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Original article

# Pre-eclampsia, eclampsia and adverse maternal and perinatal outcomes: a secondary analysis of the World Health Organization Multicountry Survey on Maternal and Newborn Health

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**Objective** To assess the incidence of hypertensive disorders of pregnancy and related severe complications, identify other associated factors and compare maternal and perinatal outcomes in women with and without these conditions.

**Design** Secondary analysis of the World Health Organization Multicountry Survey on Maternal and Newborn Health (WHOMCS) database.

**Setting** Cross-sectional study implemented at 357 health facilities conducting 1000 or more deliveries annually in 29 countries from Africa, Asia, Latin America and the Middle East.

**Population** All women suffering from any hypertensive disorder during pregnancy, the intrapartum or early postpartum period in the participating hospitals during the study period.

**Methods** We calculated the proportion of the pre-specified outcomes in the study population and their distribution according to hypertensive disorders' severity. We estimated the association between them and maternal deaths, near-miss cases, and severe maternal complications using a multilevel logit model.

**Main outcome measures** Hypertensive disorders of pregnancy. Potentially life-threatening conditions among maternal near-miss cases, maternal deaths and cases without severe maternal outcomes.

**Results** Overall, 8542 (2.73%) women suffered from hypertensive disorders. Incidences of pre-eclampsia, eclampsia and chronic hypertension were 2.16%, 0.28% and 0.29%, respectively. Maternal near-miss cases were eight times more frequent in women with pre-eclampsia, and increased to up to 60 times more frequent in women with eclampsia, when compared with women without these conditions.

**Conclusions** The analysis of this large database provides estimates of the global distribution of the incidence of hypertensive disorders of pregnancy. The information on the most frequent complications related to pre-eclampsia and eclampsia could be of interest to inform policies for health systems organisation.

**Keywords** Eclampsia, incidence, near miss, pre-eclampsia, risk factors, severe maternal outcomes.

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## Introduction

An estimated 287 000 maternal deaths occurred in 2010,[1] with a wide variation across regions with regard to their lifetime risk (from 1 in 3800 in developed countries to 1 in 39 in sub-Saharan Africa).[1] Hypertensive disorders of pregnancy (HDP) account for nearly 18% of all maternal deaths worldwide, with an estimated 62 000–77 000 deaths per year.[2] HDP fall into four categories: chronic (pre-existing) hypertension, gestational hypertension or pregnancy-induced hypertension (PIH), pre-eclampsia/eclampsia and pre-eclampsia superimposed on chronic hypertension.[3] Data

on the incidence of HDP are scarce, as shown in a recently published systematic review,[4] where just 74 studies from 40 countries reported the incidence of pre-eclampsia and eclampsia, only seven of these with data on national coverage.

For every woman who dies, it is estimated that 20 others suffer severe morbidity or disability.[5] The proportion of women surviving severe maternal complications (also called 'near-miss' cases) has been proposed as a useful gauge for the evaluation of the quality of maternal health care and its determinants, with the potential to complement the information obtained from the reviews of maternal deaths.[6,7]

The present analysis has the following specific objectives: to assess the incidence and severity of HDP and related severe complications; to describe the maternal characteristics and perinatal outcomes of women suffering HDP; to identify other factors associated with pre-eclampsia and eclampsia; and to compare maternal and perinatal outcomes in women with and without HDP.

## Methods

### Study design, setting and participants

The World Health Organization (WHO) developed and tested standard definitions of maternal near miss based on markers of organ dysfunction (i.e. survivors of organ dysfunction during pregnancy, childbirth or postpartum are classified as maternal near-miss cases).[8] The World Health Organization Multicountry Survey on Maternal and Newborn Health (WHOMCS) characterised the severe maternal, perinatal and neonatal morbidity taking place in a worldwide network of health facilities using this approach.[9] The study protocol and other methodological details of the WHOMCS have been published previously.[9,10]

Briefly, this was a cross-sectional study implemented at health facilities in 29 countries from Africa, Asia, Latin America and the Middle East. The majority of participating centres had also taken part in the previous WHO Global Survey on Maternal and Perinatal Health (2004–2008).[11] With a probability proportional to their populations, countries, provinces and health facilities conducting 1000 or more deliveries annually and capable of performing caesarean section were randomly selected through a stratified, multi-stage cluster sampling strategy. All women giving birth at participating hospitals (together with their respective newborns) and all women with severe maternal outcomes (SMO) constituted the study population. Women with SMO were defined as maternal deaths or maternal near-miss cases occurring up to seven days postpartum/after termination of pregnancy, regardless of gestational age or delivery status. Maternal near-miss cases were defined as women who survived a life-threatening condition (as identified by any marker of organ dysfunction defined by WHO; Table S1). Women with HDP had a documented diagnosis in the medical record according to the treating clinician. The study definition for pre-eclampsia was the presence of hypertension (blood pressure >140/90 mmHg) associated with proteinuria in women known to be previously normotensive. Eclampsia was defined as the occurrence of convulsions and/or coma unrelated to other cerebral conditions in women with signs and symptoms of pre-eclampsia. Seizures are of grand mal type and may first appear before labour, during labour or up to 48 hours postpartum. Chronic hypertension was defined as a blood pressure >140/90 mmHg diagnosed prior to the onset of pregnancy or before the 20th week of gestation. Data were collected for a period of 2 months in facilities conducting 6000 or more deliveries annually and for 3 months in facilities with <6000 annual deliveries. In countries in which the anticipated sample size was estimated to be <3000 deliveries, data collection was extended to 4 months in all health facilities. Data were entered onto a web-based data management system developed by the Centro Rosarino de Estudios Perinatales (CREP, Rosario, Argentina). This study was approved by the WHO Ethical Review Committee and the relevant ethical clearance mechanisms in all countries.

