White Ribbon Alliance Pakistan
For Safe Motherhood

RAF
Working Towards Millennium Development Goals
Research & Advocacy Fund

USE OF MAGNESIUM SULPHATE AS A FIRST LINE TREATMENT IN SEVERE PRE-ECLAMPSIA AND ECLAMPSIA

CLINICAL GUIDELINES/PROTOCOLS FOR HEALTHCARE PROFESSIONALS

Saving Mother's Life: Addressing Barriers to the Use of Magnesium Sulphate

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Dr. Amanullah Khan
President, White Ribbon Alliance-Pakistan

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METHODOLOGY

a- Literature Review

Global evidence for effective use of magnesium sulphate and its impact on reducing maternal mortalities was searched through extensive literature review in order to get an insight of the success stories regarding use of Magnesium Sulphate in countries having contexts similar to Pakistan.

b- Review of Existing Documents/Policies

Existing health/MNCH policy level documents were reviewed extensively, both of federal and provincial levels to look into barriers in use of magnesium sulphate as effective remedy to avert eclampsia related maternal deaths. Apart from recent health policy drafts, provincial PC-1 documents of MNCH and LHW programs were reviewed to identify barriers and opportunities for promoting use of magnesium sulphate. Minimum Services Delivery Packages (MSDP) documents for Punjab, Khyber Pakhtunkhwa and Sindh governments were reviewed to look into gaps regarding the use of Magnesium Sulphate. While reviewing all these documents, special emphasis has been kept on post devolution scenario i.e. delegation of health care services responsibilities to the provinces after recent 18th amendment in constitution of Pakistan.

c- Consultative Process

A series of consultative meetings was held by the WRA-P to share the draft documents developed by the consultants. The meetings were attended by the representatives of the Provincial Departments of Health (DoHs), Research and Advocacy Fund, well-renowned Gynaecologists, WRA-P consultants and project staff. The documents were discussed in detail, further refined with consensus and endorsed by the DoHs.

BACKGROUND

Eclampsia and pre-eclampsia are morbid complications of pregnancy. They account for a large number of deaths in mothers. Since these are avoidable causes of death, as expected they are maximum in under privileged and under resourced countries and in the under resourced areas and more so in the poor people of those countries.

The definition of pre-eclampsia has always been inconsistent in the past and due to this confusion in comparing results of various treatments and outcomes has always been there. There is now a widely accepted classification system of hypertensive disorders in pregnancy.

Pre-eclampsia is a multiple organ disorder of unknown aetiology associated with raised blood pressure and proteinuria in pregnancy after 20 weeks gestation, while eclampsia is its progression to a state when a woman develops fits or convulsions and advanced disease is associated with multiple organ involvement such as renal failure, pulmonary oedema, cerebral oedema, cerebral haemorrhage, hepatic failure and rupture and clotting disturbances especially thrombocytopenia. In addition aspiration pneumonia and injury due to unconsciousness may be important causes of morbidity and mortality both in the mother and foetus. Blindness, temporary or permanent may be one of the complications. 25% of eclamptic seizures occur during the postpartum period especially in the first 24 hours[1].

Pre-eclampsia and eclampsia accounts for about 50,000 deaths each year[2] that is; about 10%-12% of all maternal deaths[3] and majority of these occur in the developing countries. There is a very striking difference, being 1per100 in low income countries compared to 1per2000 in countries like UK[4]. Maternal mortality results after a patient develops complications of pre-eclampsia. The incidence of gestational hypertension and development of pre-eclampsia is similar in the developed and the developing countries but the striking difference in the maternal mortality between the two worlds is because of lack of recognition of signs and symptoms of severe pre-eclampsia thus resulting in death of the patient. This obviously is because of poor antenatal care available in the low resourced areas of low resourced countries. Pre-eclampsia can neither be predicted nor prevented but its complications can definitely be prevented by proper antenatal care.

Eclampsia and pre-eclampsia are conditions of unknown aetiology. The level of antenatal, intrapartum and postpartum care a woman receives is vital for the survival of mother and foetus. Identifying the risk factors and diagnosing the condition and its severity is of utmost importance. Once it becomes severe enough so as to increase the risk of eclampsia the only treatment available is delivery after stabilizing the patient. Understanding the different types of hypertension in pregnancy is important to make important decisions at an appropriate time.

Eclampsia may occur for the first time during intrapartum and even postpartum. There is a 25% risk after delivery especially in the first 24hours.

Risk factors for pre-eclampsia

Primigravida
Multigravida with
- Previous history of pre-eclampsia
- Previous delivery more than 10 years
- Advancing age more than 40 years

BMI of more than 35
Family history of pre-eclampsia or eclampsia
Chronic hypertension
Multiple pregnancy
Molar pregnancy
Chronic renal disease
Diabetes Mellitus
Anti-phospholipid antibodies

Pre-eclampsia occurs only when trophoblastic tissue provides stimulus for the disorder. Trophoblastic invasion is patchy and incomplete in pre-eclampsia and the spiral arteries retain their muscular walls which are thought to prevent the development of a high flow low impedance uteroplacental circulation. The reason for this is unknown but it is an abnormal adaption of maternal immune response. This defective invasion of trophoblast results in relative under perfusion of placenta which release factors into the maternal circulation targeting the vascular endothelium. Pre-eclampsia is multi-system disease effecting multiple organs simultaneously.

It is important to accurately identify women with hypertension and more important to accurately classify them as having pre-existing hypertension or gestational hypertension as the prognosis and then obviously the management is different in both cases and then further division of gestational hypertension into proteinuric and aproteinuric hypertension where again the prognosis and management is variable.

Hypertension labelled as chronic is present before 20 weeks of gestation and about 95% of these are cases of essential hypertension, however if diagnosed as chronic HT the underlying cause especially renal disease must be ruled out. Women with co-morbid conditions such as renal disease are at significant risk in pregnancy.

Blood pressure should be measured with an appropriate size cuff and korotokoff 5 should be taken as diastolic blood pressure. Korotokoff 5 is taken as the point where the sounds disappear. Previously korotokoff 4 was taken which was the point where sounds became muffled. Diagnosis is made if the B.P is greater or equal to 140/90mmHg. These measurements should be at least two readings taken several hours apart. If B.P is raised proteinuria should be assessed on every visit or if the patient is admitted then it should be assessed daily. If proteinuria is more than 3+ then the woman is at high risk of developing seizures. The risk of dying from eclampsia is about 14 times higher in a developing as compared to a developed country [5].

Worldwide the incidence of gestational hypertension is about between 10-15%; 3-4% of them develop pre-eclampsia and eclampsia.

Pre-eclampsia is more common in primigravida. It is thought that the normal fetal-maternal transfusion that occurs during pregnancy and particularly during delivery exposes the mother to products of the fetal (and hence paternal) genome, protecting her in subsequent pregnancies. In line with this, the protective effect of first pregnancy seems to be lost if a woman has a child with a new partner. Overall the recurrence risk in a subsequent pregnancy is 20 per cent, but is much higher if severe pre-eclampsia developed at an extremely early gestation in the first pregnancy. There also appears to be a maternal genetic predisposition to pre-eclampsia as there is a three- to four-fold increase in the incidence of pre-eclampsia in the first degree relatives of affected women.

