



# Recent advances in management of pregnancy induced hypertension



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# Classification-National High Blood Pressure Education Program Working

## Group

Diagnosis of Hypertensive Disorders Complicating  
Pregnancy

## Gestational Hypertension:

- 1/ BP 140/90 -1<sup>st</sup>- pregnancy /no proteinuria
- 2// BP returns to normal before 12 weeks postpartum . Final diagnosis made only postpartum
- 3/ May have other signs or symptoms of preeclampsia, for example, epigastric discomfort or thrombocytopenia

# Diagnosis of Hypertension

- Appropriately taken blood pressure exceeds
  - 140 mm Hg systolic or
  - 90 mm Hg diastolic.
  - Korotkoff phase V is used to define diastolic pressure.

appearance of proteinuria remains an important objective diagnostic criterion

1/ 24-hour urinary protein excretion  $> 300$  mg,

A urine protein:creatinine ratio of  $\geq 0.3$ , or

Persistent  $30$  mg/dl (1 dipstick) protein in random urine

.2/urine concentrations vary widely during the day, and hence too will dipstick readings. Thus, assessment may even show a 1 to 2 value from concentrated urine specimens from women who excrete  $\leq 300$  mg/day.

3/ spot urine protein :creatinine ratio will be a suitable replacement for a 24-hour measurement.

# preeclampsia

## :Minimum criteria

: BP 140/90 mm Hg  
after 20 weeks'  
gestation

• Proteinuria 300mg/24  
hrs or 1 dipstick

- Increased certainty of preeclampsia:
- BP 160/110 mm Hg
- Proteinuria 2.0 g/24 hours or 2 dipstick
- Serum creatinine 1.2 mg/dL
- Platelets 100,000/L
- i ncreased LDH
- Elevated ALT or AST
- Persistent headache or other cerebral or visual disturbance
- Persistent epigastric pain



# Eclampsia:

Seizures that cannot be attributed to other causes in a woman with preeclampsia



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### Superimposed Preeclampsia On Chronic Hypertension

- • New-onset proteinuria 300 mg/24 hours in hypertensive women but no
- proteinuria before 20 weeks' gestation
- • A sudden increase in proteinuria or blood pressure or platelet count 100,000/L
- in women with hypertension and proteinuria before 20 weeks' gestation

### Chronic Hypertension:

- • BP 140/90 mm Hg before pregnancy or diagnosed before 20 weeks' gestation
- not attributable to gestational trophoblastic disease
- or
- • Hypertension first diagnosed after 20 weeks' gestation and persistent after
- 12 weeks postpartum

# Indicators of Severity of Gestational Hypertensive Disorders

## Nonsevere

- Diastolic < 110
- Systolic <160 mm Hg
- Proteinuria= $\leq$ 2+
- Headache Absent
- Visual disturbances Absent
- Upper abdominal pain Absent
- Oliguria Absent
- Convulsion (eclampsia) Absent
- Serum creatinine Normal
- Thrombocytopenia Absent
- Serum transaminase elevation Minimal
- Fetal-growth restriction Absent
- Pulmonary edema Absent

## Severe

- >110 mm Hg
- >160
- PROTEINURIA $>3=$
- Present
- Present
- Present
- Present
- ELEVATED
- OBVIOUS
- present

# Epidemiology- preeclampsia/eclampsia

- Major cause of maternal & perinatal morbidity & mortality –worldwide-
- 15% -24% direct maternal death
- 5 fold increase in perinatal mortality—iatrogenic prematurity
- PNMR—59,90,400/1000 births in mild, moderate & severe preeclampsia respectively
- Different m/n would have altered outcome in 46% mat deaths

# Risk factors for PIH

## *Maternal Considerations*

- Inherent  
Age < 20 or 35–40 years/long interval between 2 pregnancies
- Nulliparity
- Afro-Caribbean origin
- Prior or family history of PE or cardiovascular disease
- Woman born small for gestational
- Obesity-BMI>35kg/m<sup>2</sup>-before pregnancy/at booking
- Mat low birth, PCOS, migrain,

