RISK FACTORS FOR HYPERTENSIVE DISORDERS IN MYANMAR PREGNANT WOMEN

EI WAH PHYU THET

**A THESIS SUBMITTED IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF
NURSING SCIENCE (MIDWIFERY)
FACULTY OF GRADUATE STUDIES
MAHIDOL UNIVERSITY
2016**

Thesis
entitled

RISK FACTORS FOR HYPERTENSIVE DISORDERS IN MYANMAR PREGNANT WOMEN

.....
Miss. Ei Wah Phyu Thet
Candidate

.....
Asst. Prof. Piyanun Limruangrong,
Ph.D. (Nursing)
Major advisor

.....
Assoc. Prof. Nittaya Sinsuksai,
Ph.D. (Nursing)
Co- advisor

.....
Prof. Patcharee Lertrit,
M.D., Ph.D. (Biochemistry)
Dean
Faculty of Graduate Studies
Mahidol University

.....
Assoc. Prof. Nittaya Sinsuksai,
Ph.D. (Nursing)
Program Director
Master of Nursing Science
Faculty of Nursing, Mahidol University

Thesis
entitled

RISK FACTORS FOR HYPERTENSIVE DISORDERS IN MYANMAR PREGNANT WOMEN

was submitted to the Faculty of Graduate Studies, Mahidol University
for the degree of Master of Nursing Science (Midwifery)
on
July 22, 2016

.....
Miss Ei Wah Phyu Thet
Candidate

.....
Asst. Prof. Ameporn Ratinthorn,
Ph.D. (Nursing)
Chair

.....
Asst. Prof. Piyanun Limruangrong,
Ph.D. (Nursing)
Member

.....
Assoc. Prof. Ratsiri Thato,
Ph.D. (Nursing)
Member

.....
Assoc. Prof. Nittaya Sinsuksai,
Ph.D. (Nursing)
Member

.....
Prof. Patcharee Lertrit,
M.D., Ph.D. (Biochemistry)
Dean
Faculty of Graduate Studies
Mahidol University

.....
Assoc. Prof. Yajai Sitthimongkol,
Ph.D. (Nursing)
Dean
Faculty of Nursing
Mahidol University

ACKNOWLEDGEMENTS

First and foremost, I would like to express my heartfelt thanks to Ministry of Health and Sports, Norwegian Government and Mahidol University for awarding me with the scholarship for Master of Nursing Science in Midwifery. I am also thankful to all authorized personnel and Daw Htay Htay Hlaing (Deputy Director-Nursing) from Department of Health Professional Resource Development and Management, Ministry of Health and Sports for their kind administrative support.

I am very grateful to Assoc. Prof. Dr. Yajai Sitthimongkol (Dean) and Assoc. Prof. Dr. Fongcum Tilokskulchai (Consultant), Faculty of Nursing, Mahidol University for their kind emotional and administrative support throughout my study.

In addition, the success of this thesis would not be achieved without support from Asst. Prof. Dr. Piyanun Limruangrong, my major advisor and Assoc. Prof. Dr. Nittaya Sinsuksai, my co-advisor. I deeply thank them for their kind guidance, great effort, enthusiastic motivation and valuable advices in my study. Also, I would like to express my special gratitude to Asst. Prof. Dr. Ameporn Ratinthorn, the chair and Assoc. Prof. Dr. Ratsiri Thato, the member of thesis committee for giving clear cut comments and suggestions in this research. Moreover, I would like to express my grateful appreciation to Rector Prof. Dr. Myat Thandar, the chair and other members of Ethical and Research Committee, University of Nursing, Yangon for their constructive comments. Furthermore, I would like to give my sincere thank to the Professors who validated the research instrument, and my Teachers who translated the research instrument and corrected the Grammar. I also would like to state my appreciation to the individual pregnant women who participated in my study.

Last, but not the least, I would like to express my gratitude to my beloved family, my teachers, my best friends and colleagues for their love, understanding and support which enhanced my strength and honor.

Ei Wah Phyu Thet

RISK FACTORS FOR HYPERTENSIVE DISORDERS IN MYANMAR PREGNANT WOMEN

EI WAH PHYU THET 5737124 NSMY/M

M.N.S (MIDWIFERY)

THESIS ADVISORY COMMITTEE: PIYANUN LIMRUANGRONG, Ph.D., NITTAYA SINSUKSAI, Ph.D.

ABSTRACT

Hypertensive disorders were responsible for 21% of all maternal death in Myanmar. This predictive study aimed to identify the significant risk factors that contribute to hypertensive disorders in Myanmar pregnant women depending on extreme age, nulliparity, body mass index $\geq$ 23kg/m^2, family history of hypertension and gestational diabetes mellitus. The sample was composed of 388 pregnant women with 36 to 42 weeks of gestation who visited the antenatal clinic of Central Women's Hospital and North Okkalapa General Hospital, Yangon. Data were collected using a questionnaire and were analyzed using binary logistic regression analysis.

The results show that these risk factors except age could explain 56.1% of the variance in the development of hypertensive disorders with 92.5% overall rate of correct classification. The risk of hypertensive disorders was 2.6 times higher in nulliparous women, 14.8 times higher in women who had BMI $\geq$ 23 kg/m^2, 3.3 times higher in women who had family history of hypertension, and 24.6 times higher in women diagnosed with gestational diabetes mellitus.

This study is useful for nursing and midwifery practice in screening and monitoring risks of hypertensive disorders in nulliparous women, women who had body mass index $\geq$ 23 kg/m^2, women with family history of hypertension, and women diagnosed with gestational diabetes mellitus. Pregnant women who are at risk of hypertensive disorders should be advised to adjust their lifestyle and to control their body weight with diet and physical activity.

KEY WORDS: HYPERTENSIVE DISORDERS / RISK FACTORS / PREGNANT WOMEN

113 pages

CONTENTS

CONTENTS (cont.)

LIST OF TABLES

LIST OF FIGURES

CHAPTER I
INTRODUCTION

Background and Significance of the Study

Hypertensive disorders of pregnancy (HDP) are common medical complications for pregnant women that contribute to global burden of diseases in both developed and developing countries (Vogel et al., 2014). Hypertensive disorders of pregnancy are classified into four categories as chronic hypertension, gestational hypertension, preeclampsia-eclampsia, and chronic hypertension with superimposed pre-eclampsia (American College of Obstetericians & Gynaecologists, 2013).

Globally, hypertensive disorders are complicated in 5% to 10% of pregnancies, and approximately 1% of pregnancies are complicated by chronic hypertension, 5% to 6 % are complicated by gestational hypertension, and 3% to 5% are complicated by preeclampsia (Carson, 2015; Singh, 2013). The incidence of hypertensive disorders in the obstetric admission of North Okkalapa General Hospital, Yangon was 6.6% (North Okkalapa General Hospital, 2013). Likewise, the incidence of hypertensive disorders in obstetric admission of Central Women's Hospital, Yangon was 7.7% and 7.4% for the year of 2014 and 2015 respectively (Central Women's Hospital, 2014; Central Women's Hospital, 2015).

Hypertensive disorders of pregnancy are associated with serious complications to mother and fetus in both acute and long-term (Abalos et al., 2014). Acute serious complications include eclampsia, hemolytic, elevated liver enzymes, low platelets (HELLP syndrome), disseminated intravascular coagulation (DIC), placental abruption, post-partum hemorrhage, pulmonary edema, acute renal failure, stroke, intrauterine growth restriction, and preterm birth (Ghulmiyyah & Sibai, 2012; Hutcheon, Lisonkova, & Joseph, 2011; Ye et al., 2014) . These complications can be life threatening to both mother and fetus, and may contribute to increased rate of cesarean delivery (Póvoa, Costa, Rodrigues, Patrício, & Cardoso, 2008; Ye et al., 2014). In addition, women who had hypertensive disorders of pregnancy are at

increased risk of recurrent complications in future pregnancy (Van Oostwaard et al., 2012). Moreover, they may develop cardiovascular diseases, cerebrovascular diseases, peripheral artery diseases, type 2 diabetes mellitus and renal diseases in later life, and there is an increased risk of shorter life expectancy from these conditions (Carson, 2015; Leffert, Clancy, Bateman, Bryant, & Kuklina, 2015; McCarthy & Kenny, 2015; Yang et al., 2015).Moreover, the offspring of women with hypertensive disorders are more vulnerable to hypertension, diabetes mellitus, neurological problems, and stroke in their future life (Davis et al., 2015; McCarthy & Kenny, 2015).

The risk of death in women with hypertensive disorders is four times higher than normal pregnancies (Abalos et al., 2014). World Health Organization's Review identified hypertensive disorders as the second leading cause of maternal mortality with 14% of all maternal deaths worldwide (Say et al., 2014). It was also responsible for 12.9 % of all maternal deaths in developed countries (Say et al., 2014), 14.5 % of all maternal deaths in Southeast Asia and 21% of all maternal deaths in Myanmar (Maternal and Reproductive Health Division, 2013).

In addition, hypertensive disorders are also the leading cause of increased perinatal morbidity and mortality including stillbirth, neonatal death, preterm birth, intrauterine growth restriction, small for gestational age, low Apgar score, seizure, neonatal encephalopathy, and neonatal intensive care admission (Abalos et al., 2014; Magee, Pels, Helewa, Rey, & Von Dadelszen, 2014; Vogel et al., 2014). Approximately, hypertensive disorders of pregnancy are responsible for 9% to 20% of all perinatal deaths (Abalos et al., 2014), 11% of still birth (Lawn et al. 2011), 8% to 10% of preterm births (National Collaborating Centre for Women's and Children's Health, 2010), and 25.3% of small for gestational age infants (McCowan et al., 2010).

Several factors have been found to be significantly associated with the risk of hypertensive disorders, including body mass index (BMI), maternal age, nulliparity, multiple pregnancies, preexisting diabetes mellitus, gestational diabetes mellitus, renal diseases, autoimmune disease, hypertensive disorders in previous pregnancy, family history of preeclampsia, family history of cardiovascular disease, and pregnancy interval of more than 10 years (Carson, 2015; Magee et al., 2015; Rich Edwards, Ness, & Roberts, 2015; Tranquilli et al., 2014; Ye et al., 2014). The risk of hypertensive disorders increased two to fourfold in woman with one or more of these risk factors

(Magee et al., 2015). Among these risk factors, extreme maternal age which younger than 20 years or older than 35 years is a significant risk factor for hypertensive disorders in pregnancy (Abalos et al., 2014; Lisonkova & Joseph, 2013; Liu et al., 2014; Ye et al., 2014). Previous studies have shown that the risk of hypertensive disorders was 2.6 times higher in those aged 13 to 16 years, 1.8 times higher in those aged 35 to 39 years and 2.4% higher in those aged over 40 years (P<.001) (Ye et al., 2014). In addition, nulliparity is also a significant risk factor for hypertensive disorders during pregnancy (Abalos et al., 2014; Lisonkova & Joseph, 2013; McCarthy & Kenny, 2015). It was reported that the risk of hypertensive disorders range from 1.4 to 5.5 times increase in primiparas compared with multiparous women (Trogstad, Magnus & Stoltenberg, 2011). Moreover, the risk of hypertensive disorders was 1.8 times higher in overweight women, and 3.1 times higher in obese women compared to women with normal pre-pregnancy BMI (Ye et al., 2014). In a large cohort study of Alves, Azevedo, Rodrigues, Santos, & Barros (2013) reported that obesity is responsible for 30.6% and 36.5% of hypertensive disorders in primipara and multipara respectively. Furthermore, the risk of hypertensive disorders is two times higher in women who had family history of hypertension (Lee et al., 2014). The risk of hypertensive disorders is four times higher in women whose mother or sister had a history of hypertension, and eight times higher in women whose father had a history of hypertension compared to women with no family history of hypertension (Bezerra et al., 2010; Mehta, Kumar, Chawla, Sachdeva, & Mahopatra, 2015). Additionally, gestational diabetes mellitus (GDM) was associated with 75% increased risk of hypertensive disorders in pregnancy. It was indicated that women with gestational diabetes mellitus were 2.45 times more likely to develop hypertension compared with women without GDM (Bentley-Lewis et al., 2014). Depending on the severity of diabetes mellitus, the occurrence of hypertensive disorders in women with gestational diabetes mellitus varies from 9 % to 60 % (Moussa & Sibai, 2015).

By reviewing the previous literature, it was found that age, parity, body mass index, family history of hypertension and gestational diabetes mellitus were not only the strong risk factors but also cause joint affect on hypertensive disorders during pregnancy (Alves et al., 2013; North et al., 2011; Ye et al., 2014). Although several studies focused on magnitude of the relationship between risk factors and the

occurrence of hypertensive disorders, and the impact of hypertensive disorders on adverse pregnancy outcomes was conducted in Myanmar, studies examined the joint impact of several risk factors, and the causality of these risk factors to hypertensive disorder are still limited (Esther Tin Htet, 1980; Khin Ohn Chit, 1983; Naw Mary Paw, 1995; Swe Swe Hlaing, 2001; Than Than Oo, 2001). Therefore, this study is developed to predict the risk of hypertensive disorders in Myanmar pregnant women by using the combination of significant risk factors in previous studies. In addition, it was found that universally applied BMI cut-off points have been used to classify overweight and obesity in most of the previous studies (Campbell et al., 2013; Deborah, Claudine, Matthew, Xiaozhang, & William, 2011; Hogan et al., 2012; Than Than Oo, 2001). Generally, there is a difference in association of BMI and body fat between Asian and non-Asian population. The magnitude of the association of body mass index and risk of hypertensive disorders was stronger in Asian population than non-Asian population with lower BMI cut-off point (World Health Organization, 2004; Savitz et al., 2014; Misra, 2015). Recent studies suggested the BMI cut-off point 23 kg/m^2 for overweight and obesity in Asian population which will be used as a reference in this study (Douketis, Paradis, Keller, & Martineau, 2005; Misra, 2015; World Health Organization, 2004).

Research Question

What are the risk factors as regards with extreme age, nulliparity, body mass index $\geq 23kg/m^2$, family history of hypertension and gestational diabetes mellitus that contribute to hypertensive disorders in Myanmar pregnant women?

Specific Aims

To identify the significant risk factors that contribute to hypertensive disorders in Myanmar pregnant women depending on extreme age, nulliparity, body mass index $\geq 23kg/m^2$, family history of hypertension and gestational diabetes mellitus.

Hypothesis

Extreme age, nulliparity, body mass index ≥ 23kg/m^2, family history of hypertension and gestational diabetes mellitus are the significant risk factors for the development of hypertensive disorders in Myanmar pregnant women.

Conceptual Framework

The conceptual framework of this study is based on pathophysiological concept of hypertensive disorders by Two-stage model (Roberts & Hubel, 2009). According to this model, hypertensive disorders of pregnancy occur in Two-stage processes (Roberts & Hubel, 2009). The first stage is reduced placenta perfusion which results from physiologic increase in uterine arterial resistant and defective invasion of the spiral arteries by cytotrophoblasts. The second stage is endothelial dysfunction with clinical manifestation of hypertensive disorders which results from interaction of maternal constitutional factors with reduced placenta perfusion. Maternal constitutional factors included genetic, behavioral, and environmental factors such as obesity, diet and physical activity. It was postulated that women with extensive constitutional factors could develop endothelial dysfunction with mildly reduced placental perfusion. In contrast, women with severely reduced placental perfusion could develop endothelial dysfunction with very little constitutional factors (Figure 1.1).