### Analysis and statistical methods

We used frequencies to describe maternal characteristics, modes of onset of labour and delivery, and the perinatal outcome with stratification by the maternal outcome. We used frequencies to describe the proportion of women affected by HDP and assessed the distribution of selected pregnancy-related complications (i.e. potentially life-threatening conditions) among women without SMO, maternal near-miss cases and maternal deaths.

Considering that the health facilities are the primary sampling unit of this study, we assumed that the individual-level analyses may be affected by cluster effects.[12] Consequently, all estimates of association were calculated using a multilevel logit model which includes country and facility (nested within country) as random effects. Other potential confounder variables (such as maternal age, marital status, schooling years, number of pregnancies, number of previous births, number of neonates delivered, infant sex, chronic hypertension, pyelonephritis, other systemic infections/sepsis, anaemia, heart disease, renal disease and hepatic disease) were also included in the model. We used the Glimmix procedure from SAS 9.3 (SAS Institute, Cary, NC, USA) software to adjust the logit mixed models.[13]

## Results

Overall, 8542 (2.73%) women, from a total of 313 030 in the database, were recorded as suffering from any

hypertensive disorder during pregnancy and/or the intrapartum and early postpartum periods. Of these, 914 women (0.29%) had chronic hypertension, 6753 (2.16%) were pre-eclamptic and 875 (0.28%) had eclamptic fits (Table 1). As a result of the pragmatic design of WHOMCS (only short-term outcomes, maximum of 7 days), we were unable to collect information about PIH or gestational hypertension (a retrospective diagnosis that could be reliably confirmed after the sixth week postpartum).[3] The incidences of pre-eclampsia and eclampsia varied between and within regions, with the highest values for pre-eclampsia and eclampsia in the American and African regions, respectively. When grouped by income, the highest incidences of pre-eclampsia were found in upper middle income countries, whereas eclampsia appeared to be more frequent in lower middle income countries (Table 2).

Table 3 summarises the characteristics of women according to the final diagnosis of pre-eclampsia or eclampsia. The proportion of women older than 35 years in the pre-eclamptic group was approximately double that found in the group without pre-eclampsia or eclampsia. Moreover, adolescents of <17 years were three times more frequent in the group of women with eclampsia than in the reference population. Primigravids, as well as a lack of for-

**Table 1.** Description of incidence of chronic hypertension, pre-eclampsia and eclampsia by country and region

| Region | Country | No. of women (*N*) | Chronic hypertension *n* (%) | Pre-eclampsia *n* (%) | Eclampsia *n* (%) |
|---|---|---|---|---|---|
| AFRO | Angola | 10 414 | 19 (0.18) | 237 (2.29) | 79 (0.78) |
| | Democratic Republic of the Congo | 8700 | 0 (0.0) | 71 (0.82) | 17 (0.20) |
| | Kenya | 20 280 | 21 (0.10) | 398 (1.97) | 63 (0.32) |
| | Niger | 10 963 | 41 (0.37) | 50 (0.46) | 52 (0.48) |
| | Nigeria | 12 585 | 70 (0.56) | 289 (2.33) | 166 (1.35) |
| | Uganda | 10 828 | 4 (0.04) | 103 (0.95) | 21 (0.20) |
| Total AFRO | | 73 770 | 155 (0.21) | 1148 (1.56) | 398 (0.55) |
| AMRO | Argentina | 9797 | 46 (0.47) | 257 (2.63) | 22 (0.23) |
| | Brazil | 7052 | 57 (0.81) | 324 (4.60) | 11 (0.16) |
| | Ecuador | 10 224 | 34 (0.33) | 356 (3.49) | 32 (0.32) |
| | Mexico | 13 273 | 110 (0.83) | 509 (3.84) | 19 (0.15) |
| | Nicaragua | 6472 | 35 (0.54) | 494 (7.67) | 28 (0.47) |
| | Paraguay | 3607 | 7 (0.19) | 65 (1.80) | 2 (0.06) |
| | Peru | 15 181 | 9 (0.06) | 537 (3.5) | 20 (0.14) |
| Total AMRO | | 65 606 | 298 (0.45) | 2542 (3.88) | 134 (0.21) |
| EMRO | Afghanistan | 25 913 | 20 (0.08) | 252 (0.97) | 32 (0.12) |
| | Jordan | 1166 | 9 (0.77) | 55 (4.72) | 1 (0.09) |
| | Lebanon | 4042 | 9 (0.22) | 41 (1.02) | 5 (0.12) |
| | Occupied Palestinian Territory | 980 | 11 (1.12) | 23 (2.35) | 1 (0.10) |
| | Pakistan | 13 122 | 69 (0.53) | 155 (1.19) | 47 (0.36) |
| | Qatar | 3950 | 11 (0.28) | 155 (3.93) | 3 (0.08) |
| Total EMRO | | 49 173 | 129 (0.26) | 681 (1.39) | 89 (0.18) |
| SEARO | India | 31 168 | 65 (0.21) | 610 (1.97) | 131 (0.43) |
| | Nepal | 11 239 | 12 (0.11) | 66 (0.59) | 26 (0.23) |
| | Sri Lanka | 18 108 | 46 (0.25) | 173 (0.96) | 9 (0.05) |
| | Thailand | 8942 | 32 (0.36) | 198 (2.22) | 11 (0.13) |
| Total SEARO | | 69 457 | 155 (0.22) | 1047 (1.51) | 177 (0.26) |
| WPRO | Cambodia | 4691 | 1 (0.02) | 109 (2.34) | 23 (0.50) |
| | China | 13 273 | 79 (0.60) | 275 (2.07) | 12 (0.09) |
| | Japan | 3534 | 13 (0.37) | 42 (1.19) | 1 (0.03) |
| | Mongolia | 7343 | 7 (0.10) | 492 (6.71) | 8 (0.12) |
| | Philippines | 10 762 | 71 (0.66) | 386 (3.60) | 29 (0.28) |
| | Vietnam | 15 421 | 6 (0.04) | 31 (0.20) | 4 (0.03) |
| Total WPRO | | 55 024 | 177 (0.32) | 1335 (2.43) | 77 (0.14) |
| Overall | | 313 030 | 914 (0.29) | 6753 (2.16) | 875 (0.28) |

