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Pre-eclampsia (PE)

"A women is never closer to death than when giving a life"

Lev Nikolayevich Tolstoy

- The multisystem disorders of PE continue to be a massive cause of maternal and perinatal morbidity and mortality. It's complicates an estimated 2–30% of pregnancies and it is a major cause of maternal morbidity, prenatal death and premature delivery, although outcome for most women is good;
- Over 4 four million women will develop the disorder worldwide every year, 50.000-100.000 women die from the PE each year, and it's responsible for approximately 300.000 perinatal deaths;

Pre-eclampsia (PE)

- Women with PE usually develop hypertension, proteinuria, and varying degrees of ischemic end-organ damage, caused by widespread endothelial dysfunction;
- PE is associated with abnormalities of coagulation system, disturbed liver function, renal failure and cerebral ischemia.

Definition

The presence of hypertension of at least 140/90 mm Hg recorded on two separate occasions at least 4 hours apart and in the presence of at least 300 mg protein in a 24 hours collection of urine arising de novo after the 20th week gestation in a previously normotensive women and resolving completely by the sixth postpartum week.

- New onset after 20 weeks of gestation, or
- Early post-partum, previously normotensive
- Resolves within 48 hrs postpartum
- With the following (Renal or other systemic)

Classification of hypertensive disorders of pregnancy

- Preeclampsia / eclampsia
- Chronic hypertension
- Chronic hypertension with superimposed preeclampsia
- Gestational or transient hypertension

Risk factors

- Nuliparity (7%)
- Previous preeclampsia
- Age (<18 or >35)
- Family history of PE
- Preexisting diseases: chronic and /or severe hypertension (15-40%) , vascular, immune or renal disease (25%)
- Pre-gestational Diabetes mellitus (up to 50%)
- Multifetal pregnancies (for gemelar 20%)
- Polihydramnion
- Molla hydatidosa (up to 70%)
- Hydrops fetalis (up to 50%)
- Unexplained intrauterine growth restriction

Etiology and Patogenesis

Zweifel (1916.) described preeclampsia as a "disease of theories", because the cause is unknown.

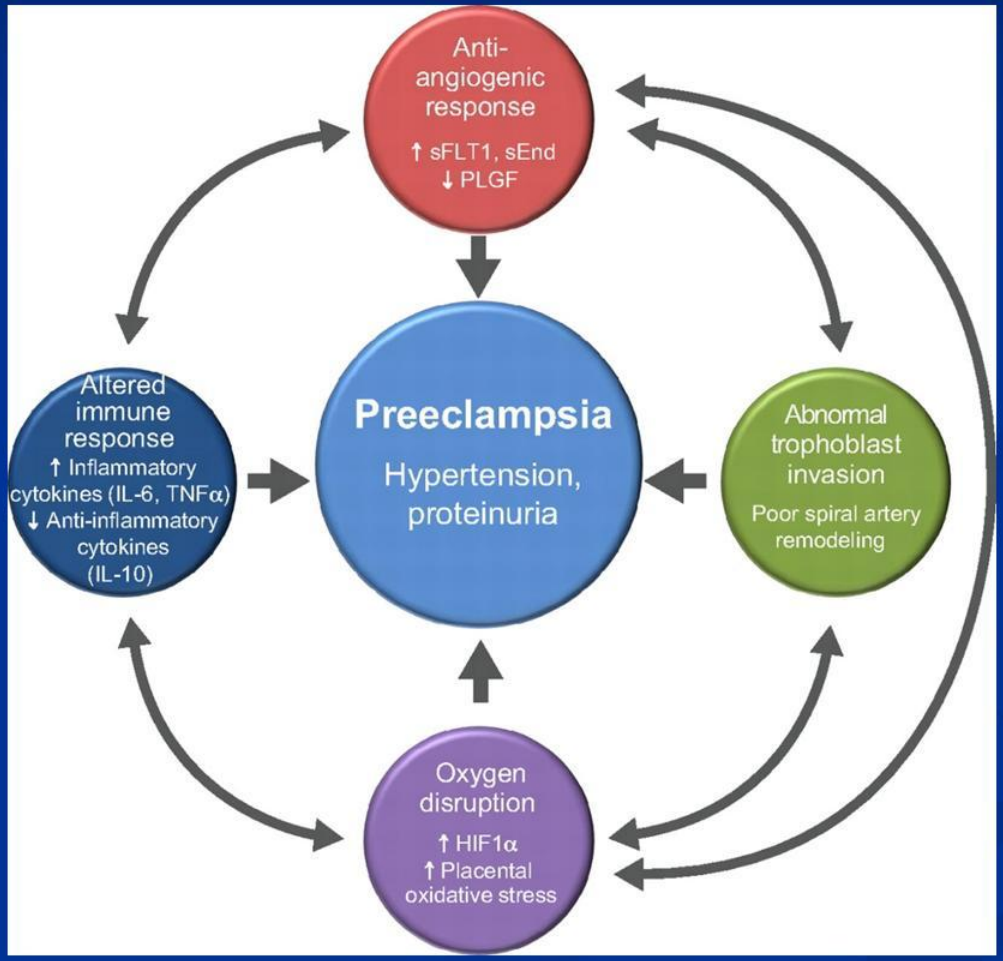
- Genetic predisposition
- Abnormal immunological response
- Deficient trophoplast invasion
- Hypoperfused placenta
- Circulating factors
- Vascular endothelial cell activation
- Clinical manifestations of the disease

