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Description of the contributing factors to deaths secondary to hypertensive disorders associated with pregnancy in Antioquia, Colombia (2012-2020).

Descripción de los factores contribuyentes a las muertes secundarias a trastornos hipertensivos asociados al embarazo en Antioquia, Colombia (2012-2020)

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Abstract

OBJECTIVE: To describe the characteristics of the affected population and the delays which contributed to maternal mortality, secondary to hypertensive disorders of pregnancy.

MATERIALS AND METHODS: Descriptive and retrospective study based on the epidemiologic surveillance of sentinel cases of early maternal deaths of women residing in Antioquia, Colombia, during pregnancy, delivery and the 42 days after delivery, occurring in the period 2012-2020. A database was created in Microsoft Access 2007 (Microsoft, Redmond, WA, USA), and data was analyzed in Microsoft Excel and SPSS version 22.

RESULTS: There were 266 maternal deaths, 38 of which were secondary to hypertensive disorders of pregnancy. Eclampsia was the cause of 15 deaths; 12 due to HELLP syndrome, 9 due to intracerebral hemorrhage, and 2 due to placental abruption and disseminated intravascular coagulation. In 13 of the 38 cases, there was no adequate magnesium sulfate regimen, 19 did not receive indicated antihypertensive treatment, and 17 did not have adequate antihypertensive control.

CONCLUSION: Antenatal care is a critical opportunity for detection, prevention, and risk stratification. All obstetric care centers should be prepared to manage emergencies associated with hypertensive disorders of pregnancy. Outcomes improve with the use of standardized, organized emergency protocols and the participation of multidisciplinary teams that ensure quality care and a positive impact on preventable maternal morbidity and mortality.

KEYWORDS: Maternal mortality; Hypertensive disorders of pregnancy; Maternal deaths; Pregnancy; Eclampsia; HELLP syndrome; Intracerebral hemorrhage; Placental abruption; Magnesium sulfate; Antihypertensive.

Resumen

OBJETIVO: Describir las características de la población afectada y los retrasos que contribuyeron a la mortalidad materna, secundaria a los trastornos hipertensivos del embarazo.

MATERIALES Y MÉTODOS: Estudio descriptivo y retrospectivo efectuado con base en la vigilancia epidemiológica de casos centinela de muertes maternas tempranas de mujeres residentes en Antioquia, Colombia, durante el embarazo, el parto y los 42 días siguientes a éste ocurridas en el periodo 2012-2020. Se creó una base de datos en Microsoft Access 2007 (Microsoft, Redmond, WA, USA) y los datos se analizaron en Microsoft Excel y SPSS versión 22.

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RESULTADOS: Se registraron 266 muertes maternas, de las que 38 fueron secundarias a trastornos hipertensivos del embarazo. La eclampsia fue causa de 15 fallecimientos; 12 por síndrome HELLP, 9 por hemorragia intracerebral y 2 por desprendimiento prematuro de placenta y coagulación intravascular diseminada. En 13 de los 38 casos no hubo una pauta adecuada del sulfato de magnesio, 19 no recibieron tratamiento antihipertensivo, que estaba indicado y 17 no tuvieron un control antihipertensivo adecuado.

CONCLUSIÓN: La atención prenatal es una oportunidad decisiva para la detección, prevención y estratificación del riesgo. Todos los centros de atención obstétrica deben estar preparados para gestionar urgencias asociadas con los trastornos hipertensivos del embarazo. Los desenlaces mejoran con la aplicación de protocolos de emergencia estandarizados, organizados y la participación de equipos multidisciplinarios que garanticen una atención de calidad y un efecto positivo en la morbilidad y mortalidad materna susceptible de prevención.

PALABRAS CLAVE: Trastornos hipertensivos del embarazo; muertes maternas; embarazo; eclampsia; síndrome HELLP; hemorragia intracerebral; desprendimiento de placenta; sulfato de magnesio; antihipertensivos.

