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Review Article

Diagnosis and management of preeclampsia in community settings in low and middle-income countries

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Abstract

Hypertensive disorders of pregnancy contribute significantly to maternal mortality and morbidity. Preeclampsia belongs to the spectrum of hypertensive disorders of pregnancy and if undiagnosed and/or untreated leads to fatal consequences for both the mother and the baby. Early detection and prevention of preeclampsia is limited by uncertainty in the knowledge about its etiopathogenesis. While much work has been done in establishing clinical guidelines for management of preeclampsia in the hospital or tertiary care settings, there is considerable lack of work in the domain of evidence-based guidelines for screening, identification and management of preeclampsia at the community-level. The article reviews these issues with special considerations and to challenges faced in low and middle-income countries. There is a need to focus on low-cost screening and interventions in the community to achieve a significant impact on preventable maternal and fetal mortality in order to control the burden of preeclampsia significantly as well as investing on more research at primary care level to improve the evidence base for community-level interventions.

Keywords: Eclampsia, preeclampsia, health system, magnesium sulphate

Introduction

Preeclampsia is a condition, within the spectrum of hypertensive disorders of pregnancy, characterized by elevated blood pressure and proteinuria, which can progress to involve multiple organ systems.[1] The Royal College of Obstetricians and Gynecologists clinically defines preeclampsia as the presence of pregnancy-induced hypertension (blood pressure ≥ 140/90 mmHg after 19 weeks of gestation) and significant proteinuria (>0·3 g/24 h).[2] Preeclampsia can be further categorized as mild or severe, depending upon the classification system that is used.[3] Severe preeclampsia includes severe hypertension (≥170/110 mmHg) and heavy proteinuria, and may also include other maternal signs of end-organ dysfunction.[2]

Across the globe, approximately 800 women die due to preventable causes of pregnancy and childbirth; 99% of these deaths occur in low and middle-income countries (LMICs).[4] In the early years of the 21st century, the millennium development goals explicitly placed maternal health at the core of the struggle against poverty and inequality.[5] Hypertensive disorders of pregnancy are an important cause of severe morbidity and mortality among mothers and infants;[6] and 10% of all women experience it during pregnancy.[7] Globally, preeclampsia is the second-leading cause of maternal mortality, resulting in an estimated 76,000 maternal deaths annually.[6] In addition, 500,000 fetal and newborn lives are lost annually due to the perinatal consequences of preeclampsia.[6] Moreover, preeclampsia complicates 2–8% of all pregnancies, and 10–15% of direct maternal deaths are associated with preeclampsia and eclampsia.[7] The syndrome of hemolysis, elevated liver enzymes and low platelets is a severe manifestation of preeclampsia and complicates approximately 0.5–0.9% of all pregnancies and 10–20% of cases with severe preeclampsia.[8] A 20-fold increase in maternal mortality is associated with preeclampsia arising at < 32 weeks compared with that at ≥ 37 weeks.[9] According to a systematic review and meta-analysis published in 2007, preeclampsia is associated with increased risk of having hypertension, ischemic heart disease and

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stroke in later life.[10,11] Overall mortality among women several years later was also greater in those who had preeclampsia.[10,12] Preeclampsia is also an important cause of fetal and neonatal mortality. Hypertension and/or proteinuria during pregnancy have also been associated with stillbirth[13] while preeclampsia is strongly associated with fetal growth restriction, low birth weight, preterm delivery, respiratory distress syndrome, and admission to neonatal intensive care.[14]

There are a number of hypotheses attempting to explain the pathogenesis of preeclampsia. The definitive cause of preeclampsia is generally unknown. Preeclampsia is generally considered a two-stage disorder.[15] It is hypothesized that inadequate trophoblast invasion in early pregnancy results in impaired placental perfusion, leading to an increase in oxidative stress.[16] According to one of the hypotheses, impaired remodeling of the spiral artery is the basis for this stage of the disease.[17] The later stage of the disease is the development of systemic endothelial dysfunction, which is responsible for the characteristic clinical manifestations of preeclampsia.[16] Underlying metabolic and cardiovascular conditions carry risks for endothelial dysfunction themselves, which is why they are postulated to play an important role in the pathogenesis of late-onset preeclampsia.[17] It has been proposed that reduced placental perfection due to oxidative stress causes endothelial dysfunction, hence linking the two stages of the syndrome.[15] There is also a genetic association with a multifactorial polygenic inheritance, suggested to play a role in the development of this disease.[16]

Most of the maternal deaths in LMICs occur at the community-level where the majority of women do not have access to the health care facility. Failure to identify preeclampsia along with a delay in responding to the clinical signs and symptoms is responsible for nearly half of maternal deaths and more than half of fetal deaths.[13] In community setups, determining the cause of death is difficult, and often reliance is placed on the relatives' or caretakers' recall of the symptoms experienced by the women prior to death.[18] Hence, there is a need for laying the extensive groundwork in development and implementation of guidelines and protocols at the community-level especially in LMICs. Screening and early detection of preeclampsia in the community could lead to a decrease in the preventable mortality of mother and the fetus. Guidelines could be also useful for establishing thresholds for referral to specialist care, and assessment procedures for suspected preeclampsia cases.

