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Review Article

Prevalence, Incidence, and Temporal Trend of Hypertensive Disorders of Pregnancy and Its Association with Adverse Perinatal Outcomes in High and Low-Middle Income Countries: A Narrative Review

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Abstract

Hypertensive disorders of pregnancy (HDP) are the predominant pregnancy complication in both high and low-middle-income countries. The age-standardized incidence rate and the absolute incidence number of HDP in low-middle-income countries are 2-fold and 4-fold higher than in high-income countries in 2021, respectively. However, the reduction in the age-standardized prevalence rate (-41.1% vs. -8.7%) and incidence rate (-40.8% vs. -7.1%) of HDP is ≈5-fold faster in low-middle income countries compared with high-income countries between 1990 and 2021. Moreover, HDP is significantly associated with the increased risk of adverse perinatal outcomes, including preterm birth, low birth weight, and perinatal mortality in both high and low-middle-income countries. In the current review, we have highlighted the prevalence, incidence, and temporal trend of HDP and its association with adverse perinatal outcomes in high and low-middle-income countries.

Keywords: Hypertensive disorders of pregnancy; Prevalence; Incidence; Adverse perinatal outcomes; Socioeconomic status

Introduction

Hypertensive disorders of pregnancy (HDP), including preeclampsia, eclampsia, and gestational hypertension, are significant contributors to maternal and perinatal morbidity and mortality worldwide. HDP complicates approximately 5-10% of all pregnancies, representing one of the most common pregnancy complications during gestation (1). The pathophysiology of HDP involves a complex interplay between maternal vascular health, placental function, and immune regulation, often leading to multisystemic maternal dysfunction and adverse perinatal outcomes. Adverse perinatal outcomes associated with HDP include preterm birth, low birth weight, perinatal mortality, neonatal intensive care unit (NICU) admission, and long-term neurodevelopmental challenges in infants (2). The risk of adverse perinatal outcomes varies considerably between high-income countries (HICs) and low-and middle-income countries (LMICs), influenced by dispari-

ties in access to healthcare, antenatal surveillance, and management protocols (3).

Over the past few decades, evidence suggests that the burden of HDP and its associated adverse perinatal outcomes has demonstrated a concerning temporal trend, particularly in low- and middle-income countries (LMICs), where healthcare disparities exacerbate the challenges (4). In HICs, while improvements in antenatal care and advanced obstetric interventions have reduced perinatal mortality, the rising prevalence of risk factors such as obesity, advanced maternal age, and metabolic disorders has contributed to a persistent rate of adverse outcomes related to HDP (1). In contrast, LMICs experience a disproportionate burden due to delayed diagnosis, inadequate prenatal care, and limited access to life-saving interventions such as antihypertensive therapies and timely delivery. These systemic barriers, coupled with insufficient healthcare infrastructure, drive the temporal increase in adverse perinatal outcomes associated with HDP (3).

Prevalence and trend of preterm births

Preterm birth is defined as a neonate born before 37 completed weeks or fewer than 259 days from the first date of a woman's last menstrual period (5). More than 90% of all preterm births occur in low- and middle-income countries. Its prevalence rate is approximately 12% in low-income countries, 9.4% in middle-income countries, and 9.3% in high-income countries (6). Among these preterm births (n= 14.84 million), 81.1% (12.0 million) preterm births occurred in sub-Saharan Africa and Asia. Disparities in preterm birth rates by region were observed. It ranges from 13.4% in North Africa to 8.7% in Europe. Countries including Indonesia, Nigeria, India, Bangladesh, and Pakistan accounted for 44.6% (6.6 million) of preterm births globally (7).

The trend in preterm birth is rising worldwide. The trend of preterm births increased from 9.8% in 2000 to 10.6% in 2014 across the globe. However, in sub-Saharan Africa, the trend in preterm births decreased from 13.1% in 2000 to 12.0% in 2014. In 2014, the estimated global preterm birth rate was 10.6%, representing 14.84 million live preterm births (7). In the United States, the preterm birth rates increased by 3% from 9.57% to 9.63% in 2015 and 9.85% in 2016, during 2014-2016. The late preterm birth rates increased by 4% from 6.82% in 2014 to 7.09% in 2016. The rates of neonates born at 36 weeks, 35 weeks, and 34 weeks rose from 3.69% to 3.86%, from 1.87% to 1.90%, and from 1.27% to 1.32%, respectively during 2014-2016. (8). In China, the pooled incidence of preterm births was 6.09% and increased from 5.36% in 1990-1994 to 7.04% in 2015-2016, with an annual rate of increase of 1.05% (9).