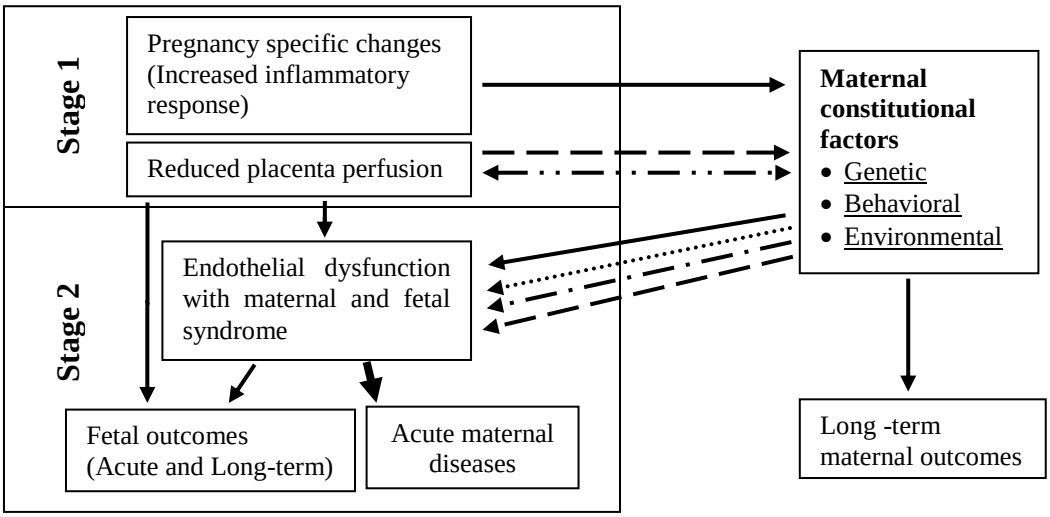

Fig1.1: Two-stage Model (Roberts & Hubel, 2009)

There are several maternal constitutional factors which strongly associated with the development of hypertensive disorders including extreme maternal age, nulliparity, high body mass index, family history of hypertension and gestational diabetes mellitus (Campbell, Lynch, Esterman, & McDermott, 2013; Liu et al., 2014; Lisonkova & Joseph, 2013; McCarthy & Kenny, 2015; Mehta et al., 2015).

According to the physiology of extreme age, it is considered as a genetic factor which is related to the development of hypertensive disorders during pregnancy. Puberty is a period of transient increased in insulin resistance secondary to dynamic metabolic, hormonal, and body composition changes (Amiel, Sherwin, Simonson, Lauritano, & Tamborlane, 1986). The physiologic metabolic changes of pregnancy may be exacerbated by puberty-related insulin resistance, leading to increase risk of developing hypertensive disorders (Liu, Ruan, Liu, & Zhang, 2015). Likewise, the physiologic changes of advancing age such as anthropometric changes, neuro-hormonal variations, deterioration of pancreatic β cell function and oxidative stress may contribute to increased insulin resistance, and subsequently increases risk of hypertensive disorders during pregnancy (Barzilai & Ferrucci, 2012; Barbieri, Rizzo, Manzella, & Paolisso, 2001; Møller, Gormsen, Fuglsang, & Gjedsted, 2003).

High body mass index is associated with both local adipose inflammation and systemic inflammation caused by metabolic cells response to excess nutrients and energy. The inflammatory response in women with high body mass index may contribute to increased insulin resistance, dyslipidemia, oxidative stress, and ultimately resulting hypertensive disorders of pregnancy (Jeyabalan, Hubel, & Roberts, 2015). The risk of obesity-induced hypertensive disorders could be prevented by lifestyle therapy such as weight control before pregnancy, exercise and healthy diet. Nearly 50% risk of developing hypertensive disorders during pregnancy could be reduced by lowering BMI from 29 to 27.4 kg/m^2 before pregnancy (Bodnar, Ness, Markovic, & Roberts, 2005). Therefore, high body mass index is considered as a behavioral factor for the development of hypertensive disorders during pregnancy.

By considering the role of placenta derived hormones to increased insulin resistance, gestational diabetes mellitus is considered as one of the maternal genetic constitutional factors. During pregnancy, the adipokines secreted from the placenta such as tumor necrosis factor alpha (TNFα), human placental lactogen, progesterone,

cortisol, growth hormone and prolactin contribute to increased insulin resistance (Beck & Daughaday, 1967; Handwerger & Freemark, 2000). Insulin resistance is normally compensated by considerable increased in insulin secretion, but the pregnant women do not have the capacity to increase the insulin secretion to such extent develop gestational diabetes mellitus (Kühl, 1991). Increased insulin resistance leads to activation of sympathetic nervous system, hyperinsulinemia, adipocytes dysfunction, alteration in angiogenic growth factors, thereby resulting endothelium dysfunction with manifestation of hypertensive disorders (Kaaja, 1998; Levine et al., 2004; Thadhani et al., 2014).

In addition, nulliparity is also considered as a genetic factor which contributes to hypertensive disorders during pregnancy. Maternal immune-maladaptation to fetal antigen is one of the key issue for the development of hypertensive disorders in nulliparous women (Redman, Sargent, & Taylor, 2015; Trogstad et al., 2011). During placentation, the uterine Natural Killer (NK) cells are activated to produce cytokines and angiogenic growth factors that, in turn, attract and instruct maternal immune system to release antigen-specific response by means of antibodies (Redman, Sargent, & Taylor, 2015). The systemic or vascular inflammation caused by maladaptive immune response produce antiangiogenic growth factors; soluble fms-like tyrosine kinase 1(sFlt-1). Increased concentration of sFlt-1 inactivates vascular endothelial growth factor (VEGF) and placental growth factor (PIGF) which lead to atherosis and thrombosis within placental circulation, and ultimately resulting in manifestation of hypertensive disorders (Levine et al., 2004; Thadhani et al., 2004).

Finally, family history of hypertension is also considered as a genetic factor for the development of hypertensive disorders. The offspring of hypertensive parents are more likely to develop hypertensive diseases in their future (Mongeau, 1987). In addition, the women who had genetic predisposition of chronic hypertension have greater risk for poor vascular compliance during pregnancy (Bernstein, Meyer, Osol, & Ward, 1998; Roes, Sieben, Raijmakers, Peters, & Steegers, 2005; Hale et al., 2010). Chronic hypertension and hypertensive disorders during pregnancy have similar heritable physiologic characteristics including reduce plasma volume, increased sympathetic tone, increased vascular resistance, and peripheral vasoconstriction (Hays, Cruikshank, & Dunn, 1985; McBride, Hale, Subramanian,

Badger, & Bernstein, 2014; Tihtonen, Koobi, & Uotila, 2006). During pregnancy, these predisposing vascular abnormalities precipitate the defective trophoblastic invasion and remodeling of spiral arteries. The abnormal implantation invokes inflammatory factors and oxidative stresses, contributing to reduced placental perfusion and endothelial dysfunction with manifestation of hypertensive disorders subsequently (Bernstein, Meyer, Osol, & Ward, 1998; Karumanchi, Rana, & Taylor, 2015). Based on these evidences of relationship between maternal constitution factors and hypertensive disorders, the conceptual framework of this study is developed as in Fig 1.2.

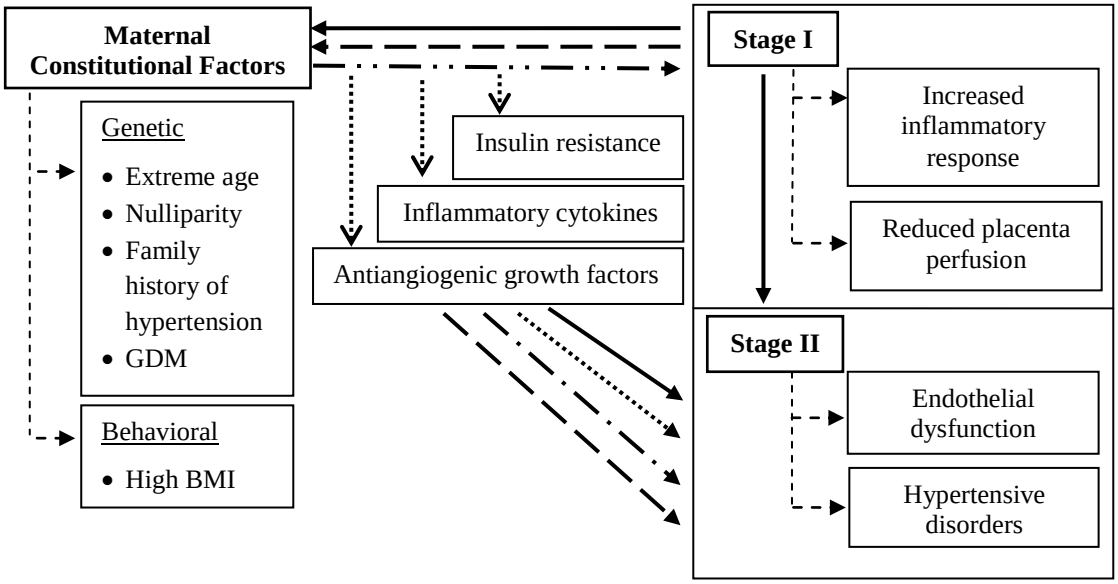

Fig 1.2: Conceptual Framework

Definitions of Terms

Hypertensive Disorder of Pregnancy refers to the abnormal condition associated with increased blood pressure ≥ 140/90 mmHg. The diagnosis of hypertensive disorders is made by the obstetrician according to ACOG criteria (ACOG, 2013; Cunningham et al., 2014). Thus, in this study, the diagnosis of hypertensive disorders is recorded from the women's antenatal record sheet.

Hypertensive disorders of pregnancy are classified into four categories including chronic hypertension, gestational hypertension, preeclampsia-eclampsia, and chronic hypertension with superimposed preeclampsia. In this study, women with chronic hypertension are not categorized as those diagnosed with hypertensive disorders unless they develop superimposed pre-eclampsia. The subjects are followed up by telephone six weeks after delivery to rule out the possibility of chronic hypertension.

Gestational hypertension is defined as increased blood pressure ≥ 140/90 mmHg for the first time after 20 weeks of gestation in the absence of proteinuria, which returns to normal within 12 weeks postpartum. This diagnosis is made retrospectively in the postpartum period.

Preeclampsia is defined as increased blood pressure ≥ 140/90 mmHg for the first time after 20 weeks of gestation with proteinuria (urinary excretion of protein ≥ 300mg in 24 hour urine collection, or ≥ 1+ on urine dipstick examination). In the absence of proteinuria, preeclampsia is diagnosed as gestational hypertension with thrombocytopenia, impaired liver function, the new development of renal insufficiency, pulmonary edema, or new-onset cerebral or visual disturbances. Eclampsia is neurologic involvement characterized by generalized tonic-clonic convulsions in women with preeclampsia after exclusion of any other causes such as epilepsy, cerebral infection, tumor or ruptured aneurysm.

Chronic hypertension with superimposed preeclampsia is defined as the new onset of either proteinuria or end organ dysfunction after 20 weeks of gestation in a woman with preexisting hypertension.

The pregnant women diagnosed with any of these three categories are coded as ‘Yes=1’ and others are coded as ‘No=0’.

Age refers to the number of years the pregnant women have lived. It is calculated by subtracting the birth date from the date of the study. If the period between the date of previous birthday and the date of data collection is exceeded more than six months, it was counted as one year. Age was recorded by self-administered questionnaire. The predictor variable of age is dichotomous variable (extreme age; < 20 years or ≥ 35 years = 1, 20-34 years = 0).

Parity refers to the number of giving birth by the women. It includes still birth, live birth, or preterm birth. Parity was recorded by self-administered questionnaire. The predictor variable of parity is dichotomous variable (nulliparity = 1, multiparity = 0).

Body Mass Index (BMI) refers to the measurement of women's body fat based on self-reported pre-pregnancy weight in kilograms divided by the square of the height in meters (kg/m^2). Pre-pregnancy weight was recorded by self-administered questionnaire. If pre-pregnant weight is not known, the BMIs were calculated from the height and weight measured at the booking visits during the first trimester. Women were categorized by BMI for Asian populations; underweight (BMI $\leq$ 18.49 kg/m^2), normal weight (BMI 18.50-22.99 kg/m^2), overweight (BMI 23.00-27.49 kg/m^2), and obese (BMI $\geq$ 27.5 kg/m^2) (World Health Organization, 2004). The predictor variable of BMI is dichotomous variable (BMI $\geq$23 kg/m^2 = 1, BMI <23 kg/m^2 = 0).

Family History of Hypertension refers to the first degree relatives of pregnant women who had suffered from chronic hypertension. Family history of hypertension was recorded by self-administered questionnaire. The predictor variable of family history of hypertension is dichotomous variable (Yes = 1, No = 0).

Gestational Diabetes Mellitus (GDM) refers to the glucose intolerance that occurs as the first time during pregnancy. In Myanmar, the cost effective method of selective screening strategy for risk factors or random blood glucose measurement is used as a preliminary test of glucose tolerance. The low risk pregnant women or women with normal random plasma glucose level were exempted from the glucose tolerance test. The diagnosis of gestational diabetes is made by the clinician according to WHO criteria (International Association of Diabetes and Pregnancy Study Groups, 2010; World Health Organization, 2013). Thus, in this study, the diagnosis of gestational diabetes mellitus was recorded from the women's antenatal record sheet. The predictor variable of gestational diabetes mellitus is dichotomous variable (Yes = 1, No = 0).

CHAPTER II
LITERATURE REVIEW

This study aims to determine the possible predictive factors of hypertensive disorders in Myanmar pregnant women which are extreme age, nulliparity, body mass index ≥ 23 kg/m^2, family history of hypertension and gestational diabetes mellitus. Therefore, literature is reviewed as regards with hypertensive disorders with the emphasis on definition and classification, incidence, pathogenesis, risk factors, complications, management, and nursing and midwifery implications.

Definition and Classifications of Hypertensive Disorders

American College of Obstetricians and Gynecologists (ACOG) classified hypertensive disorders into four categories; chronic hypertension, gestational hypertension, preeclampsia-eclampsia, and chronic hypertension with superimposed pre-eclampsia (ACOG, 2013; Cunningham et al., 2014). However, there is a difference between the pathophysiology of chronic hypertension and pregnancy induced hypertension. Therefore, gestational hypertension, preeclampsia-eclampsia, and chronic hypertension with superimposed preeclampsia are implied to hypertensive disorders, and chronic hypertension is excluded from hypertensive disorders in this study.

1. Gestational Hypertension

Gestational hypertension is defined as increased blood pressure ≥140/90 mmHg on two occasions at least 4 hours apart in the absence of proteinuria, edema or symptoms of preeclampsia. It occurs after 20 weeks of gestation in women without preexisting hypertension. This diagnosis is made retrospectively when the blood pressure returns to normal within 12 weeks postpartum (ACOG, 2013; Cunningham et al., 2014).