Early Identification and Diagnosis

Prompt diagnosis of preeclampsia in community settings is necessary to ensure maternal and fetal well-being. Unlike women with severe preeclampsia, women with moderate preeclampsia generally have no symptoms.[7] Therefore, delays in diagnosis, adequate primary care, and referral to a specialist are likely to be important contributors of adverse maternal and fetal outcomes.[19]

While there are numerous clinical guidelines for diagnosis and management of preeclampsia in specialist or tertiary care centers,[20,21] such is not the case for primary care settings in the community.[2] Preeclampsia community guidelines (PRECOG) were published in 2005, after having been formulated following the National Institute for Clinical Excellence's (NICE) recommendations for the development of guidelines.[2] This guideline makes provisions for assessing risk based on evidence, and gives clear criteria for referral to specialist centers, and also establishes a schedule for monitoring women in the community after 20 weeks' gestation. Criteria of referral for step-up care are also given.[2] However, it is important to note that these guidelines work best only in health systems of developed nations, and there is a need to contextualize it as per those of LMICs.

Perhaps the most important initial step toward a diagnosis of preeclampsia in community settings is the assessment of risk. A meta-analysis by Duckitt and Harrington showed that the risk of preeclampsia is increased in women with a previous history of preeclampsia (relative risk 7.19) and in those with anti-phospholipids antibodies (relative risk 9.72) and preexisting diabetes (relative risk 3.56).[22] Patients with multiple pregnancy, nulliparity, family history, raised body mass index before pregnancy and maternal age > 40 for multiparous women were shown to have increased the risk for preeclampsia as well.[22] A population-based retrospective study from Canada also concluded an approximately seven-fold higher risk of recurrent severe preeclampsia among women who has severe preeclampsia in previous pregnancy (6.8%; 95% confidence interval 5.7–7.9%).[23] Moreover, a history of early-onset preeclampsia is associated with increased odds of adverse pregnancy outcomes despite a normotensive second pregnancy.[24]

According to the PRECOG assessment of risk should be performed before 20 weeks of gestation and women should be referred for expert evaluation by specialist if they have either had a previous preeclampsia, a multiple pregnancy, preexisting underlying medical conditions like renal disease or chronic hypertension or any two other risk factors from a list.[2] Complete absence of antenatal care is known to be strongly associated with fetal death.[25] However, there is no evidence to recommend special antenatal care in addition to routine, to women who might be at risk for preeclampsia but otherwise do not qualify for specialist referral according to PRECOG criteria.[26] It is possible for women with no risk factors for preeclampsia to develop the condition. NICE recommends assessment for preeclampsia at weeks 16, 28, 34, 36, 38, 40, and 41 for healthy parous women with a single fetus.[27] However, such rigorous schedule of hospital visits might not be implementable in a LMIC nation where health systems are overburdened at one end and patients themselves find it difficult to visit healthcare facilities due to cost and distance considerations. There is an immense role that community healthcare workers can play in this arena and future research should be directed to this issue.

Assessments done after 20 weeks' gestation, by identifying possible onset of preeclampsia from signs and symptoms including new hypertension, new proteinuria, symptoms of headache, visual disturbance, epigastric pain, vomiting, reduced fetal movements, and an infant that is small for gestational age can help identifying high-risk cases for referral to specialist care.[28] In the community, fetal compromise is usually assessed by asking women about reduced fetal movements or by assessment for small for gestational age fetus.[2]

The World Health Organization (WHO) antepartum care model calls for a blood pressure check in the second antenatal visit in addition to testing for proteinuria in nulliparous women or in women with previous preeclampsia.[29] The method of measuring blood pressure is critical: Errors have been implicated in maternal deaths.[2] Regular maintenance and calibration checks are vital in ensuring that blood pressure is measured as accurately as possible. A large of number of devices in use may have an unacceptable calibration error.[30] The effective management requires measurement and monitoring of blood pressure. Low-cost self-measurement oscillometric devices, with features suitable for use in an adult population in a low-resource setting in the LMICs, have shown to be acceptable.[31] While both inflationary and deflationary oscillometry devices are acceptable for measuring blood pressure, it is possible that inflationary oscillometry is more accurate for screening for hypertension in pregnant women with preeclampsia.[32] In conclusion, measuring blood pressure and proteinuria is challenging in low-resource settings due to the financial cost and lack of training. Significant training is needed to measure blood pressure accurately, along with the availability of well-maintained equipment, both of which pose a challenge to the early identification of preeclampsia in community settings. A detection tool that is affordable and can be easily applied is needed.[33]