Prevalence and trend of low birth weight (LBW)

According to the WHO, LBW is defined as birth weight ≤2500 g (10). Approximately 15% (20.5 million) of the total babies are born with LBW worldwide. In 2015, the highest prevalence of LBW was observed in Asia with 17.3% (12.8 million) followed by Africa with 13.7% (5.7 million), Oceania with 9.9% (1.4 million), Latin American and Caribbean with 8.7% (0.9 million), and more developed regions with 7.2% (1.0 million). The prevalence of LBW in Southern Asia (26.4%) is five times higher than reported in Eastern Asia (5.1%). Of the 20.5 million LBW babies, Asia accounts for more than half of all LBW babies in the world (11).

In the USA, the number of LBW babies declined from 37,603 to 33,447 during one decade (2005-2104); however, the prevalence of LBW did not change significantly (i.e., 6.9% in 2005 to 6.7% in 2014) (12). In Japan, the proportion of LBW increased by 99% from 4.2% in 1980 to 6.1% in 1990 and 8.3% in 2000 (13). In the Korean population, the trend in prevalence of LBW rate increased by 2.3-fold from 2.6% in 1993 to 5.9% in 2016 (14). In China, the proportion of LBW increased by 46% from 7.7% in 2005 to 11.3% in 2011 and by 5.1% from 7.7% to 8.1% during 2005-2017 (15).

Prevalence and trend of perinatal mortality

In 2017, the estimated neonatal mortality incidence was 2.5 million worldwide. The neonatal mortality rate decreased by 51% from 36.6 deaths

per 1,000 live births to 18.0 deaths per 1,000 live births during 1990-2017. The estimated number of neonatal mortality decreased from 5.0 million in 1990 to 2.5 million in 2017. The highest reduction in neonatal mortality was reported in East Asia and the Pacific (71.0%), from 27.4 deaths per 1,000 live births to 7.8 deaths per 1,000 live births followed by Eastern Europe and Central Asia (68·0%) from 20.6 deaths per 1,000 live births to 6.5 deaths per 1,000 live births and the lowest reduction in neonatal mortality was reported in West and central Africa (38.0%) from 48.6 deaths per 1,000 live births to 30.2 deaths per 1,000 live births followed by Sub-Saharan Africa (44%) from 45.7 deaths per 1,000 live births to 27.2 deaths per 1,000 live births during 1990-2017. South Asia accounted for 38% of neonatal deaths and, together with sub-Saharan Africa, accounted for 79% of the total neonatal mortality (16).

In the Netherlands population, the perinatal mortality decreased by 21.7% from 5.6 in 2010 to 4.6 per 1,000 live births in 2015 (17). In 2014, in the Korean, Japanese, and American populations, the neonatal mortality rate was 7.4, 6.9, and 5.9 per 1,000 live births, respectively. In Korea, the fetal mortality rate declined by 32.9% from 11.0 to 7.4 per 1,000 live births during 2009-2014. In Japan, the fetal mortality decreased by 5.6% from 7.3 in 2009 to 6.9 in 2014. However, no decline in fetal mortality rate was observed in the Unites Stated (18). In Bangladesh, the perinatal mortality rate significantly declined from 64 deaths per 1,000 live births to 41 deaths per 1,000 live births during one decade (2004-2014) (19). In Qatar, over the three decades (1977-2007), the neonatal mortality rate decreased from 14.1 to 5.1 per 1,000 live births, the early neonatal mortality rate from 12.5 to 2.3 per 1,000 live births, and the perinatal mortality rate declined from 24.7 to 10.3 per 1,000 live births (20). In China, during 1997-2014, the neonatal mortality rate significantly decreased by 75.34% from 7.57 to 1.87 per 1,000 live births or 7.04% per year (21).

Prevalence, incidence, and trend of HDP

Over the last three decades, the number of maternal hypertensive disorders (MHD) cases has increased by 15.8% from 15.5 million in 1992 to 18.0 million in 2021. However, the age-standardized incidence rate decreased by 13.40% from 533.44 per 100,000 populations in 1992 to 461.94 per 100,000 populations in 2021 worldwide. Moreover, across Brazil, Russia, India, China and South Africa (BRICS), the overall annual percentage change in the incidence of MHD has significantly increased in Russia (0.42%) and China (2.38%) but decreased in Brazil (-1.34%), India (−4.25%) and South Africa (-2.01%) between 1992 and 2021 (22).