## CONTD

- *Paternal Considerations*
- Limited sperm exposure
- Barrier contraception
- First-time father
- Donor insemination
- Change of partner

# CONTD

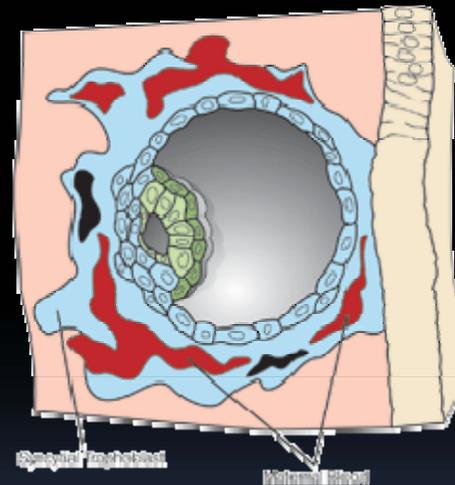
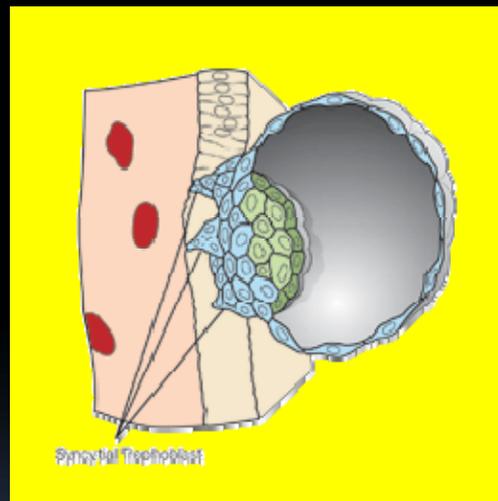
## Medical conditions

- ∅ Obesity
- ∅ Chronic hypertension
- ∅ Chronic renal disease
- ∅ Diabetes mellitus (insulin resistance, type 1, and gestational)
- ∅ Antiphospholipid antibody syndrome
- ∅ Connective tissue diseases
- ∅ Thrombophilia
- ∅ Stress

## CONTD

- Pregnancy specific
- Ø Multiple gestation
- Ø Oocyte donation
- Ø New partner
- Ø Urinary tract infection
- Ø Congenital conditions affecting the fetus
- Ø Hydatidiform mole
- Ø Hydrops fetalis
- Ø Structural anomalies

# Normal placentation



# similar pathogenesis –varying severity–abnormal invasion of trophoblasts

- 1. Placental implantation with abnormal trophoblastic invasion of uterine vessels
- 2. Immunological maladaptive tolerance between maternal, paternal (placental), and fetal tissues
- 3. Maternal maladaptation to cardiovascular or inflammatory changes of normal pregnancy
- 4. Genetic factors



# Endothelial Cell Activation

unknown factors likely placental in origin—are secreted into the maternal circulation and provoke activation and dysfunction of the vascular endothelium.

The clinical syndrome of preeclampsia is thought to result from these widespread endothelial cell changes



# Leads to

- Vasospasm –contracted vascular tree
  - Decreased plasma volume
  - Endothelial cell activation
- 



# women with new-onset hypertension

1/Hospitalization

2/daily scrutiny - headache, visual disturbances, epigastric pain, and rapid weight gain

3/Weight determined daily

4/ Analysis for proteinuria on admittance and at least every 2 days thereafter

5/Blood pressure--n the sitting position with an appropriate-size cuff every 4 hours, except between 2400 and 0600 unless previous readings had become elevated

6/ Measurements of plasma or serum creatinine and liver transaminase levels, and hemogram to include platelet quantification.

7/The frequency of testing is determined by the severity of hypertension.

