



Perinatal Outcome and Factors Associated with Hypertensive Disorders in Pregnancy in Yaoundé-Cameroon: A Retrospective Case-Control Study

Fouedjio JH^{1,2*}, Mbongo JA³, Ngoune-Tegofack DS⁴, Ebong C^{1,2}, Dohbit JS^{4,5}, Fouelifack YF², Nguefack-Tsague G⁶, Mekdes-Daba⁷ and Mbu RE^{1,5}

¹Department of Obstetrics and Gynecology, University of Yaoundé I, Cameroon

²Yaounde Central Hospital, Cameroon

³Department of Obstetrics and Gynecology, Marien Ngouabi University, Congo Brazzaville

⁴Faculty of Health Sciences, University of Bamenda, Cameroon

⁵Yaounde Obstetrics-Gynaecology and Pediatrics Hospital, Cameroon

⁶Department of Public Health, University of Yaoundé I, Cameroon

⁷St. Paul Hospital Millennium Medical College, Ethiopia



Abstract

Background: Hypertension is the most common medical problem encountered during pregnancy complicating 10% of pregnancies. It is the third leading cause of maternal mortality and the first leading cause of perinatal mortality.

Objective: To determine the perinatal outcome and factors associated with hypertensive disease in pregnancy in Yaoundé

Materials and methods: A retrospective case-control study was carried out at the Yaounde Central Hospital. Data were extracted from files of women who presented with high blood pressure and those who had normal blood pressure during pregnancy from January 2018 to January 2019 using a structured questionnaire. A multivariate logistic regression analysis was done to determine risk factors of hypertension during pregnancy and Odds Ratio (OR), and their confidence intervals (CI) were obtained. Data were analyzed using SPSS version 20 softwares and level of significance was set at $p < 0.05$.

Results: We identified 147 cases of hypertension, a prevalence of 7.7%; and 147 cases with no hypertension, giving a total of 294 participants recruited. The proportion of preterm births was found to be 66% (97/147) in the hypertensive group compared to 19% in the non hypertensive group. There was a statistically significant association between hypertension and age between 13-19 years-old (OR:2.15 [1.16-3.96], $p = 0.014$), nulliparity (OR:2.48 [1.36-4.50], $p = 0.003$), grand multiparity (OR: 3.92 [1.24-12.39], $p = 0.02$), low socioeconomic status (OR:3.24 [1.29-8.13], $p = 0.012$), low level of education (OR: 2.08 [1.03-4.17], $p = 0.039$), History of preeclampsia (OR: 19.02 [2.41-147.96], $p = 0.005$) and gestational age between 20-23 weeks at onset of Antenatal Care (OR:2.55 [1.25-5.19], $p = 0.01$).

Conclusion: The proportion of preterm births was high in hypertensive women compared to non hypertensive women during pregnancy. Hypertensive disease risk factors in pregnant women include: teenage, nulliparity, grand multiparity, low socioeconomic status, low level of education, history of preeclampsia and advanced gestational age at onset of Antenatal care.

Keywords

Pregnancy, Hypertension, Prematurity, Yaoundé

Background

Pregnancy, although being a physiological phenomenon, can have a significant impact on the prognosis of the mother and/or the newborn when it is associated with certain pathologies. This is the case with hypertension during pregnancy. According to the World Health Organization

(WHO), hypertension in pregnancy is defined as Systolic Blood Pressure (SBP) ≥ 140 mmHg and or DBP ≥ 90 mmHg [1]. Association of hypertension and pregnancy represents in black Africa the leading group for cardiovascular pathology during pregnancy [2]. Due to the maternal-fetal complications that it causes and the complexity of its management, it is the third cause of maternal mortality (after hemorrhages and

infections) and the first leading cause of perinatal mortality [3,4]. It is a real public health problem, with great variability in the figures reported around the world. The frequency of hypertension during pregnancy is similar in most western countries; 9.3% in France, 10.8% in the United Kingdom, 10 to 15% in the United States and 10% in Australia [5,6]. In China, a national survey reported a rate of 9.4% in 1994 [7]. There is also a great disparity in occurrence in African countries: 8.90-9.66% in Guinea Conakry; 17.05% in Niger, 3% in Dakar and 2.8% in Libreville [8,9]. The rates were 4.91% in 2012 in Fomba Nianankoro hospital (Mali) and 8.2% in Yaounde Gynaeco-Obstetric and Pediatric Hospital in 2006 (Cameroon) [10,11].