The all-ages, age-standardized, and age-specific (15-49 years) prevalence and incidence rate of MHD in low-middle sociodemographic index (SDI) countries are almost 2-fold higher than high SDI countries in 2021. Moreover, the all-ages prevalence number and incidence number of MHD in low-middle SDI countries are 3.7-fold and 4.2-fold higher than high SDI countries in 2021, respectively. However, low-middle SDI countries showed the fastest reduction in the all-ages prevalence rate (-35.1% vs. -18.9%), incidence rate (-35.6% vs. -18.4%), age-standardized prevalence rate (-41.1% vs. -8.7%), incidence rate (-40.8% vs. -7.1%), age-specific (15-49 years) prevalence rate (-41.1% vs. -7.8%) and incidence rate (-41.8% vs. -6.4%) of MHD compared with high SDI countries between 1990 and 2021 (GBD 2021, http://ghdx.healthdata.org/gbd-results-tool) (23) as shown in Fig. 1 and Table 1.

Table 1: Prevalence and incidence of maternal hypertensive disorders in 2021 and its temporal trend between 1990 and 2021 in high and low-middle-income countries

Maternal hypertensive disorders		High SDI 2021	% change 1990-2021	Low-middle SDI 2021	% change 1990-2021
All-ages rate					
	Prevalence (95%UI)	47.3 (30.6-68.8)	-18.9% (-21.8 to -18.9)	98.2 (63.8-142.4)	-35.1% (-36.1 to -35.1)
	Incidence (95%UI)	225.2 (186.6- 275.9)	-18.4% (-23.8 to -13.8)	534.1 (449.2- 633.7)	-35.6% (-37.3 to -35.4)
Age standardize rate					
	Prevalence (95%UI)	52.5 (33.8-76.5)	-8.7% (-10.5 to -8.3)	89.7 (57.8- 130.3)	-41.1% (-41.1 to -40.0)
	Incidence (95%UI)	250.3 (208.3-304.8)	-7.1% (-13.8 to -1.4)	487.2 (411.4-575.5)	-40.8% (-41.8 to -40.2)
Aged 15-49 years rate					
	Prevalence (95%UI)	106.6 (69.0-155.2)	-7.8% (-9.8 to -5.4)	185.0 (120.2-268.3)	-41.1% (-42.1 to -40.5)
	Incidence (95%UI)	507.3 (420.2-621.6)	-6.4% (-12.4 to -0.9)	1004.9 (844.8-1193.3)	-41.8% (-43.3 to -41.7)

Note: Sociodemographic index (SDI)