2. Preeclampsia-Eclampsia

Preeclampsia is defined as increased blood pressure ≥140/90 mmHg on two occasions at least 4 hours apart. It occurs after 20 weeks of gestation in women without preexisting hypertension. It is usually accompanied by proteinuria (≥ 300 mg protein in 24 hours urinary excretion, or a urine protein: creatinine ratio ≥0.3 or persistent 30 mg/dl protein or ≥ 1^{+} dipstick in random urine examination) (ACOG, 2013; Cunningham et al., 2014).

In the absence of proteinuria, preeclampsia is defined as the new onset of hypertension (increased blood pressure ≥140/90 mmHg) in association with thrombocytopenia (platelet count < 100 000/ μL), renal insufficiency (serum creatinine > 1.1 mg/dl or a doubling of baseline), impaired liver function (elevated serum transaminase; aspartate aminotransferase (AST), or alanine aminotransferase (ALT) twice than normal concentration), cerebral symptoms (headache, visual disturbances, convulsions), and pulmonary edema (ACOG, 2013; Cunningham et al., 2014).

Severe preeclampsia is defined as severe hypertension (systolic blood pressure ≥160 mmHg, and/or diastolic blood pressure ≥110 mmHg) in association with thrombocytopenia, renal insufficiency, impaired liver function, severe persistent epigastric or right upper quadrant pain, cerebral symptoms (headache, visual disturbances, convulsions), and pulmonary edema (ACOG, 2013; Cunningham et al., 2014).

Eclampsia is neurologic involvement characterized by generalized tonic–clonic convulsions in women with preeclampsia after exclusion of any other causes such as epilepsy, cerebral infection, tumor or ruptured aneurysm (ACOG, 2013).

Table 2.1 Normal Laboratory Value of Creatinine and Serum Transaminase in Pregnancy

Test	**Value**		
	First trimester	**Second trimester**	**Third trimester**
Creatinine	35-62 μmol/L	35-71 μmol/L	35-80 μmol/L
AST (SGOT)	3-23 U/L	3-33 U/L	4-32 U/L
ALT (SGPT)	3-30 U/L	2-33 U/L	2-25 U/L

(Abbassi-Ghanavati, Greer, & Cunningham, 2009)

3. Chronic hypertension with superimposed preeclampsia

Chronic hypertension with superimposed preeclampsia is defined as increased blood pressure ≥140/90 mmHg before pregnancy, or before 20 weeks of gestation in association with proteinuria, edema, or any other systemic features of pre-eclampsia. This diagnosis is made retrospectively when there is increase in blood pressure of more than 12 weeks postpartum (ACOG, 2013; Cunningham et al., 2014).

Incidence of Hypertensive Disorders

The World Health Organization's estimated prevalence of hypertensive disorders was 0.29% chronic hypertension, 2.16% pre-eclampsia, and 0.28% eclampsia for all delivery with wide variations across 29 countries in the different regions (Abalos et al, 2014). Hypertensive disorders of pregnancy occurred in 5.22% of Chinese, 6.4% of African-American, 7.5% of Brazilians, 7.5% of Australians and 6% of Portuguese women (Alves et al., 2013; Leung, 2015; Ye et al., 2014). The WHO collaborative study of incidence of hypertensive disorders in Myanmar showed that hypertensive disorders of pregnancy occurred in 7% of women aged 20-24 years and 10.2% of women aged 25-29 years with overall prevalence of 8.3% in all primigravida (Swe Swe Hlaing, 2001). In a study of Naw Mary Paw (1995), it was found that hypertensive disorders of pregnancy were responsible for 19.13% of preinatal mortality with 191.3 per 1000 births in North Okkalapa General Hospital. In 2013, the incidence of hypertensive disorders in obstetric admission of North Okkalapa General Hospital, Yangon was 6.6% (North Okkalapa General Hospital, 2013). Likewise, the incidence of hypertensive disorders in obstetric admission of Central Women's Hospital, Yangon was 7.7% and 7.42% for the year of 2014 and 2015 respectively (Central Women's Hospital, 2014; Central Women's Hospital, 2015). According to Nationwide Cause-specific Maternal Mortality Survey in 2004-2005, hypertensive disorders of pregnancy were responsible for 5.63% of all maternal deaths (Ministry of Health, 2008). Nowadays, hypertensive disorders of pregnancy stood at the third place among the leading cause of maternal death with 21% of all maternal deaths in Myanmar (Maternal and Reproductive Health Division, 2013).

Pathogenesis of Hypertensive Disorders

Although concise etiologies of hypertensive disorders are remained unclear, both reduced placenta perfusion and maternal constitutional factors are the fundamental cause of hypertensive disorders in Two-stage model (Roberts & Hubel, 2009). According to this model, hypertensive disorders occur in Two-stage processes. The first stage is reduced placenta perfusion which result from increase inflammatory response secondary to physiologic increased in uterine arterial resistance and defective invasion of the spiral arteries by cytotrophoblasts. The second stage is endothelial dysfunction with clinical manifestation of hypertensive disorders. Reduced placental perfusion leads to increase production of placental antiangiogenic protein such as soluble fms-like tyrosine kinase1 (sFlt-1) and soluble endoglin (sEng) into the maternal circulation. These proteins bind and inactivate placental angiogenic factors such as vascular endothelial growth factor (VEGF) and placental growth factor (PIGF) resulting the second stage of endothelial dysfunction with manifestation of hypertensive disorders. However, reduced placental perfusion is not the sufficient cause to develop hypertensive disorders during pregnancy. Maternal constitutional factors are necessary to serve as a mediator in the progression of stage one to stage two. Maternal constitutional factors included genetic, behavioral, and environmental factors such as obesity, diet and physical activity (Figure 2.1).

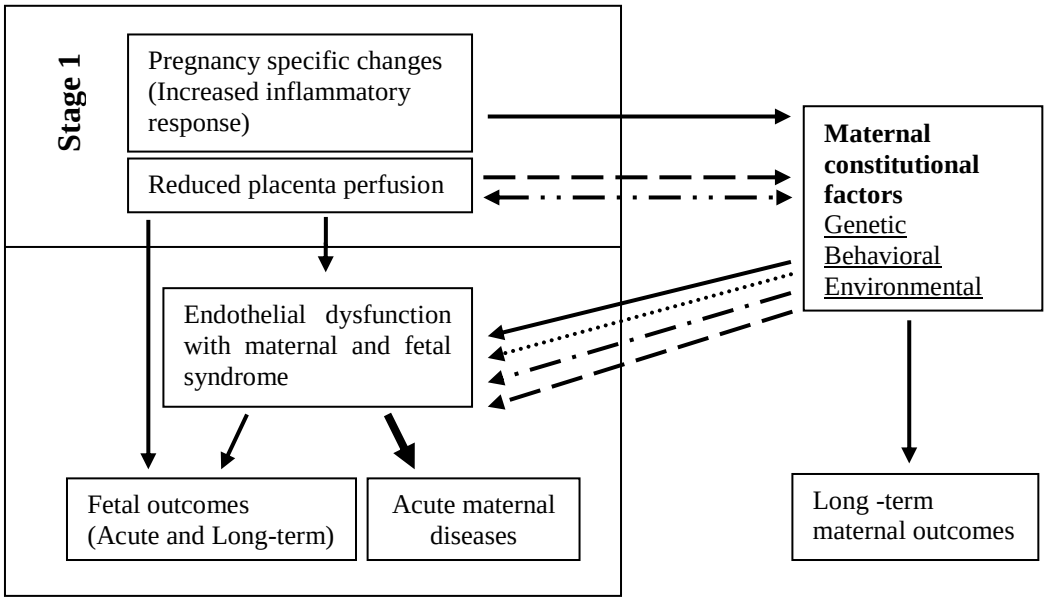

Fig 2.1: Two-stage Model (Roberts & Hubel, 2009)

There are several maternal constitutional factors which strongly associated with the development of hypertensive disorders including extreme maternal age, nulliparity, high body mass index, family history of hypertension and gestational diabetes mellitus (Campbell, Lynch, Esterman, & McDermott, 2013; Liu et al., 2014; Lisonkova & Joseph, 2013; McCarthy & Kenny, 2015; Mehta et al., 2015).

According to the physiology of extreme age, nulliparity, family history of hypertension and gestational diabetes mellitus, they are considered as the genetic factors which are related to the development of hypertensive disorders during pregnancy (Barzilai & Ferrucci, 2012; Kaaja, 1998; Liu et al., 2015; Mongeau, 1987; Redman, Sargent, & Taylor, 2015). Body mass index is considered as a behavioral factor which is related to the development of hypertensive disorders (Jeyabalan, Hubel, & Roberts, 2015).

Extreme age, high body mass index and gestational diabetes mellitus are associated with the risk of developing hypertensive disorders by means of increased insulin resistance. High body mass index leads to adverse metabolic effects on blood pressure, cholesterol, triglycerides and insulin resistance (World Health Organization, 2016). Increased cytokines and reduced adiponectin in obesity may predisposed to local tissue hypoxia and down regulation of angiogenic growth factors, and further lead to the development of hypertensive disorders (Callaway et al., 2009; Roberts et al., 2011). Advancing age is associated with increased insulin resistance due to age-related impairment of insulin-mediated glucose uptake (Fink, Kolterman, Griffin, & Olefsky, 1983). Likewise, increased secretion of growth hormone is associated with decreased insulin sensitivity; relative increased insulin secretion and increased the ratio of fat-glucose oxidation during puberty (Ball et al., 2006; Hannon, Janosky & Arslanian, 2006; Kelsey & Zeitler, 2016). According to Randle theory, increased fat oxidation competes with glucose oxidation, contributing to decreased glucose uptake and insulin resistance during puberty (Arslanian & Kalhan, 1994).

Increased insulin resistance may adversely affect on blood pressure regulation by adipocytes dysfunction, elevated free fatty acid, and hyperinsulinemia (Mastrogiannis, Spiliopoulos, Mulla, & Homko, 2009; Roberts et al., 2011). Increased insulin resistance causes increase in the secretion of proinflammatory cytokines, such as C reactive protein (CRP), interleukin-6 (IL6) tumour necrosis factor-α (TNF-α).

Cytokines stimulate the release of non-esterfied fatty acids (NEFA) from adipose tissue, which in turn worsens insulin resistance and hyperinsulinemia by release of glucose from muscle and liver. In addition, Cytokines also suppress the production and concentration of circulating adiponectin. Adiponectin is an important insulin sensitizer. So, as adiponectin is reduced, insulin resistance increases. Insulin resistance is in turn compensated by hyperinsulinemia leading to hypertension by vasoconstriction, by promoting renal tubular sodium re-absorption, and sodium retention (Callaway, O'Callaghan, & McIntyre, 2009; Roberts et al., 2011). Furthermore, cytokines mediated systemic or vascular inflammation stimulates the production of antiangiogenic protein such as soluble fms-like tyrosine kinase-1 (sFlt-1). These proteins inhabit the secretion of vascular endothelial growth factor (VEGF), and placental growth factor (PIGF) leading to endothelial dysfunction with manifestation of hypertensive disorder (Kaaja, 1998; Levine et al., 2004; Thadhani et al., 2004).

The high serum concentration of antiangiogenic protein; soluble fms-like tyrosine kinase 1 (sFlt-1) resulted from immune-mal-adaptation have the pivotal role in the development of hypertensive disorders in nulliparous women (Bdolah et al., 2014; Mijal et al., 2011; Faupel-Badger et al., 2011). Both maternal innate and adaptive immune system involve in the development of hypertensive disorders in nulliparous women. The natural killer (NK) cells of uterine endothelium are part innate immune system. The main effectors of adaptive immune system are T and B lymphocytes which activated in response to fetal Human Leukocytes Antigens (HLA). The function of adaptive immune system is depends on the signal of innate immune system (Redman, Sargent, & Taylor, 2015; Trogstad et al., 2011).

During implantation, the uterine endothelial cells (innate immune system) are activated to promote the placental angiogenesis by enhancing cytokines and angiogenic growth factors production. Consequently, increased secretion of inflammatory cytokines signifies the adaptive immune system to produce antigen-specific response by means of antibodies. The systemic or vascular inflammation caused by maternal immune response to trophoblastic invasion contributing to production of antiangiogenic growth factors; soluble fms-like tyrosine kinase 1 (sFlt-1). Increased concentration of soluble fms-like tyrosine kinase 1 (sFlt-1) inactivates

vascular endothelial growth factor (VEGF) and placental growth factor (PIGF) (Singh, 2013; Vest, & Cho, 2014). The vascular damage resulted from angiogenic imbalance lead to atherosis and thrombosis within placental circulation, ultimately resulting in manifestation of hypertensive disorders.

Family history of hypertension is significant risk factors for atherosclerosis cardiovascular diseases such as chronic hypertension, atherosclerosis and hypertensive disorders during pregnancy (Singh, Pathak, & Paul, 2015). Women who had genetic predisposition of chronic hypertension are at greater risk for poor vascular compliance during pregnancy (Bernstein, Meyer, Osol, & Ward, 1998; Hale et al., 2010). There is increased arterial stiffness in women with hypertensive disorders during pregnancy (Khalil, Jauniaux, & Harrington, 2009). Chronic hypertension, atherosclerosis and hypertensive disorders during pregnancy have certain similarities which are dyslipidemia, increased circulating levels of proinflammatory cytokines, such as IL-6 and TNF-α. Cytokines mediated oxidative stresses stimulates vascular smooth muscle cell proliferation, hypertrophy and collagen deposition, resulting in thickening of the vascular media, narrowing of vascular lumen and subsequently increased vascular resistance (Hays, Cruikshank, & Dunn, 1985; McBride, Hale, Subramanian, Badger, & Bernstein, 2014; Singh, Pathak, & Paul, 2015; Subramanian, Badger, & Bernstein, 2014; Tihtonen, Koobi, & Uotila, 2006). Therefore, women who had preexisting vascular abnormalities have prone to develop hypertensive disorders by disrupting placenta angiogenesis during pregnancy (Bernstein, Meyer, Osol, & Ward, 1998; Karumanchi, Rana, & Taylor, 2015; Singh, Pathak, & Paul, 2015).

Risk Factors of Hypertensive Disorders

Several maternal constitutional factors are associated with the development of hypertensive disorders during pregnancy including extreme age, nulliparity, high body mass index, family history of hypertension and gestational diabetes mellitus (Cunningham et al., 2014; Rich-Edwards, Ness, & Roberts, 2015). In addition, the incidence of hypertensive disorders is influenced by race, ethnicity and genetic predisposition (Myatt et al., 2013). Moreover, macro and micronutrients

imbalance could be related with hypertensive disorders of pregnancy (Mukhopadhyay et al., 2012). Other risk factors include family and personal history of gestational hypertensive disorders, multiple gestation, primipaternity, preexisting diabetes mellitus, antiphospholipid syndrome, smoking, physical activity, socioeconomic status, and even seasonal influences (Cunningham et al., 2014; Rich-Edwards, Ness, & Roberts, 2015).