Pathophysiologic Abnormalities

The efforts to unravel the pathogenesis of PE have been hampered by the lack of clear diagnostic criteria for the disease and its subtypes. However pathophysiologic abnormalities in PE are:

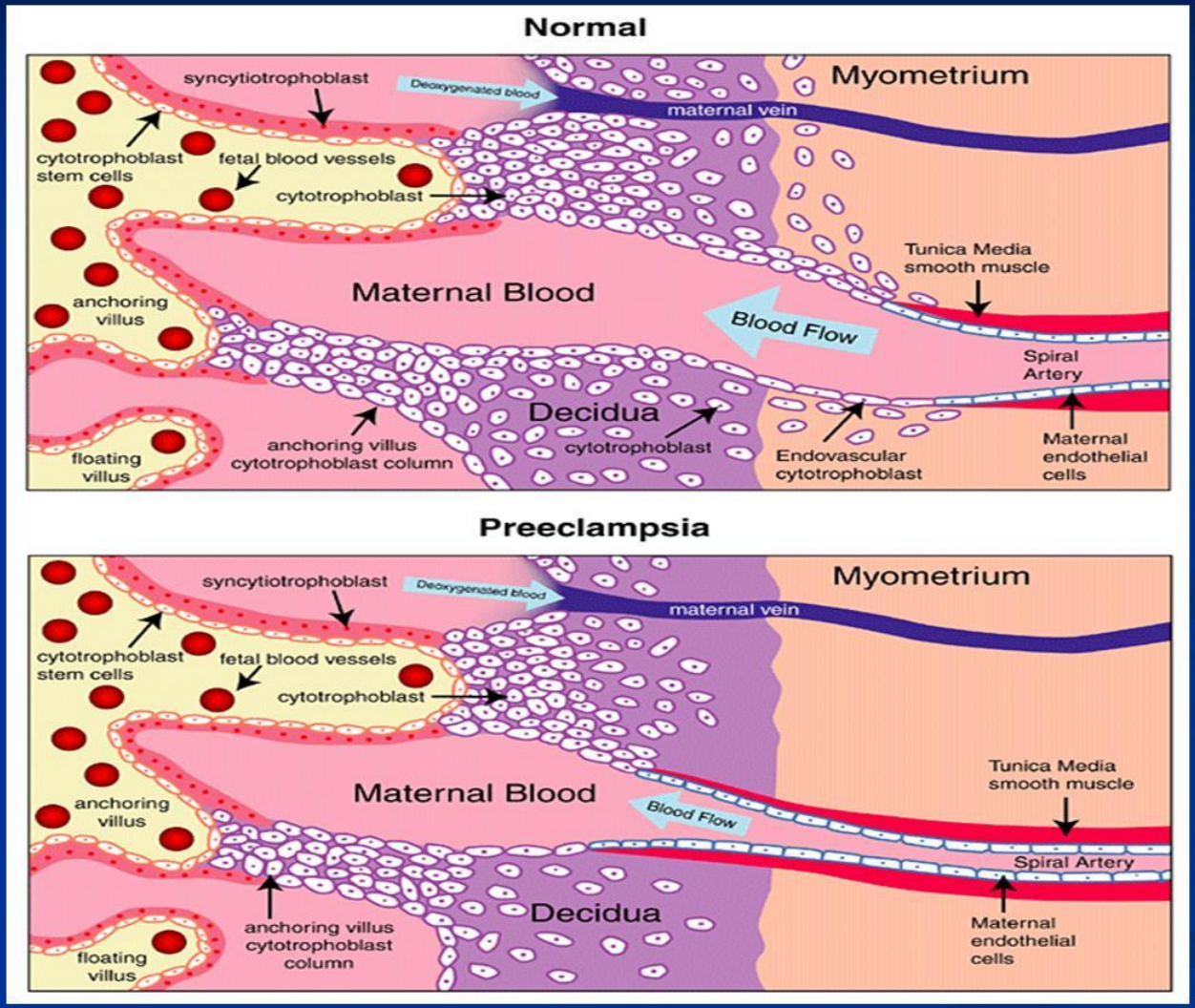
1. Generalized vasospasm
2. Activation of coagulation system
3. Abnormal hemostasis
4. Altered thromboxane-prostacyclin ratio
5. Endothelial cell injury
6. Abnormal hemodynamics
7. Reduced uteroplacental blood flow