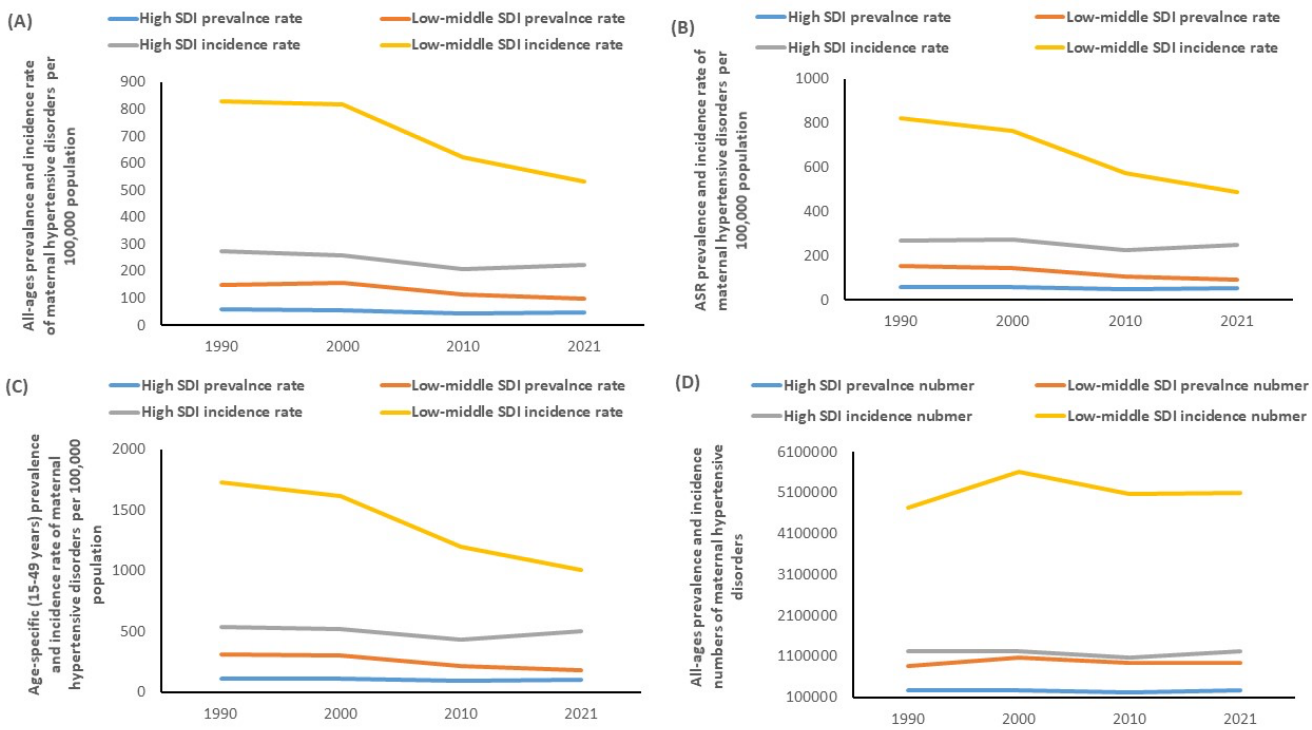

Fig. 1: Temporal trends of all-ages prevalence and incidence rate of maternal hypertensive disorders (A), age-standardized rate (ASR) of prevalence and incidence of maternal hypertensive disorders (B), age-specific (15-49 years) prevalence and incidence rate of maternal hypertensive disorders (C), and all-ages prevalence and incidence numbers of maternal hypertensive disorders (D) across high sociodemographic index (SDI) and low-middle SDI countries between 1990 and 2021

Pregnancy-induced hypertension (PIH) and adverse neonatal outcomes

PIH is a syndrome of hypertension associated with or without proteinuria and edema, usually starting after the 20th week of gestations. Several studies reported that women who had experienced PIH and high blood pressure during pregnancy had a 3-20 times higher risk of developing chronic hypertension in later life compared with women without PIH during pregnancy. Similarly, women who had recurrent PIH and eclampsia in subsequent pregnancies have a higher risk of developing chronic hypertension. Moreover, the occurrence of eclampsia in earlier gestation leads to a higher prevalence of chronic hypertension in later life. Several risk factors associated with PIH including family history, immune-response genes, parity, previous history of abortion, assisted reproductive technology, maternal age, pre-pregnancy body mass index (BMI), multiple gestations, smoking, and high altitude. PIH is a major obstetric complication, causing intrauterine growth retardation (IUGR), preterm births, placental abruption, neonatal deaths and maternal morbidity and mortality (24)

The impact of PIH on fetal growth is complex. PIH is significantly associated with an increased risk of LBW due to preterm births, IUGR or small-for-gestational-age (SGA). On the other hand, PIH is associated with an increased rate of high birthweight and large-for-gestational-age (LGA) babies. It has been found that the effect of PIH on birthweight is the function of gestational age. Babies born preterm to mothers with PIH had decreased mean birthweight, and babies born to mothers with PIH at term gestation had even higher mean birthweight compared with babies born to normotensive mothers (25).

Several studies reported that PIH is associated with an increased risk of preterm births, LBW, and SGA. On the other side, PIH is also associated with increased mean birth weight and LGA. Preterm PIH was found to be associated with shorter, lighter, and linear neonates, whereas term PIH was associated with both LGA and SGA. PIH was associated with a decreased risk of early neonatal mortality, late neonatal mortality, and infant mortality in both preterm and term SGA neonates. Moreover, PIH was associated with lower post-neonatal mortality in preterm SGA neonates. PIH was associated with decreased risks of early neonatal mortality, late neonatal mortality, post-neonatal mortality, and infant mortality in preterm appropriate-for-gestational-age (AGA) neonates. Lower early neonatal mortality and infant mortality in early preterm LGA neonates associated with PIH (26).

Bridwell et al. (27) determined the impact of HDP on adverse maternal-neonatal outcomes and observed that women with HDP had four times increased risk (adjusted odds ratio (aOR) 4.17) of LBW babies compared with women without HDP. Moreover, HDP increased the risk of stillbirths by 3-fold and maternal death by 5-fold. Among HDP, eclampsia was associated with higher odds (aOR 5.1) of LBW babies, six times the odds of stillbirths (aOR 6.3), and the risk of maternal death increased by 12-fold. In the Ethiopian population, in a prospective-based study, Berhe et al. (28) observed the impact of PIH on adverse neonatal outcomes. Women with PIH were associated with a higher incidence of adverse neonatal outcomes compared with normotensive women (66.4% vs 22.2%). After adjustment of confounding factors, women with PIH had higher risk of perinatal mortality (adjusted relative risk (aRR) 3.6), stillbirths (aRR 3.4), preterm births (aRR 5.2), LBW (aRR 5.1), birth asphyxia (aRR 2.6), SGA (aRR 3.3), and admission to neonatal intensive care unit (aRR 5.1), compared with normotensive pregnant women.