1. Age

Hypertensive disorders of pregnancy are associated with extreme maternal age younger than 20 years and older than 35 years (Abalos et al., 2014; Lisonkova & Joseph, 2013; Liu et al.,2014; Ye et al., 2014). Young women are particularly vulnerable to developing preeclampsia whereas older women are at greater risk for chronic hypertension with superimposed preeclampsia (Cunningham et al., 2014). Increased insulin resistance in puberty, and increased prevalence of chronic hypertension and other co-morbid medical diseases due to glucose intolerance in women older than 35 years may explain the increased frequency of hypertensive disorders among women with those age (Carson, 2015; Gold et al., 2014; Savitz et al., 2014). Tebeu et al. (2011) found that early teenage status (13-16 years) was associated with an increased risk for hypertensive disorders in pregnancy (OR: 2.6; 95% CI: 1.5-4.7; P=0.0005), however, the percentage of women aged 35 to 44 years old was similar in case and control group. Therefore, it was concluded that women aged 35 to 44 years were not at significant risk for hypertensive disorders during pregnancy. In contrast, a prospective cohort study of 9,149 singleton pregnancies in UK, it was found that the risk of hypertensive disorder increases by 4% every year in women over the age of 32 years (Poon, Kametas, Chelemen, Leal, & Nicolaides, 2010). Moreover, Savitz et al. (2014) also suggested that advanced maternal age was strongly associated with chronic hypertension but not any forms of pregnancy-associated hypertension.

However, there is controversy about the relation between maternal age and hypertensive disorders due to the effect of confounding factors. For example, younger women were more likely to be nulliparous, less likely to receive adequate prenatal care and seek prenatal care lately because of their desire to conceal or not to recognize the pregnancy; not realizing that prenatal care is valuable or available; and not being able

to afford prenatal care (Aliyu, Luke, Kristensen, Alio, & Salihu, 2010). In an epidemiological study of effect of age on the incidence of hypertensive disorders stratified by race and parity, it was found that the incidence of hypertensive disorders was significantly lower in multiparous women than primiparous women in the age group < 20 years ($p<.0001$). But the incidence of hypertensive disorders increases in both primiparous and multiparous women aged over 40 years ($P\leq.0001$) (Gold et al., 2014).

2. Parity

It is well known that nulliparity is a significant risk factor for hypertensive disorders during pregnancy (Abalos et al., 2014; Lisonkova & Joseph, 2013; McCarthy & Kenny, 2015). More than half of the women diagnosed with hypertensive disorders were nulliparous (Kenny et al., 2014). High level of circulating antiangiogenic protein; soluble fms-like tyrosine kinase 1 (sFlt-1) is a route cause of hypertensive disorders in nulliparous women (Kenny et al., 2014; Karumanchi, Rana, & Taylor, 2015). In addition, a retrospective cohort study of 16,582 women with singleton pregnancy observed that nulliparous women have nearly 2 fold increases in the risk of developing hypertensive disorders than multiparous women (OR: 1.89, 95% CI: 1.69-2.12, $P < .001$) (Ehrenthal, Jurkovitz, Hoffman, Jiang, & Weintraub, 2011). It was congruent with the finding of prospective observational study of 2,230 white European women with a singleton pregnancy; hypertensive disorders of pregnancy occurred in 2.1% of primigravidas and 0.3% of multigravidas (Hogan et al., 2012).

Though as mentioned in maternal age, the impact of parity on the risk of hypertensive disorders is also complex and difficult to predict due to the effect of confounding factors. In a study of Gold et al. (2014), it was shown that the incidence of hypertensive disorders of pregnancy increased in primiparous women compared to multiparous women in the age group of 16 to 19 years ($p< .0001$). On the other hand, there is higher incidence of hypertensive disorders in multiparas women aged > 40 years compared with those aged < 20 years (Gold et al., 2014). Therefore, Favilli et al. (2012) suggested that age should be combined with other maternal characteristics including parity, body mass index, and obstetric history in calculating the risk for adverse pregnancy outcomes.

3. Body Mass Index (BMI)

Obesity or high body mass index is a strong predictor for hypertensive disorders during pregnancy (Campbell et al., 2013; Gaillard et al., 2011; Shin & Song, 2014). Compared with normal weight women, overweight or obese women were significantly increased risk of hypertensive disorders during pregnancy (OR: 1.9, 99% CI: 1.7-2.3; OR: 3.5, 99% CI: 2.9-4.2) (Scott-Pillai, Spence, Cardwell, Hunter, & Holmes, 2013). In addition, there is also a dose-dependent relationship between body mass index and the risk of hypertensive disorders during pregnancy. Ehrenthal, et al. (2011) conducted a retrospective cohort study of 16,582 women with singleton pregnancy to explore the association of pre-pregnancy BMI and hypertensive disorders during pregnancy, it was identified that hypertensive disorders were more likely to develop in women with increasing pre-pregnancy BMI with the odds ratio (OR) of 1.99 for BMI 25-29.9, 2.68 for BMI 30-34.9, 3.43 for BMI 35-39.9, and 4.26 for BMI ≥ 40 (P<.0001). In a previous case-control study of Than Than Oo (2001) described that among total 1194 pregnant women, 9% was obese (BMI ≥ 29kg/m^2), and 404 pregnant women with hypertensive disorders, 75.7% was obese (BMI ≥ 29kg/m^2).

Obesity has become a worldwide epidemic along with the rate was also increased among the pregnant women (Ono, Guthold, & Strong, 2010). In United Kingdom, maternal obesity increased double during 19 years from 7.6% to 15.6% (Heslehurst, Rankin, Wilkinson, & Summerbell, 2010). In United State, 58.5% of reproductive aged women (20-39 years) were classified as overweight or obese (BMI ≥25.0 kg/m^2) (Ogden, Carroll, Kit, & Flegal, 2014). In Myanmar, the Nation Stepwise surveillance survey reported that 23.07% of female population was overweight (BMI ≥25 kg/m^2) (World Health Organization, 2009). WHO classified BMI as underweight (BMI < 18.50 kg/ m^2), normal weight (BMI 18.50-24.99 kg/m^2), overweight (BMI 25.00-29.99 kg/m^2), obese class I (BMI 30.00-34.99 kg/m^2), obese class II (BMI 35-39.99 kg/m^2), and obese class III (BMI ≥ 40 kg/m^2) (World Health Organization, 2015). However, there is evidence of increasing prevalence of cardiovascular diseases such as hypertension in Asian population where the average BMI is lower than WHO BMI cut-off point of 25 kg/m^2, and evidence of difference in the association of BMI and the percentage of body fat composition between different populations of the world (Misra, 2015). Therefore, WHO further identified BMI classification for Asian

population as underweight (< 18.5kg/m2), acceptable risk or normal weight (18.5-22.99 kg/m2), increased risk or overweight (23.00-27.49 kg/m2), and high risk or obese (≥ 27.5 kg/m2) (World Health Organization, 2004). Additional trigger points for public health action were identified as increased risk (≥23 kg/m2), and high risk (≥ 27.5 kg/m2) (World Health Organization, 2004). To achieve optimum health, an adult should maintain the medium body mass index with the range of 21 to 23 kg/ m^2 (World Health Organization, 2016). Recently, definite guidelines have been published by the Indian Consensus Group to classify a BMI of ≥ 23kg/m^2 for overweight, ≥ 25kg/m^2 for obese Asian Indians (Misra, 2015). In addition, National Institute of Health and Care Excellence (NICE) of the United Kingdom and American Diabetes Association (ADA) recommended to use a BMI of ≥ 23kg/m^2 for screening diabetes in all Asian ethnic groups (Misra, 2015). Cnossen et al. (2007) examined the accuracy of body mass index in predicting hypertensive disorders in pregnancy. The result revealed that pre-pregnancy BMI or booking BMI ≥25 kg/m^2 could predict the risk of hypertensive disorders with 47% sensitivity and 73% specificity, and pre-pregnancy or booking BMI ≥ 30 kg/m^2 could predict the risk of hypertensive disorder with 19% sensitivity and 90% specificity. It was proved that the low BMI cutoff value could predict the risk of HDP with higher sensitivity.

4. Family History of Hypertension

Family history of hypertension is also a significant risk factor for the development of hypertensive disorders during pregnancy (Mehta et al., 2015; Morgan et al., 2015; Wright et al., 2015). Previous studies showed that the prevalence of hypertension among first degree relative is significantly higher in women with hypertensive disorders than those without hypertensive disorders (Roes, Sieben, Raijmakers, Peters, & Steegers, 2005). In a case control study of 152 complicated pregnancies with hypertension and 414 uncomplicated pregnancies in Cameroon, compared to women with no hypertensive disorders, the number of women with hypertensive diseases in pregnancy was significantly higher in women with history of paternal hypertension (17.8% vs. 6.5%), history of hypertension in siblings (8.6% vs. 2.9%), however, there was no significant difference between the two groups concerning with the history of maternal hypertension (Tebeu et al., 2011). This finding

is congruent with the cross-sectional study of 1104 pregnant women in India. In this study, a stepwise logistic regression analysis was performed to predict the prevalence of hypertension in pregnancy, using family history of hypertension as one of the predictors. It was found that the incidence of hypertensive disorders during pregnancy was significantly associated with history of paternal hypertension (OR: 8.38, 95%CI: 2.09-33.55, p=0.003). However, there was no association between hypertensive disorders and history of maternal hypertension (Mehta et al., 2015).

In contrast, a case-control study of 412 pregnant women in Brazil revealed that hypertensive disorder was significantly associated with family history of hypertension defined by mother's and sister's status of systemic hypertension. The study revealed that women whose mothers had a history of hypertension were at increased risk of developing hypertensive disorders during pregnancy (OR: 1.26, 95% CI: 1.13-1.88, p= .003). Moreover, women whose sister had a history of hypertension were at increased risk of developing hypertensive disorders during pregnancy (OR: 2.60, 95%CI: 1.61-4.21, p= .001). In addition, the risk of developing hypertensive disorders was significantly higher in women of whom both mother and sister had a history of hypertension compared to women with only mother or sister had a history of hypertension (OR: 3.65, 95% CI: 1.65-8.09, p= .001; OR: 1.41; 95% CI: 1.04-1.90, p=.025) (Bezerra et al., 2010).

5. Gestational Diabetes Mellitus

Gestational diabetes mellitus (GDM) is a significant risk factor for hypertensive disorders during pregnancy (Hossein-nezhad et al., 2011; Lisonkova & Joseph, 2013; Schneider et al., 2012; Vest & Cho, 2014). Hossein-nezhad et al. (2011) studied the incidence of hypertensive disorders among the pregnant women with gestational diabetes mellitus and healthy pregnant women. The researcher recruited 615 pregnant women, among them, 293 pregnant women are diagnosed to have gestational diabetes mellitus. It was found that women with gestational diabetes mellitus had a significant higher prevalence of hypertensive disorders during pregnancy compared to healthy pregnant women(OR: 3.18, 95%CI: 1.13-8.94; PR: 1.03; 95%CI: 1.004-1.06). In addition, gestational diabetes mellitus can predict the

risk of hypertensive disorders during pregnancy after adjustment of age, BMI, and parity (p=0.03).

Gestational diabetes mellitus (GDM) was defined as carbohydrate intolerance of degree which was first recognized during pregnancy regardless of whether the condition may have predated the pregnancy or persisted after pregnancy (American Diabete Association, 2015). Increased insulin resistance and elevated non-esterfied fatty acids (NEFA) with subsequently pancreatic β cell failure to sustain insulin secretion are the leading cause of hyperglycemia and impaired glucose tolerance in gestational diabetes mellitus (Nolan, 2011). In addition, increased insulin resistance, hyperinsulinemia, high body mass index, extreme age, and parity are common underlying causes of metabolic syndrome such as hypertension and diabetes mellitus (Hossein-nezhad et al., 2011). Therefore, it can be hypothesized that increased insulin resistance and hyperinsulinemia in women with gestational diabetes mellitus could precipitate the risk of hypertensive disorders during pregnancy (Feig et al., 2013; Hossein-nezhad et al., 2011; Moussa & Sibai, 2015).

A recent survey of prevalence of GDM showed a median incidence of GDM of about 5% in all world regions and 8% in Southeast Asia (Visser & de Valk, 2013). The prevalence of GDM in the United States is 1%-25% depending on demographic characteristics and diagnostic threshold (Moyer, 2014). There was significant relative risk reduction of preeclampsia and gestational hypertension by identifying and managing women with GDM (RR: 0.61, 95% CI 0.46-0.81; RR: 0.64, 95% CI 0.51-0.81) (World Health Organization, 2013). Pregnancies diagnosed with GDM are at a higher risk for complications including preeclampsia, shoulder dystocia secondary to fetal macrosomia, preterm birth, and cesarean section. In addition, affected women were 15% -60% increased risk for type 2 DM within 5 to 15 years of delivery (IADPSG, 2010; Werner et al., 2012).

The common risk factors associated with abnormal glucose tolerance test were elevated fasting or random plasma glucose (>7 mmol/l), prior macrosomia >9 lb, previous gestational diabetes mellitus, hypertension (≥140/90 mmHg or on therapy for hypertension), overweight women (BMI≥ 25 kg/m^2 or ≥ 23 kg/m^2 in Asian Americans), first-degree relative with diabetes (American Diabete Association, 2016; Caliskan, Kayikcioglu, Ozturk, Koc, & Haberal, 2004; Hanna & Peters, 2002;

Phaloprakarn, Tangjitgamol, & Manusirivithaya, 2009; van Leeuwen et al., 2010). The low –risk group was defined as age <25 years, member of an ethnic group with low prevalence of GDM, normal pre-pregnancy weight, normal weight at delivery, no first degree relatives with diabetes, no history of abnormal glucose metabolism, and no history of poor obstetric outcomes (Metzger et al., 2007; Moyer, 2014; Phaloprakarn et al., 2009).

The commonly used screening strategies for GDM were one-step approach of 75g OGTT and two-step approach of 100g OGTT. Other methods of screening included fasting plasma glucose, random plasma glucose and risk factors based screening (Metzger, Coustan, & Committee, 1998; Metzger et al., 2007; Moyer, 2014). The risk factor-based screening strategies caused a 50%-53% reduction in the number of OGTT applied (Caliskan et al., 2004; Hanna & Peters, 2002; Phaloprakarn et al., 2009; van Leeuwen et al., 2010). It was also found that universal screening reduced missing case of GDM approximately 40% (Hanna & Peters, 2002). However, U.S Preventive Services Task Force concluded that there was insufficient evidence to recommend universal screening for GDM (Moyer, 2014).

The ADA and many other medical associations around the world followed the NDDG's recommendation of 3-h 100g OGTT (WHO, 2013). In the United States, the two step approach of 50-g 1-h glucose challenge test followed by a 100g 3-h OGTT was the commonly used strategy (ADA, 2015; ACOG, 2013; Moyer, 2014; National Diabetes Data Group, 1979). In the two step approach, firstly the 50-g oral glucose challenge test was performed in women who were not previously diagnosed with overt diabetes at 24-28 weeks of gestation in non-fasting state. If the plasma glucose level was measured 1 hour after the load was ≥ 7.8 mmol/l (140mg/dl), the women were preceded to the second step of 100-g OGTT. The ACOG recommended a lower threshold 7.5 mmol/l (135 mg/dl) in populations with higher prevalence of GDM, and some experts also recommended 7.2 mmol/l (130mg/dl). The plasma glucose levels were measured fasting and 1h, 2h, 3h after the 100-g glucose load. The pregnant women were diagnosed as gestational diabetes if at least two of the following four plasma glucose levels were met: fasting ≥ 5.8 mmol/l (105mg/dl), 1h ≥ 10.6mmol/l (190mg/dl), 2h ≥ 9.2 mmol/l (165mg/dl), 3h ≥ 8.0 mmol/l (145mg/dl) (ADA, 2015).