The main objective of the study was to determine the perinatal outcome and factors associated with hypertensive disease in pregnancy in Yaoundé.

Materials and Method

Study design

The study was a case-control study.

Study duration

We carried out this study from January 2018 to January 2019.

Study setting

Presentation of the study location

History: The study took place at the Obstetrics and Gynecology unit of the Yaounde Central Hospital (YCH), which is a referral category II hospital, in the pyramid of the health system in Cameroon. It is a social hospital which receives disadvantaged social strata. The Obstetrics and Gynecology unit has qualified staff and an adequate technical platform for the overall management of pregnancy complications.

Study population

Study population: Consist of all pregnant women followed-up at the maternity of the YCH.

Target population: Consisted of all pregnant women followed-up at the maternity between January 2018 and December 2018 who developed high blood pressure.

Inclusion and Exclusion criteria

Inclusion criteria:

Case: All pregnant women followed-up at the Yaoundé Central Hospital between January 2018 and January 2019 who developed hypertension.

Control: All pregnant women followed-up during the same period that did not develop high blood pressure.

Exclusion criteria

- Incomplete files.
- Files of pregnant women who had still born babies.
- Files of pregnant women who delivered babies with intrauterine growth retardation.

Sample size determination

The sample size was determined by using Schlesselman formula. Therefore, the minimum sample size required for this study was 294 (147 cases, 147 controls).

Recruitment process flow chart

A total of 1900 files were found among which 294 were selected. Out of the 294 files selected, 147 were hypertensive and 147 were non hypertensive (Figure 1).

Data analysis

Data were entered in SPSS version 20 software, where a page was created for the study. Categorical variables were presented as frequencies and percentages, while continuous variables were presented as means and standard deviations (SD). Chi-square test was used to compare categorical variables. Finally, multi variate analysis was performed via multiple logistic regression and refo logistic regression was expressed as adjusted odds ratio and 95% CI. A two-sided $p < 0.05$ was considered as statistically significant. The Microsoft excel 2016 software was used to design the different tables and figures for the presentation of the results.

Ethical considerations

Ethical clearance was obtained from the institutional Review Board of the Faculty of Health Sciences, University of Bamenda.

Authorization to carry out the study at Yaounde Central Hospital was acquired from the director of the hospital.

Patients confidentiality was respected as participant identity (name, phone number, identity card number) wasn't revealed and the information collected was kept secret.

Results

Proportion of preterm birth

The hypertensive women were 4.8 times at risk of delivering premature babies (Table 1).

Classification of different types of hypertensive diseases

Preeclampsia was the most frequent pathology, representing 73.5% of cases, and a total 5.6% of deliveries (Table 2).

***Corresponding author:** FOUEDJIO Jeanne Hortence, Department of Obstetrics and Gynecology, University of Yaoundé I; Yaounde Central Hospital, Cameroon, Tel: 00237-696818339/00237673795023