Muti et al. (29) assessed the prevalence and adverse effects of PIH in the Zimbabwe population. They reported a 19.4% prevalence of PIH. Women with PIH had a three times higher risk of LBW, 4.3 times stillbirths, and four times more likely to have a baby with a low Apgar score compared with normotensive women. Rahman et al. (30) observed the association between PIH and LBW in a population-based case-control study. The study was conducted during 2003-

2004 with 312 control mothers and 312 cases who delivered LBW babies. After controlling for significant confounding factors, including ethnicity, maternal age, gestational age at delivery, parity, maternal education, and previous history of abortion, PIH increased the risk of LBW by 5-fold. A significant association was found between PIH and LBW, and PIH was the independent risk factor for LBW. Women with severe PIH without proteinuria had a higher rate of LBW compared with normotensive and women with mild hypertension. However, PE and GH showed an increased rate of macrosomic babies. An incremental increase in blood pressure is associated with an increase in mean birth weight. The causes of LBW vary from population to population.

The difference in findings across studies could be attributed to the difference in the quality of health care services and management of PIH in the study areas. The higher risk of LBW and preterm births in women of PIH might be due to IUGR, placental insufficiency, and interventional delivery being carried out irrespective of gestational age to prevent maternal-neonatal morbidity and mortality.

Preeclampsia (PE), severe PE, and adverse neonatal outcomes

PE is a common pregnancy complication with a reported prevalence of 6-10% of all pregnancies. Healthy nulliparous pregnant had a higher incidence of PE (10-12%), women with multiple gestations had 25-30% PE, women with previous history of PE had 20-50% PE, women with pre-existing hypertension had 15-50% PE, and women with pre-gestational diabetes mellitus (GDM), renal disease or thrombophilia had 15-35% PE. The clinical findings of PE can be maternal syndrome (high blood pressure and proteinuria with or without multi-organ involvement) or fetal syndrome (IUGR, reduced placental growth with infarctions, and low amniotic fluid/ oligohydramnios). Despite advances in maternal health care, the prevalence of PE has not reduced. However, the prevalence of PE has increased due to changes in the demographics of pregnant women (i.e., increase in childbearing age or advanced maternal age, increase in obesity, increased nulliparity, increased rate of multiple gestation, and changes in paternity). Moreover, advances in maternal-neonatal care resulted in a reduced rate of maternal-neonatal complications associated with PE (31).

PE is associated with both maternal-neonatal short and long-term morbidities. The maternal-neonatal complications associated with PE usually depend on the severity of the disease, gestational age at the time of diagnosis, fetal growth status, and the presence of pre-existing obstetric complications. In general, healthy nulliparous pregnant women with mild gestational hypertension (GH) or mild PE after 36 weeks of gestation had healthy pregnancy outcomes. On the other hand, maternal-neonatal consequences increased in pregnant women with severe disease and with a history of previous PE. Moreover, maternal-neonatal complications increased in pregnant women with pre-existing obstetric or medical complications, multiple gestations, and the onset of PE before 35 weeks of gestation. PE can affect both the mother and fetus. No proper cure exists for PE except neonatal delivery; delivery is always an option for the mother's and fetus's safety. The primary objective of the management of preeclamptic mothers must always be the safety of the mother and then the delivery of a healthy fetus. Delivery is recommended for pregnant women who develop PE at 37 weeks of gestation or more. Due to maternal-neonatal safety, delivery is recommended for all pregnant women with severe PE at 34 weeks of gestation. Moreover, for women who develop mild PE before 35 weeks of gestation without delivery, proper and close management is recommended to prolong pregnancy for healthy neonatal outcomes (31).

