-3 and P-selectin (13-20).

•**Counsel pregnant women:** Pregnant women should be made aware of the need to seek immediate advice from a healthcare professional if they experience symptoms of pre eclampsia. Symptoms include:

• severe headache

• problems with vision, such as blurring or flashing before the eyes

• severe pain just below the ribs

• vomiting

• sudden swelling of the face, hands or feet.

•**Treat hypertension** (27) and especially systolic hypertension) quickly and effectively to prevent haemorrhagic stroke. Deaths from intracranial hemorrhage , the single largest cause of death indicate a failure of antihypertensive therapy. Ensuring effective antihypertensive therapy is the priority for improving clinical care. The NICE guideline recommends a target systolic blood pressure of150 mm Hg.

•**Establish the Criteria** for referral to Critical Care

•Referrals to specialist services in pregnancy should be prioritised as urgent

•Women with severe pre-eclampsia or potentially serious medical conditions require immediate and appropriate multidisciplinary specialist care (27)

•**Use magnesium sulphate appropriately** (9-10)

•**Abandone the use of ergometrine in routine third-stage management** to avoid the risk of Iatrogenic hypertension. İntramuscular oxytocine should be the drug of choice for the active management of the third stage of labor (28).

•**Limit maintenance fluids to 80 ml/hour** unless there are other ongoing fluid losses (for example, haemorrhage) In women with severe pre-eclampsia.

•The management of pregnant or postpartum women who present with, pre-eclampsia/eclampsia with severe arterial hypertension, requires a **team approach**. Trainees in obstetrics and/or gynaecology must request help early from senior medical staff, including advice and help from anaesthetic and critical care services. In very acute situations telephoning an experienced colleague can be very helpful.

•**Choose mode of birth for women with severe hypertension, severe pre-eclampsia or eclampsia according to the clinical circumstances .**

•**Remember the exaggerated hemodynamic response during anesthesia:** Sudden increase in blood pressure may occur in general anesthesia during either intubation or extubation, leading to a cerebrovascular event. An increase in arterial blood pressure accompanies laryngoscopy performed with or without tracheal intubation. Therefore, blood pressure should be reduced prior to intubation or extubation. This hypertensive response is prevented with a short-acting antihypertensive agent, such as nitroglycerin, sodium nitroprusside, or labetalol. Esmolol, a pure β-receptor antagonist with a rapid onset of action, is a popular agent for blunting the hypertensive response to tracheal intubation in nonpregnant patients. Unfortunately, it crosses the placenta and causes severe fetal bradycardia; hence, it is not recommended in pregnant patients but may be used in postpartum preeclampsia. Decreased sympathetic activity due to regional anesthesia leads to dilatation of the capacitance vessels that cause hypotension. Adequate intravascular volume repletion (fluid preloading) performed before initiating regional anesthesia avoids this relative hypovolemia. Management of volume status varies according to the severity of the patient's disease. Hypotension can also occur with intravenous administration of antihypertensive medication. This effect is more pronounced if the mother has been in a supine position for a long period; hence, the need to have the patient in a "tilted" position to avoid compression of the vena cava by the uterus (29).

•Difficulty with intubation: Preeclamptic women may have pharyngeal and laryngeal edema rendering intubation and ventilation difficult. A laryngeal mask airway may be a useful alternative in cases of difficult airway management and should be anticipated in severe preeclampsia.

•Magnesium sulfate interaction with neuromuscular blocking agents: Magnesium decreases the release of acetylcholine from the presynaptic portion of the myometrial junction as well as decreasing the sensitivity of the motor endplate to the effects of acetylcholine. Women receiving magnesium sulfate are more sensitive to the depolarizing and nondepolarizing neuromuscular blocking agents; therefore, the dose of muscle relaxant must be adjusted accordingly. This neuromuscular transmission defect correlates with increased serum magnesium levels and decreased serum calcium levels (30-32).

•Regional anesthesia is now established as the preferred mode of anesthesia for preeclampsia patients as long as there is no contraindication to regional anesthesia such as coagulopathy. Regional anesthesia is the anesthetic of choice in most women with preeclampsia or eclampsia, for some of the following reasons. Epidural analgesia reduces maternal plasma catecholamine levels in laboring women. This may benefit preeclamptic women who are already exhibiting increased vascular reactivity to circulating catecholamines. Compromised intervillous blood flow in preeclamptic women may be improved by lumbar epidural analgesia. In turn, lumbar epidural analgesia may improve uteroplacental perfusion by reversal of uterine arterial vasospasm (32).