In Pakistan the situation is grave. After PPH the second most common cause of death is eclampsia and pre-eclampsia which accounts for about 14% of total deaths in the Pakistan demographic health survey. It is estimated that 2000 women die of eclampsia and 8-10% women suffer from this condition during their pregnancies in Pakistan.

Optimizing healthcare to prevent deaths due to hypertension in pregnancy can go a long way in achieving the Millennium Development Goals 4 and 5. The actual scenario is that less than half of the pregnant ladies in Pakistan have only one antenatal visit while others have none. As expected most of those suffering from pre-eclampsia are never diagnosed and they are for the first time brought in a healthcare with convulsions thus enhancing the mortality and morbidity of the mother and foetus. The concern is that even when a woman is brought in with full blown eclampsia or severe pre-eclampsia which if not treated will result in eclampsia, usually no treatment is given and she is rushed to another facility and then another with no treatment offered till she finally lands in a secondary or tertiary care hospital, if she is lucky to survive till then. $MgSO_4$ is hardly used during transfer stages or even at the final facility, although it is one of essential drugs to be used.

The only cure for pre-eclampsia and eclampsia is to deliver the baby and placenta but this can be a big problem when pre-eclampsia occurs before 34 weeks. Management strategies are aimed to minimize the risk to the mother so that the pregnancy can be continued till an appropriate foetal age is reached to improve the neo-natal survival. In severe cases however it may not be possible.

This is talking of an ideal situation. The actual scenario in our country is quite disturbing. A large majority of patients who have even been to a health care provider have never had their B.P recorded and on top of that more than half of the pregnant ladies have never had even one antenatal check-up. They mostly are noticed when they develop seizures and then when seen by the first hand care providers, they are rushed to the nearby facility. This take many hours because of the identified first and second delay i.e. decision making and arranging transport and when taken to the nearest facility there is the third delay as in most of the low level facilities trained HCPs are not available. Receiving patient in a serious condition with neither human resource nor facilities they are referred to another hospital

and yet another, even good private hospitals do not cater such emergencies. The irony of the matter is that no emergency treatment is provided before rushing them from one place to another. The use of $MgSO_4$ is almost non-existent at primary and even secondary level facilities and if the patient is lucky enough to survive and reach a facility where appropriate human resource and critical care facilities are available and she by nature has not suffered any irreversible damage, may survive. According to the PDHS the main cause of maternal mortality in community was PPH, But according to a survey of eight teaching hospitals of RWP/ISB the main cause of death was eclampsia [14] The reason is that most of the cases of PPH were unable to reach these hospitals and died at their homes or on the way and those who reached these hospitals were mostly saved with vigilant treatment. In contrast most of the cases of eclampsia reached the tertiary hospitals but because of repeated fits and complications due to that, in spite of intensive care, had suffered irreversible damage and could not be saved. This is an eye opener and signifies the importance of this guideline as these patients arrive without any treatment to prevent further fits.

Principles of management of pre-eclampsia

History

History of pre-eclampsia/eclampsia in previous pregnancy
History of pre-eclampsia/eclampsia in first degree relative
History of risk factors

Examination

Proper antenatal blood pressure record
Early recognition of pre-eclampsia which is often symptomless
Awareness of the serious nature if blood pressure is associated with proteinuria

Referral

Adherence to agreed guidelines for admission to hospital and investigations

Treatment

Agreed guidelines for the use of anti-hypertensive
Agreed guidelines for the use of anti-convulsant therapy where preference should be $MgSO_4$
Delivery to prevent serious maternal and foetal complications

Follow-up

Postnatal follow-up
Appropriate contraceptive advice

Unfortunately there is currently no screening test for pre-eclampsia. No single blood biomarker has emerged which either alone or in combination with other biomarkers or clinical data possesses sufficient sensitivity and specificity to be clinically useful. Doppler ultrasound of uterine artery wave form has been analysed with variable success. Preventive intervention is probably only low dose aspirin 75mg daily. Low dose aspirin reverses the imbalance between the vasoconstrictor thromboxane and the vasodilator

prostacyclin which is known to occur in pre-eclampsia. There is a 15% relative risk reduction in pre-eclampsia with aspirin intake.

We therefore propose the following guidelines/recommendations for health care providers to prevent deaths due to eclampsia and severe pre-eclampsia both in the mother and foetus, with main focus on the use of magnesium Sulphate for the prevention of fits in severe pre-eclampsia and preventing further fits in established eclampsia.

It is now fully established that Magnesium Sulphate is the drug of choice for the treatment and prevention of fits in eclampsia and severe pre-eclampsia[6, 7]. It is included in World Health Organization's (WHO) essential medicines list since 1996 and since 2003 further reinforced for use in severe pre-eclampsia and eclampsia. However in spite of being highly effective and a cheap drug its use is still not as it should be in developing countries due to various hindrances. Scaling up its use in Pakistan by addressing the barriers can accomplish the millennium development goals to a great extent. The consumption data from the ministry displays an overall usage of $MgSO_4$ (Public and Private) for any indication in Pakistan was observed to be 0.06% of the pregnant women in 2009 and this does not even cover a 24hr administration for eclampsia alone. Women who actually need treatment for eclampsia are about 8% to 10%, so more than 10 times higher consumption is desired. In a very comprehensive article, barriers to the use of Magnesium Sulphate in Pakistan have been discussed in detail.

There are many factors responsible for its limited use.

a) Lack of proper national guideline
b) Independent procurement policy by different hospitals although it is included in the national essential medicine list (2007). It however is dependent on facility policy rather than national policy
c) $MgSO_4$ is a low cost drug with not much incentive for pharmaceuticals and the use is limited
d) Lack of knowledge, lack of proper national guidelines and fear of monitoring and serious side effects are the main factors preventing its use
e) Availability is another issue especially in smaller towns and villages and private facilities, also the antidote calcium gluconate is not available. Although in contrast to international guidelines Diazepam is usually available in the emergency tray
f) Lack of proper training of health care providers
g) Lack of champions

Addressing these problems we have devised guidelines for use of $MgSO_4$ at every level of healthcare facility.

GUIDELINES

Identification of the problem is of profound importance.

The health care providers in Pakistan fall into various categories, from highly educated professionals to almost totally illiterate, untrained traditional birth attendants (TBA's).

At community level we have

a) Traditional Birth Attendants (TBAs)
b) Lady Health Workers. (LHW)
c) Community Midwives (CMW)

At facility level we have

a) Lady Health Visitors (LHV)
b) Woman Medical Officer (WMO)
c) Gynaecologists/ Obstetricians
d) All varieties of private practitioners including general practitioners (GP), hakims, homeopathic and quakes.

Health facilities available are:

a) Civil Dispensaries/ First Aid Post
b) Basic Health Units (BHU)
c) Rural Health Centre (RHC)
d) Tehsil Headquarter Hospital (THQ)
e) District Headquarter Hospital (DHQ)
f) Teaching Hospitals
g) All varieties of private clinics and hospitals

Guidelines are being proposed for all levels of understanding and implementation.

