Mariam K. Maducolil*, Sawsan Al-Obaidly, Tawa Olukade, Husam Salama, Mai AlQubaisi and Hilal Al Rifai

Maternal characteristics and pregnancy outcomes of women with chronic hypertension: a population-based study

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Abstract

Background: We aimed to study the maternal characteristics and obstetric and neonatal outcomes in pregnant mothers with chronic hypertension (CHTN) compared to non-CHTN.

Methods: The study was a population-based cohort study, and a PEARL-Peristat Study (PPS) for the year of 2017. There were 20,210 total births including 19,762 singleton and 448 multiple births. We excluded multiple gestations from the analysis as they differ in fetal growth, duration of gestation and have a higher rate of obstetric and neonatal complications. We compared the maternal characteristics of mothers with pre-existing HTN with non-hypertensive mothers and studied the obstetric and neonatal outcomes including cesarean section, stillbirths, prematurity, macrosomia and postpartum hemorrhage (PPH).

Results: We identified 223 births of mothers with essential HTN. The overall prevalence of CHTN in our population was 1.1% (223/20,210). In regard to maternal characteristics, women with CHTN were at or above 35 years of age at the time of delivery 58.9% compared to non-CHTN women 18.7%, P-value <0.001. Pre-existing diabetes was found more in women with CHTN 15.1% compared to non-CHTN women 1.9%, P-value <0.001; while obesity was found in 64% of women with CHTN compared to 32.5% in non-CHTN women, P-value <0.001. Preterm birth was noted in 26% compared to 8% in CHTN compared to non-CHTN women, respectively, P-value <0.001. The rate of stillbirth was similar between the two groups, 0.9% compared to 0.6% in CHTN compared to non-CHTN women, respectively, P-value 0.369.

Conclusion: Hypertensive mothers have multiple other comorbidities. When compared to the general population, they are older, parous, diabetic and obese with an increased risk of preterm birth and cesarean deliveries. Lifestyle modification, extensive pre-conceptional counseling and multidisciplinary antenatal care are required for such a high-risk group.

Keywords: chronic hypertension; incidence; Middle East; outcome; pregnancy.

Introduction

Maternal chronic hypertension (CHTN) is a risk factor in pregnancy, which is becoming more common as women become pregnant in their later years. Chronic or pre-existing HTN is defined as HTN that antedates pregnancy, is present before the 20th week of pregnancy or persists longer than 12 weeks postpartum [1]. CHTN complicates 3%–5% of pregnancies [2]. The incidence is gradually rising due to various contributory factors such as increasing rates of obesity, pregnancy in advanced age and sedentary lifestyles.

Pregnancy complicated with CHTN is associated with adverse maternal and fetal outcomes with increased rates of pre-eclampsia (PET), abruptio placenta, hospitalization, adverse effect on fetal growth with iatrogenic preterm delivery and its consequences.

Despite the known complications of CHTN, establishing a diagnosis of CHTN in pregnancy is sometimes challenging as the physiological changes that occur during pregnancy especially in the second trimester reduce the blood pressure to be within the normal range which will erroneously label the patient as normotensive especially if the patient is booked during the second trimester of pregnancy. Therefore, a subset of patients are diagnosed as gestational hypertensive once the physiologic reduction in blood pressure ends in the third trimester of pregnancy [1, 3]. This may also lead to a lost opportunity for close monitoring in order to prevent the consequences associated with CHTN in pregnancy on both the fetal and the maternal health.

***Corresponding author: Mariam K. Maducolil,** Associate Consultant, Women's Wellness and Research Center, Hamad Medical Corporation, PO Box 3050, Doha, Qatar,
E-mail: mariamroy@gmail.com
Sawsan Al-Obaidly, Tawa Olukade, Husam Salama, Mai AlQubaisi and Hilal Al Rifai: Women's Wellness and Research Center, Hamad Medical Corporation, Doha, Qatar

There are many studies on gestational HTN and PET, but there is a lack of significant international data or data from the Middle East on CHTN and its effect on pregnancy especially among a multiethnic population. This article aims to provide an understanding of maternal characteristics, perinatal outcomes and the current trend in CHTN in pregnancy when compared to non-hypertensive mothers from a middle-eastern perspective.

