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## OBSTETRICS

# Hypertensive Disorders in Pregnant Women with One or More Abnormal Values of Oral Glucose Tolerance Test

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**ABSTRACT**

**Objective:** To determine the incidence of hypertensive disorders in singleton women with one or more abnormal values of oral glucose tolerance test (OGTT) and to evaluate the association between characteristics of these women and hypertensive disorders in pregnancy.

**Materials and methods:** The retrospective study conducted at the Department of Obstetrics and Gynecology, BMA Medical College and Vajira Hospital. The study group consisted of singleton women who had one or more abnormal values of OGTT between July 2006 and December 2007. The incidence and risk factors for development of hypertensive disorders were determined.

**Results:** Of the 434 women studied, the incidence of hypertensive disorders was 12% (8.6%, 12.3%, 17.2% and 20% in women with 1, 2, 3 and 4 abnormal values of OGTT, respectively). Thus the number of abnormal values of OGTT tended to have higher prevalence of hypertensive disorder but not reach statistical significance. Pre-pregnancy body mass index (BMI) was the significant characteristic that associated with the development of hypertensive disorders.

**Conclusion:** The incidence of hypertensive disorders in singleton women with one or more abnormal values of OGTT was 12%. Women who have high pre-pregnancy BMI were at increased risk of developing hypertensive disorders in pregnancy.

**Keywords:** hypertensive disorders, oral glucose tolerance test, pre-pregnancy BMI

## Introduction

Pregnancy-induced hypertension (PIH) is a common complication of pregnancy. This condition is associated with an increased risk of maternal and fetal morbidity and mortality. Hypertension in pregnancy comprises several disorders including preeclampsia (proteinuric hypertension), gestational (non-proteinuric) hypertension, and chronic hypertension with or without superimposed preeclampsia.[1] Focusing on the former two hypertensive conditions (preeclampsia and gestational hypertension), extensive research has been conducted to search for their precise etiology. Nevertheless, this is still unknown at the present time.

Despite a poor understanding in the

pathophysiology of PIH, many studies reported a significant increase in the incidence rates of PIH in women with gestational diabetes mellitus (GDM) or gestational mild hyperglycemia (GMH).[2-4] Some authors proposed that the mechanism might be related to insulin resistance.[5-7] In addition, some characteristic features of women who were affected by GDM or GMH were demonstrated to be independently associated with the development of preeclampsia or gestational hypertension, including high body mass index (BMI) and severity of GDM.[8-10]

Although several authors reported the association between GDM or GMH and risk of PIH the data are still limited in the Southeast Asians particularly in Thai people. Thus, the aim of this study was to search for the incidence of pregnancy-induced hypertension in Thai women who had relative glucose intolerance (GDM and GMH). Further aim was to explore the characteristics of these women, which would be related to the development of hypertensive disorders in pregnancy.

## Materials and Methods

The study was conducted after the approval of the Bangkok Metropolitan Administration (BMA) Ethics Committee for Researches Involving Human Subjects. Singleton pregnancies, who presented for antenatal booking at BMA Medical College and Vajira Hospital, consecutively underwent 100-gram oral glucose tolerance test (OGTT) between July 2006 and December 2007, and who had one or more abnormal values of OGTT were enrolled. Exclusion criteria were those who had chronic hypertension, overt diabetes, or other chronic diseases which may be related to the occurrence of hypertension, such as renal, connective tissue or thyroid diseases. The women who delivered elsewhere and had incomplete obstetric charts were also excluded from the study.

From pilot study, the prevalence of PIH among pregnant women with one or more abnormal values of OGTT was 10%. With 95% confidence interval and maximum allowable error of 3%, 385 women were needed. We added 10% of the sample size in the event that the enrolled subjects met any of the exclusion criteria, so a total of 424 women would be required. All pregnant women in the study underwent glucose challenge test (GCT) for GDM screening. Women without any risk factors were screened at 24-28 weeks of gestation. Those with any of the risk factors (age $\geq$ 30 years, BMI $\geq$ 27 kg/m$^2$, any first-degree relatives with type 2 diabetes, history of GDM in previous pregnancy, prior delivery of a newborn weighing $\geq$ 4,000 grams, history of any adverse obstetric events [congenital fetal anomaly or unexplained intrauterine fetal demise], or glucosuria)[11] were screened at an initial visit or as soon as possible. The GCT value of $\geq$ 140 mg/dl was followed by a diagnostic OGTT. GMH was defined as one abnormal value of OGTT,[2] while GDM was diagnosed with $\geq$ 2 abnormal values using the National Diabetes Data Group criteria.[12] All women who were diagnosed as having GDM were managed with diet modification and insulin therapy if needed, under close surveillance of the endocrinologists.