These guidelines are specifically proposed to target the

a) Primary Level Care
b) Secondary Level Care
c) Tertiary Level Care

In general antenatal coverage should be provided to all pregnant ladies. Minimum of four visits are recommended. Whoever is doing the antenatal must be able to correctly take the B.P.

All health care providers should be capable of

A. Diagnosis and Identification of high risk patients
  a. History of high B.P or fits in previous pregnancy

b. Obesity or marked oedema in current pregnancy
c. B.P more than or equal to 140/90 mmHg taken as two readings four hours apart after 20 weeks of gestation
d. Proteinuria

Once the B.P is recorded to be high on two occasions, (140/90) or very high as 160/110 on a single occasion after 20 weeks of gestation, the woman is at risk of developing pre-eclampsia and eclampsia and is diagnosed as gestational hypertension. It may remain mild hypertension till term or it may just gallop to severe pre-eclampsia and eclampsia within no time thus markedly increasing the maternal and peri-natal mortality. It is difficult to predict the outcome of gestational HT in different patients but all Cases Diagnosed as Gestational Hypertension Must Be Taken Seriously. There is about 50% progression in those who develop gestational hypertension prior to 32 weeks gestation[10]. Risk of developing gestational hypertension, in future pregnancy, ranges from 16% to about 47 %[11].

Once a woman is diagnosed to have hypertension and if facilities are not available for diagnosis, she should be referred to a higher facility. However in countries like Pakistan it is easier said than done due to various reasons.

The next step at all levels once hypertension is diagnosed, is to test for proteinuria with a dipstick. A reading of 1+ or more should prompt further evaluation.

At this level when a patient is having high blood pressure in pregnancy she should be referred for antenatal care at the facility.

The focus of this guideline is mainly on preventing fits due to severe pre-eclampsia and preventing further fits if eclampsia has already occurred. It is now a proven fact that $MgSO_4$ is the drug of choice in preventing fits and is far superior to Diazepam, phenytoin and Lytic cocktail[12].

Who should receive $MgSO_4$?
It should be given to all pregnant women who develop seizures (fits) and also all those who are liable to develop fits if no treatment is given. The former is an obvious situation which anybody even a layman can recognize, the latter however requires a little knowledge about the disease and its progress.

The most important message of this guideline is that $MgSO_4$ is a cheap, available drug in Pakistan which is underutilized and about 2000 women every year are dying of eclampsia in Pakistan. It is the second most important cause of death after PPH and is totally preventable. Even with good antenatal care you cannot prevent pre-eclampsia which is a disease of theories, but with good antenatal care eclampsia can definitely be prevented. Women die of eclampsia and not pre-eclampsia or gestational hypertension.

Identification of signs and symptoms of severe pre-eclampsia:

Severe hypertension = or > 160/110 with proteinuria or mild to moderate hypertension i.e. = or >140/90 for severe hypertension = or < 160/110 and proteinuria with at least one of the features:

Symptoms

a) Severe Headache
b) Blurring of Vision
c) Severe abdominal pain or vomiting
d) Confusion and restlessness

Signs

a) Papilledema
b) Signs of clonus (>or= 3beats)
c) Liver tenderness
d) HELLP Syndrome
Low Platelet Count
Abnormal Liver Enzymes (ALT or AST rises to >70iu/ litre)

If the patient is not treated in this situation eclampsia can occur in which she develops fits. Both severe pre-eclampsia and eclampsia are grave situations. All such cases must be clearly identified by HCPs.

Once identified the HCPs should take an immediate action:
Various situations can arise:

a) If the woman is in the community and seen by an LHV or CMW/LHW
b) She is at a low resource centre such as a BHU or RHC where at least some health professional is available
c) At a private health facility
d) At THQ hospital
e) At DHQ hospital
f) At teaching or a tertiary care hospital

1. Guidelines for Community Level HCPs

a) When a woman is found to have high blood pressure in pregnancy she should be referred to the nearest facility

b) If cannot be referred then proteinuria should be checked. If proteinuria more than 2+ should be referred immediately. The family must be counselled strongly for referral

c) If seen to have very high blood pressure that is more than 160/110 mmHg and proteinuria more than 3+ or patient having signs and symptoms of severe pre-eclampsia she must be given 10 gms of $MgSO_4$ Injection as a loading dose (5gms in each buttock I/M) and then immediately referred to the highest available facility with 24 hours emergency cover

d) If the patient is seen at the time of fits then again she must be given 10 gms of $MgSO_4$ Injection as a loading dose (5gms in each buttock I/M) and then immediately referred to the highest available facility with 24hours emergency cover

e) If due to any reason the patient is still not transferred after 4 hours, then repeat 5gm deep intramuscular in the buttock. Stress on the family to take the patient to the highest facility.

Recommended antenatal visits are:

Once a month till 28 weeks
Fortnightly till 36 weeks
Weekly till birth
If this is not possible then minimum of four visits

In every visit blood pressure should be measured. Blood pressure may be normal or elevated.

2. Guidelines for Primary Health Care Facilities

a) When a woman is found to have high blood pressure in pregnancy she should be advised anti-hypertensive i.e. Methyldopa Tablet 250 mg three times a day and proteinuria should be checked. She should be called for more frequent antenatal visits

b) If blood pressure is very high i.e. ≥ 160/110 mmHg or proteinuria more than 2+ the patient should be referred immediately. Anti-hypertensive should be started. The family must be counselled strongly for referral

c) If seen to have very high blood pressure that is more than 160/110 mmHg and proteinuria more than 3+ or patient having signs and symptoms of severe pre-eclampsia she must be given 10 gms of $MgSO_4$ Injection as a loading dose (5gms in each buttock I/M) and then immediately referred to the highest available facility with 24 hours emergency cover

d) If the patient is seen at the time of fits then again she must be given 10 gms of $MgSO_4$ Injection as a loading dose (5gms in each buttock I/M) and immediately referred to the highest available facility with 24 hours emergency cover