Materials and methods

Study design

This was a population-based retrospective cohort analysis using data obtained from the PEARL-Peristat Registry of the PEARL-Peristat Study (PPS) (Perinatal Neonatal Outcomes Research Study in the Arabian Gulf), Qatar. The PPS is an ongoing population-based cohort study of mainly routinely collected hospital data from women and their neonates. The study aims to study the fetal and maternal outcomes of the perinatal-neonatal period. The study is funded by Qatar National Research Fund (Grant no. NPRP 6-238-3-059) and sponsored by the Medical Research Centre, Hamad Medical Corporation. The study was approved by the Hamad Medical Corporation Institutional Review Board, with a waiver of consent.

Setting and participants

The sample for this study comprised births from all four public maternity hospitals in Qatar. Data were collected from 20,210 total births including 19,762 singleton and 448 multiple births. All singleton pregnancies of 24 weeks or more were included in this study. Multiple gestations were excluded from the analysis as they differ in fetal growth, duration of gestation and have a higher rate of obstetric and neonatal complications.

The 19,762 singleton births at or more than 24 weeks of gestation were births from January to December 2017 in the Women's Hospital and March to December 2017 in other hospitals.

Chronic hypertension

CHTN was defined as HTN that antedates pregnancy, is present before the 20th week of pregnancy or persists longer than 12 weeks postpartum [1]. In this analysis, a history of or the presence or absence of CHTN/essential HTN in a patient was coded as yes (1) or no (0).

Covariates and outcome variables

Maternal age at delivery was grouped as <35 years and ≥35 years. Parity was grouped as nulliparous, 1–4 parous experiences and ≥5 parous experiences. Nationality was coded as Qatari or non-Qatari. Diabetes was grouped as none, overt and gestational diabetes. Early body mass index (BMI) (kg/m^2) was calculated as the ratio of first-trimester weight (kg) divided by height (m^2). This was grouped as underweight (≤18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2) and obese (≥30 kg/m^2) [4].

The presence or absence of maternal outcomes included cholestasis of pregnancy (ICP), PET, postpartum hemorrhage (PPH), intensive care unit (ICU) admission, acute maternal morbidity and in-hospital maternal mortality. Morbidities included in acute maternal morbidity included renal dysfunction/failure, acute pulmonary edema, HELLP, disseminated intravascular coagulation (DIC), shock, respiratory failure and requirement for intubation/ventilation, etc. For PPH, blood loss was defined as ≥500 mL for vaginal births or ≥1000 mL for cesarean births. Mode of delivery was grouped as vaginal and cesarean delivery. Within vaginal births studied, outcomes included induction of labor (IOL) and assisted delivery (forceps or vacuum).

Neonatal outcomes included gestational age (GA) at delivery (preterm 24–36 weeks and term ≥37 weeks), fetal death, admission to neonatal intensive care unit (NICU), fetal macrosomia (birth weight ≥4 kg), term low birth weight (<2500 g), term intrauterine growth restriction (IUGR) (<5th centile) and 5-min Apgar <7.

Statistical analysis

Descriptive statistics was used to show the distribution of variables using numbers and percentages. The differences in observed proportions between the hypertensive and non-hypertensive groups were compared using chi-square (χ^2) test or Fisher's test as appropriate. Statistical significance was set at $P < 0.05$. Statistical analysis was performed using the IBM SPSS Statistics for Windows, version 22 (IBM Corp., Armonk, NY, USA).

Results

We identified 223 births of mothers with CHTN. The overall prevalence of CHTN in our population was 1.1% (223/20,210). The majority of cases were in singleton gestations (219/19,762) also giving us a prevalence rate of 1.1%.