Obstetric records of the eligible women were reviewed. Data collection included maternal demographics, risk factors for GDM, gestational ages (GA) at which screening and diagnostic tests were performed, 50-gram GCT and all four OGTT values, and insulin use. BMI was determined as pre-pregnancy BMI. Pregnancy-induced hypertension was diagnosed using the criteria of the National High Blood Pressure Education Program Working Group.[1] Gestational hypertension was defined as hypertension (blood pressure $\geq$ 140/90 mmHg) without proteinuria after the 20$^{th}$ week of gestation while preeclampsia referred to gestational hypertension with proteinuria ($\geq$ 300 mg in 24 hours or dipstick $\geq$ 1+).

Data were analyzed using the SPSS software package version 11.5 (SPSS Inc., Chicago, IL, USA). Incidence of PIH and categorical variables were reported as number with percentage. Factors associated with PIH in women with one or more abnormal values of OGTT were evaluated by the $\chi^2$ test or Fisher's exact test as appropriate. P-value of $< 0.05$ was considered statistically significant.

## Results

During the study period, 2,196 women had abnormal GCT screening, 1,908 women underwent

OGTT, 288 women were loss to follow up, 575 women had one or more abnormal values of OGTT, 141 women delivered elsewhere, finally 434 pregnant were included for the analysis. Of these, mean age and mean pre-pregnancy BMI were 31.5 ± 5.4 years and 23.7 ± 4.7 kg/m$^2$ respectively. 177 (40.8%) women were nulliparity, 92 (21.2%) women had family history of diabetes. No data were recorded regarding previous history of GDM, while only 7 (1.6%) had prior macrosomia. None had previous history of congenital fetal anomaly or unexplained intrauterine fetal demise.

Overall, mean GCT value of the study group was 177 ± 37 mg/dl. The mean gestational age (GA) at OGTT testing was 27.8 ± 6.6 weeks; 55 (12.7%) women underwent OGTT before 24 weeks of gestation. A total of 198 women (45.6%) had one abnormal value of OGTT while 138 (31.8%), 58 (13.4%) and 40 (9.2%) women had 2, 3 and 4 abnormal values of OGTT. One hundred and seventy-one women (39.4%) were diagnosed with GDM of class $A_1$ and the remaining 65 women (15.0%) were diagnosed with class $A_2$. Details of clinical characteristics of the studied population are presented in Table 1.

The incidence of PIH in women with one or more abnormal values of OGTT was 12.0% (52/434); 10 (2.3%) had gestational hypertension, 27 (6.2%) developed mild preeclampsia, while 15 (3.5%) had severe preeclampsia. The mean GA at which hypertensive disorders were diagnosed was 37.0 ± 2.1 weeks.

Various factors of these 434 women were evaluated for the association with the occurrence of PIH. In a univariable analysis, high BMI (≥ 27 kg/m$^2$), earlier GA at diagnosis of GDM or GMH, and insulin use were significantly associated with the development of PIH. Women who were older and had increasing numbers of abnormal values of OGTT tended to have increased incidence of PIH, however, statistical analysis did not reach significant level (Table 1). In a multivariable analysis, age, gestational age at OGTT, severity of abnormal glucose values and insulin use were not identified as predictors for PIH. High prepregnancy BMI was the only independent factor related to this hypertensive disorder. The result demonstrated that women with abnormal glucose intolerance (GDM or GMH) who had BMI ≥ 27 kg/m$^2$ had a 3.1-fold risk of developing PIH as compared to those whose BMI was < 27 kg/m$^2$. (Table 2)