Numerous clinical, biophysical, and biochemical screening tests have been proposed for the early detection of preeclampsia over the past decades. However, discrepancies have been reported in their sensitivity and predictive value. No single screening test used for preeclampsia prediction has gained widespread acceptance into clinical practice.[34] It is important to identify at-risk women in the community and building the capacity of the caregivers in community and staff at the primary health centers to manage women with preeclampsia and eclampsia at the primary care level itself. Only those that develop complications should be referred to prevent overburdening of tertiary care facilities.

Prevention

The causes of preeclampsia are still largely debatable and mostly unknown. Hence, it is difficult to formulate strategies for effective primary prevention at this stage. Research in the past decade has identified some major risk factors for preeclampsia, and identification and modification of these factors might result in a decrease in its frequency.[35,36] Advanced maternal age, obesity, and no utilization of prenatal care are the risk factors identified for preeclampsia.[37] Overweight and obese women have an increased risk for preeclampsia, while underweight women have an increased risk for preterm delivery.[38] There is some evidence that secondary prevention with calcium supplementation and aspirin administration during pregnancy are beneficial in women with low calcium intake, and at a very high risk of developing severe early onset disease, respectively.[35]

Anti-platelet agents, especially low-dose aspirin, have small-moderate benefits when used for prevention of preeclampsia. When anti-platelet agents were compared to placebo or no agent, there was a 17% reduction in the risk of preeclampsia associated with the use of anti-platelet agents.[39] There was a small (8%) reduction in the risk of delivery before 37 completed weeks. Overall there was a 14% reduction in baby deaths in the anti-platelet group. There was a 10% reduction in risk of small-for-gestational age babies. There is a need for further research to assess women, which are likely to benefit most from such interventions and to identify best time of starting treatment, as well as optimal dosing.[39] A meta-analysis that assessed the influence of starting aspirin before 16 weeks of gestation found a 52% reduction in the risk of preeclampsia compared with the control group, however no difference was observed when started after 16 weeks.[40]

Calcium supplementation during pregnancy, when compared with placebo, appears to approximately halve the risk of preeclampsia.[41] It also reduces the risk of preterm birth and occurrence of death or serious morbidity.[41] However, it is of note that existing evidence shows that only women with a low dietary calcium intake are likely to benefit from calcium supplementation.[36] Since most pregnant women in LMICs are deficient in calcium, calcium supplementation is an intervention of interest for LMICs.[33] Other dietary nutritional measures, including administration of Vitamin C and other anti-oxidants, or drugs have not shown clear, irrefutable benefit, and there is insufficient evidence to recommend clinical use.[35]

Management

The goal of managing preeclampsia is to keep blood pressure of woman in the normal range with anti-hypertensives and prevent the development of complications like eclampsia. Delivery of the fetus and placenta is the only definitive treatment for preeclampsia but the option, is sadly not available for most patients who are diagnosed before the baby is full-term. Treatment is largely symptomatic with monitoring for development of complications. Once blood pressure increases above a certain level, it may lead to direct vascular damage, which in turn leads to life-threatening complications such as renal failure, stroke, and fetal distress.[7] Thus for women with severe preeclampsia, before 34 weeks of gestation, expectant management is recommended, such that maternal hypertension is under control, and maternal organ dysfunction or fetal distress is absent and can be monitored. However, the evidence-based behind expectant management for decreasing neonatal morbidity is small and based on data from only limited number of trials.[42]

There is no clear drug of choice for use during hypertensive disorders of pregnancy. In contrast to nonsevere hypertension, severe hypertension (defined as systolic blood pressure 160 and/or diastolic blood pressure 110) must be treated. The Confidential Inquiry into Maternal and Child Health highlighted the importance of treating severe hypertension and demonstrated that the failure of anti-hypertensive therapy was the most common source of sub-standard care even in high resource settings.[13] The choice of anti-hypertensive however is largely guided by the clinicians experience and familiarity with a particular drug[43] and on what is known about adverse effects and teratogenic potential due to lack of good quality evidence from trials.