The maternal characteristics are presented in Table 1. There was no significant difference in the nationality of those women with CHTN and those without, 71.7% (157/219) of women with CHTN were non-Qatari compared to 74.4% (14,474/19,452) in the non-CHTN group ($P = 0.36$). There was a significant difference observed between women with CHTN and those without for age, BMI, parity, pre-existing and gestational diabetes and previous poor obstetric history. Maternal age at delivery ≥35 years was significantly more common in the CHTN group [129/219 (58.9%) vs. 3648/19,543 (18.7%); $P < 0.001$]. The early pregnancy BMI was only recorded in 27% (5296/19,762) of the cohort; however, women in the CHTN group were significantly more likely to be obese with a BMI more than 30

Table 1: Baseline maternal characteristics.

Variables	No HTN (n=19,543)		HTN (n=219)		P-value
	n	%	n	%	
Maternal age (≥35 years)	3648	18.7	129	58.9	**<0.001**
Nationality[a]					
Qatari	5041	25.8	62	28.3	0.403
Non-Qatari	14,482	74.2	157	71.7	
Early pregnancy obesity[b]	1695	32.5	55	64.0	**<0.001**
Parity[a]					
Nulliparous	5548	28.4	39	17.8	
Parity 1–4	12,647	64.7	147	67.1	**<0.001**
Parity ≥5	1344	6.9	33	15.1	
History of stillbirth[a]	280	1.4	7	3.3	**0.028**

[a]Variables with missing data: nationality (20), parity (4), history of stillbirth (131). [b]Data available for 26.8% of samples. Bold text indicates values <0.05.

Table 2: Maternal outcomes in 19,762 births.

Variables	No HTN (n=19,543)		HTN (n=219)		P-value
	n	%	n	%	
Diabetes status					
No DM	14,074	72.0	107	48.9	**<0.001**
GDM	5102	26.1	79	36.1	
Overt DM	367	1.9	33	15.1	
Cholestasis of pregnancy	248	1.3	1	0.5	0.533
Cesarean	6025	30.8	122	55.7	**<0.001**
IOL[a]	2200	16.3	32	33.0	**<0.001**
Assisted birth[a]	1194	8.8	5	5.2	0.203
GA at birth					
24–36 weeks	1569	8.0	57	26.0	**<0.001**
≥37 weeks	17,974	92.0	162	74.0	**<0.001**
PPH	988	5.1	11	5.0	0.982
Acute maternal morbidity	18	0.1	1	0.5	0.191
Admission to ICU	65	0.3	3	1.4	**0.040**

DM, diabetes mellitus; GDM, gestational diabetes mellitus. [a]Applicable to vaginal births only (n=13,615). Bold text indicates values <0.05.

[55/86 (64%) vs. 1695/5210 (32.5%); P<0.001] compared to the non-CHTN group. Women with CHTN were also significantly more likely to be parous when compared to non-CHTN women [180/219 (82.2%) vs. 13,991/19,539 (71.6%); P<0.001], and more likely to have pre-existing diabetes [33/219 (15.1%) vs. 367/19,543 (1.9%); P<0.001] and gestational diabetes [79/219 (36.1%) vs. 5102/19,543 (26.1%); P<0.001] than the non-CHTN women.

The rate of stillbirth in a previous pregnancy was noted to be more common in CHTN group [7/219 (3.3%) vs. 280/19,543 (1.4%)] when compared to non-CHTN women (P=0.028).

Tables 2 and 3 demonstrate the perinatal outcomes for the two comparative groups. There was a significantly higher cesarean section rate in women with CHTN [122/219 (55.7%)] compared to non-CHTN women [6025/19,543 (30.8%) (P<0.001)]. There was no difference in PPH between the two groups [5% (11/219) vs. 5.1% (988/19,543)].