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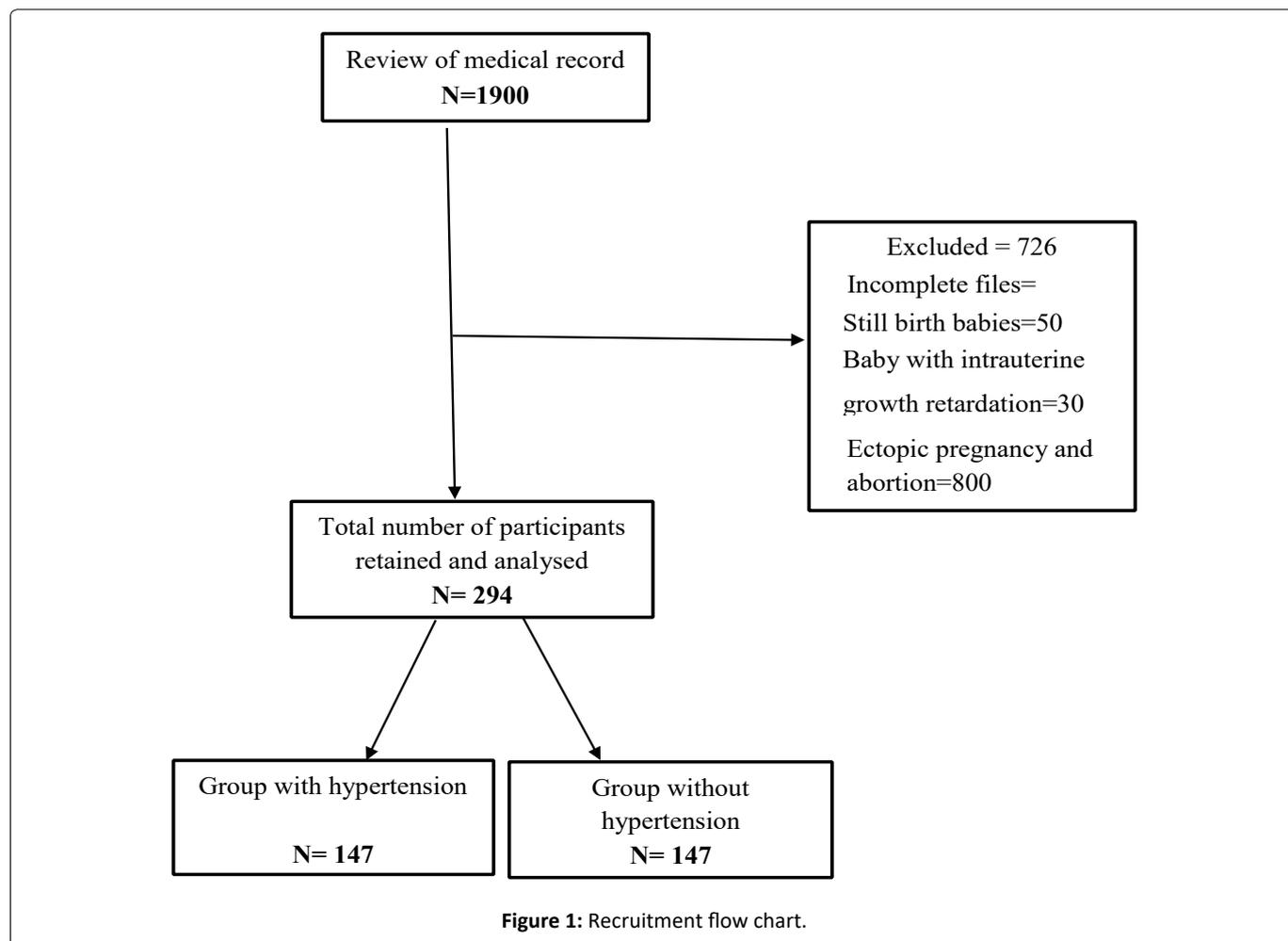


Table 1: Association between hypertension in pregnancy and premature birth.

Prematurity	HTN+ n (%)	HTN n (%)	OR (95% CI)	P value
Yes	97 (66.0)	28 (19.0)	4.38 (2.8-6.8)	0.001
No	50 (34.0)	119 (69.3)	Ref	Ref

HTN+: Hypertensive; HTN-: non hypertensive; OR: Odds Ratio; n: Frequency; %: percentage

Table 2: Distribution of the study population with respect to hypertensive disease entity.

Hypertensive diseases	Frequency	Percentages
	N	%
Preeclampsia	108	73.5
Gestational hypertension	27	18.37
Superimposedpreeclampsia	7	4.76
Chronic hypertension	5	3.4
Total	147	100

Factors associated with hypertensive disease in pregnancy

Sociodemo graphics characteristics and gestational age: Sociodemographics characteristics associated with hypertensive disease are: Adolescent (teenage) group, primary and secondary level of education and the self-

employed group (Table 3).

Obstetrical and family history

The frequency of primigravid a was much higher in the hypertensive group compared to non hypertensive.

The nulliparous and grand multiparous women were more at risk of developing hypertension,

Women with obstetrical history of preeclampsia were more at risk of developing hypertension during pregnancy (Table 4).

Follow up of the pregnancy

The majority of patients in the two groups had more than four Antenatal Clinic (ANC) contacts.

The most frequent pathology in our study population was malaria with occurrence of 13.6% in the hypertensive group and 46.2% in the non hypertensive group (Table 5).

Table 3: Distribution of the study population according to sociodemographics characteristics and gestational age.