Pathology of PE



Pennington K, et al. Preeclampsia: multiple approaches for a multifactorial disease. Dis. Mod. Mech. Jan 2012

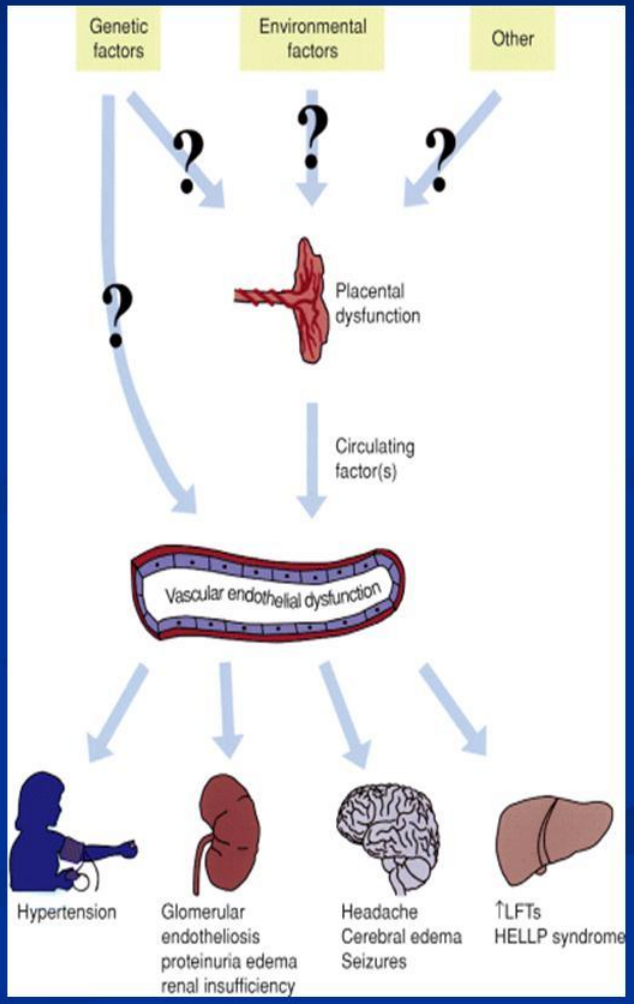
Abnormal Placentation



Bdolah Y, Karumachi SA, Sach PB: Recent Advances in Understanding of Preeclampsia. Croat Med J. 2005;46(5):728-36