The incidence of major maternal morbidity associated with acute organ failure, disseminated intravascular coagulation or uncontrolled blood pressure requiring ICU admission was low in both groups (0.1% in the CHTN group and 0.5% in the non-CHTN group). There was a maternal death in the chronic hypertensive group due to superimposed PET with severe features.

With regard to neonatal outcomes, preterm birth (24–36 weeks) occurred in 26% (57/219) of CHTN women compared to 8% (1569/19,543) of women with no CHTN (P<0.001). Similarly, more neonates of CHTN women were admitted to the NICU than those of non-CHTN women (26.9% vs. 13.4%; P<0.01). Macrosomic infants were less likely to occur with women with CHTN (5.1% vs. 1.8%; P=0.03). The rate of stillbirth was similar between the CHTN group [2/219 (0.9%)] and the non-CHTN group [114/19,543 (0.6%)].

Table 3: Neonatal outcomes.

Variables	No HTN (19,429)		HTN (217)		P-value
	n	%	n	%	
Stillborn	114	0.6	2	0.9	0.369
Low Apgar at 5 min	49	0.3	2	0.9	0.109
NICU admission	2610	13.4	58	26.9	**<0.001**
Preterm	1569	8.0	57	26.0	**<0.001**
Macrosomic baby	985	5.1	4	1.8	**0.027**
IUGR (<5th centile)[a]	889	5.0	10	6.2	0.477
Birth weight <2500 g[a]	597	3.1	10	4.6	0.194

[a]Term babies. Low Apgar at 5 min, NICU admission, preterm, macrosomic baby, IUGR and birth weight 2500 g were examined in livebirths. Bold text indicates values <0.05.

Discussion

Hypertensive disorders in pregnancy are a wide spectrum of disorders and still a complex disorder in pregnancy despite recent advances in screening, monitoring and treatment. Definition of certain hypertensive disorders in pregnancy such as PET and gestational HTN has gone

through major changes over the last decade but there is no significant change in the definition of CHTN in pregnancy.

The prevalence of CHTN in pregnancy varies in different study populations but the worldwide prevalence rate is between 0.5% and 5% in pregnancies [2]. According to a nationwide sample analyzing the trends and prevalence of CHTN, 1995–1996 through 2007–2008 in the USA, it was noted that the prevalence is gradually increasing from 0.9% to 1.8%, respectively [5].

The incidence of CHTN in a population is influenced by the ethnicity and prevalence of modifiable risk factors such as obesity and smoking among the studied population. The prevalence of CHTN in our multiethnic population was 1.1% and it is comparatively less than the prevalence rates published by the studies from the Western population. This lesser prevalence rate may be because the majority of women in the gulf region conceive before 35 years of age and because the prevalence of smoking, drug abuse and intake of alcohol is very low in this population for a variety of social and cultural factors. The World Health Organization (WHO) Global Survey on Maternal and Perinatal Health performed in 2010 stated that the prevalence of CHTN in Qatar was 0.28% [6]. The results of our study, despite presenting a low incidence of CHTN amongst pregnant women, do suggest an upward trend in incidence of CHTN over the past 7 years since the WHO survey.

According to a secondary analysis of the WHO Global Survey on Maternal and Perinatal Health, one of the major risk factors for PET and eclampsia was CHTN [7]. It is therefore important that women with CHTN are known promptly, treated with appropriate medication and monitored closely for the wide spectrum of maternal and fetal signs and symptoms of superimposed PET as it is significantly associated with adverse perinatal outcomes.

CHTN can be classified into primary HTN, without an underlying cause, and secondary HTN, developed due to underlying causes, e.g. diabetes mellitus, autoimmune disorders and chronic kidney disease, with the prevalence of primary and secondary HTN reported at 88.8% and 11.2%, respectively [5]. We have reviewed the pregnancy outcomes of women with CHTN in general without sub-classifying HTN into primary or secondary based on causative factors.