BACKGROUND

The hypertensive disorders associated with pregnancy complicate 2 to 4% of pregnancies, and they are the cause of approximately 14% of direct maternal deaths in the world, and of 26% in Latin America and the Caribbean.[1-4] In Colombia, in the year 2022, there were 433 maternal deaths, 148 of which were direct deaths, and hypertensive disorders were the first cause of direct maternal mortality with 26.7%.[5]

Preeclampsia is a disease of theories and pathogenic overlap between endothelial dysfunction, vasospasm, placental abnormalities, angiogenic-antiangiogenic imbalance, oxidative stress, changes in the immune response, and general inflammation.[6] Mild preeclampsia implies the coexistence of hypertension ((≥ 140-159/90-109 mmHg) or proteinuria (≥ 300 mg in 24 h). Severe preeclampsia is when tension parameters go over 160-110 mmHg, there is multi-organ involvement with paraclinical evidence of target organ damage, seizures, or de novo neurological symptoms.[2,3] Gestational hypertension is characterized by elevated tensional readings without proteinuria, target organ damage, after 20 weeks of gestation . Hypertension that starts before 20 weeks of gestation is considered chronic arterial hypertension.[3] This hypertensive disease of pregnancy requires quality prenatal care, early diagnosis, adequate treatment, and timely delivery.[7]

Several strategies have been used for the prevention of preeclampsia and its complications, among them the administration of aspirin and calcium at the end of the first trimester in patients at risk,[2,8] close monitoring of the disease, magnesium sulphate to prevent eclamptic seizures, and a strict control of arterial pressure to prevent strokes.[2] Low quality care seems to be the main contributor to a lack of decrease of mortality due to preeclampsia.[9]

Due to the aforementioned, the objectives of the present study were to describe the characteristics of the affected population, and the delays which contributed to maternal mortality secondary to pregnancy hypertensive disorders.

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MATERIALS AND METHODS

Observational, retrospective study carried out based on epidemiologic monitoring of sentinel cases of early maternal deaths, of patients who lived in Antioquia, Colombia, during pregnancy, delivery, and 42 days post-delivery, between 2012 and 2020. The cases were collected from the Population Census which contains mandatory reports from health care institutions sent to the public health monitoring system, and all the death certificates of women in reproductive age. The clinical information was obtained from the databases of mortality analyses, from the epidemiologic surveillance reports by the research committee of the *NACER* group of the University of Antioquia, who are in charge of monitoring and analyzing cases for the Regional Department of Health and Social Protection of Antioquia, who granted authorization to carry out the research.

There were no interventions, nor modifications of biological, physiological, psychological, or social variables of the patients. Confidentiality of the databases was guaranteed. *Variables*: age, access to prenatal control, area of residency, level of education, place of death, and moment of death with respect to delivery, childbirth type, weeks of pregnancy at the end of gestation, known preeclampsia risk factors history. Age, parity, and prenatal control are reported as means. The rest of the variables are reported in number. To describe the factors which contributed to maternal mortality, the "three delays" model was considered, as it was described by Maine in 1994.[10,11] **(Table 1)** Medical records and family interviews were used.

To analyze and evaluate delays, the recommendations and international guidelines were standardized by consensus among the evaluators, based on the best scientific evidence available, when analyzing medical records. A case was considered to have "delay of detection"

Table 1. The "three delays" model

Delay 1: Delay in the decision to seek help due to a lack of recognition of pregnancy risk factors, or the patient's perception of the severity of the disease, family or community factors, economic status, perception of the distance to the health center, potential cost, and previous experiences with the health system.
***Delay 2*:** Challenges of access because of distance, health center distribution near patient's location, state of roads and communication, availability, and real cost of transportation
Delay 3: Delay in the attention and adequate treatment received at health center. It addresses the care received at the health center. It can be insufficient in terms of equipment, provide hostile service, or have inadequately trained staff.

Source: Thaddeus S, Maine D. Too To Walk : Maternal Mortality in. Soc Sci Med. 1994;38(8):1091-110.[10]

of preeclampsia when in the medical records there were elevated tensional parameters, and premonitory signs or symptoms, or if there was a delay in the clinical suspicion by the time the patient presented with some complication. Cases of incomplete paraclinical data, inadequate vital signs monitoring, lack of monitorization or detection of signs and symptoms of toxicity due to magnesium sulphate, inadequate treatment of complications secondary to preeclampsia, and lack of identification of the degree of severity of preeclampsia, were considered "inadequate clinical surveillance".