8/ Evaluation of fetal size and well-being and amnionic fluid volume either clinically or using sonography.

# What after admission

- Reduced physical activity - is likely beneficial. Absolute bed rest is not necessary.
- Ample protein and calories should be included in the diet, and sodium and fluid intake should not be limited or forced.

role of antihypertensive drugs is limited in mild to moderate preeclampsia

- Fortunately, many cases are sufficiently mild and near
- enough to term that they can be managed conservatively until labor commences spontaneously or until the cervix becomes favorable for labor induction.

# Goals of such management

- 1/early identification of worsening preeclampsia
- 2/development of a management scheme that includes a plan for timely delivery If any of these observations lead to a diagnosis of severe preeclampsia

# If fetus is preterm

- the tendency is to temporize in the hope that a few more weeks in utero will reduce the risk of neonatal death or serious morbidity from prematurity
- . justified in milder cases. Assessments of fetal well-being and placental function are performed, especially when the fetus is immature
- . Most recommend frequent performance of various tests-- include the *nonstress test* or the *biophysical profile*
- *Measurement* of the lecithin-sphingomyelin (L/S) ratio in amnionic fluid may provide evidence of lung maturity .

# Preeclampsia – Delivery Indications

- Mild Preeclampsia

- Expectant
  - Stable
  - Preterm
- Deliver
  - Term
  - Unstable preterm
  - Fetal compromise
    - GR/OH/abnormal Umbilical Doppler

Induced delivery  
(PG, Oxytocin, Amniotomy) unless  
obstetric indication

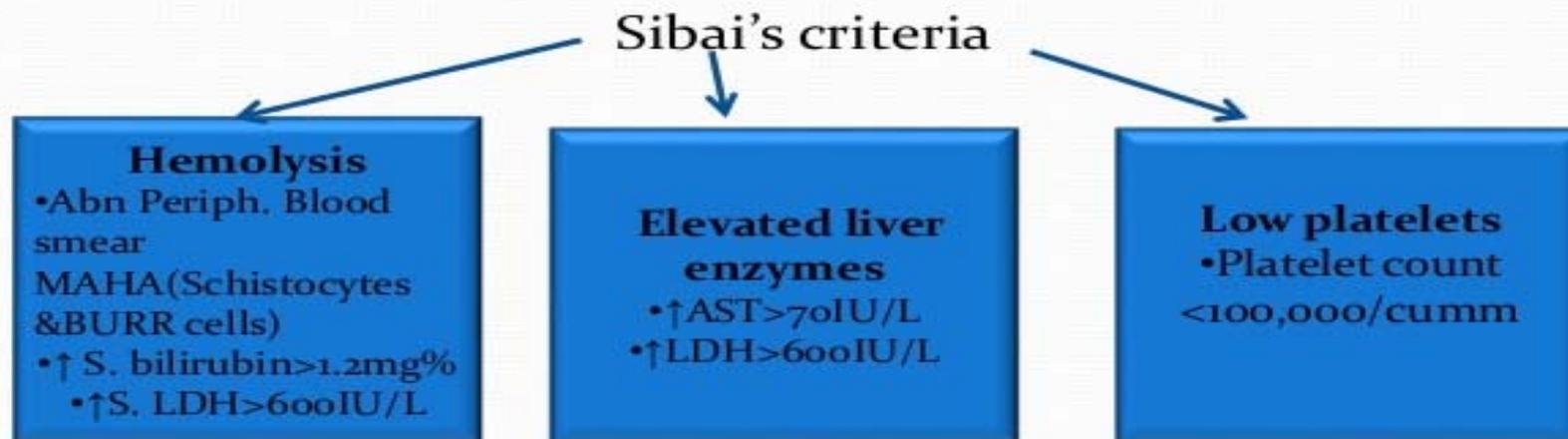
- Severe Preeclampsia

- Expectant (Betamethasone + MgSO<sub>4</sub>)
  - GA 24-32/52
- Deliver
  - GA > 32/52
  - Patient presenting with
    - Uncontrollable BP
    - Symptoms
      - Headache, RUQ, Visual
    - Hyperreflexia
    - Complications
      - HELLP or LP
      - Renal Failure
      - Hepatic Injury
      - Pulmonary Edema
      - DIC



# HELLP syndrome

- ❑ Variant of severe preeclampsia
- ❑ Maternal mortality ↑↑ (DIC, pulmonary edema, APH, Liver failure etc.)