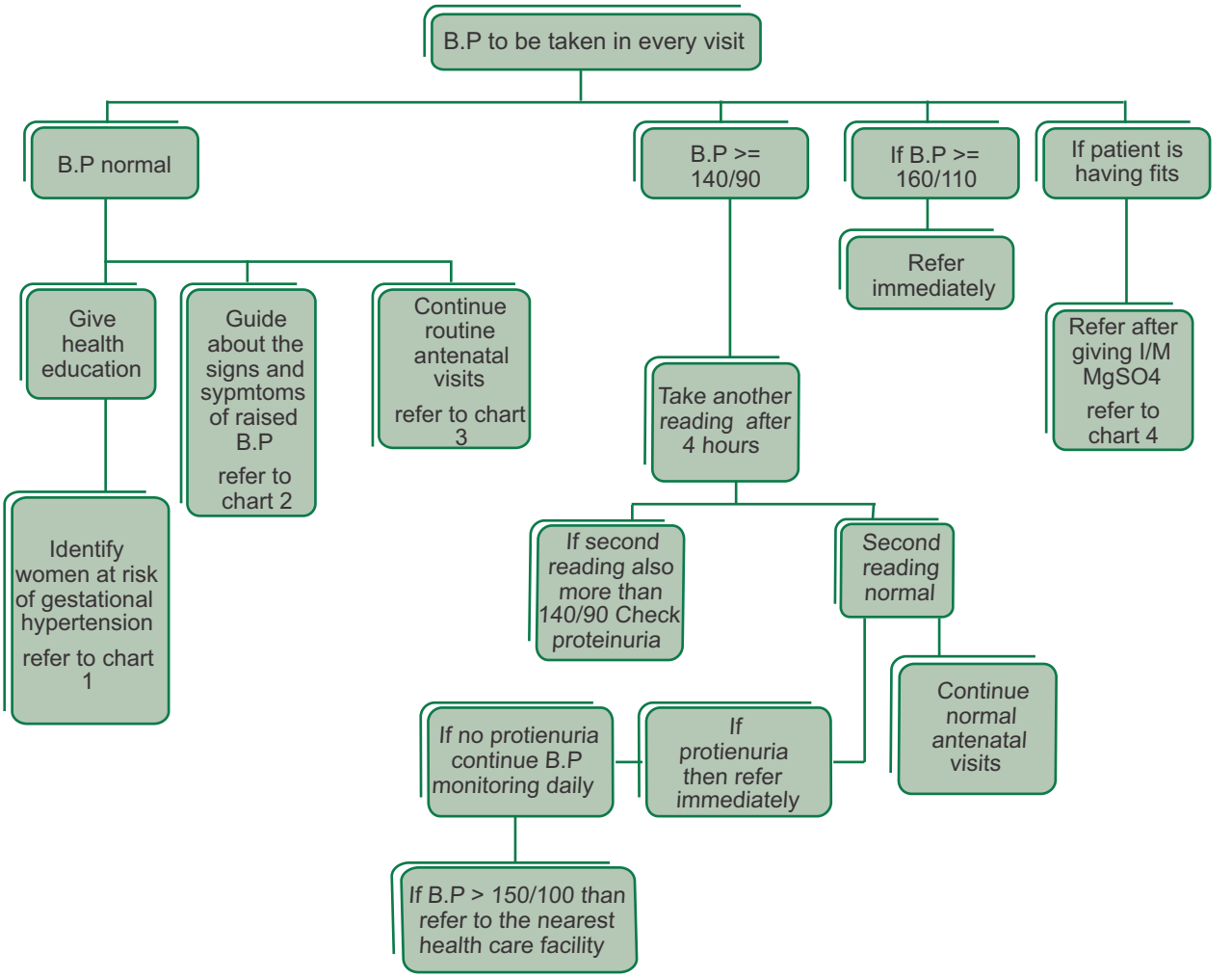
e) If due to any reason the patient is still not transferred after 4 hours, then repeat 5gm deep intramuscular in the buttock. Stress on the family to take the patient to the highest facility

We recommend that when a patient is recognized as a case of severe pre-eclampsia or Eclampsia at primary health care facility, she must be given anti-convulsant treatment and then immediately referred to the nearest highest facility available. At this level 1 care, our recommendation is for intramuscular regimen as recommended by The Oxford Group:

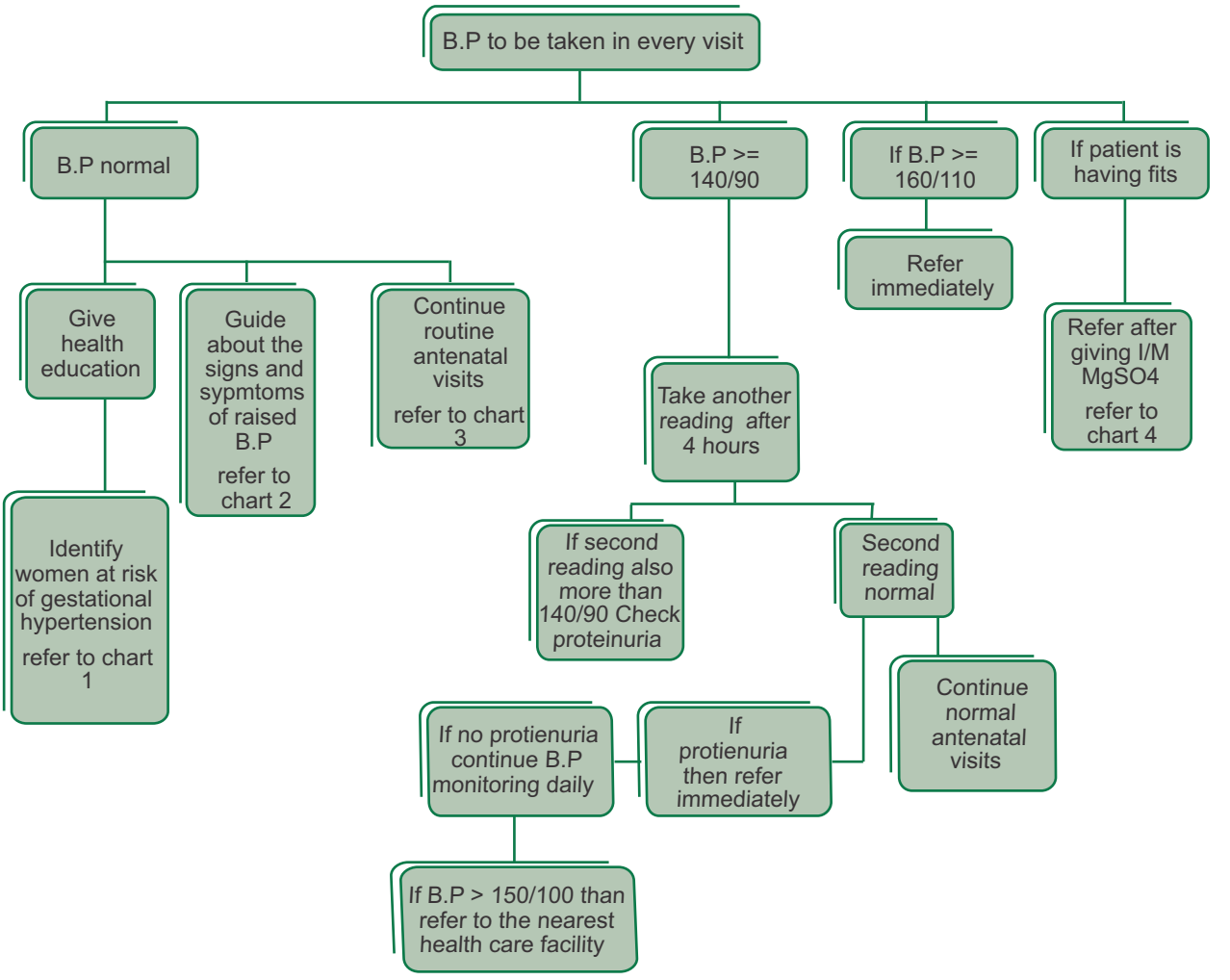
> After the loading dose patient should be referred immediately to the highest available facility which can cater for critically ill patients and neonates, with written notes of dose and route given.
> This should be followed by 5gm deep I/M injection in each buttock at a 4 hourly interval

$MgSO_4$ can be administered by anyone trained in I/M injection and has fewer side effects. The I/M regimen practice is very important in a variety of care settings by paramedics and medical personnel and for wider use rather than allowing the women to die by denying treatment. This regimen was shown to be effective in Ghana and Bangladesh[14].