**Table 2.** Description of incidence of chronic hypertension, pre-eclampsia and eclampsia by income group[14]

| Income group* | No. of women (*N*) | Chronic hypertension *n* (%) | Pre-eclampsia** *n* (%) | Eclampsia *n* (%) |
|---|---|---|---|---|
| Low income | 92 614 | 99 (0.11) | 1049 (1.14) | 234 (0.26) |
| Lower middle income | 119 568 | 387 (0.32) | 2718 (2.27) | 425 (0.35) |
| Upper middle income | 93 364 | 404 (0.43) | 2789 (2.99) | 212 (0.23) |
| High income | 7484 | 24 (0.32) | 197 (2.63) | 4 (0.05) |
| Overall | 313 030 | 914 (0.29) | 6753 (2.16) | 875 (0.28) |

*Low income: Afghanistan, Cambodia, Democratic Republic of the Congo, Kenya, Nepal, Niger, Uganda. Lower middle income: India, Mongolia, Nicaragua, Nigeria, Occupied Palestinian Territory, Pakistan, Paraguay, Philippines, Sri Lanka, Vietnam. Upper middle income: Angola, Argentina, Brazil, China, Ecuador, Jordan, Lebanon, Mexico, Peru, Thailand. High income: Qatar, Japan.
**Excludes eclampsia.

mal education, were more frequent in the group of eclamptic women. In both the pre-eclamptic and eclamptic groups, the induction of labour, caesarean sections and preterm births were relatively more frequent than in the group of women without these conditions. In accordance with maternal figures, the proportions of stillbirths, low birthweight, low Apgar score at birth and neonatal complications were more frequent among the group of babies born from pre-eclamptic and eclamptic mothers (Table 4).

Figures 1 and 2 illustrate the associations of several conditions with pre-eclampsia and eclampsia, respectively. Chronic hypertension was robustly associated with pre-eclampsia with an adjusted odds ratio (OR) of 8.32 and 95% confidence interval (CI) of 7.13–9.72. Similar figures were found for eclampsia (OR = 12.06; 95% CI, 8.40–17.31). Pre-eclampsia and eclampsia were also significantly allied to renal and hepatic disease, anaemia and systemic infections or sepsis, as well as to other maternal conditions, such as nulliparity, multiple pregnancies and lack of formal education (defined as zero schooling years). With regard to maternal age, being older than 35 years was significantly associated with pre-eclampsia, but not with eclampsia. On the contrary, adolescence (<19 years of age) did not seem to be associated with pre-eclampsia, but was a risk for eclampsia. A woman's marital status and the sex of the baby did not appear to be associated with any of these conditions.

Markers of coagulation dysfunction were more frequently found among maternal near-miss cases in women with pre-eclampsia (Table 5), followed by respiratory,