# Complications of HELLP Syndrome

- Acute renal failure in 7% (usually ATN)
- Hepatic compromise is common
- Maternal mortality 1-3%
- Perinatal mortality 7-30%
- Resolves after delivery

## Complications

- ❖ **The mortality rate for women with HELLP syndrome is approximately 1.1 %**
- ❖ **From 1 to 25 % of affected women develop serious complications such as DIC, placental abruption, adult respiratory distress syndrome, hepatorenal failure, pulmonary edema, subcapsular hematoma and hepatic rupture.**
- ❖ **A significant percentage of patients receive blood products.**



With moderate or severe preeclampsia that does not improve after hospitalization, delivery is usually advisable for the welfare of both mother and fetus

- Labor induction is carried out, usually with preinduction cervical ripening with a prostaglandin
  - .
  - Whenever it appears that induction almost certainly will not succeed, or attempts have failed, cesarean delivery is indicated for more severe cases.
  - For a woman near term, with a soft, partially effaced cervix, even milder degrees of preeclampsia probably carry more risk to the mother and her fetus-infant than does induction of labor.
- 

# Mode of delivery-elective LSCS

Once severe preeclampsia is diagnosed, labor induction and vaginal delivery have traditionally been considered ideal.

- Temporization with an immature fetus is considered subsequently.
- Several concerns, including an unfavorable cervix, a perceived sense of urgency because of the severity of preeclampsia, and the
- need to coordinate neonatal intensive care, have led some to advocate cesarean delivery.

# Mode of delivery

- Following a seizure, labor often ensues spontaneously or can be induced successfully even in women remote from term .
- An immediate cure does not promptly follow delivery by any route, but serious morbidity is less common during the puerperium in women delivered vaginally.
- To avoid maternal risks from cesarean delivery, steps to effect vaginal delivery are used initially in women with eclampsia.

# LSCS in critical condition

- Skilled operative delivery may give better result than prolonged vaginal delivery
- **much less tolerant of even normal blood loss**
- **an appreciable** fall in blood pressure soon after delivery most often means excessive blood loss and not sudden resolution of vasospasm and endothelial damage.
- When oliguria follows delivery, the hematocrit should be evaluated frequently to help detect excessive blood loss. If identified, hemorrhage should be treated appropriately by careful blood transfusion.

## Severe preeclampsia, eclampsia , HELLP

- Confirmed Clinical diagnosis and lab evaluation
- Anticonvulsant t/t
- Antihypertensive m/n
- Fluid therapy
- Mode of delivery
- Component therapy

## Anticonvulsant treatment- -Magsulf regime

- 1/ Effective anticonvulsant - significantly lower incidence of recurrent seizure & maternal MORTALITY
- 2/ avoids CNS depression in - mother / infant.
- 3/ Intravenously / intramuscularly
- 4/ **The dosages** for severe preeclampsia/ eclampsia are SAME
- 5/ during labor and for 24 post partum

# Dosage Schedule-Intermittent Intramuscular Injections

- 4 g- 20% -IV - 10 g of 50% IM, DIVIDED - in the upper outer quadrant of both buttocks through a 3-inch-long 20-gauge needle.
- If convulsions persist after 15 min, give up to 2 g more intravenously as a 20% solution . if the woman is large, up to 4 g may be given slowly
- 3. Every 4 hr thereafter give 5 g of a 50% sol IM, but only after ensuring a/ patellar reflex is b. Respirations are not depressed c/ Urine output the previous 4 hr exceeded 100 ml