Variables	HTN+ n (%)	HTN- n (%)	Total n (%)	OR (95% CI)	P value
Age					
13-19	34 (23.1)	19 (13.0)	53 (18.0)	2.15 (1.7-3.9)	0.014
20-26	49 (33.3)	58 (39.5)	107 (36.4)	Ref	Ref
27-34	47 (32.0)	56 (38.0)	103 (35.0)	1.04 (0.6-1.7)	0.89
35-47	17 (11.6)	14 (9.5)	31 (10.5)	1.5 (0.7-3.1)	0.27
Gestational age					
28-36 weeks	97 (66.0)	28 (19.0)	125 (42.5)	1.7 (0.8-2.4)	0.34
37-42 weeks	50 (34.0)	119 (81.0)	169 (57.5)	Ref	Ref
Level of education					
Primary	22 (15.0)	17 (11.6)	36 (13.3)	2.08 (1.0-4.1)	0.039
Secondary first cycle	62 (42.2)	52 (35.4)	114 (38.8)	1.85 (1.1-3.0)	0.018
Secondary second cycle	26 (17.7)	21 (14.3)	47 (16.0)	1.9 (1.0-3.6)	0.05
University and higher	37 (25.8)	57 (38.8)	94 (32.0)	Ref	Ref
Marital Status					
Single	96 (65.3)	92 (62.6)	188 (64.0)	1.46 (0.4-1.8)	0.24
Married	51 (34.7)	55 (37.4)	106 (36.0)	Ref	Ref
Occupation					
House wife	48 (32.7)	47 (32.0)	95 (32.3)	1.1 (0.6-1.7)	0.69
Self-employed	19 (13.0)	5 (3.4)	24 (8.7)	3.24 (1.3-8.1)	0.012
Civil servant	39 (26.5)	56 (38.1)	95 (32.3)	0.77 (0.4-1.1)	0.14
Student	41 (27.9)	39 (26.5)	80 (27.2)	Ref	Ref
Religion					
Christian	142 (96.6)	140 (95.2)	282 (96.0)	1.38 (0.5-4.1)	0.55
Muslim	5 (3.4)	7 (4.8)	12 (4.0)	Ref	Ref

HTN+: Hypertensive; HTN-: non hypertensive; OR: Odds Ratio; n: Frequency; %: percentage; CI: Confidence Interval

Table 4: Distribution of the study population according to obstetrical and family history.

Variables	HTN+ n (%)	HTN- n (%)	OR (95% CI)	P value
Parity				
Nulliparas	73 (49.7)	52 (35.4)	2.48 (1.36-4.50)	0.003
Primiparas	21 (14.3)	37 (25.2)	Ref	Ref
Pauciparas	29 (19.73)	43 (29.3)	1.31 (0.66-2.56)	0.432
Multiparas	15 (10.2)	13 (8.8)	2.06 (0.89-4.80)	0.091
Grand multiparas	9 (6.12)	2 (1.4)	3.92 (1.24-12.39)	0.02
Gravidity				
Primigravida	58 (39.5)	52 (35.4)	Ref	Ref
Paucigravida	40 (27.2)	48 (32.6)	0.81 (0.44-1.25)	0.273
Multigravida	30 (20.4)	29 (19.7)	1.12 (0.51-1.63)	0.561
Grand multigravida	19 (12.9)	18(12.2)	0.96 (0.48-1.89)	0.701
History of preeclampsia				
History of Abortion	12 (8.16)	1 (0.46)	19.02 (2.41-34.96)	0.005
Family history				
Hypertension	49 (33.3)	64 (29.8)	1.18 (0.75-1.85)	0.472
Diabetes	6 (4.08)	11 (7.48)	1.09 (0.08-14.66)	0.948
	3 (2.04)	7 (4.76)	0.64 (0.10-4.09)	0.64

HTN+: Hypertensive; HTN-: non hypertensive; OR: Odds Ratio; n: Frequency; %: percentage; CI: Confidence Interval

Table 5: Association between hypertension in pregnancy and antenatal care, pathologies.