Flowchart for Community Level HCPs



Flowchart for Primary Health Care Facilities

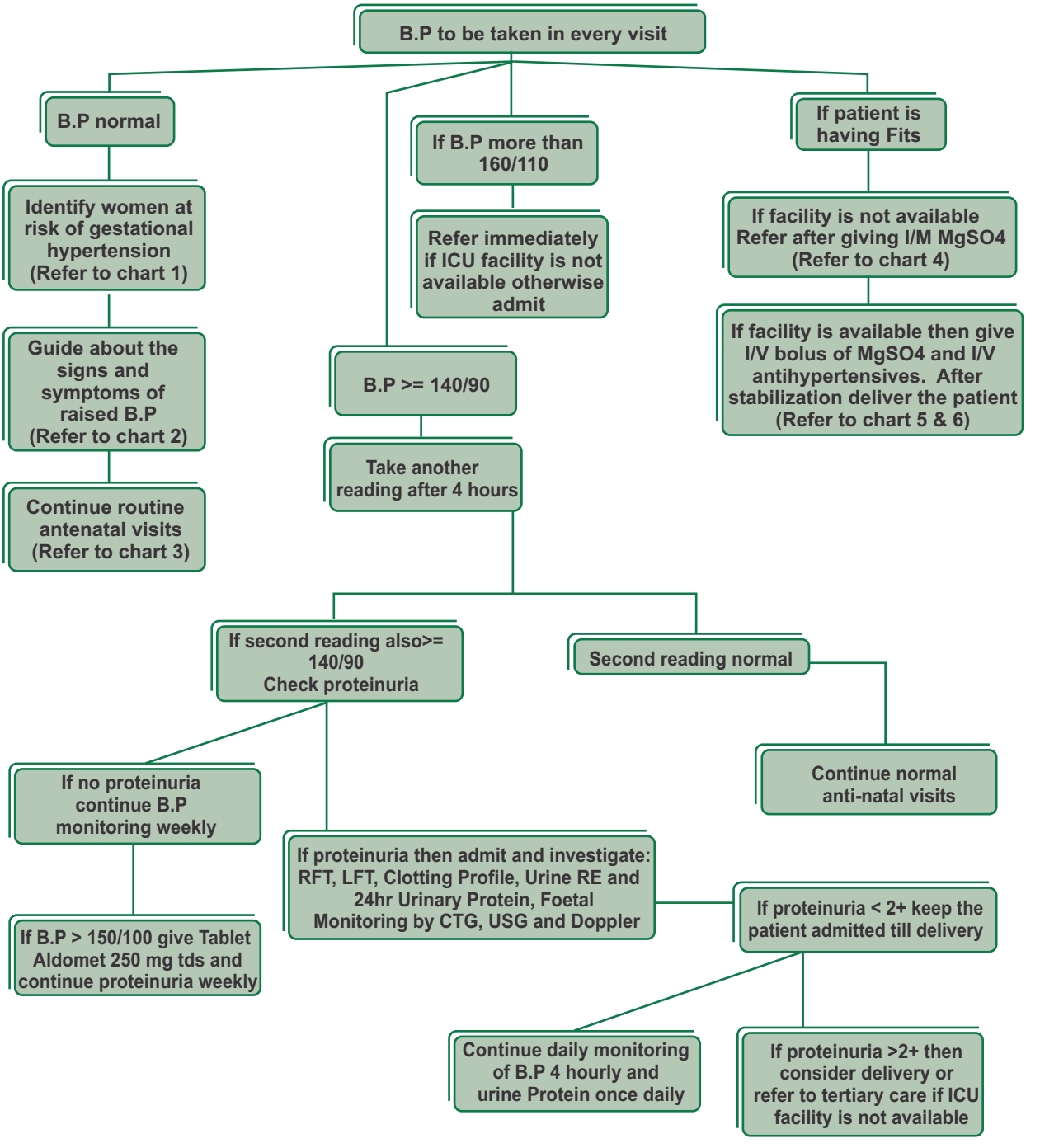


3. Guidelines for Secondary Health Care Facilities

Once the patient arrives at secondary care facility then she should be assessed properly, all investigations taken and send to the lab.

If facility is available to cater for emergency obstetrics 24 hours and receives a critically ill patient then the patient should be retained, otherwise should be referred to a tertiary care facility. If the patient is retained at secondary level then manage as guideline no 4, which is the same for secondary and tertiary care facilities.

Flowchart for Secondary Health Care Facilities



Guidelines for Secondary and Tertiary Health Care Facilities

In case of severe pre-eclampsia and eclampsia investigation should be sent immediately, patient assessed and then appropriate treatment given.

Management of High Blood Pressure

Anti-hypertensive should be given to lower the blood pressure. B.P must be controlled with Labetalol, Hydralazine or Nifedipine. I/V therapy is usually required.

Management of Fits

Anti-convulsants should be given to prevent further fits by giving:

A loading dose of 4 gms(8 ml of 10 ml vial) of $MgSO_4$ in 50 ml of solution over 10 minutes by an intravenous infusion

Followed by I/M Injection of 5gms (10 ml or 1 vial) of $MgSO_4$ mixed with 1ml of 2% lignocaine injection first in one buttock and then the other making a total of 14gms.

Maintain dose of 5 gms (10 ml or 1 vial) of $MgSO_4$ mixed with 2% lignocaine 1 ml is then given 4 hourly I/M in alternate buttock for 24hours (Pritchard regimen) after delivery.

Management of $MgSO_4$ Therapy

Once $MgSO_4$ is given, monitoring of the patient should be done by

Urine output (more than 25mls/ hour)
knee jerk (should be present)
Respiratory rate (more than 16/ min)

If either of these is disturbed $MgSO_4$ should be stopped immediately. Antidote is calcium gluconate Injection given slowly I/V.