•Bleeding problems: Decreased platelet count and function occur in up to 18% of women with preeclampsia. Epidural anesthesia is safe for women with platelet counts ≥ 100000/μL in the peripartum period. The rate of fall in platelet count is equally important because a rapid fall in platelet count may be indicative of severe disease. It is, important to check other indicators of coagulopathy, including prothrombin time partial thromboplastin time and international normalized ratio, especially if there are clinical signs of coagulopathy. If an epidural catheter is already in place, then the platelet count should be checked before removal of the epidural When there is significant impairment of coagulation, not uncommon in severe hypertensive disease, regional blocks are contraindicated for fear of producing an epidural hematoma and neurologic damage.

•Specialist clinical care: On rare occasions, pregnant women may present with life threatening conditions that requre immediate control of blood pressure, such as hypertensive encephalopathy, acute left ventricular failure, acute aortic dissection, or increasing levels of catecholamines (pheochromocytoma, clonidine withdrawal). Patients at the highest risk of these complications include those with underlying cardiac disease, chronic renal disease, hypertension requiring multiple dugs to achieve control, superimposed pre-eclampsia in the second trimester, and abruptio placenta with DIC.

Correct referral to critical care and multidisciplinary approach are the mainstay of management.

•Serious Incident Reporting and Maternal Deaths: All maternal deaths must be subject to a high quality local review. The results of this high quality reviews must be disseminated and discussed with all maternity staff and their recommendation implemented and audited at regular intervals

•Pathology: The standarts of maternal autopsy must be improved. There should be a complementary major input by clinicians into obtaining more consented hospital autopsies.

References

1.Duley L: The global impact of pre-eclampsia and eclampsia: Semin Perinatol 2009, 33 (3); 130-7

2.Redman CWG, Jacobson Sl, Russell R: Hypertension in pregnancy in de Swiet's Medical Disorders in Obstetric Practice (Raymond O Powrie, Michael F Greee, William Camannn eds) page 153-81, Fifth edition, 2010. McMillan Company, Singapore

3.Barış E, Mollahaliloğlu S, Aydın S: Healthcare in Turkey: from laggard to leader: BMJ 2011, 342, c 7456 doi 10.1136/bmj c 7456:

4.WHO and UNICEF estimation of maternal mortality for 2000 and 2003 and 2010 maternal mortality projected by Turkish Ministry of Health

5.WHO Statistics, 2010

6.Centre for Maternal and Child Enquiries(CMACE): Saving Mother's Lifes: reviewing maternal deaths to make motherhood safer:2006-08. The Eighth Report on Confidential Enquiries into Maternal Deaths in the United Kingdom. BJOG 2011; 118(Suppl. 1) 1:203

7.Brown MA, Lindheimer MD, de Swiet M, Van Assche A, Moutquin JM The classification and diagnosis of hypertensive disorders of pregnancy: statement from the international society for the study of hypertension in pregnancy(ISSHP). Hypertens Foundation, 2011: (Charity No: 1037116).

8.National Collaborating Centre for Women's and Children's Health. Hypertension in Pregnancy: The Management of Hypertensive Disorders During Pregnancy. National Institute for Health and Clinical Excellence Guideline 107. London: RCOG. August 2010. [www.guidance. nice.org.uk/CG107/]. Accessed 5 October 2010.

9.The Magpie Trial Collaborative Group. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. Lancet 2002;

359: 1877-1890

10.The Eclampsia Trial Collaborative Group: Which anticonvulsant for women with eclampsia? Evidence from the Collaborative Eclampsia Trial. Lancet 1995; 345:1455-63

11.Baxter JK, Weinstein L: HELLP syndrome: the state of the art. Obstet Gynecol Surv 2004, 59:838-845.

12.Knight M, Nelson-Piercy C, Kurinczuk JJ, Spark P, Brocklehurst P. A prospective national study of acute fatty liver of pregnancy in the UK. Gut 2008;57:951–6

13.Akolekar R, Syngelaki A, Sarquis R, Zvanca M, Nicolaides KH.: Prediction of early, intermediate and late pre-eclampsia from maternal factors, biophysical and biochemical markers at 11-13 weeks. Prenat Diagn. 2011 Jan;31(1):66-74. doi: 10.1002/pd.2660

14.Akolekar R, Zaragoza E, Poon LCY, Pepes S, Nicolaides KH:. Maternal serum placental growth factor (PlGF) at 11 to 13 weeks of gestation in hypertensive disorders of pregnancy. Ultrasound Obstet Gynecol 2008 32:732–739.