Certain maternal characteristics such as age, BMI and ethnicity are known risk factors predisposing women to CHTN. Advancing maternal age has been found to be a strong predictor of CHTN. A large 5-year epidemiological study in the US concluded a strong association of CHTN with maternal age [8]. Similar results were seen in a prospective screening study in the UK where high booking blood pressure was associated with advancing maternal age [9].

The confirmation of CHTN in pregnancy results in an increased risk of adverse pregnancy outcomes. Superimposed PET, cesarean delivery, PPH and placental abruption all increased in pregnancies affected by CHTN, which can all impact maternal morbidity and mortality which may affect the quality of women's long-term health.

In an analysis of outcomes for 763 women with CHTN enrolled into a multicenter trial of low-dose aspirin for the prevention of PET [10], the incidence of superimposed PET was 25%, a figure increased in women with more than 4-year history of CHTN. Panaitescu et al. [11] also reported a similar incidence of superimposed PET in women with CHTN, 22% [11].

The incidence of superimposed PET in our study is 7.5%, which is significantly less than the figure quoted internationally [10, 11]. We are unable to explain this low incidence. It may be related to the complex nature of our population, in terms of parity or ethnicity, and further prospective work is needed to explore this further, and identify any modifiable factors that can have adverse synergistic effects on patients with CHTN [11].

In this study, there was a near doubling of cesarean section rates amongst women with CHTN (56%) compared to non-hypertensive women (30%). Sibai et al. [12] in a comparative study of singleton term (>36 weeks) deliveries noted that pregnancies complicated with CHTN had statistically higher rates of cesarean deliveries [odds ratio (OR) = 2.7; 95% confidence interval (CI) 2.4–3.0] [11]. Again similar associations between CHTN and cesarean delivery rates have been reported elsewhere [5] and are a result of high incidence of induced preterm delivery due to uncontrollable HTN, superimposed PET, IUGR and abruptio placentae.

Bateman et al. [5] reported that the incidence of pregestational diabetes among patients with CHTN was 6.6% compared to 0.7% in non-hypertensive women ($P < 0.001$) and that this risk increased with lengthening duration of HTN over 12 years [5]. Whilst our incidence of diabetes is much higher, due in part to screening criteria, we have also seen an increase in diabetes in women with pre-existing HTN.

In a retrospective cohort study of 532,088 singleton pregnancies [8], the rate of preterm birth was 25.5%, while the rate of small for GA was 18.3% in patients with CHTN. The same study also reported that the rate of stillbirths was 2.5 times higher in the group with CHTN compared to controls. A very similar figure for an increased risk of stillbirth was also reported for women with CHTN. According to a prospective study, Yerlikaya et al. [9] examined 113,415 singleton pregnancies and found the

OR of still birth to be increased (OR 2.6) in patients with CHTN [9]. Our study has demonstrated similar associations between preterm birth, still births and IUGR in addition to increased neonatal care admission in women with CHTN than those without.

Conclusion

It is advisable that women in the reproductive age group with CHTN be offered pre-pregnancy counseling, close monitoring of blood pressure, lifestyle modification such as diet and weight reduction and commencement of safe antihypertensive medications which can continue during any planned pregnancy. It would also be the time to investigate and determine whether the HTN is primary or secondary as management becomes much more complex requiring a multi-disciplinary team for those with secondary causes. Once pregnancy is confirmed, the importance of aspirin therapy, detection and monitoring of any new onset of albuminuria and the regular assessment of the fetal growth and well-being should be emphasized.

We have done a preliminary evaluation of incidence and risk factors associated with CHTN in pregnancy in a middle-eastern population. One notable finding is that superimposed PET was less common than described in previous studies in other parts of the world. This study will be the foundation on which we will be evaluate further the causes and co-morbidities of CHTN among this population. This study confirmed the depth of associated maternal and fetal adverse outcomes to enable targeted antenatal care for pregnant women with CHTN.

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