## Discussion

In this Thai population-based study, we found a 12.0 % incidence rate of PIH in GDM or GMH-affected gravidas; 17/198 (8.6%) in GMH and 35/236 (14.8%) in GDM women. The incidence was slightly lower than that 14.7% in previous study of Vambergue, et al[2] which was conducted in French people, but was higher than the 9.0 % incidence rate in Japanese population-based study of Miyakoshi, et al.[3] A variety of the incidence rates among these three studies may lie on the differences of population characteristics, ethnicity, as well as criteria used for GDM screening and diagnosis. Nevertheless, the results from the present and previous studies were in the same direction that the incidence of PIH in women with GDM or GMH was higher than those reported in general population. [2-4]

In the present study, we found that obesity was the only independent factor associated with development of PIH in women affected by GDM or GMH. Some authors hypothesized that such association might be related to the mechanism of insulin resistance. In support of this hypothesis, several studies demonstrated that pregnant women who developed hypertension in pregnancy were relatively hyperinsulinemic and had lower insulin sensitivity.[13-15] Based on the finding that obesity was an independent risk factor for preeclampsia or gestational hypertension, we propose that women who are obese should therefore be encouraged to achieve an ideal body weight before becoming pregnant. Likewise, according to the results of the present study that the incidence of PIH in women with GDM was higher than that in individuals with GMH (14.8% and 8.6% respectively), we suggest that the obstetricians should closely monitor and control plasma glucose levels of the GMH women in an attempt to avoid their condition to turn out to be GDM.

In conclusion, the present study demonstrated a 12.0% incidence rate of PIH in singleton women with GDM or GMH. It is interesting to determine

whether severity of insulin resistance or GDM would be associated with severity of preeclampsia. Further studies with larger number of women are warranted to determine this issue.

**Table 1.** Association of various characteristic factors and hypertensive disorders in abnormal OGTT women by univariable analysis (n = 434)

| Characteristic factors | | Hypertensive disorders (n) (%) | p-value |
|---|---|---|---|
| Age | <30 years (n= 140) | 12 (8.6%) | 0.13 |
| | ≥30 years (n= 294) | 40 (13.6%) | |
| Parity | Nulliparity (n= 177) | 19 (10.7%) | 0.50 |
| | Multiparity (n= 257) | 33 (12.8%) | |
| Pre – pregnancy BMI (kg/m$^2$ ) | | | |
| | <27 (n=340) | 28 (8.2%) | <0.001* |
| | ≥27 (n=94) | 24 (25.5%) | |
| Family history of DM | | | |
| | Absence (n=342) | 42 (13.3%) | 0.71 |
| | Presence (n=92) | 10 (10.9%) | |
| Gestational age at OGTT (weeks) | | | |
| | <24 (n=55) | 14 (25.5%) | 0.001* |
| | ≥24 (n=379) | 38 (10%) | |
| Number of abnormal value of OGTT | | | 0.09 |
| | 1 value (n=198) | 17 (8.6%) | |
| | 2 values (n=138) | 17 (12.3%) | |
| | 3 values (n=58) | 10 (17.2%) | |
| | 4 values (n=40) | 8 (20%) | |
| Diagnosis | | | |
| GMH (n=198 ) | | | 0.06 |
| | Abnormal fasting blood sugar (n= 8) | 1 (12.5%) | |
| | Abnormal 1 hour value (n=61) | 6 (9.8%) | |
| | Abnormal 2 hour value (n=42) | 2 (4.8%) | |
| | Abnormal 3 hour value (n=87) | 8 (9.2%) | |
| GDM A1 (n=171) | | 20 (11.7%) | |
| GDM A2 (n=65) | | 15 (23.1%) | |
| Insulin treatment | | | |
| | Yes (n=29) | 8 (27.6%) | 0.007* |
| | No (n=405) | 44 (10.9%) | |

BMI =Body mass index, OGTT=Oral glucose tolerance test, GMH = Gestational mild hyperglycemia, GDM= Gestational diabetes mellitus, DM=Diabetes mellitus