**Table 3.** Description of women's characteristics

| | Women without pre-eclampsia/ eclampsia* (*N* = 305 402) *n* (%) | Pre-eclampsia** (*N* = 6753) *n* (%) | Eclampsia (*N* = 875) *n* (%) |
|---|---|---|---|
| **Age (years)*** ** | | | |
| <17 | 5346 (1.7) | 174 (2.6) | 53 (6.1) |
| 17–19 | 25 871 (8.5) | 545 (8.1) | 175 (20.1) |
| 20–35 | 247 471 (81.3) | 5027 (74.5) | 593 (68.1) |
| >35 | 25 796 (8.5) | 997 (14.8) | 50 (5.7) |
| **Marital status (without partner)**** ** | 30 528 (10.1) | 931 (13.9) | 115 (13.3) |
| **No. of years attended school***** ** | | | |
| 0 | 46 517 (16.6) | 630 (9.9) | 280 (34.4) |
| 1–4 | 10 230 (3.7) | 270 (4.3) | 33 (4.0) |
| 5–8 | 63 750 (22.8) | 1449 (22.8) | 197 (24.2) |
| 9–11 | 71 281 (25.4) | 1949 (30.7) | 144 (17.7) |
| >11 | 88 405 (31.5) | 2054 (32.3) | 161 (19.8) |
| **Number of pregnancies****** ** | | | |
| 1 | 110 508 (36.3) | 2831 (42.0) | 537 (61.6) |
| 2–4 | 158 107 (51.9) | 3077 (45.6) | 256 (29.4) |
| ≥5 | 36 264 (11.9) | 841 (12.5) | 79 (9.1) |
| **Number of previous births******* ** | | | |
| 0 | 128 175 (42.1) | 3402 (50.4) | 580 (66.4) |
| 1–3 | 148 069 (48.6) | 2783 (41.2) | 225 (25.8) |
| ≥4 | 28 515 (9.4) | 563 (8.3) | 68 (7.8) |
| **Gestational age at delivery (weeks)******** ** | | | |
| ≤32 | 5639 (1.9) | 701 (10.4) | 151 (17.7) |
| 33–36 | 15 802 (5.2) | 1378 (20.5) | 188 (22.1) |
| ≥37 | 280 718 (92.9) | 4652 (69.1) | 512 (60.2) |
| **Onset of labour********* ** | | | |
| Spontaneous | 237 921 (78.1) | 3264 (48.4) | 455 (52.5) |
| Induced | 31 363 (10.3) | 1248 (18.5) | 154 (17.8) |
| No labour | 35 465 (11.6) | 2233 (33.1) | 258 (29.8) |
| **Final mode of delivery (caesarean)********** ** | 84 664 (27.7) | 4107 (60.8) | 505 (58.0) |
| **Other maternal conditions identified** | | | |
| HIV/AIDS | 1261 (0.4) | 31 (0.5) | 6 (0.7) |
| Anaemia | 3796 (1.2) | 528 (7.8) | 67 (6.7) |
| Malaria/dengue | 313 (0.1) | 25 (0.4) | 18 (2.1) |
| Cancer | 38 (0.01) | 13 (0.2) | 0 (0.0) |
| **Income group** | | | |
| Low | 91 331 (29.9) | 1049 (15.5) | 234 (26.7) |
| Lower middle | 159 188 (52.1) | 3839 (56.9) | 560 (64.0) |
| Upper middle | 47 600 (15.6) | 1668 (24.7) | 77 (8.8) |
| High | 7283 (2.4) | 197 (2.9) | 4 (0.5) |

*Includes women with chronic hypertension.
**Excludes eclampsia.
***928 missing values.
****3653 missing values.
*****25 620 missing values.
******527 missing values.
*******647 missing values.
********3265 missing values.
*********661 missing values.
**********148 missing values.

**Table 4.** Description of babies' characteristics

| | Women without pre-eclampsia/ eclampsia* (*N* = 305 402) *n* (%) | Pre-eclampsia** (*N* = 6753) *n* (%) | Eclampsia (*N* = 875) *n* (%) |
|---|---|---|---|
| **No. of neonates delivered (singleton)*** ** | 300 748 (98.6) | 6471 (95.9) | 830 (95.5) |
| **Infant sex (male)**** ** | 156 268 (51.3) | 3445 (51.2) | 432 (49.8) |
| **Birthweight (g)***** ** | | | |
| <1500 | 3640 (1.2) | 553 (8.2) | 117 (14.0) |
| 1500–2499 | 28 582 (9.4) | 1756 (26.1) | 257 (30.6) |
| ≥2500 | 272 057 (89.4) | 4412 (65.6) | 465 (55.4) |
| **Neonatal conditions at birth (stillbirth)****** ** | 5714 (1.9) | 429 (6.4) | 133 (15.3) |
| **Apgar score at 5 minutes******* ** | | | |
| ≥7 | 290 624 (97.4) | 5822 (92.1) | 578 (79.8) |
| 4–6 | 5966 (2.0) | 389 (6.2) | 115 (15.9) |
| ≤3 | 1665 (0.6) | 108 (1.7) | 31 (4.3) |
| **Neonatal complications (at least one)** | 16 293 (5.3) | 1388 (20.6) | 223 (25.5) |

*Includes women with chronic hypertension.
**Excludes eclampsia.
***236 missing values.
****648 missing values.
*****1155 missing values.
******358 missing values.
*******7581 missing values.

cardiovascular and hepatic clinical, laboratory or management indicators (Table S1). For eclamptic women, maternal indicators of organ dysfunction in near-miss cases were mostly related to the neurological and respiratory system (Table 5).

The risk of death was nearly four times higher for women with pre-eclampsia when compared with non pre-eclamptic women (Table 6) and, for those with eclampsia, this risk increased exponentially (adjusted OR = 42.38; 95% CI, 25.14–71.44). Moreover, the risk of being a survivor of a life-threatening condition (that is, a maternal near-miss case) was eight and 60 times higher in women with pre-eclampsia and eclampsia, respectively.