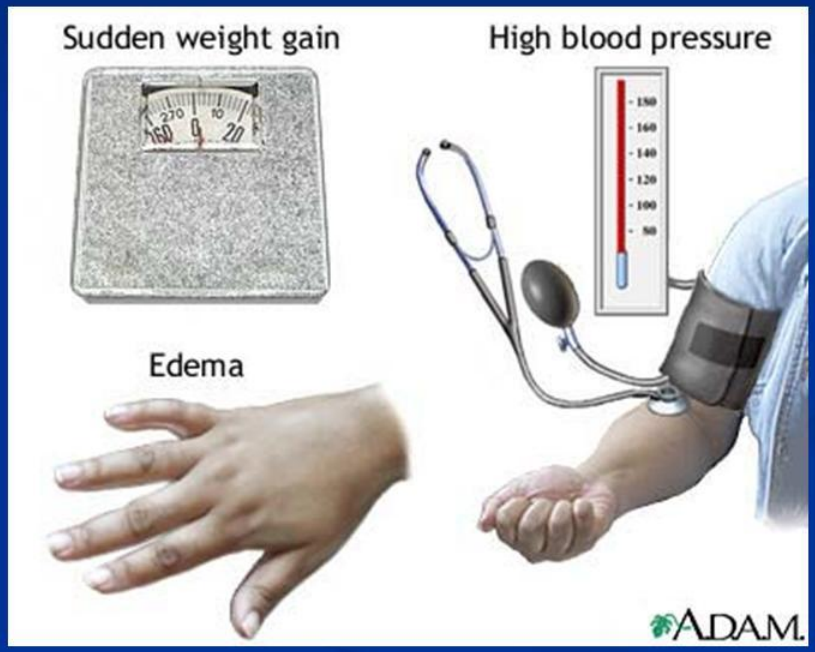
Clinical Presentation of Pre-eclampsia

- **Hypertension-**is the most important criteria for the diagnosis of PE. May occur suddenly. An increase of 15mmHg (for diastolic BP) or 30 mmHg (for systolic BP) should be considered ominous. In patients with severe PE，BP may increase during sleep.
- **Proteinuria-**is the last sign to develop. Eclampsia may occur without proteinuria. In PE, it's an indicator of fetal jeopardy. The incidence of SGA infants and perinatal mortality is markedly increased in patients with proteinuric PE.
- **Edema-** PE may occur without edema. Weight gain in excess of 2kg/week or particularly sudden weight gain over 1 or 2 days should raise the suspicion of PE.



Mild Forms of Preeclampsia

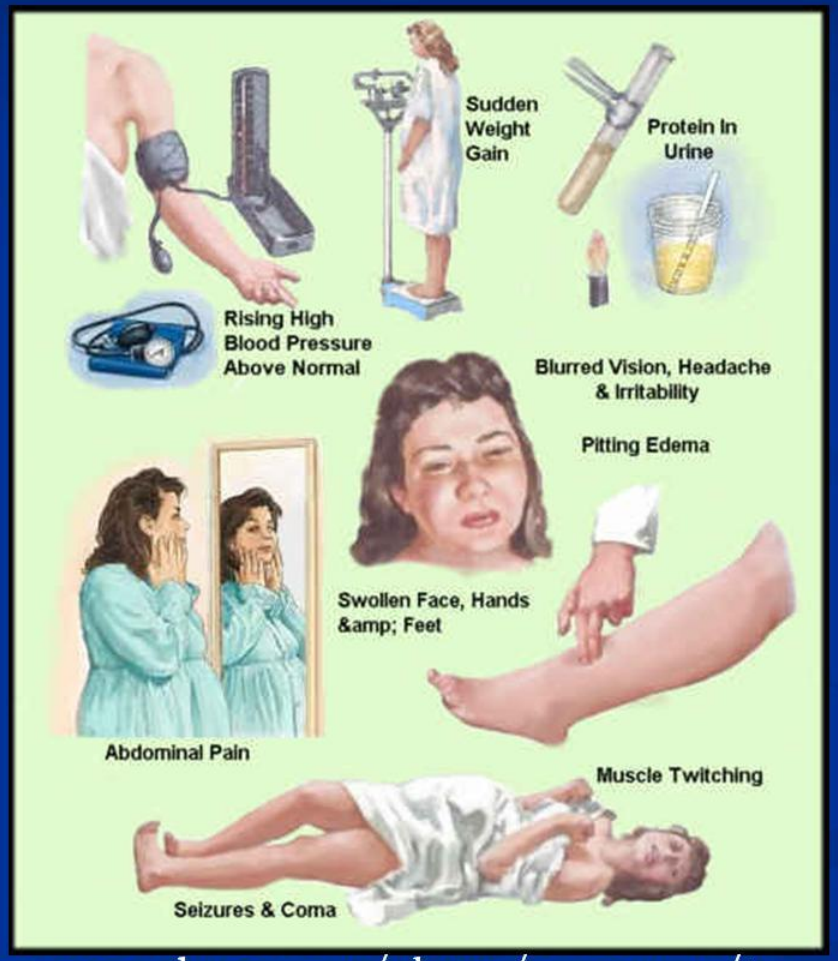
- **Hypertension -**a systolic blood pressure of 140 mmHg or above, or a diastolic blood pressure of 90mmHg or above (on two occasions 6 hours apart)
- ***Abnormal proteinuria*** the excretion of 300 mg or more of protein in 24 hours
- ***Edema-*** weight gain <2kg