The full intravenous or intramuscular regimen of magnesium sulfate is the drug of choice for both prevention of eclampsia in severe preeclampsia cases as well as treatment of eclampsia. In the United Kingdom, widespread uptake of magnesium sulfate is thought to account for the decline in the incidence of eclampsia.[44] In LMICs healthcare access is poor and routine antenatal coverage is not universal or of poor quality resulting in most patients visiting a clinician at the stage of severe preeclampsia or eclampsia. Such cases are an obstetric emergency considering the impending danger to the mother and the baby. Magnesium sulfate has been found to be beneficial to use in terms of significantly decreased the risk of eclampsia (about half) and risk of placental abruption (more than half) when compared with placebo or no anti-convulsant.[44,45] Use of magnesium sulfate in the community is however limited because of apprehension among healthcare workers about its safety. This, despite its clear effectiveness, low-cost, and being on the essential medicines for most countries, if not all.[46,47] Toxicity can be monitored clinically by respiratory rate, urine output and deep tendon reflexes. Limited provider knowledge and training, and lack of national guidelines and protocols and sociocultural factors and various other factors for underutilization of magnesium sulfate has already been identified.[33,48] For primary care facilities where full schedule of magnesium sulfate cannot be given or when development of further complications is anticipated, WHO recommends giving the loading dose of magnesium followed by referral to a higher level health-care facility.[49] Health care worker training and confidence building measures are hence an important part of the strategy for controlling the problem of preeclampsia. Trials comparing alternative regimens of magnesium sulfate for preeclampsia are of poor quality-too small and unreliable for making any conclusions and hence its clinical use not recommended.[50]

Conclusions

Evidence exists that a series of strategies including standardized assessment and surveillance, adequate management of severe hypertension, and prevention of eclampsia have the potential for reducing risks of adverse maternal outcomes in women with preeclampsia.[51] However, this involves a full detailed work-up in addition to the routine clinical tests done and hence might be not feasible in terms of costs as well as implementation in LMICs. Furthermore, intervention delivery and targeting the ones at high risk are a major issue in many LMICs. Despite the existing proven interventions to prevent and manage preeclampsia and eclampsia, effective delivery strategies still remain unexplored. Access to health care, distance, and cost are major obstacles for women in LMICs to seek care for preeclampsia. Antenatal care utilization is around 68% in LMICs compared with 98% in high resource settings.[33] The region of the world with the lowest levels of use is South Asia, where only 54% of pregnant women have at least one antenatal care visit.[52] Though the principles of care for women with preeclampsia remain the same globally, there is a need to adapt guidelines in the context of these and other problems unique to LMICs. Delays in identification, transport, and initiation of treatment because of number of factors lead to additional health system issues and this need to be accounted when contextualizing evidence regarding preeclampsia in LMICs.

One of the ways forward, especially for the LMICs, could be scaling up of existing community-based delivery platforms for screening and delivering intervention strategies. Many LMICs have an existing cadre of community health workers (CHWs) for example Shasthyo Sebikas (Bangladesh), Village Health Worker (Bhutan), Village Health Guide (India), Female Community Health Volunteer (Nepal), and Lady Health Visitor (Pakistan). These existing cadres could be utilized for screening and early referrals to prevent delays in identification and treatment. Evidence from Bangladesh, a typical LMIC, clearly indicates that outcomes were better for community-based maternal care programs implemented by posting trained midwives posted in villages at primary health care system.[53] There are successful examples from Pakistan where CHWs workers and midwives have been trained to administer misoprostol in women with postpartum hemorrhage.[54] This is supportive to of the recommendation that with proper training, it is feasible to incorporate even emergency medication administration in community settings where accessibility and availability are an issue.

Such an approach is also reasonable as CHWs are already functioning within the communities to deliver health promotion, preventive care and essential curative maternal, newborn child health services. Furthermore, there is a significant amount of community acceptability of these workers. However, there is a need to train these CHWs on the concepts related to the prevention and management of preeclampsia and eclampsia specifically. There is also a need for focused primary care funding to evaluate success of such programs before large-scale implementation can be done – especially with regard to conditions like preeclampsia and eclampsia, which turn to emergencies within a very short span of time. Such efforts thus need to be supplemented by the development of rapid and effective emergency care facilities and capacity building of health facilities where women are being referred to.

It is important to note that there is a need to shift from the current approach of either 'vertical' programs (which only aim at reducing disease-specific targets) or "horizontal" programs (which only aim at solving health system issues and consequently more time consuming and difficult to implement).[55] For better maternal and child care it is important to take a "diagonal approach" as of now and also aim at focused research at primary care level to improve the evidence base for it.

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