The risk of fetal and neonatal deaths, as well as preterm birth and admission to a Neonatal Intensive Care Unit (NICU), was, in general, similarly increased in both conditions, albeit slightly higher in eclampsia (Table 7).

## Discussion

### Summary of main findings, strengths and limitations

The analysis of this large database with the data from 29 countries in five WHO regions provides estimates of the global distribution of the incidence of HDP. The overall figures for chronic hypertension, pre-eclampsia and eclampsia are 0.29%, 2.16% and 0.28% of all deliveries, with wide variations across countries in the different regions. Pre-eclampsia is the condition showing the greatest disparities, from an incidence of 0.20% in Vietnam to 6.71% in Mongolia. This could represent different risks for the development of pre-eclampsia in some countries, albeit the limitation of misclassification or under-reporting of HDP, particularly pre-eclampsia, must be considered, given the pragmatic nature of data collection in this study.

Even when the diagnosis of pre-eclampsia was standardised in the study protocol, incidences by countries and regions were based on the data reported by attending clinicians in the selected hospitals, which were not systematically confirmed. Definitions could differ among settings and the sample hospitals in the study may not be representative of the whole region, and may not reflect global proportions. The pragmatic approach of the WHOMCS may also explain the relatively lower incidence of pre-eclampsia found in this analysis when compared with other studies,[4,15,16] where the criteria for defining pre-eclampsia cases could be stricter, and the proportion of women with risk factors among the population studied (according to the objectives of the original studies: randomised controlled trials for pre-eclampsia prevention, diagnostic test evaluations, etc.) was probably higher. Variations found in the incidence of eclampsia may also reflect different management of pre-eclampsia cases across countries. The WHOMCS study shows that the use of magnesium sulfate in eclamptic women ranged from 40% in Ecuador to 100% in Brazil, Jordan, Mongolia, Occupied Palestinian Territory, Paraguay and Qatar.[9] However, the incidence of eclampsia in these countries also varied (from 0.06% in Paraguay to 0.16% in Brazil).

In line with published reports, pre-eclampsia and eclampsia were associated with a maternal age over 35 years, nulliparity, multiple pregnancies, poor socioeconomic conditions and poor education.[17–19] Although evidence for the contribution of young maternal age as an independent risk factor for pre-eclampsia is still controversial,[20–22] our data confirm that a maternal age below 19 years, and even lower than 17 years, does not seem to be a risk factor for pre-eclampsia. However, we found that an age below 17 years is highly associated with eclampsia (adjusted OR = 1.73; 95% CI, 1.23–2.43). As eclampsia is a more severe stage of pre-eclampsia, this apparent