15.Akolekar R, Minekawa R, Veduta A, Romero XC, Nicolaides KH.. Maternal plasma inhibin A at 11 to 13 weeks of gestation in hypertensivedisorders of pregnancy. Prenat Diagn 2009a 29: 75 3–760.

16.Akolekar R, Etchegaray A, Zhou Y, Maiz N, Nicolaides KH. Maternal serum activin A at 11 to 13 weeks of gestation in hypertensive disorders of pregnancy. Fetal Diagn Ther 2009b.25: 322–327.

17.Akolekar R, Casagrandi D, Livanos P, Tetteh A, Nicolaides KH. Maternal plasma pentraxin 3 at 11 to 13 weeks of gestation in hypertensive disorders of pregnancy. Prenat Diagn2009c. 29: 934–938.

18.Akolekar R, Syngelaki A, Beta J, Kocylowski R, Nicolaides KH.. Maternal serum placental protein 13 at 11–13 weeks of gestation in preeclampsia. Prenat Diagn 2009d 29: 1103–1108.

19.Akolekar R, Veduta A, Minekawa R, Chelemen T, Nicolaides KH..Maternal plasma P-selectin at 11 to 13 weeks of gestation in hypertensive disorders of pregnancy. Hypertens Pregnancy 2010 DOI: 10.3109/106419509032 42683.

20.Levine RJ, Lindheimer MD.. First-trimester prediction of early preeclampsia: a possibility at last! Hypertension 2009: 53: 747–748.
21.Foidart JM, Manuat C, Akolekar R, Cruz J, Nicolaides KH.. Maternal plasma soluble endoglin at 11–13 weeks of pregnancy in preeclampsia. Ultrasound Obstet Gynecol 35: 680–687.

22.Giguere Y, Charland M, Bujold E, et al. Combining biochemical and ultrasonographic markers in predicting preeclampsia: a systematic review.Clin Chem 2010 56: 361–374.

23.Plasencia W, Maiz N, Bonino S, Kaihura C, Nicolaides KH.. Uterine artery Doppler at 11 + 0 to 13 + 6 weeks in the prediction of preeclampsia. Ultrasound Obstet Gynecol 2007; 30: 742–749.

24.Poon LC, Kametas NA, Chelemen T, Leal A, Nicolaides KH.. Maternal risk factors for hypertensive disorders in pregnancy: a multivariate approach. J Hum Hypertens 2010a 24: 104–110.

25.Poon LC, Kametas NA, Valencia C, Chelemen T, Nicolaides KH. Hypertensive disorders in pregnancy: screening by systolic diastolic and mean arterial pressure at 11–13 weeks. Hypertens Pregnancy 2010b DOI: 10.3109 / 10641955.2010.484086

26.Bujold E, Roberge S, Lacasse Y, et al. Prevention of preeclampsia and intrauterine growth restriction with aspirin started in early pregnancy: a metaanalysis Obstet Gynecol 2010 116: 402–414.

27.Şen C: Management of Severe Pre-eclampsia and Eclampsia (Chapter 202) in Textbook of Perinatal Medicine(Asım Kurjak, Frank A Chervenak eds), pp 2688-97, Second Edition, Informa Healthcare, 2006, UK

28.McDonald SJ, Abbott JN, Higgins SP. Prophylactic ergometrine-oxytocin versus oxytocin for the third stage of labour. Cochrane Database Syst Rev 2004;Issue 1:CD000201

29.Frederick U. Eruo and Baha M. Sibai : Hypertensive diseases in pregnancy in Clinical Obstetrics(E.Albert Reece, John C Hobbins eds) Clinical Obstetrics: The Fetus and Mother Blackwell Publishing Third Edition, Hong Kok, 683-99, 2007

30.Douglas KA, Redman CW. Eclampsia in the United Kingdom. BMJ 1994;309:1395–400.

31.Knight M. Eclampsia in the United Kingdom 2005. BJOG 2007;114:1072–8.

32.Sibai BM: Hypertensive Emergencies(chapter 5) in Obstetric Intensive Care Manual (Michael Foley, Thomas R Strong, Thomas J Garite eds), pp 49-60, McGraw Hill, New York 2011:

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