Severe Forms of Preeclampsia

- ✓ Blood pressure: > 160 mmHg systolic or > 110 mm Hg diastolic
- ✓ Proteinuria: > 5 g in 24 hours
- ✓ Epigastric pain or right upper quadrant pain (hepatocellular damage)
- ✓ Oliguria- <500 ml/24 h
- ✓ Thrombocytopenia- < 100,000/mm^3
- ✓ IUGR
- ✓ Headache, visual disturbances, CNS hyperexcitability and hyperreflexia (Hypertensive encephalopathy and loss of cerebral autoregulation when MAP exceeds a critical value.)
- ✓ Other: Pharyngolaryngeal edema, Pulmonary edema.

Severe Forms of Preeclampsia



http://www.moondragon.org/obgyn/pregnancy/toxemia.html

Management of Hypertensive Disorders in Pregnancy

- **Anamnesis**
  - **History of PE in previous pregnancy**
  - **History of chronic diseases**
  - **Family history**
  - **Social status**
  - **Risk factors for PE**
- **Physical examination**
  - **Maternal**
  - **Fetal**

Management of PE- Symptoms

- Visual disturbances typical of PE are scintillations and scotomata (cerebral vasospasm.
- Headache (frontal, throbbing, or similar to a migraine headache, but no classic headache)
- Epigastric pain is due to hepatic swelling and inflammation, with stretch of the liver capsule
- Rapidly increasing or nondependent edema may be a signal of developing PE
- Rapid weight gain is a result of edema due to capillary leak as well as renal sodium and fluid retention

Management of PE- Physical Findings

General Principles

- early recognition of the symptomless syndrome
- awareness of serious nature of the condition in its severe form without over-reacting to mild disease
- agreed guidelines for admission to hospital, investigation, and use of anti hypertensive and anticonvulsant therapy
- well-timed delivery to pre-empt serious maternal or fetal complications • postnatal follow-up and counseling for future pregnancies.

Management of PE- Physical Findings

- Blood Pressure
- Proteinuria
- Retinal vasospasm or Retinal edema
- Right upper quadrant abdominal tenderness stems from liver swelling and capsular stretch

Treatment

GOAL: TO PREVENT ECLAMPSIA AND OTHER SEVERE COMPLICATIONS

- **Prevention of PE**
- **General procedures**
- **Drugs**

1. Antihypertensive Therapy: Hydralazine, Labetolol, Nifedipine
2. Seizure Prophylaxis & Treatment **:** Magnesium sulfate, Phenytoin, Diazepam
3. Antiagregation therapy: Aspirin, Calcium, Heparin

Prevention of preeclampsia

- Detection of women at risk: multifetal gestation, vascular or renal disease, previous severe preeclampsia-eclampsia, abnormal uterine artery Doppler velocimetry
- antihypertensive drugs
- magnesium
- zinc
- fish oil
- calcium
- low-dose aspirin

Treatment

When To Hospitalize?

- Often, hospitalization recommended with new-onset preeclampsia to assess maternal and fetal conditions.
- Hospitalization for duration of pregnancy indicated for preterm onset of severe gestational hypertension or preeclampsia.
- Ambulatory management at home or at day-care unit may be considered with mild gestational hypertension or preeclampsia remote from term

Antepartum Testing And Treatment

- Ultrasound every 4-6 weeks after 28-32 weeks to assess fetal growth
- If IUGR is suspected, testing should include umbilical artery Doppler flow studies
- Weekly NST for gestational hypertensive patients in good control are not indicated
- Antenatal corticosteroids
- If delivery seems imminent (between 24- 34 weeks), steroids should be initiated. Delivery should not be delayed for steroids if immediate delivery is necessary
- Treatment should consist of either two doses of betamethasone or four doses

Timing and Mode Of Delivery

❖**Delivery is the only effective treatment for PE, and despite the fact that clinical symptoms and laboratory abnormalities usually regress in the hours afterwards, the risk of complications persists for some time following delivery.**