On the other hand, WHO suggested the use of a one step approach of 75-g, 2-h OGTT for all pregnant women between 24 and 28 weeks gestation and earlier screening in the first trimester for those considered to be at high risk (IADPSG, 2010; WHO, 2013). In the United Kingdom, 80% of perinatal units utilized the method of screening by risk factors and the one step approach of 75-g OGTT (Crete & Anasti, 2013). Risk factors based screening caused a 50%-53% reduction in the number of OGTT and diagnosed 85% to 100% of women who had gestational diabetes mellitus (Caliskan et al., 2004). In addition, screening strategies based on maternal characteristics and history could detect about 75% of cases with false positive rate of 40% (Syngelaki et al., 2015). A national survey from the UK showed that 52% of the respondents used random glucose measurement as preliminary test of glucose tolerance (van Leeuwen et al., 2011). Therefore, these screening strategies appeared to be useful to identify a good proportion of women with GDM without the need for universal screening with an OGTT (Cuschieri, Craus, & Savona-Ventura, 2016; Meek, Murphy, & Simmons, 2016; Phaloprakarn et al., 2009; van Leeuwen et al., 2010).

In Myanmar, most of obstetricians and physician agreed on selective screening strategy by risk factors or random blood glucose measurement for cost-effectiveness. The pregnant women at low risk for GDM were exempted from the OGTT. The clinicians obtained random plasma glucose value at booking visit. If this value was ≥ 10 mmol/l (180 mg/dl) and the pregnant women not previously diagnosed with overt diabetes were proceeded a one-step 75-g, 2-h OGTT after overnight fasting (8-14 hours) by giving 75g anhydrous glucose in 250-300ml water. Plasma glucose levels were measured fasting, after 1 and 2 hours. Pregnant women were diagnosed to have gestational diabetes mellitus at anytime in pregnancy if one or more of the following criteria were met: fasting: 5.1-6.9 mmol/l (92-125mg/dl), 1-h ≥ 10.0 mmol/l (180mg/dl), 2-h: 8.5-11.0 mmol/l (153-199mg/dl). The pregnant women were diagnosed as overt DM if the random plasma glucose ≥ 11.1 mmol/l (200mg/dl) in the presence of diabetes symptoms, fasting plasma glucose ≥ 7 mmol/l (126 mg/dl), and 2-h plasma glucose ≥ 11.1 mmol/l (200mg/dl) (IADPSG, 2010; WHO, 2013).

6. Other Risk Factors

In addition to the risk factors used to predict the risk of hypertensive disorders in this study, there are other risk factors significantly related to the risk of developing hypertensive disorders which are diet and nutritional intake, multiple gestations, hypertensive disorders in previous pregnancy, socioeconomic status and racial differences (Cunningham et al., 2014; Mukhopadhyay et al., 2012; Myatt et al., 2013; Rich-Edwards, Ness, & Roberts, 2015).

6.1 Diet and Nutritional Intake

By considering the oxidative stress as a key mediator in the development of hypertensive disorders, it can be hypothesized that macro and micronutrients imbalance could be related with hypertensive disorders of pregnancy (Roberts & Hubel, 1999). This hypothesis is also supported by strong evidence of increased concentration of biomarkers of oxidative stress and decreased concentration of antioxidants in the serum and tissue of women with hypertensive disorders compared to those without disorders (Mukhopadhyay et al., 2012) . Previous research studies on diet and nutritional intake during pregnancy proved that energy, calcium and fiber intake were significantly associated with the risk of hypertensive disorders of pregnancy.

Energy Intake**:** It was found that excessive energy intake is associated with increased oxidative stress which could contribute to hypertensive disorders (Clausen et al., 2001; Van Gaal, Mertens, & De Block, 2006). In a study of Savica, Bellinghieri, & Kopple (2010), it was found that the mean calorie intakes of the women with hypertensive disorders are higher than normotensive women. Energy is not a nutrient but it is produced from dietary source of carbohydrates, proteins, fats and alcohol by oxidation. Excessive energy and gycemic intake stimulates more insulin production, and subsequently increases eicosanoid production (thromboxane A2, PGE2, PGF2a and leukotrienes) (Barger, 2010; Ludwig, 2002). Oxidative stress from an imbalance of prooxidant and proinflammatory eicosanoids cause inflammatory responses and endothelial dysfunction, and subsequently the development of hypertensive disorders (Barger, 2010; Cunningham, 2005; Mayret-Mesquiti, Perez-Mendez, & Rodriguez, 2007; Vadachkoria, Woelk, & Mahomed,

2006). The energy balance of an individual depends on his or her dietary energy intake and energy expenditure. The American Dietetic Association's recommendation of energy intake for an adult is 2,200–2,900 kcal/day (Abu-Saad & Fraser, 2010; Kaiser & Allen, 2008; Kolasa & Weismiller, 2014). Additional energy is also needed in pregnancy and lactation to fulfill the needs of the growing fetus, the placenta and expanding maternal tissues and additional maternal effort at rest and in physical activity, as well as the production of breast milk (Food and Agriculture Organization, 1985). The recommended Dietary Reference Intakes (DRIs) of additional energy intake during pregnancy is nil in the first trimester, 200 to 300 kcal/ day in the second trimester, and 200 to 500 kcal/ day in the third trimester (Kolasa & Weismiller, 2014). However, the requirement of energy intake during pregnancy also depends on pre-pregnancy body fat (Goldberg et al., 1993). UK Committee on Medical Aspects of Food Policy suggested that underweight pregnant women require more energy than normal weight women. However, the committee did not describe the possibility of lower requirement in overweight or obese women (Department of Health, 1991).

Calcium Intake: Low calcium intake causes to increase in blood pressure through stimulating the release of rennin and parathyroid hormones which lead to increased intracellular calcium concentration in vascular smooth muscle cells and causes vasoconstriction (Belizan & Villar, 1980; Imdad, Jabeen, & Bhutta, 2011; Villar, Repke, Belizan, & Pareja, 1987). Also, ACOG (2013) recommended that pregnant and lactating women should take calcium 1000 milligrams (mg) per day by serving of dairy products and calcium rich foods three to four times per day or daily calcium supplementation. World Health Organization (2011), also recommended daily supplementation with 1.5 mg to 2.0 g of calcium during pregnancy to prevent pre-eclampsia for the pregnant women who live in the area where dietary calcium intake is low, especially in those at high risk of developing pre-eclampsia. There is a lower rate of hypertensive disorders among pregnant women who had had a diet rich in calcium (Hamlin, 1962; Niromanesh, Laghaii, & Mosavi-Jarrahi, 2001). However, in a previous case control study of 172 women with preeclampsia, 251 women with gestational hypertension, and 505 controls subjects ,it was found that dietary calcium intake was not associated with the risk of preeclampsia, however it was inversely associated with the risk of gestational hypertension (Marcoux, Brisson, & Fabia,

1991). In a meta-analysis of Bucher et al. (1996) calcium supplementation is found to be highly effective in preventing preeclampsia (OR 0.38, CI 0.22-0.65). In contrast, Calcium for Preeclampsia Prevention Trial indicated that there is no reduction of preeclampsia risk in healthy nulliparous women due to calcium supplementation (RR 0.94, CI 0.76 - 1.16) (Levine et al., 1997). Therefore, DerSimonian and Levine (1999) tried to resolve discrepancies between these two studies by classifying in terms of high risk, and low risk populations. The result showed that calcium supplementation does not prevent preeclampsia in healthy nulliparous women, but the beneficial effect of calcium supplementation was found in high risk population groups. A previous review of Imdad et al. (2011) also showed that calculation supplementation during pregnancy is significantly associated with reduction of hypertensive disorders in developing countries where the baseline calcium intake was low. In addition, in a review of Trumbo and Ellwood (2007) ,it was also evidenced that the beneficial effect of calcium supplementation could only be shown in populations whose baseline calcium is inadequate. In recent Cochrane systematic review of 13 randomized controlled trials, it was found that there was significant reduction of the risk of preeclampsia in the women who took calcium supplementation at least 1000 mg per day during pregnancy (RR 0.45, CI 0.31 to 0.65). The effect was greatest for the women with low baseline dietary calcium intake less than 900 mg per day (RR 0.36, CI 0.31 to 0.65), and for the women with high risk of pre-eclampsia (RR 0.22, CI 0.12 to 0.42) (Hofmeyr, Lawrie, Atallah, Duley, & Torloni, 2014). However, in the WHO trial of calcium supplementation in women with low calcium intake, it was revealed that there was no significant reduction in the incidence of preeclampsia but the frequency of serious complications was significantly reduced about 30% (Roberts & Bodnar, 2007; Villar et al., 2006).

Fiber Intake: Since insulin resistance and hyperlipidemia has been suggested as a major underlying pathogenic mechanism for the development of hypertension (Callaway et al., 2009), it can be hypothesized that dietary fiber has beneficial effect on the development of hypertensive disorders. This hypothesis has been proved by many previous research studies that dietary fiber has beneficial effects on plasma lipid and lipoprotein profiles, postprandial glucose metabolism, insulin sensitivity, and blood pressure (Biggs, 2008; Qiu, Coughlin, Frederick, Sorensen, &

Williams, 2008; Wallis & Saftlas, 2008; Whelton et al., 2005). Dietary Fiber is defined as non-digestible carbohydrates and lignin that are intrinsic and intact in plants. Functional Fiber is defined as isolated, non-digestible carbohydrates that have been shown to have beneficial physiological effects in humans. Total Fiber is the sum of Dietary Fiber and Functional Fiber. The Dietary Reference Intakes (DRIs) of fiber for pregnant women aged 19 to 50 years is 28 g/ day (Institute of Medicine, 2005). The association between dietary fiber and hypertensive disorders of pregnancy has been studied by many observational, case control, and prospective cohort studies. Most of the studies proved that increase risk of preeclampsia with decrease intake of dietary fiber, and fiber intake was inversely associated with the risk of preeclampsia (Ascherio et al., 1996; Brantsæter et al., 2009; Frederick et al., 2005; Qiu et al., 2008; Sacks & Kass, 1988; Wallis & Saftlas, 2008). A large prospect case control study of Biggs (2008) showed that the highest quartile of fiber consumption (≥21g/day) were 67% less likely to develop preeclampsia than were women with the lowest quartile (<11.9 g/day). On the other hand, Skajaa, Dorup, and Sandstrom (1991) also found that there was no difference in mean daily fiber intake during the third trimester between preeclampsia case and control groups.

6.2 Multiple Gestations

Multiple gestations are also a well known risk factor for hypertensive disorders during pregnancy (Cunningham et al., 2014). In an Australian study of 214 women with twin pregnancies compared to 3,942 women with singletons pregnancy, it was found that the incidence of gestational hypertension was 35% in twin pregnancies and 60% in singleton pregnancies. Also, the incidence of preeclampsia is 65% in twin pregnancies and 40% in singleton pregnancies. In addition, it has been shown that the risk of progression from gestational hypertension to preeclampsia for twins was twice of singleton pregnancies ($p<.001$) (Foo, Mangos, & Brown, 2013).

6.3 Hypertensive Disorders in Previous Pregnancy

Women with preeclampsia in the first pregnancy have 18% risk of recurrent preeclampsia in the second pregnancy (Carson, 2015), and women with gestational hypertension in the first pregnancy have 16% risk of recurrent gestational hypertension in the future pregnancy (National Institute for Health and Clinical Excellence, 2014). Conversely, the incidence of hypertensive disorders in women without hypertensive disorders in the first pregnancy is lower than women with preeclampsia during the first pregnancy, with the rate of 1.8% and 3% respectively (Cunningham et al., 2014). A retrospective cohort study of van Oostwaard et al. (2012) provided that chronic hypertension and maternal age were the strongest predictors for recurrence of hypertensive disorders during pregnancy (OR 7.9, 95% CI 2.6-24; OR 1.1, 95% CI 1.02-1.2). Moreover, it was found that women with hypertensive disorders in previous pregnancy were 50% increased risk of developing hypertensive disorders in subsequent pregnancy ($P<.05$).

6.4 Socioeconomic Status

Hypertensive disorders of pregnancy were also associated with poor socioeconomic condition of pregnant women (Abalos et al., 2014). It may be due to inadequate health related knowledge and poor utilization of preventive-curative health care services in women with lower socioeconomic conditions. Jwa et al. (2013) found that there is higher level of blood pressure during pregnancy in women with low educational level compared to women with higher educational level (OR 1.24, 95% CI 0.44-3.44, $p<.05$). In addition, a case-control study of Tebeu et al. (2011) also revealed that the risk of having hypertensive disorders of pregnancy is greater in women with no school education (OR: 1.6; 95% CI: 1.0-2.3; P=0.0117), and in women with no occupation/housewives (OR: 2.8; 95% CI: 1.1-6.9; P=0.0167).

6.5 Racial Differences

Regarding racial differences in the risk of developing hypertensive disorders during pregnancy, a descriptive epidemiology study of 2.3 million births over the period 1995-2004 in New York state, it was found that risk of hypertensive disorders during pregnancy were strongly associated with pre-pregnancy

weight of Asian population and weakly associated with black population (Savitz et al., 2014). Likewise, Gong, Savitz, Stein, & Engel (2012) studied the association between racial differences and the occurrence of hypertensive disorders in 902,460 singleton births in New York City. There was increased risk of preeclampsia in foreign-born South-East Asian and Pacific Islanders women compared to women born in US (OR:1.8, 95%CI 1.0-3.1). In addition, it was found that there was a slightly decreased risk for hypertensive disorders in East Asian women (OR: 0.8, 95% CI: 0.7-0.8), similar risk for North African women (OR: 1.1, 95%CI: 0.9-1.3), and highest risk for Mexican women (OR: 2.9, 95%CI: 2.7-3.1) compared to non-Hispanic White women.

Complications of Hypertensive Disorders

Women with severe preeclampsia have a 70% higher risk of placental abruption, and also increased risk of serious complications such as acute renal failure, disseminated intravascular coagulation, HELLP syndrome, liver failure, eclampsia, stroke and pulmonary edema (Vogel et al., 2014). The risk of death was nearly four times higher for women with hypertensive disorders compared to women without hypertensive disorders during pregnancy (Abalos et al., 2014). Approximately, hypertensive disorders of pregnancy are responsible for 9% to 20% of all perinatal deaths (Abalos et al., 2014), 11% of still birth (Lawn et al., 2011), 8% to 10% of preterm births (National Collaborating Centre for Women's and Children's Health, 2010), and 25.3% of small for gestational age infants (McCowan et al., 2010).

The most common fetal and neonatal complications include severe intrauterine growth restriction and premature birth (Vintzileos & Ananth, 2014). Other complications include oligohydramios, hypoxia-acidosis, neurologic injury, and intrauterine fetal death. The risk of neonatal intensive care unit admission also increases due to small for gestational age, low Apgar scores, febrile seizures, encephalopathy, and metabolic disorders. In addition, offspring of pregnancies complicated by preeclampsia have higher levels of systolic and diastolic blood pressure in childhood and adolescence than the offspring of uncomplicated pregnancies (Abalos et al., 2014; Magee et al., 2014; Vogal et al., 2014).