Cases when the initial treatments were not prescribed at the right time, or in the right dose, or if medications other than the indicated ones were prescribed for the emergency treatment of hypertension or preeclampsia, were considered "inadequate treatment". A "lack of magnesium sulphate prophylaxis" was considered if there was no indication of an initial intravenous bolus of 4 to 6 g per hour, when there were tensional readings in severity limits, or signs and symptoms of cortical irritation, if a maintenance dose of 1 to 2 g per hour was not considered after the initial bolus, if prophylaxis was not continued in the first 24 hours of postpartum, or if an

additional bolus of magnesium sulphate was not administered to eclamptic patients. Fluid administration was evaluated, and if the patient was admitted, or not, to the intensive care unit, when indicated. Regarding an "inadequate decision to refer", we assessed if after stabilization, the staff continued treatment in the initial care center. A lack of resources was considered if the medical centers of a given level did not have the required treatment. Administrative difficulties were considered for treatment authorizations, referral decision, and transportation on the side of the health care providers.

Additionally, we used the evaluation method proposed by the Scottish group to evaluate the care received by each case, according to the categories shown in **Table 2**.[12]

A database was created with Microsoft Access 2007 (Microsoft, Redmond, WA, U.S.A.) and the data was analyzed with Microsoft Excel and SPSS, version 22.

RESULTS

There were 671,906 births and 266 maternal deaths in Antioquia, Colombia in the years considered for the study, meaning a maternal death ratio of 39.58 for every 100,000 newborns.[13] We included the cases where pregnancy hypertensive disorders had contributed directly to maternal mortality, as assessed by the research committee, and 38 deaths (14.29%) were associated to this cause. The sociodemographic and clinical characteristics of the deceased women are shown in **Table 3**. The causes of death associated with pregnancy hypertensive disorders are shown in **Figure 1**.

Regarding the delays described by Maine,[11] the factors identified as contributing to maternal mortality due to hypertensive disorders are shown in **Table 4**. It is evident that the three delays were present, and the third one was a common denominator in more than half of the cases. Of the 15 cases who died because of eclampsia, 5 received medication which was not recommended, one patient received 30 mg of nifedipine and diazepam, another patient received only midazolam, two patients received midazolam and diazepam, and another patient received diazepam and phenytoin. Suboptimal treatment was identified in 37 of the 38 cases.

Table 2. Evaluation of health care according to assessment model for extreme maternal morbidity

Adequate care: The patient was treated adequately, adhering to health care standards and guidelines.
Incidental suboptimal: There was a situation not considered in protocols, but without direct relation with the complication. Learning to be gained from the case, but without impacting evolution.
Minor suboptimal: the care for the complication did not adhere to the protocols but did not impact the outcome. The patient's evolution was not affected but it might have been.
Major suboptimal: a different care might have favored a more positive evolution. The treatment contributed in a significant way to the patient's mortality.

Source: Scottish Program for Clinical Effectiveness in Reproductive Health, Adamson L, Penney G. Scottish confidential audit of severe maternal morbidity: 4th annual report 2006. Edinburgh: Scottish Program for Clinical Effectiveness in Reproductive Health; 2007[12]

DISCUSSION

Maternal mortality is one of the most important health indicators of a population, because it reflects equity and timely access to services, as part of the advances that a society has made socioeconomically and educationally.[14] The rate of morbidity and perinatal-maternal mortality secondary to preeclampsia has risen in developing countries,[4,15] becoming the first cause of direct maternal mortality in Colombia, according to the National Health Institute reports of recent years.[5,16]

The literature shows that the patients with preeclampsia have a 3 to 25 times higher risk of complications such as eclampsia, cerebral hemorrhage, HELLP syndrome, placental abruption,

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Table 3. Sociodemographic and clinical characteristics of the population

Characteristic	
Age (mean)	26,94 years
Women with prenatal control	31
Prenatal control median	5 (1-9)
Parity mean	2,1 gestations
Relevant medical records	**Value n/38**
Chronic hypertension	1
Previous preeclampsia	2
Overweight	3
Obesity	5
Diabetes	1
Area of residence	**Value n/38**
Rural	15
Urban	22
No information	1
Education	**Value n/38**
Primary	9
Secondary	16
Higher education	4
No information	8
Place of death	**Value n/38**
Home	3
Transit	1
Level 1 hospital	3
Level 2 hospital	2
Level 3 hospital	29
Moment of death with regards to delivery	**Value n/38**
Under 24 h postpartum	9
2-7 days postpartum	17
8-42 days postpartum	4
Birth route	**Value n/38**
Vaginal	4
C-section	26
Not pertinent	8
Weeks of pregnancy at termination	**Value n/38**
Under 34 weeks	12
Over 34 weeks	25
No information	1

thrombocytopenia, disseminated intravascular coagulation, and pulmonary edema,[7,14] which are considered preeclampsia complications and can explain the annual death of 50,000 women in the world,[14,15] all of which is in line with what we found in the present study.