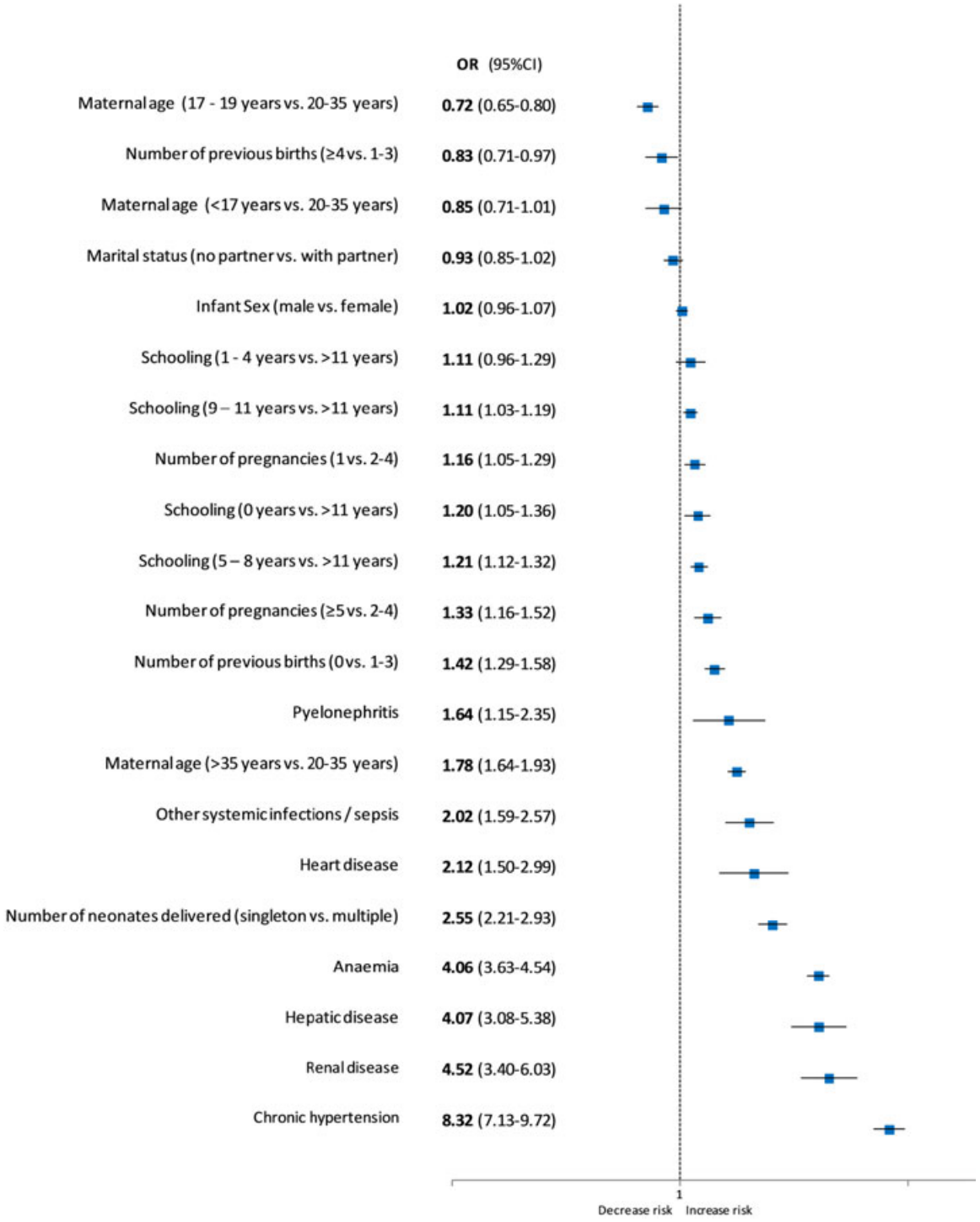


**Figure 1.** Factors associated with pre-eclampsia. The odds ratio (OR) was calculated based on a multivariate logit model that includes all risk factors (as fixed effects) and countries and hospitals within countries (as random effects).

discrepancy could indicate an increased lability of the central nervous system response in teenage mothers. Concomitant renal disease and chronic hypertension are strongly correlated with pre-eclampsia and eclampsia, as reported in the literature.[23,24] We found chronic hypertension to be the factor with the strongest association with both pre-eclampsia (adjusted OR = 8.32; 95% CI, 7.13–9.72) and eclampsia (adjusted OR = 12.06; 95% CI, 8.40–17.31),