❖**<u>Vaginal delivery is preferable.</u>**

❖**The mode of delivery (caesarean section versus vaginal) depends on:**

- the seriousness of the situation
- the gestational age
- the degree of fetal/maternal compromise.
- Epidural analgesia is the method of choice for labour (as long as a coagulation defect has been excluded).
- Appropriate facilities for the care of the newborn available

Delivery

- Prompt delivery is curative and avoids possible bad consequences to mom and baby. (abruption, seizures…)
- Prompt delivery may cause significant morbidity or mortality to baby due to prematurity

Newborns from PE pregnancies

- Fetal complications in PE are directly related to gestational age and the severity of maternal disease and include increased rates of preterm delivery, intrauterine growth restriction, placental abruption, and perinatal death.

- The major complications for the newborn are related to prematurity, although the data on the morbidity and outcome for preterm infants of women who have PE are conflicting, and few studies address this issue

Newborns from PE pregnancies

- ***Early Onset Complications***

- **Low Birth Weight Infant**
- Asfiksija
- Acidosis
- Hyperbilirubinemia
- Hypoglicemia
- Respiratory distress syndrom
- Infections

- ***Late onset complications***

- Respiratory complications
- Cerebral palsy
- Mental disorders
- Visual and acoustic disorders
- Delayed growth
- Increased risks for adult diseases

Conclusions

- ***For clinical management, PE should be over diagnosed to prevent maternal and perinatal morbidity and mortality – primarily through timing of delivery***
- To reduce the level of perinatal morbidity and mortality in PE, a regular and organized surveillance of every pregnancy is necessary.
- An integrated first hospital visit at first trimester combining data from maternal characteristics and history and maternal blood pressure measurement can define the patient at risk for PE

Conclusions

- For women who have experienced a pregnancy complicated by preeclampsia, a systemic evaluation for underlying risk factors may identify a specific pathway suitable for a specific intervention. Although some progress has been made developing potentional options to prevent preeclampsia recurrence, there is a great need for better data to determine who will benefit most from any specific therapy

Conclusions

- Prediction and prevention of PE is very important contribution for maternal health.
- Primary prevention:

1. Identification of women at high risk of PE
2. Blood pressure measurement
3. Doppler ultrasonography
4. Biochemical markers as potential predictors (PAPP-A, PlGF, PP13, sEndoglin, Inhibin-A, Activin-A, Pentraxin 3 and P-Selectin)

Conclusions

- Secondary prevention:

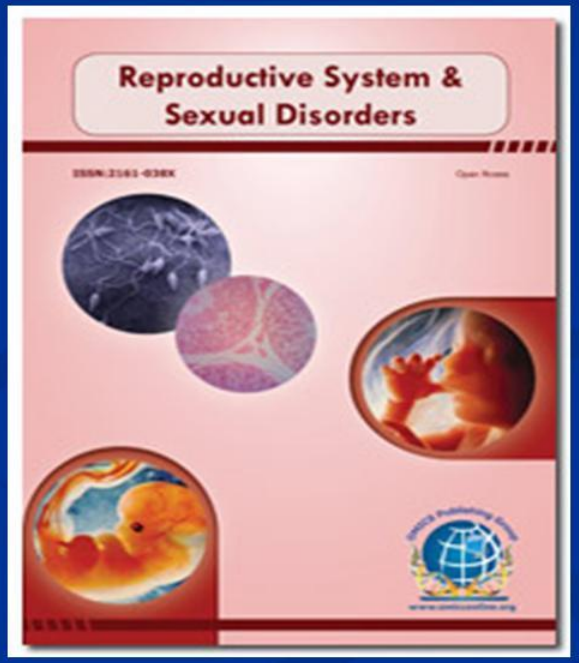
1. Antiplatelet aspirin therapy (before 12–14 weeks)
2. Calcium supplementation
3. Omega-3 (n-3) fatty acids

Conclusions

- The delivery of the hypertensive pregnancies needs to be performed in institution that can provide intensive care and adequate therapy for the newborn if needed.
- ***Counseling regarding future pregnancies.***
- Future research should concentrate on the development of algorithms that combine biochemical and biophysical markers, including blood pressure measurement—a diagnostic process used in clinical care. These may help improve the predictive accuracy of the tests to clinically important values.

Reproductive & Sexual Disorders Related Journals

- Andrology
- Journal Of Pregnancy And Child Birth
- Journal of Women's Health Care
- Gynaecology & Obstetrics



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