Hypertensive disorders of pregnancy can be life threatening condition to both mother and fetus with various organ system involvements, including cardiovascular system, circulatory system, central nervous system, respiratory system, hepatic system, and renal system (Cunningham et al., 2014; Magee et al., 2014). These complications are as follows.

1. Cardiovascular System

Vasospasm and endothelial dysfunction with extravasation of intravascular fluid in women with hypertensive disorders lead to increased cardiac load, and ultimately resulting in symptoms of cardiomyopathy, left ventricular failure, and pulmonary edema (Cunningham et al., 2014; Magee et al., 2014).

2. Circulatory System

Increase in peripheral vascular resistance, and decrease in the level of some plasma clotting factors in women with hypertensive disorders cause several hematological abnormalities, including thrombocytopenia, low platelets count, low fibrinogen levels, prolonged prothrombin time, microangiopathic hemolysis, disseminated intravascular coagulation, and occluded blood flows to kidneys, liver, brain, and placenta. In addition, reduced uterine blood flow secondary to vasoconstriction in women with hypertensive disorders could lead to placental abruption, intrauterine growth restriction, and oligohydramios (Cunningham et al., 2014; Magee et al., 2014).

3. Central Nervous System

Cerebral vasospasm, hemorrhage, ischemia, and edema of cerebral hemispheres lead to the neurological manifestations of hypertensive disorders in women with hypertensive disorders. The neurological complications of hypertensive disorders included persistent headache, visual disturbance, seizure, stroke, clonus hyperreflexivity, and hemiplegia (Cunningham et al., 2014; Magee et al., 2014).

4. Respiratory System

Increased capillary permeablility in women with hypertensive disorders also causes respiratory complications, including dyspnea, chest pain, cyanosis, acute respiratory distress, and pulmonary edema (Cunningham et al., 2014; Magee et al., 2014).

5. Hepatic System

Vasospasm and increased inflammatory factors could lead to hepatic complications in hypertensive disorders. The symptoms of hepatic dysfunction included elevated liver enzymes (aspartate aminotransferase/AST and alanine aminotransferase/ALT), right upper quadrant or midepigastric pain and tenderness, hemorrhagic infarction, subcapsular hematoma, and liver rupture. Hepatocellular necrosis combined with hemolysis and thrombocytopenia were collectively known as HELLP syndrome, and it is the most serious life threatening complications of hypertensive disorders (Cunningham et al., 2014; Magee et al., 2014).

6. Renal System

Damage to the endothelial cells of the glomerular capillaries secondary to reduced renal perfusion and glomerular filtration cause proteinuria, oliguria, reduced creatinine clearance, increased serum creatinine, increased uric acid levels and acute tubular necrosis in women with hypertensive disorders (Cunningham et al., 2014; Magee et al., 2014).

Management of Hypertensive Disorders

The management of hypertensive disorders is based on the severity of disease condition, gestational age and presence of preeclampsia. There are three basic objectives for management of any hypertensive disorders; termination of pregnancy with the least possible trauma to mother and fetus; birth of the infant who subsequently thrives; and complete restoration of health to the mother (Alexander & Cunningham, 2015; Cunningham et al., 2014).

Outpatient management with more frequent antenatal visit is recommended for women with suspected pre-eclampsia with the goal of early identification of worsening preeclampsia and development of a management plan for timely delivery (Alexander & Cunningham, 2015; Cunningham et al., 2014). In women with preeclampsia or mild to moderate stable hypertension, conservative management can be continued in hospital or at home until labor commences spontaneously or achievement of fetal lung maturity. Conservative management includes;

1. Restricted activity
2. Close observation of maternal blood pressure and urine protein
3. Weekly check for platelet count and liver enzymes
4. Evaluation of fetal status with ultrasonography at the time of diagnosis and every 3 weeks, and non-stress testing
5. The patient should be instructed to remain alert for symptoms of preeclampsia (i.e., headache, blurred vision, epigastric or abdominal pain, nausea or vomiting, contractions, and vaginal bleeding) and count the fetal kick.

Indication of delivery included,

1. Gestational age ≥ 37 weeks with ripe cervix
2. Onset of labor or rupture of membranes at gestational age ≥ 34 weeks
3. Onset of persistent headaches or visual symptoms
4. Epigastric or right upper quadrant pain
5. Abdominal tenderness or vaginal bleeding
6. Thrombocytopenia
7. Severe oligohydramios
8. Severe intrauterine growth restriction, and
9. Abnormal fetal heart rate

Hospital maternal and fetal surveillance is considered initially for women with persistent or worsening hypertension and severe preeclampsia. In severe preeclampsia, the first steps in management are administering magnesium sulphate to prevent convulsions and antihypertensive drugs to control extreme levels of hypertension (Alexander & Cunningham, 2015; Cunningham et al., 2014). Prompt delivery with induction of labor or cesarean section is recommended for pregnant

women with severe preeclampsia before 34 weeks gestation when the following symptoms occur; uncontrolled severe hypertension, eclampsia, pulmonary edema, disseminated intravascular coagulation, placental abruption, severe oligohydramios, rupture membrane, and nonreassuring fetal test (Alexander & Cunningham, 2015; Cunningham et al., 2014).

Medications

Corticosteroids are used in women with gestational age between 24 weeks and 34 weeks to increase fetal lungs maturity, and to reduce neonatal mortality and morbidity (ACOG, 2013; Cunningham et al., 2014). Anticonvulsant and antihyper - tensive are used in women with severe hypertensive disorders to prevent convulsions, intracranial hemorrhage, and serious damage to other vital organs, and to deliver a healthy newborn. Most commonly used antihypertensive medications are methyldolpa, nifedipine, labetalol, and hydralazine (Danso & Opare-Addo, 2010). Labetalol should be avoided in women with asthma or heart failure. In addition, Labetalol can cause fetal bradycardia and treatment induced adverse fetal growth. The frequency of growth restricted infants was double in women who have been treated with labetalol compared to women without being treated with labetelol (Cunningham et al., 2014). International Society for the Study of Hypertension in Pregnancy (ISSHP) recommended that antihypertensive therapy does not prevent complications of hypertensive disorders (RR 0.99, 95% CI 0.84-1.18). However, it reduces half of the risk of severe hypertension (RR 0.52; 95% CI 0.41-0.64) (Cunningham et al., 2014; Magee et al., 2014).

Magnesium sulfate is the most commonly used anticonvulsant for hypertensive disorders during pregnancy. A Cochrane review also provided that magnesium sulfate can reduce half the risk of eclampsia (Duley, Matar, Almerie, & Hall, 2010). Magnesium sulfate is contraindicated in women with pulmonary edema or congestive heart failure, renal failure or poor urinary output, and myasthenia gravis. Women with hypertensive disorders are at increased risk of convulsion during labor and first 12 to 24 hours postpartum. Therefore, magnesium sulfate should be started at least 2 hours before delivery until 12 hours postpartum. The continuous intravenous

infusion or intermittent intramuscular injections of magnesium sulfate is recommended for women with severe preeclampsia and eclampsia (Cunningham et al., 2014).

Continuous Intravenous Infusion

The pregnant women are administered a loading dose of 4-6 g magnesium sulfate diluted in 100 ml of 5% Dextrose or Lactate Ringer's intravenous solution over 15-20 minutes, followed by a maintenance dose of 2 g per hour in 100 ml intravenous solution. Magnesium sulfate should be given by a standard infusion pump because excessive dose of magnesium sulfate can lead to toxicity. Magnesium sulfate must be discontinued immediately if the women develop respiratory difficulties, shallow or absent respiratory effort, muscle weakness, double vision, and inappropriate speech. The women should be administered 1 g calcium gluconate intravenously over 5 to 10 minutes, and incubated or ventilated artificially.

Intermittent Intramuscular Injections

The pregnant women are administered 4 g of magnesium sulfate ($MgSo_4 7H_2O$ USP) as a 20% solution intravenously at a rate of 1g/min, and followed by deep injection of total 10 g $MgSo_4$ as a 50% solution intramuscularly with a separate dose of 5 g in each buttock. To minimize discomfort, 1ml of 2% lidocaine can be used. If convulsions persist after 15 minutes, the pregnant women are administered a booster dose of 2 to 4 g $MgSo_4$ (20%) solution intravenously at a rate of 1g/min. Every 4 hours thereafter, the pregnant women are administered 5g $MgSo_4$ (50%) solution intramuscularly, and closely monitored for the signs of magnesium sulfate toxicity. The treatment is discontinued at 24 hours after delivery.

Nursing and Midwifery Implications

The nurses-midwives are responsible for checking the blood pressure of pregnant women diagnosed with hypertensive disorders using correct technique, appropriate cuff size and properly functioned equipment on each prenatal visit. Before the procedure, the nurses-midwives should check the electronic or manual blood pressure monitors to ensure the measurements begin from a starting point of zero. The

choice of cuff size is based on the arm circumference of women (12×23 for normal weight, 15×33 cm for overweight). The nurses-midwives must instruct the clients to avoid the caffeine in the preceding hour. After five minutes rest, the nurses-midwives must measure the blood pressure using the following correct technique; sit in upright position without leg crossing, support the arm at heart level, encircle the bladder cuff at 80% of the arm circumference with the lower edge is 3 cm above the elbow crease, lower the mercury column at a rate of 2 to 3 mmHg/second, take the first and last audible sounds as systolic and diastolic blood pressure, either the client or the observer don't talk during the procedure (Register Nurse Association of Ontario, 2005).

In addition, the nurses-midwives are responsible to help the women diagnosed with hypertensive disorders in examining their lifestyles and recognizing potential area for changes such diet, weight and physical activity. The nurses-midwives should assess the client's current eating habits using a food diary and the body mass index should be measured using appropriate BMI cut-off points. Moreover, pre-conception weight reduction program should be considered for the women with high body mass index. The nurses-midwives should provide the clients the appropriate education and intervention programs for life style modification in collaboration with other members of the health care team. Before providing appropriate education and intervention programs, the nurses-midwives should assess the client's level of knowledge. Furthermore, the nurses-midwives should advocate the clients who are receiving antihypertensive treatment in clarifying the information about the medications regimens such as doses, effects and side-effects which will help in promoting the client's compliance to therapeutic regimens (Register Nurse Association of Ontario, 2005).

Lastly, the nurses-midwives play an important role in documenting the information of pregnant women who diagnosed with hypertensive disorders and sharing information regarding hypertensive management between these pregnant women and other members of the health care team. These documents will support the health care team in continuing and ongoing monitoring the progress of pregnant women who diagnosed with hypertensive disorders toward the treatment goals (Register Nurse Association of Ontario, 2005).

Conclusion

Hypertensive disorders are common medical complications during pregnancy, and it can be categorized into four categories including chronic hypertension, gestation hypertension, preeclampsia-eclampsia, and chronic hypertension with superimposed pre-eclampsia. Abnormal placentation along with increased insulin resistance, oxidative stress, and endothelium dysfunction are the underlying causes of hypertensive disorders during pregnancy. However, placenta is not the sufficient cause for the development of hypertensive disorders, but also maternal constitutional factors (genetic, behavior, and environmental) are necessary to interact with reduced placental perfusion for the development of hypertensive disorders during pregnancy.

From reviewing literature, it was found that several maternal risk factors are significantly associated with the development of hypertensive disorders during pregnancy. However, most of the studies were focused on the magnitude of the relationship between risk factors and the occurrence of hypertensive disorders, and only few studies examined the predictive value of these risk factors. By considering the role of maternal risk factors in the development of hypertensive disorders, it can be hypothesized that the risk of developing hypertensive disorders could be reduced to certain extent by modification of life styles such as eating well balanced diet and maintaining appropriate body weight.

CHAPTER III
MATERIALS AND METHODS

This chapter includes the research materials and methods that are used in this study. These are research design, research setting, population and sample, instrumentation, protection of human subjects, procedures for data collection, and data analysis.

Research Design

This study was a predictive study design aimed at identifying the significant risk factors for hypertensive disorders in Myanmar pregnant women.

Research Setting

This study was conducted at antenatal clinic of two tertiary teaching hospital; Central Women's Hospital, and North Okkalapa General Hospital in Yangon. These two hospitals used the same standard screening and diagnosis criteria for hypertensive disorders and gestational diabetes mellitus. Hypertensive disorders of pregnancy were diagnosed by the obstetrician when the systolic and diastolic blood pressure was ≥ 140/90 mmHg according to ACOG's criteria. In addition, these two settings had the similar routine care for all pregnant women. The number of pregnant women who visited antenatal clinic of Central women's hospital and North Okkalapa General Hospital in the year 2015 was 12992 and 6356 pregnant women respectively.

Population and Sample

The population was comprised of pregnant women who visited antenatal clinic of Central Women's Hospital and North Okkalapa General Hospital in Yangon, Myanmar.

Sample

The sample was selected from the population of pregnant women by using convenient sampling method. The pregnant women who met the inclusion criteria were eligible to be sample as followed.

Inclusion criteria

1) Singleton pregnancy
2) Gestational age between 36 weeks and 42 weeks
3) Age ≥18 years
4) Burma language literacy, and able to read and write Burma language
5) Well-oriented and able to communicate

Sample Size

The sample size was calculated by using General power analysis (G* Power 3.1) with power (1-β error probability) of 0.8, an alpha probability of .05 (Faul, Erdfelder, Buchner, & Lang, 2009). A previous retrospective cohort study of Ehrenthal et al. (2011) explored the association of maternal demographic characteristics and medical risk factors with pregnancy induced hypertension by using logistic regression. Therefore, the effective size (Pr: H_0 =0.62, Pr: H_1=0.68, OR=1.30) was calculated based on the odds of pre-pregnancy BMI and parity in this study with the formula of OR/1 + OR. Based on the calculation, the total sample size of 388 pregnant women was needed to predict the risk of hypertensive disorders in Myanmar pregnant women. The samples were selected using convenient sampling method as follows: 120 pregnant women from Central Women's Hospital and 268 pregnant women from North Okkalapa General Hospital who met the inclusion criteria.

Instrumentation

The personal data questionnaire was developed by the researcher in English language. It was divided into two parts. The first part was self-administered questionnaire. It was used to collect information including socio-demographic characteristics such as age, race, education, occupation and family income, history of previous pregnancy, medical history, and family history. The second part of questionnaire was used to collect information from the women's antenatal record sheet by the researcher and research assistant, including gestational age at the time of data collection, pre-pregnancy body weight, height, body mass index, and pregnancy complications. The research instrument was validated by the three experts from Obstetric and Gynaecological Department, Faculty of Nursing, Mahidol University (Appendix D). After getting validation, the research instrument was revised by the researcher as an expert recommended. After revised the research instrument, it was translated from the English version into Myanmar Language by Mrs. Lwe Say Paw Hla, Lecturer, Adult Health Nursing Department, University of Nursing, Yangon. And then, both versions of questionnaires was review and revised by the bilingual expert; Ms. Khin Thandar Aung, Head of Critical Care Nursing Department, Faculty of Nursing, International Islamic University, Malaysia. Then, the finalized back-translated instrument in English was developed (Appendix C).