Li et al. (32) observed that PE caused around 5.4% of perinatal deaths. Moreover, women with early-onset PE had a higher rate of perinatal deaths (9.1%). A significant difference was observed among three PE groups for preterm births: IUGR, very LBW, fetal distress, and neonatal asphyxia. Pregnant women with early-onset PE had higher rates (49.9%) of preterm births (<34 weeks), very LBW (31.3%), fetal distress

(6.3%), and neonatal asphyxia (3.3%). Moreover, pregnant women with superimposed PE had 39.5%, pregnant women with late-onset PE had 6.4%, and pregnant women with early-onset PE had 61.1% of at least one adverse perinatal outcome. In the Iranian population, Omani-Samani et al. (33) found that after adjustment of confounding factors, the risk of preterm births increased by 4.1-fold in women with PE compared with normal pregnant women. Higher rate of neonates born with LBW in women with PE (15.32% vs 4.93%) compared with normal pregnant women. PE increased the risk of LBW by 1.19-fold.

Early-onset PE caused perinatal mortality and morbidity. Pregnant women with PE had a higher rate of perinatal mortality (13% vs. 7%), infant mortality (16% vs. 9%), and 20% lower birth weight (1150g vs. 1430g) compared with pregnant women without PE. Neonates born to mothers with PE were more often SGA (22% vs. 9%) compared to neonates born to mothers without PE. The early onset of PE increased the risk of perinatal mortality by 2.03-fold and infant mortality by 1.96-fold. PE is associated with 1.6 times increased risk of perinatal mortality in neonates born SGA. It suggests that the effect of early-onset PE on perinatal mortality is partially due to SGA. Moreover, a higher incidence of infant respiratory distress syndrome (IRDS) (62% vs. 50%) and sepsis (43% vs. 30%) were observed in neonates born to mothers with early onset of PE compared with mothers without this complication. Adverse neonatal outcomes caused by PE are often related to gestational age at delivery, and gestational age is the significant marker of perinatal morbidity and mortality. The early onset of PE is a strong factor for adverse neonatal outcomes in preterm neonates. PE causes a reduced uteroplacental flow and leads to impaired fetal growth (34).

Liu et al. (35) investigated the relationship between severe PE and adverse perinatal outcomes in Taiwanese pregnant women. In a univariate analysis, severe PE increased the risk of preterm births by 3.18-fold, LBW by 3.46-fold, very LBW by 3.14-fold, extremely LBW by 4.1-fold, 1 mint Apgar score <5 by 2.95-fold, 5 mint Apgar score <7 by 2.96-fold, IUGR by 1.53-fold, and intrauterine fetal demise by 2.56-fold. In multiple logistic regression models, including both severe PE and GH, women with severe PE had higher odds of extreme LBW (aOR 2.86) and IUGR (aOR 2.16). Women with severe PE are at higher risk of developing maternal complications and having adverse neonatal outcomes, in particular, if they have no prenatal care.

In the Ethiopian population, Tlaye et al. (36) determined the impact of PE and severe PE on perinatal mortality. Women with severe PE had a higher rate of LBW babies compared with mild PE (54.7% vs 32%). The perinatal mortality rate was 197 per 1,000 live births. Of this, 57.4% were stillbirths, and 42.6% were early neonatal mortality. Women with severe PE had a higher rate of perinatal mortality than their mild counterparts (76.59% vs. 23.4%). The perinatal mortality rate among preeclamptic mothers ranged from 47 per 1,000 live births to 416 per 1,000 live births. The difference in perinatal mortality rate among studies could be attributed to the cutoff points of gestational age used in studies, the severity and type of HDP, and the healthcare facilities of the hospitals where pregnant women with PE were managed.

Conclusion

HPD is a significant pregnancy complication among women of childbearing age across the globe. Over the last three decades, the absolute number of HDPs has markedly increased, whereas the age-standardized rate of HDPs has significantly decreased worldwide. Moreover, the age-standardized and age-specific (aged 15-49 years) prevalence and incidence rate of HDP in low-middle SDI countries is almost 2-fold higher than high SDI countries in 2021. The all-ages prevalence number and incidence number of HDP in low-middle SDI countries are 3.7-fold and 4.2-fold higher than high SDI countries in 2021, respectively. HDP is significantly associated with the increased risk of adverse perinatal outcomes,

including preterm birth, low birth weight, and perinatal mortality in both high and low-middle-income countries regardless of healthcare settings. The slowest reduction in the all-ages, age-standardized, and age-specific prevalence rate and incidence rate of HDP in high SDI countries and the 2-fold higher burden of HDP in the low-middle SDI countries underscores the urgent need for targeted strategies to address the inequities in maternal and neonatal care, optimize HDP management, and ultimately mitigate the adverse perinatal outcomes associated with HDP.

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Conflict of interest

The authors have no conflict of interest regarding this review.

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