# Dosage Schedule-Continuous Intravenous Infusion

—

- 1. Give 4- to 6-g loading dose of magnesium sulfate diluted in 100 mL of IV fluid administered over 15–20 min
- 2. Begin 2 g/hr in 100 mL of IV maintenance infusion. Some recommend 1 g/hr
- 3. Monitor for magnesium toxicity:
  - a. Assess deep tendon reflexes periodically
  - b. Some measure serum magnesium level at 4–6 hr and adjust infusion to maintain levels between 4 and 7 meq/L (4.8 to 8.4 mg/dL)
  - c. Measure serum magnesium levels if serum creatinine  $\geq 1.0$  mg/dL
- 4. Magnesium sulfate is discontinued 24 hr after delivery

# Pharmacology and Toxicology

- $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$
- total clearance by renal excretion,
- Magnesium intoxication is unusual when the glomerular filtration rate is maintained or only slightly decreased.
- Adequate urine output usually correlates with preserved glomerular filtration rates. Thus, serum creatinine levels must be measured to detect signs of declining glomerular filtration rate.
- Eclamptic convulsions are almost always prevented or arrested by plasma magnesium levels maintained at 4 to 7 meq/l, 4.8 to 8.4 mg/dl, or 2.0 to 3.5 mmol/L. to determine if either measurement provides a superior

# TOXICITY

Patellar reflexes disappear plasma  $\text{mgso}_4$  10 meq/L—presumably because of a curariform action. This sign serves to warn of impending magnesium toxicity.

above 10 meq/L, breathing becomes weakened, at 12 meq/L or more, respiratory paralysis and respiratory arrest follow.

- **Treatment with calcium gluconate or calcium chloride,**
- **1 g intravenously, along with withholding further magnesium sulfate, usually reverses mild to moderate respiratory depression.**

For severe respiratory depression and arrest, prompt tracheal intubation and mechanical ventilation are lifesaving.

# Magnesium is anticonvulsant and neuroprotective .

- Some proposed mechanisms of action include:
- (1) reduced presynaptic release of the neurotransmitter glutamate, (2) blockade of glutamatergic *N-methyl-D-aspartate*
- (NMDA) receptors, (3) potentiation of adenosine action, (4) improved mitochondrial calcium buffering, and (5) blockage of calcium entry via voltage-gated channels central anticonvulsant effect

# Clinical Efficacy of Magnesium Sulfate Therapy.

- magnesium sulfate therapy was associated
- with a significantly lower incidence of recurrent seizures compared with women given an alternative anticonvulsant—9.7 versus 23 percent. Importantly, the maternal death rate of
- 3.1 percent with magnesium sulfate was significantly lower than for the other regimens.

# magnesium & Uterine Effects

- 1/ high conc depress myometrial contractility both in vivo and in vitro.
- 2/With the regimen no evidence of myometrial depression (transient decrease in activity during and immediately after the initial intravenous loading dose).
- 3/ No alteration in the need for oxytocin stimulation of labor, admission- to-delivery intervals, or route of delivery.
- 4/Inhibition of uterine contractility - dose dependent, and serum levels of at least 8 to 10 meq/L are necessary to inhibit uterine contractions by .

# Mg sulfate - fetal heart

- Whether magnesium sulfate affects the fetal heart rate pattern—specifically beat-to-beat variability—is controversial.
- In a randomized investigation, Hallak and colleagues (1999b) compared an infusion of magnesium sulfate with saline and reported that magnesium was associated with a small and clinically insignificant decrease in heart rate variability.