Delivery

As soon as the patient is stabilized delivery should be planned immediately

Monitoring

Monitor:

- Blood pressure
- Pulse
- Respiratory Rate
- Fits
- Intake / Output

Post-natal

Post-natal monitoring should continue for at least 24 hours after delivery

Contraceptive advice must be given

Blood pressure should be checked again after six weeks of delivery

Guidelines for Tertiary Care 1

Gestational Hypertension (Hypertension without Proteinuria)

Mild hypertension without proteinuria (140/90 to 149/99)

Admission not required
Treatment not required
Weekly visits to check for blood pressure
Weekly check for proteinuria

Moderate hypertension without proteinuria (150/100 to 159/109)

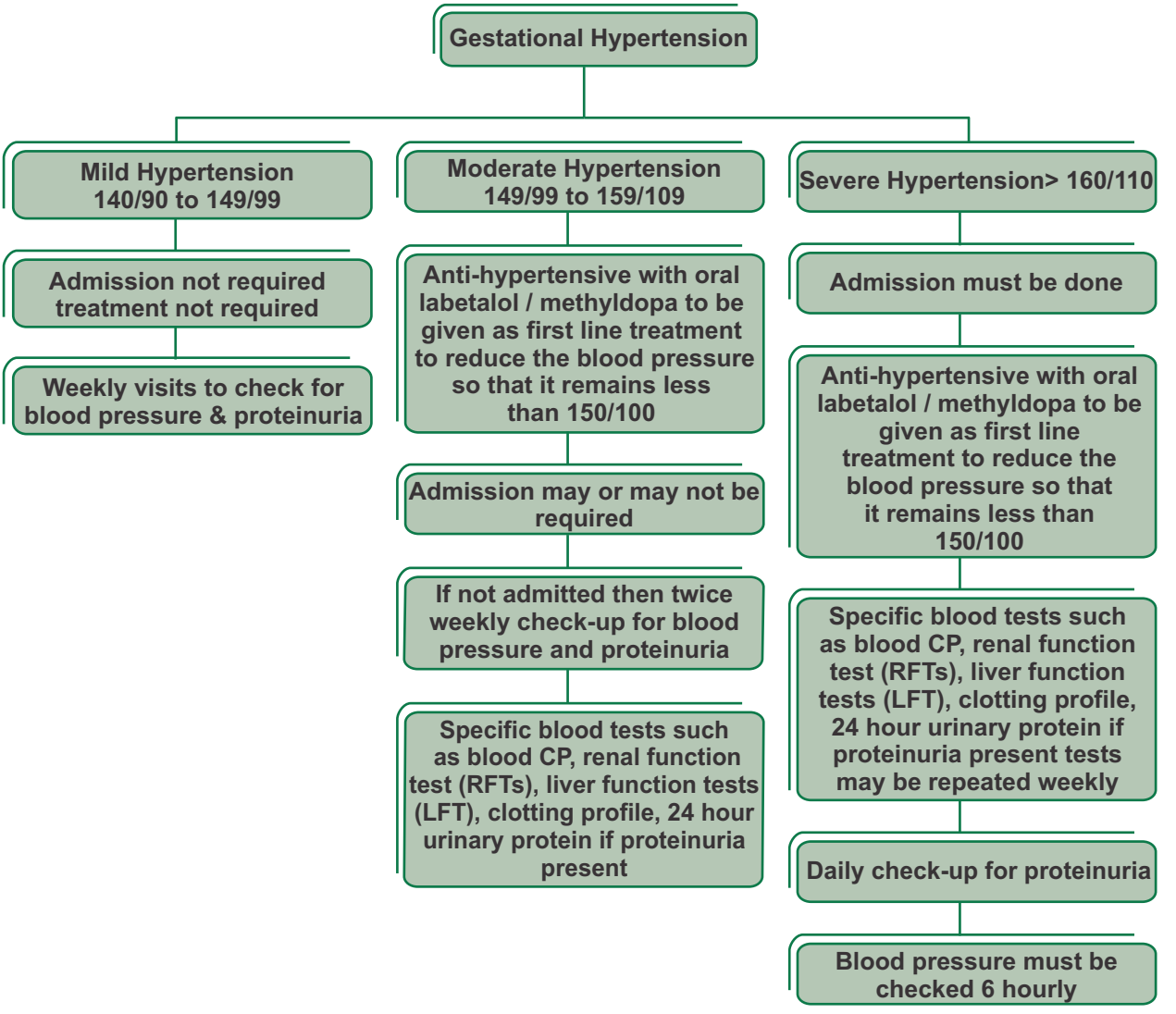
Admission may be required
Anti-hypertensive with oral labetalol / methyldopa to be given as first line treatment to reduce the blood pressure so that it remains less than 150/100
If not admitted then twice weekly check-up for blood pressure and proteinuria
Specific blood tests such as blood CP, renal function test (RFTs), liver function tests (LFT), clotting profile, 24 hour urinary protein if proteinuria present
Tests may be repeated weekly if proteinuria appears, otherwise monthly

Severe Hypertension without proteinuria (160/110 or more)

Admission must be done
Anti-hypertensive with oral labetalol/ methyldopa to be given as first line treatment to reduce the blood pressure so that it remains less than 150/100
Blood pressure must be checked 6 hourly
Daily check-up for proteinuria
Specific blood tests such as blood CP, renal function test (RFTs), liver function tests (LFT), clotting profile, 24 hour urinary protein if proteinuria present
Tests may be repeated weekly

Flowchart For Tertiary Care 1

Gestational Hypertension (Hypertension without Proteinuria)



Guidelines for Tertiary Care 2

Pre-eclampsia (Hypertension with proteinuria)

All cases of pre-eclampsia must be admitted

Mild hypertension does not require anti-hypertensives

Moderate and severe hypertension require anti-hypertensives such as oral labetalol or methyldopa to keep the blood pressure lower than 150/100

Blood pressure must be checked 4 times a day or more if required

Proteinuria daily but quantification is required only once

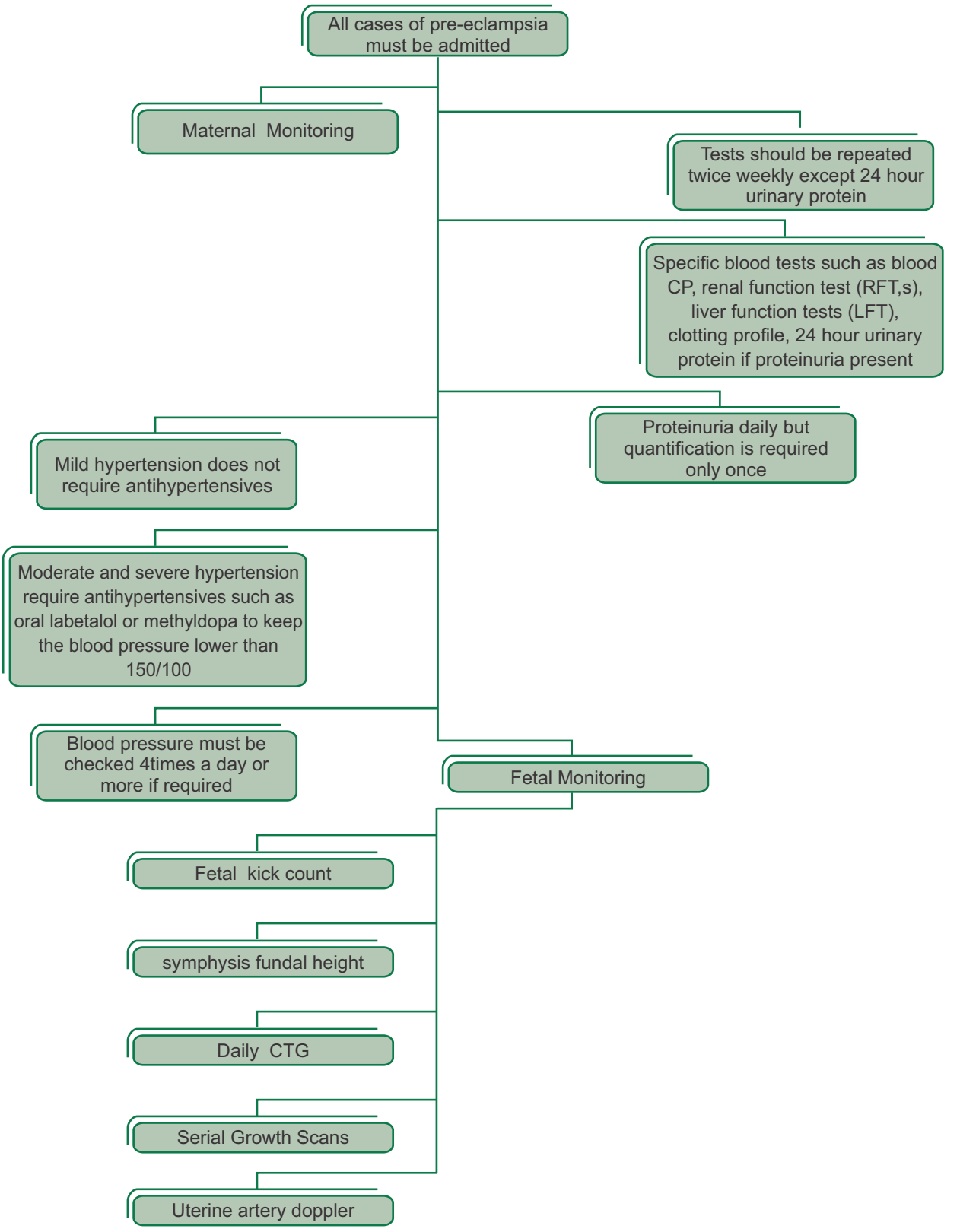
Specific blood tests such as blood CP, renal function test (RFTs), liver function tests (LFT), clotting profile, 24 hour urinary protein if proteinuria present