* Statistical significant

**Table 2.** Association of various characteristic factors and hypertensive disorders in abnormal OGTT women by multivariable analysis (n = 434)

| Characteristic factors | Odds ratio | 95% CI | p-value |
|---|---|---|---|
| Age (<30 years/>30 years) | 1.420 | 0.69 -2.88 | 0.331 |
| Prepregnancy BMI (<27 / ≥27 kg/m$^2$ ) | 3.190 | 1.70-5.99 | <0.001* |
| Gestational age at OGTT (<24 / ≥24 weeks) | 0.551 | 0.25-1.19 | 0.131 |
| Diagnosis (GMH / GDM values) | 1.213 | 0.61-2.42 | 0.581 |
| Insulin treatment (no/yes) | 2.020 | 0.77-5.25 | 0.150 |

BMI =Body mass index, OGTT=Oral glucose tolerance test, GMH= Gestational mild hyperglycemia, GDM= Gestational diabetes mellitus

* Statistical significant

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## *ภาวะความดันโลหิตสูงในสตรีตั้งครรภ์ที่ตรวจพบค่าการทดสอบความทนน้ำตาลกลูโคสที่มีความผิดปกติตั้งแต่หนึ่งค่าขึ้นไป*

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***วัตถุประสงค์*** *: เพื่อหาอุบัติการณ์การเกิดความดันโลหิตสูงขณะตั้งครรภ์ในสตรีครรภ์เดี่ยวที่มีค่าความทนน้ำตาลกลูโคส 100 กรัม ผิดปกติตั้งแต่หนึ่งค่าขึ้นไปและศึกษาความสัมพันธ์ระหว่างข้อมูลพื้นฐานกับการเกิดความดันโลหิตสูงขณะตั้งครรภ์ในสตรีกลุ่มนี้*

***วัสดุและวิธีการ*** *: เป็นการศึกษาวิจัยแบบย้อนหลัง ณ ภาควิชาสูติศาสตร์-นรีเวชวิทยา, วิทยาลัยแพทยศาสตร์กรุงเทพมหานครและวชิรพยาบาล กลุ่มศึกษาประกอบด้วยสตรีตั้งครรภ์เดี่ยวที่มีผลการตรวจค่าความทนน้ำตาลกลูโคส 100 กรัม พบความผิดปกติตั้งแต่ 1 ค่าขึ้นไประหว่างเดือน ก.ค. 2549 – ธ.ค. 2550 โดยศึกษาอุบัติการณ์และปัจจัยเสี่ยงของการเกิดความดันโลหิตสูงขณะตั้งครรภ์*

***ผลการศึกษา*** *: จากสตรีกลุ่มศึกษาจำนวน 434 ราย พบอุบัติการณ์ความดันโลหิตสูงขณะตั้งครรภ์เท่ากับร้อยละ12 โดยพบว่าร้อยละ 8.6, 12.3, 17.2 และ 20 อยู่ในกลุ่มที่มีความผิดปกติ 1, 2, 3 และ 4 ค่า ตามลำดับ จำนวนค่าความผิดที่เพิ่มขึ้นมีแนวโน้มที่จะมีความเสี่ยงต่อการเกิดความดันโลหิตสูงขณะตั้งครรภ์มากขึ้นแต่มิได้มีนัยสำคัญทางสถิติ และพบว่าดัชนีมวลกายก่อนการตั้งครรภ์มีความสัมพันธ์กับการเกิดภาวะความดันโลหิตสูงขณะตั้งครรภ์ในสตรีกลุ่มนี้อย่างมีนัยสำคัญทางสถิติ*

***สรุป*** *: อุบัติการณ์ความดันโลหิตสูงขณะตั้งครรภ์ในสตรีครรภ์เดี่ยวที่ตรวจพบค่าความทนน้ำตาลกลูโคส 100 กรัม ผิดปกติ ตั้งแต่ 1 ค่าขึ้นไป เท่ากับร้อยละ 12 และพบว่าดัชนีมวลกายก่อนการตั้งครรภ์ที่สูงเพิ่มความเสี่ยงต่อการเกิดภาวะความดันโลหิตสูงขณะตั้งครรภ์*