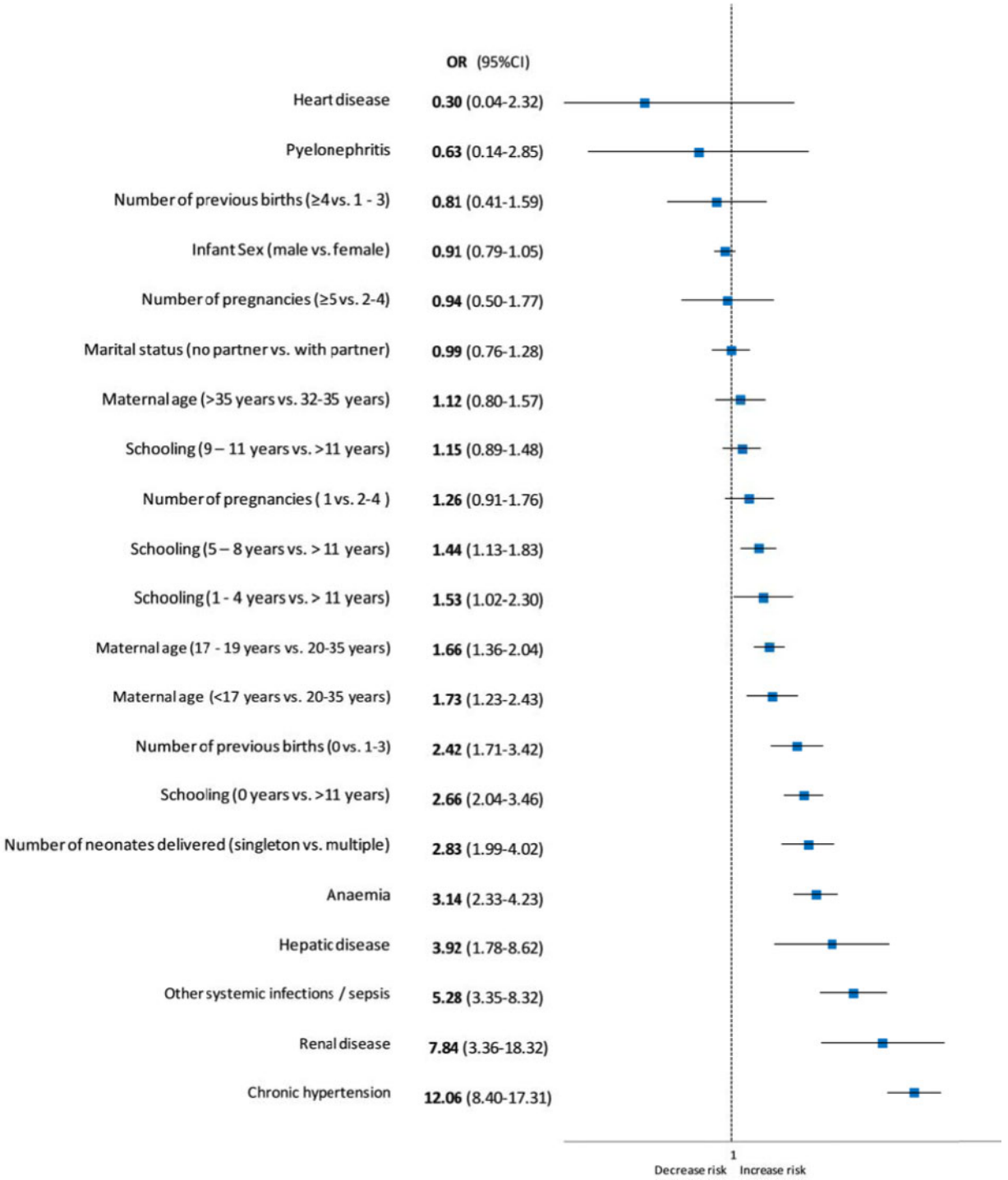


**Figure 2.** Factors associated with eclampsia. The odds ratio (OR) was calculated based on a multivariate logit model that includes all risk factors (as fixed effects) and countries and hospitals within countries (as random effects).

both of clinical relevance for management guidance.[25] The association of pre-eclampsia and eclampsia with systemic infections or sepsis and anaemia is more controversial, although they have been reported by others.[26–28] A systematic review of daily oral iron supplementation in pregnancy showed that it did not reduce the incidence of pre-eclampsia in the four studies (1704 women) evaluating this outcome;[29] thus, the role of type I error cannot be discarded.

**Table 5.** Organ dysfunction in women with pre-eclampsia and eclampsia who suffered maternal near miss

| Organ dysfunction | Pre-eclampsia (*N* = 262) *n* (%) | Eclampsia (*N* = 126) *n* (%) |
|---|---|---|
| Coagulation dysfunction | **115 (43.9)** | 23 (18.3) |
| Respiratory dysfunction | 65 (24.8) | 42 (33.3) |
| Cardiovascular dysfunction | 63 (24.0) | 24 (19.0) |
| Hepatic dysfunction | 63 (24.0) | 16 (12.7) |
| Renal dysfunction | 44 (16.8) | 24 (19.0) |
| Uterine dysfunction | 27 (10.3) | 4 (3.2) |
| Neurological dysfunction | 9 (3.4) | **66 (52.4)** |

Highest values in bold

Maternal near-miss cases are eight times more frequent in women with pre-eclampsia, increasing to up to 60 times more frequent if eclampsia occurs, when compared with women without these conditions. In eclampsia, most of these potentially life-threatening conditions involve the central nervous system, as observed by the markers of neurological dysfunction involved: coma or loss of consciousness lasting 12 hours or more; metabolic coma (loss of consciousness and the presence of glucose and ketoacids in the urine); stroke; or status epilepticus, uncontrollable fits or total paralysis. Eclamptic encephalopathy is essentially a vasogenic oedema with disruption of the blood–brain barrier. Magnetic resonance imaging (MRI) abnormalities include both white and grey matter, commonly as bilateral hypodensities in the occipital, posterior parietal or high frontal lobe. In most cases, these abnormalities are reversible, together with the clinical symptoms, if adequate treatment (mainly a decrease in blood pressure and the administration of magnesium sulfate) is started.[30]

Near-miss cases related to pre-eclampsia were more frequently identified by markers of coagulation/haematological dysfunction [clotting failure, transfusion of ≥5 units of blood/red cells and acute thrombocytopenia (<50 000 platelets)]. Although not specific to pre-eclampsia,[31] low platelet count is associated with an increased risk of abnormal coagulation and maternal adverse outcomes in these women.[32,33] Prompt recognition and treatment with the timely administration of blood products are crucial in the management of such life-threatening complications.[34,35] We also found markers of respiratory, cardiac and liver dysfunction in one in four near-miss women. Altered pulse oximetry, serum creatinine and liver enzymes were also found in women developing severe complications and ominous maternal outcomes;[36,37] thus, the monitoring of these indicators was proposed as a useful marker to stratify maternal risk during the assessment and surveillance of women admitted with pre-eclampsia.[38,39] The excessive mortality in relation to maternal near-miss cases found by WHOMCS in some settings may reflect inappropriate recognition of these indicators or inadequate or delayed management of associated complications.[9] An accurate diagnosis and assessment of these clinical, laboratory and management indicators is essential for the development of specific plans for antenatal interventions and for the management of the delivery and postpartum periods, including prompt and appropriate referral to third-level facilities.