To test the reliability of the research instrument, the researcher explained the research assistant regarding the contents of questionnaire and method of data collection on the day before collecting data. And then, the research assistant collected the data using this research instrument from 20 pregnant women who attended the Antenatal Clinic of North Okkalapa General Hospital. After that, the researcher checked the collected data for their reliabilities and consistencies with the questionnaire. After checking the data, the researcher discussed with the research assistant regarding inconsistent data and explained the research assistant again until the data are clearly understood.

Protection of Human Subjects

The study proposal was submitted to the Institutional Review Board (IRB) of the Faculty of Nursing, Mahidol University in Bangkok, Thailand for approval prior data collection. After getting the approval from the IRB-NS, an introduction letter from Faculty of Graduate Studies, Mahidol University was sent to the Director General of Department of Health Professional Resource Development and Management, and the Director General of Department of Medical Services, Ministry of Health and Sports in Nay Pyi Taw, Myanmar to request the permission for conducting research in Central Women's Hospital, and North Okkalapa General Hospital in Yangon. The study proposal was also submitted to the Ethical and Research Committee, University of Nursing in Yangon, Myanmar for their approval.

The tentative participants who met the study criteria were informed of the purpose, procedures, benefits and the risks of the study. The risks resulting from participating in the study were not greater than minimal. The participants were informed about the method of completing personal data questionnaire and they can ask any questions regarding the study. The participants were assured that they could withdraw from participating in the study at anytime of data collection without any affect on the health care services they would receive in the hospital. The participant was not responsible for any expense to participate in this research. The confidentiality of the participants was carefully protected. The code number was used on the questionnaire to identify the participants. The researcher kept the participants' personal data in a private computer, which had a password that only the researcher knows. The participants' personal data were not individually made known to the public, and only group data was published. However, the participants' personal data might be viewed by a related third party investigator such as the researcher's supervisor or ethics committees in case of necessity. The identified information would be destroyed when the study was completed.

Procedures for Data Collection

1. After approval was given by the Institutional Review Board (IRB) of the Faculty of Nursing, Mahidol University, Bangkok, Thailand, the researcher submitted an introduction letter from the Faculty of Graduate Studies, Mahidol University to the Director General of Department of Health Professional Resource Development and Management, and the Director General of Department of Medical Services, Ministry of Health and Sports in Nay Pyi Taw to request the permission for conducting research in Central Women Hospital, and North Okkalapa General Hospital in Yangon. The study proposal was also submitted to the Ethical and Research Committee, University of Nursing, Yangon for their approval.

2. After the permission was granted, the researcher informed the Medical Superintendents (MS), Nursing Superintendents (NS) and Head Nurses of antenatal clinic of Central Women Hospital, and North Okkalapa General Hospital in Yangon for the research objective and process of data collection, and asked for their help in facilitating the data collection procedure. And then, the Head Nurses of Antenatal Clinic in two hospitals gave the information to their nurses for their help in facilitating the data collection procedure.

3. Before the data collection was commenced, the researcher explained the research assistant regarding the contents of questionnaire and method of data collection. And then, the research assistant collected the data from 20 pregnant women who attended the Antenatal Clinic of North Okkalapa General Hospital using this research instrument. After that, the researcher checked the collected data for their reliabilities and consistencies with the questionnaire. After checking the data, the researcher discussed with the research assistant regarding inconsistent data and explained the research assistant again until the data are clearly understood. A research assistant was Mrs Ni Ni, Assistant Lecturer of Central Midwifery Training School with Bachelor Degree in Nursing.

4. The researcher and research assistant collected the data at two research settings from 9th March to 31st March, 2016.

5. The processes of data collection were as followed.

5.1 The antenatal clinic nurse introduced the researcher and research assistant to the tentative participants.

5.2 The researcher and research assistant enrolled the tentative participants by inclusion criteria.

5.3 After finished the antenatal care procedure, the tentative participants were informed of the purpose, procedures, benefits, and risks of the study in the private room of antenatal clinic.

5.4 The tentative participants read the information sheet for 15 minutes and were given time for questions.

5.5 The participants signed the consent form.

5.6 The participants were explained the method of completing the questionnaire and given time to answer the first part of questionnaire for 15 to 20 minutes.

5.7 The researcher and research assistant completed the second part of questionnaire using the information from the participant's antenatal record sheet.

Data Analysis

The collected data was analyzed using the following statistics,

1. Descriptive statistics was used to describe the demographic characteristics of pregnant women

2. Chi-square test or Fisher's exact test was used to compare the variables among pregnant women with hypertensive disorders and those without hypertensive disorders.

3. The risk factors related to the development of hypertensive disorders were examined using the binary logistic regression analysis with a significant level of .05.

CHAPTER IV
RESULTS

This chapter presents the results of the study 'Risk factors for hypertensive disorders in Myanmar pregnant women'. The results are presented in two parts as follows:

Part I: The descriptive data of the participants were analyzed using chi-square test or fisher's exact test. The results were shown in Table 4.1 and Table 4.2.

Part II: Factors predicting the risk of hypertensive disorders were examined using binary logistic regression analysis. The results were illustrated in Table 4.3.

Part I: Descriptive Data of the Participants

1.1. General Characteristics of the Participants

The pregnant women with gestational age between 36 weeks and 42 weeks were invited to participate in the study during their regular antenatal visit at two tertiary teaching hospitals in Yangon in March, 2016. 120 pregnant women from Central Women Hospital and 268 pregnant women from North Okkalapa General Hospital who met the inclusion criteria were recruited in this study. In 388 pregnant women, there were 52 (13.4%) pregnant women diagnosed with hypertensive disorders. Of these patients, 31 (8%) was diagnosed with gestational hypertension, 20 (5.1%) was diagnosed with preeclampsia, and only 1 (0.3%) was diagnosed with superimposed preeclampsia. The subjects were followed by telephone 6 weeks after delivery to rule out the possibility of chronic hypertension. The blood pressure of these women had returned to normal which was lower than 140/90 mmHg. This meant all 52 pregnant women were correctly diagnosed as hypertensive disorders of pregnancy defined by this study. No participants dropped out from the study.

1.2 Demographic Characteristics of the Participants

Chi-square or Fisher's exact test were used to compare the demographic characteristics of participants including race, education, occupation, family income, gravida, complications in previous pregnancy, medical history, family history of diabetes mellitus, and family history of hypertensive disorders during pregnancy (Table 4.1).

Table 4.1 Demographic Characteristics of the Participants

Demographic Characteristics	HDP N=52 (%)	Without HDP N=336 (%)	Total N=388 (%)	χ^2	P Value
Race				1.52	.468
Burma	39 (75)	262 (78)	301 (77.6)		
Karin,Chin,Mon,Rakhine,Shan	7 (13.5)	28 (8.3)	35 (9.0)		
Indian	6 (11.5)	46 (13.7)	52 (13.4)		
Education				1.68	.641
Elementary	11 (21.2)	72 (21.4)	83 (21.4)		
Middle	13 (25.0)	74 (22.0)	87 (22.4)		
High	14 (26.9)	118 (35.1)	132 (34.0)		
≥ Diploma	14 (26.9)	72 (21.4)	86 (22.2)		
Occupation					.794 [F]
Home maker	37 (71.2)	244 (72.6)	281 (72.4)		
Employed for Wages	5 (9.6)	38 (11.3)	43 (11.1)		
Self-employed	10 (19.2)	49 (14.6)	59 (15.2)		
Student	0 (0)	5 (1.5)	5 (1.3)		
Family Income(MMK)				2.93	.231
< 150,000	6 (11.5)	38 (11.3)	44 (11.3)		
150,000-300,000	36 (69.2)	261 (77.7)	297 (76.5)		
>300,000	10 (19.2)	37 (11.0)	47 (12.1)		
Mean (±SD)	262500 (±135832.58)	37098.21 (±140181.61)	240502.58 (±139703.24)		
Minimum	100,000	100,000	100,000		
Maximum	600,000	150,000,0	150,000,0		
Gravida				9.73	.002
Primigravida	31 (59.6)	123 (36.6)	154 (39.7)		
Multigravida	21 (40.4)	213 (63.4)	234 (60.3)		
- 2 times	8 (15.4)	133 (39.6)	141 (36.4)		
- 3 times	7 (13.5)	56 (16.7)	63 (16.2)		
- ≥4 times	6 (11.5)	24 (7.1)	30 (7.7)		
Minimum	0	0	0		
Maximum	7	7	7		

[F]= Fisher's exact test; Abbreviation: MMK= Myanmar Kyat (1200 MMK equal to 1 USD), HDP= Hypertensive Disorders of Pregnancy

Table 4.1 Demographic Characteristics of the Participants (cont.)

Demographic Characteristics	HDP N=52 (%)	Without HDP N=336 (%)	Total N=388 (%)	χ^2	P Value
Complications in Previous Pregnancy					.000[F]
No	42 (80.8)	324 (96.4)	366 (94.3)		
Yes	10 (19.2)	12 (3.6)	22 (5.7)		
- GH	6 (11.5)	1 (0.3)	7 (1.8)		
- PE	4 (7.7)	5 (1.5)	9 (2.3)		
- GDM	0 (.0)	6 (1.8)	6 (1.6)		
Medical History					.181 [F]
No	45 (86.5)	310 (92.3)	355 (91.5)		
Yes#	7 (13.5)	26 (7.7)	33 (8.5)		
- HTN	7 (13.5)	8 (2.4)	15 (3.8)		
- RD	0 (.0)	1 (0.3)	1 (0.3)		
- DM	1 (1.9)	2 (0.6)	3 (0.7)		
- CVD	0 (.0)	10 (2.9)	10 (2.6)		
- Asthma	0 (.0)	1 (0.3)	1 (0.3)		
- Athritis	0 (.0)	2 (0.6)	2 (0.5)		
- TB	0 (.0)	1 (0.3)	1 (0.3)		
- SLE	0 (.0)	1 (0.3)	1 (0.3)		
Family History of DM				7.36	.004
No	36 (69.2)	287 (85.4)	323 (83.2)		
Yes#	16 (30.8)	49 (14.6)	65 (16.8)		
- Father	5 (9.6)	15 (4.5)	20 (5.1)		
- Mother	12 (23.1)	26 (7.7)	38 (9.8)		
- Siblings	0 (.0)	3 (0.9)	3 (0.8)		
Family History of HDP					.155[F]
No	47 (90.4)	322 (95.8)	369 (95.1)		
Yes	5 (9.6)	14 (4.2)	19 (4.9)		
- Mother	4 (7.7)	6 (1.8)	10 (2.6)		
- Siblings	0 (.0)	8 (2.4)	8 (2.1)		

[F]= Fisher's exact test; # 1 participant has more than one disease; Abbreviation: HDP= Hypertensive Disorders of Pregnancy, GH= Gestational Hypertension, PE= Preeclampsia, GDM=Gestational Diabetes Mellitus, HTN=Hypertension, RD= Renal Diseases, DM=Diabetes Mellitus, CVD=Cardiovascular Diseases, TB=Tuberculosis, SLE= Systemic Lupus Erythematosus

Table 4.1 showed the demographic characteristics of women diagnosed with hypertensive disorders and those who without hypertensive disorders as followed. Statistically significant differences were found in gravida, complications in previous pregnancy, and family history of diabetes mellitus between pregnant women diagnosed with hypertensive disorders and those who without hypertensive disorders ($p<.05$) (Table 4.1). The results showed that 59.6% of women diagnosed with hypertensive disorders were primigravida whereas 63.4% of pregnant women who without hypertensive disorders were multigravida. The pregnant women diagnosed with hypertensive disorders had more complications in previous pregnancies than those who without hypertensive disorders (19.2% Vs 3.6%). Likewise, family history of diabetes mellitus was greater in pregnant women diagnosed with hypertensive disorders than those who without hypertensive disorders (30.8% Vs 14.6%).

On the other hand, there were no significant differences between two groups in race, education, occupation, family income, medical history and family history of hypertensive disorders in pregnancy ($p>.05$) (Table 4.1). The majority (77.6%) of women in this study was Burmese. The education levels between two groups were equal. About 75% of pregnant women in both groups were home makers who had monthly family income of 150,000-300,000 Myanmar Kyats (approximately 125-250 USD) with a mean of 240,502 Myanmar Kyats (SD: 139703, min: 100,000, max: 1,500,000). The majority (91.5%) of pregnant women in this study were free from medical diseases previously. Likewise, only a small number of women (4.9%) had family history of hypertensive disorders during pregnancy.

1.3 Characteristics of Independent Variables

Chi-square or Fisher's exact test were used to compare the characteristics of independent variables including age, parity, body mass index, family history of hypertension and gestational diabetes mellitus (Table 4.2).

Table 4.2 Characteristics of Independent Variables

Demographic Characteristics	HDP N=52 (%)	Without HDP N=336 (%)	Total N=388 (%)	χ^2	P value
Age (years)				33.77	.000
< 20	0 (.0)	19 (5.6)	19 (4.9)		
20-34	26 (50)	264 (78.6)	290 (74.7)		
≥ 35	26 (50)	53 (15.8)	79 (20.4)		
Mean (±SD)	34.6 (±6.06)	28.4 (±5.77)	29.2 (±6.18)		
Minimum	20	19	19		
Maximum	47	47	47		
Parity				6.14	.013
Nullipara	32 (61.5)	145 (43.2)	177 (45.6)		
Multipara	0 (38.5)	191 (56.8)	211 (54.4)		
-1 time	9 (17.3)	126 (37.5)	135 (34.8)		
-2 times	7 (13.5)	44 (13.1)	51 (13.2)		
-≥3 times	4 (7.7)	21 (6.2)	25 (6.4)		
Minimum	0	0	0		
Maximum	4	7	7		
Body Mass Index (kg/m^2)				97.06	.000
- Underweight (≤18.49)	0 (.0)	32 (9.5)	32 (8.2)		
- Normal weight (18.50-22.99)	2 (3.8)	157 (46.7)	159 (41.0)		
- Over weight (23.00-27.49)	18 (34.6)	114 (33.9)	132 (34.0)		
- Obese (≥27.5)	32 (61.5)	33 (9.8)	65 (16.8)		
Mean (±SD)	28.90 (±3.89)	22.82 (±3.56)	23.64 (±4.16)		
Minimum	21.8	15.9	15.9		
Maximum	38.6	37.7	38.6		
Family History of HTN				27.40	.000
No	13 (25.0)	213 (63.4)	226 (58.2)		
Yes#	39 (75.0)	123 (36.6)	162 (41.8)		
- Father	16 (30.8)	40 (11.9)	56 (14.4)		
- Mother	23 (44.2)	70 (20.8)	93 (24.0)		
- Sibling	3 (5.8)	9 (2.7)	12 (3.1)		
GDM					.000^F
No	24 (46.2)	329 (97.9)	353 (91.0)		
Yes	28 (53.8)	7 (2.1)	35 (9.0)		

^{F}= Fisher's exact test; # 1 participant has more than one disease; Abbreviation: HDP= Hypertensive Disorders of Pregnancy, HTN=Hypertension, GDM=Gestational Diabetes Mellitus, BMI=Body Mass Index

Table 4.2 showed the characteristics of independent variables as followed. Statistically significant difference were found in characteristics of independent variables between the pregnant women diagnosed with hypertensive disorders and those who without hypertensive disorders ($p<.05$). The results showed that 78.6% of

women without HDP and 50 % of women with HDP were aged 20 to 34 years. The mean age was 29.20 years (SD: 6.18, min: 19 years, max: 47 years). Similarly, the percentage of nulliparous women was greater in women with hypertensive disorders than women without hypertensive disorders (61.5% Vs 43.2%). Moreover, family history of chronic hypertension was greater in women with hypertensive disorders than those without hypertensive disorders (75% Vs 36.6%). Additionally, the percentage of pregnant women who had body mass index $\geq$ 23 kg/m^2 was significantly higher in women with hypertensive disorders than women without hypertensive disorders (96.2% Vs 43.8%). The mean BMI was 23.64 (SD=4.16) with the minimum BMI of 15.9 kg/m^2 and the maximum BMI of 38.6 kg/m^2. Lastly, more than half of the women with hypertensive disorders (53.8%) had been diagnosed as gestational diabetes mellitus. However, almost all of those without hypertensive disorders (97.9%) had not been diagnosed as gestational diabetes mellitus.