Tests should be repeated twice weekly except 24 hour urinary protein

Foetal monitoring by daily foetal kick count, daily CTG, fortnightly symphysis fundal height, fortnightly growth scans and Doppler when required

Flowchart for Tertiary Care 2

Pre-eclampsia (Hypertension with proteinuria)



Guidelines for Tertiary Care 3

Severe pre-eclampsia / eclampsia (Fits)

Do not leave the patient alone
Call for help
Inform, consultant obstetrician, anaesthetist and paediatrician
Do ABC i.e. check for Airway, Breathing and Circulation
Check for pulse and blood pressure
Artificial ventilation may be required
Secure two I/V lines
Catheterize the patient
Control fits
Control blood pressure
After stabilization deliver the patient

Investigation

Blood CP
Urine R/E
Renal function tests
Liver function tests
Coagulation screening
24 hour Urinary Protein
Blood group & Rh factor
ECG if required

Deliver the patient

Once the mother is stable consider delivery either by induction or caesarean section if baby is alive and has a chance of survival
Ergometrine should not be used
Thromboprophylaxis should be considered
Maintain vigilance for BP in the postpartum period

Flowchart for Tertiary Care 3

Severe Pre-eclampsia/Eclampsia

Do ABC

- Place in semi-prone position
- Call for help
- Inform consultants

Air way

- Assess
- Maintain patency
- Apply oxygen

Breathing

- Assess
- Protect airway
- Ventilate as required

Circulation

- Evaluate pulse and BP
- If absent, initiate CPR and call for help
- **Secure two I/V lines**

Control Seizures

- **Loading dose $MgSO_4$**

4 gm $MgSO_4$ in 50% solution IV over 10-15 minutes and 5 g in each buttock making a total of 14 g.

- **Maintenance dose $MgSO_4$:**
- 5 gm I/M injection in alternate buttocks 4 hourly till 24 hours after delivery. **If seizures continue or recur:**

$MgSO_4$ 2gm≤70 kg; 4gm≥70 kg IV as per loading dose over 5-10 minutes. If this fails: diazepam 10 ml IV or thiopentone 50 mg IV paralyse and intubate

- **Monitor**

Urine output hourly
Patellar reflexes
Respiratory rate

Every 10 minutes for first 2 hours and then every 30 minutes

Check serum magnesium if toxicity is suspected on clinical grounds

- **Stop infusion**

Check magnesium levels and review management with consultant if:

Urine output<25ml in 1 hour
Or if Patellar reflexes are absent
Or if Respiratory rate<16/minutes
Or if oxygen saturation <90%

Always get suppression of reflexes before respiratory depression

Antidote: 10% calcium gluconate 10 ml IV over 10 minutes

Control Hypertension

- **Treat Hypertension**

If systolic BP > 160 mmHg or diastolic BP> 110 mmHg then give

- **HYDRALAZINE**

10 mg IV slowly. repeated doses of HYDRALAZINE 5 mg IV 20 minutes apart may be given if necessary or

- **LABETALOL**

50 mg IV slowly if BP still uncontrolled

If necessary repeat after 20 minutes or start IV infusion: 200 mg in 200 ml physiological saline at 40 mg/hour, increasing dose at half hourly intervals as required to a maximum of 160 mg/hour

- **NEFIDIPINE SUBLINGUAL**

As soon as stable then deliver

- Once the mother is stable consider delivery either by induction or caesarean section if baby is alive and has a chance of survival
- Ergometrine should not be used
- Thromboprophylaxis should be considered
- Maintain vigilance for BP in the postpartum period

Investigations

- ► Blood CP
- ► Renal function tests
- ► Coagulation screening
- ► Blood group & Rh factor
- ► Urine R/E
- ► Liver function tests
- ► 24 hour Urinary Protein
- ► ECG if required

DISCUSSION AND RECOMMENDATIONS

Maternal mortality is far from satisfactory in Pakistan. Year 2015 is just around the corner and we are still far from achieving the Millennium Development Goals 4 and 5 in spite of pledging to do so. Eclampsia and severe Pre-eclampsia are the second leading causes of death in Pakistan. Every year about 50,000 women develop hypertension in pregnancy and 2000 of them die. Majority of these deaths are preventable by simple measure as preventing fits and delivering the patient at an appropriate time and monitoring and treating complications. In spite of the fact that $MgSO_4$ is one of the essential drugs even so declared in Pakistan, it is cheap, it is readily available but people are scared to use it. Furthermore where it is being used, every unit is following their own protocols and on top of that different protocols in the same hospital. This is because of lack of proper guidelines in the country. We hope to make these guidelines which are simple, be accepted as national guidelines for the use of $MgSO_4$ to prevent fits in pre-eclampsia and eclampsia.

Refresher courses are essential for all HCPs. Referral guidelines should also be available where necessary. Its use in the private sector should also be enhanced and encouraged. A standard treatment box must be available which contains $MgSO_4$, lignocaine and calcium gluconate etc. It is very important to translate evidence based medicine into country policies and their dissemination for a purposeful outcome. It is important to propagate the use of this cost effective drug in low resource areas and outside teaching hospitals as a large number of these women die of multiple seizures outside the hospital. In Pakistan although human resource for health is not as much as is required for the population but still training the available resource can go a long way in reducing maternal mortality and morbidity. The misconception of getting Magnesium levels in blood and intensive monitoring should be dispelled and we should move forward to bring its use at the grass root level if we want to save our mothers.