The factors associated with morbidity and maternal mortality in developing countries are delay in diagnosis and treatment, lack of prenatal control, of adequate care, of access to health care services, of transportation to reach tertiary care centers, of adequately trained staff, of resources, of medication, of laboratories, and of equipment.[11,14,17] Thirty-seven of the 38 patients who died due to hypertensive disorders had deficient health care services or did not receive the necessary care to stabilize their condition. This finding is in line with studies made in Norway[18] and Netherlands[19], from 1993 to 2002, where 87 and 90% of women, respectively, who died due to pregnancy hypertensive disorders, did not receive adequate care.

Some of the women in the study published here did not seek medical care when they had signs or symptoms of risk, and those who sought medical care at an early stage of the disease, did not get adequate treatment, either due to omissions or mistakes in the identification or approach, which is a phenomenon observed also by Verona, in Peru.[20] Inadequate diagnosis, treatment, or referral practices are known to contribute, directly, to more than a third of global maternal deaths.[21,22] The cause of mortality most commonly associated to eclampsia is when the patient has seizures before admittance, and she lacks prenatal control.[21] Actions taken at a primary level must be oriented at early diagnosis, stabilization, and timely referral of women with complications.[22]

There is evidence that up to 60% of preeclampsia cases in the postpartum, don't have previous diagnosis, and that they contribute heavily to

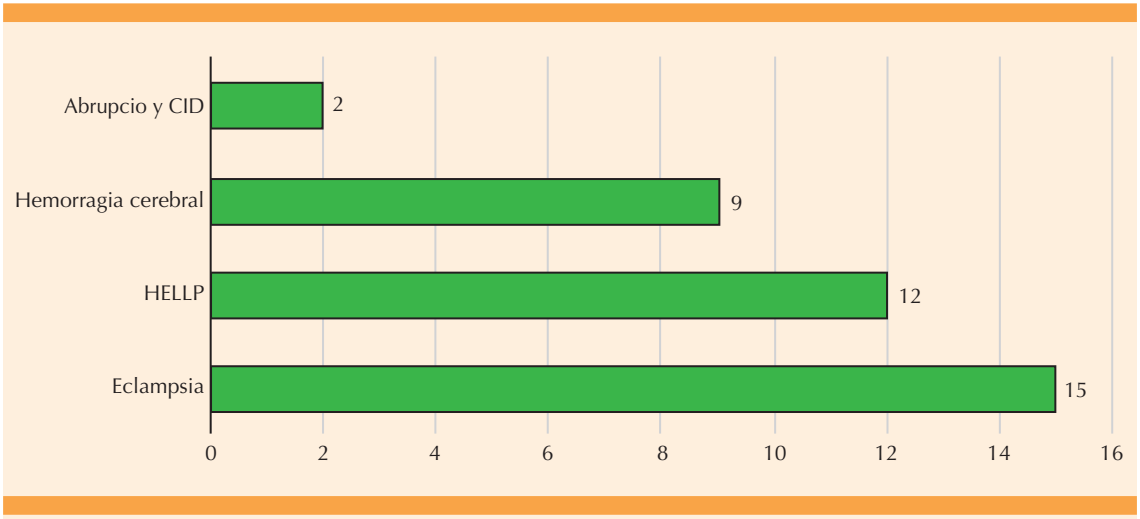


Figure 1. Causes of death due to pregnancy hypertensive disorders. Total deaths: 38.

maternal morbidity and mortality.[23] Moreover, higher arterial pressure readings tend to happen 3 to 6 days after delivery, when patients have already been discharged. [24] The present study had the same finding, as 17 patients form the cohort died between the second and the seventh postpartum day.