Variables	HTN+ n (%)	HTN- n (%)	OR	CI	P value
Number of ANC					
One	12 (8.16)	14 (9.5)	0.60	0.25-1.38	0.23
Two	21 (14.3)	25 (17.0)	0.81	0.43-1.51	0.51
Three	45 (30.6)	42 (28.6)	1.01	0.61-1.65	0.97
≥ Four	69 (46.9)	66 (44.9)	Ref	Ref	Ref
Gestational age at onset of ANC (Weeks)					
< 10	17 (11.6)	34 (23.1)	Ref	Ref	Ref
11-15	37 (25.2)	33 (22.5)	2.52	1.22-5.15	0.012
16-19	38 (25.8)	26 (17.7)	3.33	1.60-6.92	0.001
20-23	39 (26.5)	35 (23.8)	2.55	0.78-4.35	0.01
≥ 24	15 (10.2)	19 (13.0)	1.85	0.78-4.35	0.158
Type of pregnancy					
Single	130 (88)	147 (93.2)	Ref	Ref	Ref
Twin	17 (12)	10 (6.8)	2	0.83-3.59	0.095
Pathologies					
Malaria	20 (13.6)	68 (42.6)	0.039	0.019-0.08	0.001
UTI	1 (0.7)	6 (4.0)	0.09	0.01-0.76	0.027
STI	1 (0.7)	15 (10.2)	0.032	0.004-0.24	0.001

UTI: Urinary Tract Infection; STI: Sexually Transmitted Diseases

Table 6: Distribution according to birth weight, sex and APGAR score.

Variables	HTN+ n (%)	HTN- n (%)	OR	CI	P
Birth weight					
< 1000g	2 (2.06)	1 (3.6)	2.2	0.17-28.25	0.542
1000-1500g	11 (11.3)	4 (14.3)	1.22	0.35-4.23	0.752
1600-2100g	52 (53.6)	8 (28.6)	1.95	0.68-5.58	0.209
2200-5500g	32 (33.0)	15 (53.6)	Ref	Ref	Ref
Sex					
Male	60 (61.9)	12 (42.9)	1.58	0.96-2.57	0.068
Female	37 (38.1)	16 (57.1)	Ref	Ref	Ref
Apgar score					
1st minute					
3-6	11 (11.3)	0 (3.6)	2	0.60-651	0.26
7-10	86 (88.7)	27 (96.4)	Ref	Ref	Ref
5th minute					
< 7	9 (9.3)	5 (2.32)	1.25	0.39-390	0.70
8-10	88 (90.7)	61 (28.37)	Ref	Ref	Ref

HTN+: Hypertensive; HTN-: non hypertensive; OR: Odd Ratio; n: Frequency; %: percentage; CI: Confidence Interval; %: percentage; OR: Odds Ratio; n: Frequency

Characteristics of preterm birth

There was no statistically difference in the two groups according to the characteristics of the preterm birth (Table 6).

Discussions

Proportion of preterm birth

Following our analysis, the proportion of preterm birth was found to be 66% in the hypertensive group compared to 19% in the non hypertensive group. Thus, Hypertensive women were more at risk of delivering premature babies and the risk was statistically significant. This can be explained by

the fact that Yaoundé Central Hospital is a Referral hospital that receives patients from the city of Yaoundé and its environs. This is close to the results of Iouta, et al., study in Congo who reported 45% of premature babies in hypertensive group compared to 16.7% in the non hypertensive group [12]; with hypertension being a risk factor for prematurity which was statistically significant. Lower figures were reported in a 2016 publication by Davies, et al. in the United Kingdom [13]. The aim of their study was to determine the contribution of preeclampsia to preterm birth in primiparous women. The values observed were: 78.5% of premature babies in the hypertensive group compared to 85% in the non hypertensive group and this difference was statistically significant (p value = 0.001).

Factors associated of hypertension disease

During the course of our study we found that adolescents were more at risk of developing hypertension during pregnancy and the risk was statistically significant (OR: 2.15, and p value = 0.014). This is close to the results obtained by Dao, et al. in Mali who found a statistically significant association between adolescence and hypertension during pregnancy [14]. Similarity was also seen in the 2013 study by Iouta, et al. in Congo [15], where adolescents were at risk of developing hypertension and the risk was statistically significant (OR: 2.44, p value = 0.0032). This can be explained by the concept of duration of exposure to sperm and paternal antigens, which can modify the immunological response. In fact, the shorter this duration, the higher the risk of hypertension in pregnancy and preeclampsia [15].

From our analysis, there was a statistically significant association between hypertension and low level of education (OR: 2.08 p value = 0.039). This is close to the results of Iouta, et al. in Congo who found a statistically significant association between hypertension and low level of education (OR: 5, p value = 0.001) [12]. In a study by Mboudou, et al. in Cameroon, participants with low level of education were the most represented in the two groups; There was a statistically significant association between hypertension and low level of education (p value = 0.001) [16].