Recommendation is to do capacity building especially of the providers who are in contact with the woman first hand so that they are able to identify and pick the cases of severe pre-eclampsia before they develop eclampsia and after identifying they should be able to prevent the occurrence of fits by appropriate medication and proper and timely referral. For this regular updates are necessary. Staff of private hospitals must be included in trainings as majority of the women first seek their help. Provision of $MgSO_4$ and its antidote is essential and at lower facility level we must advocate the Oxford Group intramuscular regimen only. To avoid drug prescription and administration errors, Magnesium Sulphate should be available in pre-mixed solutions.

CHART 1 Risk Factors for Pre-Eclampsia

Primigravida
Multigravida with
- Previous history of pre-eclampsia
- Previous delivery more than 10 years
- Advancing age more than 40 years

BMI of more than 35
Family history of pre-eclampsia or eclampsia
Chronic hypertension
Multiple pregnancy
Molar pregnancy
Chronic renal disease
Diabetes Mellitus
Anti-phospholipid antibodies

CHART 2 Symptoms and Signs

Symptoms:

Severe headache
Blurring of vision
Severe abdominal pain or vomiting
Confusion and restlessness
Severe oedema

Signs:

Papilledema
Signs of clonus (>or= 3beats)
Liver tenderness
HELLP Syndrome

- Low Platelet Count
- Abnormal Liver Enzymes (ALT or AST rises to >70iu/ litre)

CHART 3 Recommended Antenatal Visits

Recommended antenatal visits are:

Once a month till 28 weeks
Fortnightly till 36 weeks
Weekly till birth
If this is not possible then minimum of four visits

- One in 1st trimester
- Second between 20 till 28 weeks
- Third between 28 & 36 weeks
- Fourth after 36 weeks

CHART 4 Dosage of Magnesium Sulphate I/M Loading Dose

10 gms (10 ml or 01 ampule) of $MgSO_4$ Injection given as a loading dose (5gms in each buttock I/M) and dilute this with 10 ml of normal saline and 2 % xylocaine injection i.e. total of 10 gms is given.

CHART 5 Use of Magnesium Sulphate

Loading Dose of $MgSO_4$

- A loading dose of 4 gms(8 ml of 10 ml vial) of $MgSO_4$ in 50 ml of solution over 10 minutes by an intravenous infusion
- Followed by I/M Injection of 5gms (10 ml or 1 vial) of MgSO4 mixed with 1ml of 2% lignocaine injection first in one buttock and then the other making a total of 14gms.

Maintenance dose of $MgSO_4$

- Maintenance dose of 5 gms (10 ml or 1 vial) of $MgSO_4$ mixed with 2% lignocaine 1ml is then given 4 hourly I/M in alternate buttock for 24 hours (Pritchard regimen) after delivery.

If seizures continue or recur

- $MgSO_4$ 2 g I/V can be repeated when required. If this fails then diazepam 10 ml I/V or thiopentone 50 mg I/V

Monitoring of $MgSO_4$ therapy

- Once $MgSO_4$ is given monitoring of the patient should be done every 10 minutes for first 2 hours and then every 30 minutes by:
  - Urine output (more than 25mls/ hour)
  - Knee jerk (should be present)
  - Respiratory rate (more than 16/ min)

If either of these is disturbed $MgSO_4$ should be stopped immediately.

Antidote is Calcium Gluconate Injection 10 ml given slowly I/V over 10 minutes.

CHART 6 Use of Anti - hypertensive

- **Treat Hypertension**
  If systolic BP > 160 mmHg or diastolic BP> 110 mmHg aim to reduce BP to around 130-140/90-100 mmHg **beware of maternal hypotension & FHR abnormalities –** monitor FHR with continuous CTG

- **Injection Hydralazine**
  10 mg IV slowly
  Repeated doses of injection Hydralazine 5 mg IV 20 minutes apart may be given if necessary

- **Injection Labetalol**
  50 mg IV slowly
  If BP still uncontrolled
  Repeat after 20 minutes or start IV infusion: 200 mg in 200 ml physiological saline at 40 mg/hour, increasing dose at half hourly intervals as required to a maximum of 160 mg/hour

- **Sublingual Nefidipine**
  Only if above two are not available

ACRONYMS AND ABBREVIATIONS

HT	Hypertension
BP	Blood Pressure
$MgSO_4$	Magnesium Sulphate
PDHS	Pakistan Demographic and Health Survey
PPH	Postpartum haemorrhage
RWP/ISD	Rawalpindi/Islamabad

DEFINITIONS

1. **Chronic Hypertension** is defined as a blood pressure of 140/90 mmHg or more existing prior to pregnancy or detected for the first time before 20 weeks of pregnancy. Mostly it is essential hypertension but sometimes associated with chronic renal disease. The pregnancy is poor in the later stage but even otherwise chronic hypertension can predispose to the later development of superimposed pre-eclampsia. Even in the absence of superimposed pre-eclampsia, chronic hypertension is associated with increased maternal and foetal morbidity and pregnancies complicated by chronic hypertension should therefore be regarded as high risk.

2. **Gestational hypertension** is defined as hypertension arising for the first time after 20 weeks of pregnancy but without proteinuria and is not associated with adverse pregnancy outcome. Every effort therefore should be made to clearly distinguish it from pre-eclampsia.

3. **Pre-eclampsia** is defined as hypertension of at least 140/90 mmHg recorded on at least two separate occasions and at least 4 hours apart or single reading of B.P160/110 and in the presence of proteinuria, arising for the first time after the 20th week of pregnancy in a previously normotensive woman and resolving completely by the sixth postpartum week.

4. **Severe Pre-eclampsia** is pre-eclampsia with severe hypertension and/or with symptoms, and/or biochemical and/or haematological impairment.

5. **Eclampsia** is defined as the occurrence of fits with hypertension in pregnancy, labour or postpartum.

6. **Hellp Syndrome** is haemolysis, elevated liver enzymes and low platelet count.

7. **Hypertension in pregnancy:**

   Diastolic BP≥110 mmHg on any one occasion OR

   Diastolic BP≥90mmHg on 2 or more consecutive occasions≥4hours apart

   Systolic BP≥160 mmHg on any one occasion OR

   Systolic BP≥140mmHg on 2 or more consecutive occasions≥4hours apart

8. **Mild Hypertension** diastolic blood pressure 90-99 mmHg, systolic blood pressure 140-149 mmHg

9. **Moderate Hypertension** diastolic blood pressure 100-109 mmHg, systolic blood pressure 150-159 mmHg

10. **Severe Hypertension** diastolic blood pressure 110 mmHg or greater, systolic blood pressure 160 mmHg or greater

11. **Proteinuria in Pregnancy:**

a. One 24 hours collection with total protein excretion≥300mg per 24hours

OR

b. Two Clean-catch-midstream or catheter specimens of urine collected≥4hours apart with ≥2+ on reagent strip

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