As shown in Tables 6 and 7, the odds of women and babies dying or developing severe complications are particularly high when pre-eclampsia and eclampsia occur. Pre-eclampsia and eclampsia are leading causes of maternal and perinatal mortality and morbidity worldwide, and their relative contribution to the total number of maternal deaths increases as other morbidities, such as postpartum haemorrhage or infections, are better managed. However, we found that maternal near-miss cases were ten and four

**Table 6.** Association between maternal outcomes and pre-eclampsia and eclampsia

| Outcome | Women without pre-eclampsia/ eclampsia (*N* = 305 402) *n* (%) | Women with pre-eclampsia (*N* = 6753) *n* (%) | Women with eclampsia (*N* = 875) *n* (%) | Adjusted odds ratio* for pre-eclampsia | Adjusted odds ratio* for eclampsia |
|---|---|---|---|---|---|
| Maternal deaths | 143 (0.05) | 29 (0.43) | 32 (3.66) | 3.73 (2.15–6.47) | 42.38 (25.14–71.44) |
| Maternal near miss | 839 (0.27) | 262 (3.88) | 126 (14.4) | 7.82 (6.49–9.42) | 59.38 (44.91–78.52) |
| Maternal severe outcomes | 982 (0.32) | 291 (4.31) | 158 (18.06) | 7.49 (6.26–8.95) | 66.78 (51.67–86.30) |

*Multilevel logit model adjusted by risk factors (fixed effect) and countries and hospitals within countries (random effects). Risk factors: maternal age, marital status (no partner versus with partner), schooling years, number of pregnancies, number of previous births, number of neonates delivered (singleton versus multiple), infant sex (male versus female), chronic hypertension (yes versus no), pyelonephritis (yes versus no), other systemic infections/sepsis (yes versus no), anaemia, heart disease, renal disease, hepatic disease.

**Table 7.** Association between baby outcomes and pre-eclampsia and eclampsia.

| Outcome | Women without pre-eclampsia/eclampsia *N* = 305 402 *n* (%) | Women with pre-eclampsia *N* = 6753 *n* (%) | Women with eclampsia *N* = 875 *n* (%) | Adjusted OR* for pre-eclampsia | Adjusted OR* for eclampsia |
|---|---|---|---|---|---|
| Fetal death** | 5714 (1.87) | 429 (6.36) | 133 (15.32) | 3.12 (2.77–3.51) | 3.92 (3.16–4.87) |
| Early neonatal death*** | 2450 (0.82) | 192 (3.04) | 63 (8.61) | 2.71 (2.28–3.21) | 6.58 (4.91–8.81) |
| Perinatal death**** | 8164 (2.68) | 621 (9.22) | 196 (22.66) | 3.02 (2.73–3.34) | 4.91 (4.08–5.91) |
| Preterm birth***** | 21441 (7.10) | 2079 (30.89) | 339 (39.84) | 4.51 (4.23–4.80) | 6.57 (5.60–7.71) |
| NICU admission****** | 18673 (6.24) | 1634 (25.84) | 235 (32.02) | 3.45 (3.21–3.71) | 7.83 (4.48–9.45) |

*Multilevel logit model adjusted by risk factors (fixed effect) and countries and hospitals within countries (random effects). Risk factors: Maternal Age, Marital status (no partner versus with partners), Schooling years, Number of pregnancies, Number of previous births, Number of neonates delivered (singleton versus multiple), Infant sex (male versus female), Chronic hypertension (yes versus no), Pyelonephritis (yes versus no), Other systemic infections/sepsis (yes versus no), Anemia, Heart disease, Renal disease, Hepatic disease.
**358 missing values.
***6680 missing values.
****537 missing values.
*****3265 missing values.
******6445 missing values.

times more frequent than maternal deaths in women with pre-eclampsia and eclampsia, respectively. Incorporating these near-miss cases into enquiries of maternal deaths may add robustness to the analysis of its determinants and the quality of care received by these women. This strategy could be particularly useful in small health centres or in areas in which maternal deaths are rare events.

The WHOMCS was conducted primarily in secondary and tertiary health centres, and the data may not be representative of outcomes in smaller facilities or in the community. The primary data source was routine hospital records, and there is a possibility of under-identification of near-miss cases and under-estimation of severity in settings in which basic laboratory tests may not be available. As a result of the pragmatic nature of this survey, and in order to ensure feasibility, only short-term (maximum 7 days) intra-hospital maternal and perinatal morbidity and mortality data were collected, and so a proportion of deaths, or near-miss cases developed or recognised later, could be missed. For the same reason, the collection of information about other HDP, such as transient or gestational hypertension, was not possible. Finally, data on associated factors or conditions must also be interpreted with caution, as temporality among events (i.e. eclampsia and neonatal mortality) was also not registered.

Despite these possible limitations, the data analysed here are robust and provide useful information that can contribute to both the filling of the gaps in the global maternal morbidity research agenda and guiding practice and policy about the most frequent complications and organ dysfunctions related to pre-eclampsia and eclampsia.

## Disclosure of interests

The authors declare that they have no conflicts of interest. Two WHO staff members are part of the team who conducted the study. The findings in this article represent the conclusions of the authors.

## Contribution to authorship

EA, GC, MW, JPV, JPS and CC conceived the general aims and objectives of the article, and agreed on the analysis plan. CC conducted the analyses and drafted the tables. EA wrote the article with contributions from all co-authors. ZQ, JPZ and JPV reviewed and edited the manuscript. All authors agreed on the final version.

## Details of ethics approval

The UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP) Specialist Panel on Epidemiological Research reviewed and approved the study protocol for technical content. This study was approved by the WHO Ethical Review Committee and the relevant ethical clearance mechanisms in all countries.

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## Supporting Information

Additional Supporting Information may be found in the online version of this article:

**Table S1.** World Health Organization (WHO) markers of maternal organ dysfunction (i.e. life-threatening conditions). ■

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