The literature mentions that lifestyle changes, weight loss, and bariatric surgery are effective measures to lower risk.[25] Three of the patients in our study were overweight, and 5 were obese, which indirectly shows the impact this variable can have in mortality. Despite the implementation of preventive measures, such as the prescription of aspirin and calcium since the first trimester in populations at risk,[26] severe preeclampsia cases continue to happen, and the morbidity and mortality associated with its complications as well.

Preventive measures specific to hypertensive patients (with or without proteinuria) seek to detect associated disorders, prescribe antihypertensives in a timely manner, and initiate magnesium sulphate once the symptoms or signs have been identified, and interrupt pregnancy, if necessary. Tertiary prevention seeks to prevent recurrence of eclamptic seizures and reduce the impact of side effects.[1] Eclamptic seizures happen in 2% of the women with severe preeclampsia who did not receive magnesium sulphate, and in under 0.6% of those who did receive it.[27]

Magnesium sulphate is better than phenytoin,[28] diazepam,[29] and nimodipine[30] for eclampsia prevention, and it is the medication of choice to prevent eclamptic seizures, and reduce the risk of maternal death, without undesirable side-effects for the mother or the fetus.[31] Therefore, the administration of magnesium sulphate is the most important action to prevent death by eclampsia, and the availability of the medication, and the competence of the health staff to use it, must be universal.[27] In the cohort of our study, a significant amount of patients did not receive magnesium sulphate or the administration was inadequately suspended, as prevention or initial treatment for eclampsia. This situation was also evident in a study conducted by Karolinski et al., about the impact of the intervention in maternal mortality and severe morbidity in 20 public hospitals (20 in Argentina and 4 in Uruguay), where magnesium sulphate was indicated as prevention of eclampsia only in 33% of the patients with

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Table 4. Factors which contribute to maternal mortality due to pregnancy hypertensive disorders

Factors which contribute to maternal mortality	Value n/38
Delay 1	
The patient does not recognize risk	7
Cultural practices	5
Delay in seeking attention due to economic reasons	2
Delay 2	
Delay in arriving at initial consultation	8
Delay 3	
No diagnosis	
No preeclampsia detection	10
Delay in suspicion	26
Defective physical examination and interview	16
Incorrect clinical and paraclinical interpretation	16
Inadequate monitoring of vital signs	21
Inadequate monitoring of magnesium sulphate and lack of toxicity detection	5
Incomplete paraclinical exams	16
Inadequate treatment of the complications secondary to preeclampsia	26
No preeclampsia severity classification	13
No hypertensive administration	19
Inadequate hypertensive administration	17
Inadequate regimen of magnesium sulphate	13
Medication not recommended to treat eclampsia	5
Inadequate indication of fluids	14
Non-admittance to ICU when needed	4
Untimely remittance to a higher level of care	15
Remission in inadequate conditions	13
Untimely gestation termination	15
Inadequate selection of birth route	6
Inadequate resources for complexity	36
Administrative difficulties	6
Suboptimal management	**37**

preeclampsia, and in 58.3% of the patients with eclampsia to treat the disease.[32] Similar results were reported in a previous study by Zuleta, in Antioquia, Colombia.[9]

While different societies have made guidelines for the timely treatment of patients with hypertension during pregnancy,[33] clear action schemes and staff training are needed, from the primary care level, in order to favor early detection and intensive treatment of hypertensive disorders, to have an impact on the prevention of adverse maternal and perinatal outcomes.

The present study has several strengths, it goes beyond the description of characteristics and

unmodifiable risk factors and analyzes the components of the medical care that contributes directly to maternal mortality, and reduces the variability of judgments on the part of the research committee, because the findings related with medical records were compared with renowned clinical practice guidelines, based on evidence. Moreover, it includes all the maternal deaths due to pregnancy hypertensive disorder in a department of Colombia, in a period of 9 years.

CONCLUSION

Pregnancy hypertensive disorders are an important cause of maternal death in Antioquia, Colombia. Prenatal care is a decisive opportunity to detect, prevent, and stratify risk. All the obstetric care centers must be prepared to manage emergencies related with pregnancy hypertensive disorders. Outcomes improve by the application of organized and standardized emergency protocols, with the participation of multidisciplinary teams, who guarantee a quality care, and a positive effect on maternal morbidity and mortality which are susceptible of prevention.

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Conflicts of interest

The authors declare no conflict of interests.

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