Low socioeconomic status was also identified as a risk factor of hypertension during pregnancy in our study, and the risk was statistically significant (OR: 3.24 p value of 0.012). This is close to the results obtained by Iouta, et al. in Congo who found an (OR: 2.04, and p value of 0.001). The same result had been found by Mboudou, et al. in Cameroon in 2009 [16]. This can be explained by the lack of financial support necessary for the proper monitoring of pregnancy and probably the lack of insurance coverage.

Indeed, in our study, nulliparas were the most affected in the two groups, 73 (49.7%) in the hypertensive group and 52 (35.4%) in the non hypertensive group. There was a statistically significant association between hypertension in pregnancy and nulliparity (p value of 0.001). This is slightly different from the results obtained by Mboudou, et al. who found 38.01% in the hypertensive group and 34.3% in the non hypertensive group [16]. There wasn't a statistically significant association between hypertension in pregnancy and nulliparity (p value

of 0.713). This can be explained by the difference in sample size of the case group 147 in this study versus 121 in their study. Added to this, in our study, grand multiparas were also at risk of developing hypertension during pregnancy and the risk was statistically significant (OR:2, p value of 0.02). This is close to the results of Iouta 2013 in Congo who found a statistically significant association between hypertension and grand multiparity (OR:3.29, and p value of 0.001).

In our study, a statistically significant association was found between hypertension and history of preeclampsia (OR: 19, p value of 0.005). A similar observation was made in a 2007 study by Dao, et al. in Mali [14].

Characteristics of preterm birth

In our study, most premature babies delivered from women who developed hypertension during pregnancy were 61.9% male; while 38.1% were female. This is close to the results obtained by Naha, et al. in their 2020 study [17]. In their study, which aimed to investigate and analyze the clinical, and the therapeutic characteristics of newborns from preeclamptic mothers with premature delivery, 35 were male (58.5%) and 25 (41.7%) were female. Several studies have examined the relationship between fetal sex and preeclampsia, but their results have led to conflicting conclusions. Some studies found that the risk of preeclampsia is higher in mothers with a male fetus [18,19], while other studies found the contrary [20-23]. Most research could not find a relationship after multivariate analyses [18,20,21]. The Apgar score of preterm babies at the first minute of life was low in 11.3% of cases, while in 88.7% cases, it was normal. The severity of the condition at birth could be explained by: the severity of hypertension (73.5% of preeclampsia in our study) and the decision to rescue a mother in danger (eclampsia or HELLP Syndrome). In El Mhamdi's series, 6% of newborns had an Apgar score less than 7 [24] and 94% of newborns who had an Apgar score greater than or equal to 7. In the Mabaga study it was reported that 37.9% of newborns from hypertensive women, had a low Apgar score during the first minute. These statements are consistent with the data demonstrated by the Schneider study: Low Apgar scores were a significant complication during child birth in hypertensive women [25].

Conclusion

- The proportion of preterm births in women with hypertensive disorders in Yaoundé Central Hospital was found to be 66%.
- Risk factors for hypertensive disorder in pregnant women include: Age from 13 to 20 years, nulliparity, grand multiparity, low socioeconomic status, low level of education, history of preeclampsia and gestational age at onset of ANC from 11 to 23 weeks.
- The majority of premature babies born to hypertensive women had a weight ranging from 1600 grams to 2100 grams whereas those born to non hypertensive women had a weight ranging from 2200 grams to 2500 grams. Most of the babies born to hypertensive women were male whereas babies born to non hypertensive

women were majority female. The majority of new borns in our study had an APGAR score less than 7.

- Premature baby's born from women who developed hypertension during pregnancy were at greater risk of having a poor Apgar score at birth.

Competing Interests

The authors have no conflicts of interest to declare for this study.