# Fetal Effects

- . **Maternal magsulf** promptly crosses the placenta to achieve equilibrium in fetal serum and less so in amnionic fluid
- Levels in amnionic fluid increase with duration of maternal infusion
- Neonatal depression occurs only if there is *severe hypermagnesemia at delivery*. Neonatal compromise after therapy with magnesium sulfate is usually not problematic
- Observational studies have suggested a protective effect of magnesium against the development of cerebral palsy in very low-birthweight
-

# Magsulf and renal effects

- *cleared almost exclusively by renal excretion,*
- *dosages - excessive if glomerular filtration is decreased substantively.*
- ***The initial 4-g loading dose of*** magnesium sulfate can be safely administered regardless of renal function.
- It is important to administer the standard loading dose and not to reduce it under the mistaken conception that diminished renal function requires it.
- This is because after distribution, a loading dose achieves the desired therapeutic level, and the infusion maintains the steady-state level.
- *Thus, only the maintenance infusion rate should be altered with diminished glomerular filtration rate. Renal function is estimated by measuring plasma creatinine. Whenever plasma creatinine levels are 1.0 mg/mL, serum magnesium levels are used to adjust the infusion rate.*

# Magnesium & CVS

- Acute cardiovascular effects of parenteral magnesium in
- women with severe preeclampsia have been studied using data
- obtained by pulmonary and radial artery catheterization
- . After a 4-g intravenous dose administered over 15 minutes, mean arterial blood pressure fell slightly, accompanied by a 13-percent
- increase in cardiac index
- . Thus, magnesium decreased systemic vascular resistance and mean arterial pressure, and at the same time increased cardiac output without evidence of myocardial depression.

# Antihypertensive treatment

- LABATOLOL
- NEFIDEPIN
- HYDRALLAZINE

# Labetalol.

## . effective antihypertensive agent

- Alfa 1 & nonselective –beta blocker.

Reg 1- 10 mg iv—10min—20mg—10min --40mg-- 40mg—80mg

Reg 2 Sibai 20 to 40 mg - 10 to 15 min-repeat same dose as needed for a max dose of 220 mg per treatment cycle.

Reg 3 The NHBPEP Working Group (2000) and the American College of Obstetricians and Gynecologists (2002a) recommend starting with a 20-mg intravenous bolus. If not effective within 10 minutes,

- this is followed by 40 mg, then 80 mg every 10 minutes but not
- to exceed a 220-mg total dose per episode treated

# Nifedipine- calcium-channel blocking agent

- Very effective for control of acute pregnancy related hypertension.
- The NHBPEP Working Group (2000) and the Royal College of Obst& Gyn recommend a 10-mg initial oral dose to be repeated in 30 minutes if necessary.
- Nifedipine given sublingually is no longer recommended.
- Randomized trials that compared nifedipine with labetalol found neither drug definitively superior to the other.



## ● Hydralazine

Commonly used in United States. Hydralazine is administered intravenously. 5-mg initial dose, 5- to 10-mg doses at 15- to 20-minute intervals until total dose to 30 mg per treatment cycle.

Remarkably effective in the prevention of cerebral hemorrhage. Its onset of action can be as rapid as 10 minutes.

The response to even 5- to 10-mg doses cannot be predicted by the level of hypertension. Uteroplacental insufficiency was evident when the pressure fell to 110/80 mm Hg.

These decelerations persisted until her blood pressure was increased with rapid crystalloid infusion. In some cases, this fetal response to diminished uterine perfusion

- May be confused with placental abruption

# Diuretics

- **Potent diuresis can further compromise placental perfusion.**
- Immediate effects include depletion of intravascular
- volume, which most often is already reduced compared with that of normal pregnancy
- before delivery, diuretics are not used to lower blood pressure
- We limit antepartum use of furosemide or similar drugs solely to treatment of pulmonary edema.

# FLUID THERAPY

- Mortality due to intracranial haemorrhages substantially reduced due to magsulf but this does not benefit overall maternal mortality and morbidity
- Pulmonary edema and acute tubular necrosis are new emerging causes of mortality
- Two schools of thought—forced diuresis  
//keep dry



# Fluid imbalance in preeclampsia

- Positive fluid balance—total body water
- Excess fluid in interstitial space—salt retention, low oncotic pressure, increased capillary permeability
- Gross haemoconcentration

# Preventing the problems

- Multiprofessional approach
- Careful vigilance to prevent disease progressing unchecked
- Timely delivery
- Strict fluid balance including hourly urometry
- Avoiding sharp fall in BP(Nefedipine & bolus iv oxytocin)
- Avoid simultaneous pharmacological interventions .avoid tocolysis /ergometrine/NSAIDS
- Replace sudden blood losses promptly but carefully

# STD PERIPARTUM OBSERVATIONS

- PR,BP,RRTemp,Oxygen saturation
- Urine output hourly
- Invasive monitoring—refractory hypertension, refractory pulmonary edema,severe oliguria in HELLP,SEVERE HAEMORRAGE, MODS
- CVP-/triple lumen

# Crystalloids or colloids-

- Colloids—1/due to-low oncotic pressure  
2/ability to increase intravascular volume 3/  
risk of extravasation
- Crystalloids—easy movement across  
endothelium-
- Standard fluid volume regime-1ml/hr/kg or  
previous hours urine output + 40ml to be  
given in next hour

# m/n of oliguria

majority cases expectant

approach—spontaneous resolution

Look for HELLP, sepsis, haemorrhage-risk of renal failure—CVP measurement

Hartman solution if intravascular depletion

Dopamine low dose –if filled intravascular compartment

# m/n of pulmonary edema

- Decreased oxygen saturation—pul edema, magsulf toxicity, aspiration, atelectasis, pneumonia, pulmonary embolism
- Cardiogenic/ noncardiogenic
- CVS/RS exam
- Plain chest Xray
- ABG, ECG, cardiac enzymes
- ECHO
- PROPPED UP, oxygen
- Frusemide if fluid overload/monitor for cardiovascular collapse if intravascular comp is depleted

# Prevention of pre-eclampsia

- no well-established measure
- High dose - Calcium .
- Low dose aspirin (antiplatelet agent)-- severe pre-eclampsia, gestational hypertension and IUGR<sup>19</sup>.
- prophylactic use of antioxidants (vitamin C, E) may be beneficial .
- lifestyle preventative interventions - rest, exercise and reduced dietary salt intake.??

# The pre-eclampsia community guideline (PRECOG)

- screening and detection of onset of pre-eclampsia in the community
- Care- Initial risk assessment at community booking using pre-determined criteria, to identify factors that predispose women to pre-eclampsia in a given pregnancy.
- referral before 20 weeks gestation for specialist input to their antenatal plan if they have been identified as high risk: this may be for clarification of risk, necessary investigations, advice on early intervention or pharmacological treatment.

# PRECOG CONTD

- Systematic assessment for onset of pre-eclampsia from 20 weeks gest
- Women with no risk factors for pre-eclampsia are offered assessments at weeks 16, 28, 34, 36, 38, 40, and 41 weeks
- .Women with one risk factor are reviewed in the community at least once every three weeks before 32 weeks, and then at least once every two weeks, until delivery.
- At every visit, recommendation is to look for presence of any signs or symptoms like new hypertension, new proteinuria, headache/visual disturbance, or both, epigastric pain/vomiting, or both, reduced fetal movements, small for gestational age infant
- . In the presence of two such, they are referred for early specialist input, individual assessment, and discussion of obstetric risk



# PRECOG

guideline for improving accuracy in blood pressure measurement, increasing reliability of proteinuria test with dipstick and community assessment of fetal growth and well being which provide the parameters for referral.

Referral is made for step-up assessment in hospital day unit within 24/48 hours or admission in accordance with set criteria. All pregnant women are also made aware that pre-eclampsia may develop between antenatal assessments, and they could self-refer at any time.

- continuity of care in the community and
- midwifery or GP care as part of their individual antenatal care plan

Thanks