References

1. Chamberlain G (1995) *Obstetrics by tenteachers: Normal pregnancy*. (16th edn), London: Edward Arnold.
2. Priya SP, Piercy CN, Heli T, et al. (2016) Physiological changes in pregnancy. *Cardiovasc J Afr* 27: 89-93.
3. Conrad KP (2011) Emerging role of relaxin in the maternal adaptations to normal pregnancy: Implications for preeclampsia. *Semin Nephrol* 31: 15-32.
4. Cheung KL, Lafayette RA (2013) Renal physiology of pregnancy. *Adv Chronic Kidney Dis* 20: 209-214.
5. Glinoe D (1997) The regulation of thyroid function in pregnancy: Pathways of endocrine adaptation from physiology to pathology. *Endocr Rev* 18: 404-433.
6. Dorr HG, Heller A, Versmold HT (1989) Longitudinal study of progesterone, mineralocorticoids and glucocorticoids throughout human pregnancy. *J Clin Endocrinol Metabol* 68: 863-868.
7. Elsheikh A, Creatas G, Mastorakos G, et al. (2001) The renin-aldosterone system during normal and hypertensive pregnancy. *Arch Gynecol Obstet* 264: 182-185.
8. Gordon MC (2012) *Maternal physiology in obstetrics: Normal and problem pregnancies*. (6th edn), Philadelphia: Saunders, Elsevier.
9. Linheimer MD, Barron WM, Davison JM (1991) Osmotic and volume control of vasopressin release in pregnancy. *Am J Kidney Dis* 17: 105-111.
10. Yazbeck C, Thiebaugeorges O, Charles Aline M, et al. (2009) Maternal blood lead levels and the risk of pregnancy-induced hypertension The EDEN Cohort Study. *Environmental Health Perspectives* 117: 1526-1530.
11. Dolea C, Abou Zahr C (2003) *Global burden of hypertensive disorders of pregnancy in the year 2000, Evidence and Information for Policy (EIP)* Geneva: World Health Organization.
12. Itoua C, Ngounda BF, Ellenga GM, et al. (2013) Hypertension artérielle et grossesse: épidémiologie et pronostic materno-fœtal au Centre Hospitalier Universitaire de Brazzaville. *Medicine d'Afrique Noire* 60: 21-29.
13. Davies EL, Bell JS, Bhattacharya S (2016) Preeclampsia and preterm delivery: A population-based case-control study. *The Journal of Hypertension in Pregnancy* 35: 510-519.
14. Dao ZS (2005) Hypertension artérielle et grossesse dans le service de gynéco-obstétrique du CHU Gabriel Touré à propos de 120 cas [Thèse de doctorat de médecine]. Bamako: FMPOS 72.
15. Robillard PY, Hulseley TC, Perianin J, et al. (1994) Association of pregnancy-induced hypertension with duration of sexual cohabitation before conception. *Lancet* 344: 973-975.
16. Mboudou ET, Foumane P, Belley Priso E, et al. (2009) Hypertension au cours de la grossesse: Aspects cliniques et épidémiologiques à l'Hôpital Gynéco-Obstétrique et Pédiatrique de Yaoundé, Cameroun. *Clinics in Mother and Child Health* 6: 1087-1093.
17. Bakker R, Steegers EAP, Hofman A, et al. (2011) Blood pressure in different gestational trimesters, fetal growth, and the risk of adverse birth outcomes the generation r study. *Am J Epidemiol* 174: 797-806.
18. Conde-Agudelo A, Belizán JM (2000) Risk factors for pre-eclampsia in a large cohort of Latin American and Caribbean women. *BJOG* 107: 75-83.
19. Magnus P, Eskild A (2001) Seasonal variation in the occurrence of pre-eclampsia. *BJOG* 108: 1116-1119.
20. Ros HS, Cnattingius S, Lipworth L (1998) Comparison of risk factors for preeclampsia and gestational hypertension in a population-based cohort study. *Am J Epidemiol* 147: 1062-1070.
21. Phillips JK, Bernstein IM, Mongeon JA, et al. (2004) Seasonal variation in preeclampsia based on timing of conception. *Obstet Gynecol* 104: 1015-1020.
22. Brettell R, Yeh PS, Impey LWM (2008) Examination of the association between male gender and preterm delivery. *Eur J Obstet Gynecol Reprod Biol* 141: 123-126.
23. Shiozaki A, Matsuda Y, Satoh S, et al. (2001) Impact of fetal sex in pregnancy-induced hypertension and preeclampsia in Japan. *J Reprod Immunol* 89: 133-139.
24. Dekker G, Robillard PY, Roberts C (2001) The etiology of preeclampsia: The role of the father. *J Reprod Immunol* 89: 126-132.
25. Schneider S, Freerksen N, Maul H, et al. (2011) Risk groups and maternal-neonatal complications of preeclampsia current results from the national german perinatal quality registry. *J Perinat Med* 39: 257-265.

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