Part II: Factors Predicting the Risk of Hypertensive Disorders

Binary logistic regression was done to examine the predictive factors related to the development of hypertensive disorders during pregnancy (Appendix F). The results were shown in Table 4.3.

Table 4.3 Binary Logistic Regression Analysis

Risk Factors	*Women with HDP N=52(%)*	*Women without HDP N=336(%)*	B	OR	95% CI	p-value
Age (years)			0.756	2.13	0.88-5.15	.093
20-34 [R]	26 (50)	264 (78.6)				
<20 or ≥ 35	26 (50)	72 (21.4)				
Parity			0.937	2.55	1.10-5.93	.030
Multiparous[R]	20 (38.5)	191 (56.8)				
Nulliparous	32 (61.5)	145 (43.2)				
Body Mass Index (kg/m^2)			2.697	14.83	3.38-65.18	.000
<23 [R]	2 (3.8)	189 (56.25)				
≥ 23	50 (96.2)	147 (43.75)				
Family history of HTN			1.207	3.34	1.40-8.00	.007
No[R]	13 (25)	213 (63.4)				
Yes	39 (75)	123 (36.6)				
GDM			3.203	24.60	8.35-72.45	.000
No[R]	24 (46.2)	329 (97.9)				
Yes	28 (53.8)	7 (2.1)				
Constant			-5.941			

Nagelkerke R^2 = 0.561; -2 LL =163.91; χ^2 =12.56, df =8, p=0.128

[R]= Reference group; Abbreviation: HDP= Hypertensive Disorders of Pregnancy; BMI= Body Mass Index; HTN= Hypertension, GDM= Gestational Diabetes Mellitus; OR= Odds Ratio; CI=Confident Interval

In Table 4.3, binary logistic regression analysis with enter method was applied to calculate adjusted odds ratio for the effect of other variables, simultaneously. The risk factors; extreme age, nulliparity, body mass index ≥ 23 kg/m^2, family history of hypertension and gestational diabetes mellitus were included in the logistic regression analysis as the binary independent variables. The development of hypertensive disorders was binary dependent variable. The level of statistical significant was .05.

The test assumptions of binary logistic regression analysis were as followed. The dependent variable of this study was a categorical variable while the independent variables of this study were a nominal. This model fit with -2 log likelihood (-2LL) was equal to 163.91, the significant model Chi-square was equal to 12.56 (df= 8, p= 0.128), and Nagelkerke R^2= 0.561. The result showed that four variables; parity, body mass index, family history of hypertension and gestational diabetes mellitus could significantly explain 56.1% of the variance in the presence of hypertensive disorders (p<.05) whereas age was not significant (p=.093). The overall rate of correct classification was 92.5%.

The logistic model for predicting the development of hypertensive disorders was shown in the linear relationship equation as followed.

Log-odds= -5.941 + 0.937 **(Nulliparity)** + 2.697 **(Body Mass Index ≥ 23 kg/m^2)** + 1.207 **(Family history of hypertension)** + 3.203 **(Gestational Diabetes Mellitus)**

Therefore, the significant risk factors for the development of hypertensive disorders in Myanmar pregnant women were nulliparity (OR: 2.55, 95% CI: 1.10-5.93, p=0.030), body mass index ≥ 23 kg/m^2 (OR: 14.83, 95% CI: 3.38-65.18, p= 0.000), family history of hypertension (OR: 3.34, 95% CI: 1.40-8.00, p=.007), and gestational diabetes mellitus (OR: 24.60, 95% CI: 8.35-72.45, p= 0.000).

CHAPTER V
DISCUSSION

This study was a predictive study design aimed at identifying the significant risk factors that contribute to hypertensive disorders in Myanmar pregnant women depending on extreme age, nulliparity, body mass index ≥ 23 kg/m^2, family history of hypertension and gestational diabetes mellitus. This chapter discusses the descriptive data of the participants and factors predicting the risk of hypertensive disorders. Limitation of the study is also described.

Descriptive Data of the Participants

1.1 General Characteristics of the Participants

Three hundred and eighty eight eligible pregnant women were enrolled in the study. Among them, fifty two pregnant women who had a blood pressure greater than or equal to 140/90 mmHg were classified as hypertensive disorders of pregnancy (HDP). The overall prevalence of hypertensive disorders in this study was 13.4%. The prevalence of HDP has been reported to occur as many as 10.5% and as few as 2.6% in previous studies (Esther, 1980; Naw Mary Paw, 1995; Saw-Lwin, Mary-Krasu & Win-Pe, 1993; Than Than Oo, 2001). The possible reason for increased prevalence of hypertensive disorders in this study is that the quality and coverage of antenatal care services were improved by upgrading the knowledge of communities and health personnel, and by enhancing national capacities of equity in health, access to services and health care financing systems (UNFPA, 2010; World Health Organization, 2014). These could lead to widespread use of quality antenatal care and resulted in early detection and diagnosis of hypertensive disorders.

1.2 Demographic Characteristics of the Participants

There were significant differences between two groups regarding gravida, complications in previous pregnancies, and family history of diabetes mellitus ($p<.05$) (Table 4.1). More than half of the participants in group of women with hypertensive disorders were primigravida, whereas in group of women without hypertensive disorders were multigravida. In addition, complications in previous pregnancies and family history of diabetes mellitus were greater in women with hypertensive disorders than those without hypertensive disorders.

On the contrary, no statistically significant difference were found in demographic characteristics of race, education, occupation, family income, medical history and family history of hypertensive disorders between women without hypertensive disorders and those with hypertensive disorders ($p>.05$) (Table 4.1). About three-quarter of pregnant women who participated in the study was Burmese who had monthly family income of 150,000 to 300,000 Myanmar Kyats (approximately 125-250 USD). The level of education between two groups was almost equal. About 75% of pregnant women in both groups were home makers. The majority of pregnant women in both groups were free from medical disease. Likewise, the majority of pregnant women in two groups had no family history of hypertensive disorders during pregnancy.

Factors Predicting the Risk of Hypertensive Disorders

This part discusses the factors associated with the development of hypertensive disorders according to the research hypothesis of extreme age, nulliparity, body mass index $\geq$ 23 kg/m^2, family history of hypertension and gestational diabetes mellitus could predict the risk of hypertensive disorders in Myanmar pregnant women.

To examine the possible risk factors related to the development of hypertensive disorders during pregnancy, five variables were entered into the binary logistic regression equation simultaneously (Table 4.3). The results illustrated that the four factors significantly predict the risk of hypertensive disorders which were nulliparity (OR 2.55, 95% CI 1.10-5.93, $p=.030$), high body mass index $\geq$ 23 kg/m^2

(OR 14.83, 95% CI 3.38-65.18, p=.000), family history of hypertension (OR 3.34, 95% CI 1.40-8.00, p=.007), and gestational diabetes mellitus (OR 24.60, 95% CI 8.35-72.45, p=.000). The only one factor of extreme age was not significantly associated with the development of hypertensive disorders (p=.093). The findings of the association of these risk factors and hypertensive disorders were discussed as followed.

Nulliparity was significantly associated with the development of hypertensive disorders (p<.05). The odds ratios indicated that nulliparous women were two fold increased the risk of developing hypertensive disorders (Table 4.2). The following possible mechanisms help to explain the development of hypertensive disorders in nulliparous women.

The high serum concentration of placenta anti-angiogenic proteins; soluble fms-like tyrosine kinase 1 (sFlt-1) in the first pregnancy may predispose to hypertensive disorders in primiparous women (Levine & Karumanchi, 2005; Wolf et al., 2005). The soluble fms-like tyrosinekinase 1 (sFlt-1) is a receptor for placental growth factors (PIGF) and vascular endothelial growth factors (VEGF). Increased maternal sFlt-1 levels cause decrease in concentration of circulating free PIGF and VEGF which leading to failure of placental angiogenesis and thereby, endothelial dysfunction with manifestation of hypertensive disorders (Singh, 2013; Vest, & Cho, 2014). The other possible mechanism is insulin resistance. Wolf et al. (2002) reported that insulin resistance was independent risk factors for hypertensive disorders in primiparous women but not in multiparous women. In addition, maternal immune maladaptation to fetal alloantigens may play a role in the development of hypertensive disorders in nulliparous women (Cudihy & Lee, 2009; Cunningham et al., 2014; Redman & Sargent, 2007). Abnormally activated neutrophils, cytokines and other immune effectors could lead to vascular damage themselves and could interact with platelets and coagulation systems. This exaggerated immune response inhibits trophoblast invasion to certain extent and which may lead to very poor trophoblast invasion of the arteries, defective remodeling, constricted blood flow, hypoxia, and resulting in endothelial dysfunction with the development of hypertensive disorders (Raghupathy, 2010). The result of this study was congruent with the findings of previous studies which showed that the risk of hypertensive disorders was higher in

nulliparous women than multiparous women (Abalos et al., 2014; Coghill et al., 2011; Morikawa et al., 2012; Savitz et al., 2014; Tebeu et al., 2011).

In addition, high body mass index was strongly associated with hypertensive disorders (p=.000). The result showed that body mass index ≥ 23 kg/m^2 were an important predictor of hypertensive disorders of pregnancy with adjusted OR of 14.83, 95% CI 3.38-65.18 (Table 4.2). Increased insulin resistance in obesity could precipitate the risk of hypertensive disorders (Roberts et al., 2011). Tilg & Moschen (2006) illustrated that insulin resistance is more a function of fat content than of absolute weight. It was congruent with the findings of previous studies. Than Than Oo (2001) studied the determinant of hypertensive disorders of pregnancy in Mandalay General Hospital using the body mass index ≥ 29 kg/m^2 as a case. It was revealed that the risk of hypertensive disorders was significantly associated with high body mass index (OR 7.37, 95% CI 4.53-12.06, p<.001). Ye et al (2014) conducted survey on hypertensive disorders of pregnancy using the BMI cutoff point of 24.0-27.9 kg/m^2 for overweight and ≥ 28 kg/m^2 for obese in Chinese population. The result showed that the risk of HDP was 1.8 times higher in those who were overweight (95% CI 1.63-1.96, p<.001) and 3.1 times higher in those obese (95% CI 2.71-3.56, p<.001).

However, there was a difference in magnitude of the association of body mass index and the risk of hypertensive disorders between the recent and previous studies. It was assumed due to discrepancy in BMI categories (Misra, 2015; WHO, 2004; WHO, 2015). In general, a mean BMI of Asian population is lower than non-Asian population (WHO, 2010). Savitz et al (2014) also confirmed that the magnitude of the association of body mass index and risk of hypertensive disorders was stronger among Asian population though high pre-pregnancy weight was rare. This may reflect the fact that body mass index is more sensitive than weight in shorter Asian women (Misra, 2015). Therefore, the previous studies could underestimate the magnitude of the association of body mass index and hypertensive disorders in Asian population by using universally applied BMI.

Similarly, family history of hypertension was significantly associated with the risk of hypertensive disorders (p<.05). The women who had family history of hypertension were 3.3 fold higher the risk of developing hypertensive disorders compared to those without family history of hypertension (Table 4.2). A case-control

study in Brazil also reported that family history of hypertension could predict the risk of hypertensive disorders with adjusted OR 7.05 (95% CI 1.99-24.93, p=.002) (Dalmáz et al., 2011). An explanation of the relationship between the family history of hypertension and the development of hypertensive disorders described as followed.

Familial predisposition of hypertension is a known risk factor for alterations in structural and physical properties of resistant arteries which resulting in endothelial diseases such as atherosclerosis. Atherosclerosis is an artery wall thickness as a result of accumulation of substances including active white blood cells, cholesterol and triglycerides (Maton, 1993). Changes in vascular wall thickness are predisposed to increase peripheral vascular resistance resulting in increased blood pressure **(**Dreisbach, 2015**).** Khalil et al. (2009) also found that there is increased arterial stiffness in women with hypertensive disorders during pregnancy. Atherosclerosis and hypertensive disorders have certain similarities. Both are associated with dyslipdemia, endothelial dysfunction and an increase in the circulating levels of proinflammatory cytokines, such as IL-6 and TNF-α. Endothelial alteration in atherosclerosis invokes oxidative stress. Oxidative stress promotes vascular smooth muscle cell proliferation, hypertrophy and collagen deposition which leading to thickening of the vascular media and narrowing of the vascular lumen, and resulting in decreased placental perfusion and manifestation of hypertensive disorders with endothelial dysfunction (Singh et al., 2015).

The result was congruent with the findings of previous studies which described that family history of hypertension is a significant risk factor for the development of hypertensive disorders during pregnancy (Mehta et al., 2015; Morgan et al., 2015; Wright et al., 2015). Than Than Oo (2001) stated that familial predisposition of hypertension on either maternal or paternal side had a significant effect on the development of hypertensive disorders of pregnancy in their offspring (OR 13.12, 95% CI 8.58-20.14, p<.001). Moraes, Fuchs, Dalla Costa, & Moreira (2000) also evidenced that they were strongly predisposed to HDP when two or more first-degree relatives had a diagnosis of hypertension. Therefore, women who had familial predisposition of hypertension should receive prenatal life style education to prevent vascular diseases.

In addition, the pregnant women who had gestational diabetes mellitus had significantly higher risk of hypertensive disorders compared to those without gestational diabetes mellitus ($p < .05$) (Table 4.2). The metabolic syndrome-related factors of two diseases such as insulin resistance and elevated non-esterfied fatty acids (NEFA) could be the link between gestational diabetes mellitus and hypertensive disorders (Jeyabalan, Hubel, & Roberts, 2015). According to Pedersen's hypothesis, pregnancy is associated with a physiological state of increased insulin resistance. However, this could lead to hyperinsulinemia and gestational diabetes mellitus in vulnerable pregnant women (Catalano & Hauguel-De, 2011). An explanation of the relationship between the gestational diabetes mellitus and hypertensive disorders described as followed.

Insulin has powerful anti-lipolytic effects. Therefore, increased insulin resistance cause increased in the secretion of proinflammatory cytokines and adipocytokines, such as interleukin-6 (IL6) and tumour necrosis factor-α (TNF-α). Cytokines stimulate the release of non-esterfied fatty acids (NEFA) from adipose tissue, and which in turn worsening insulin resistance and hyperinsulinemia by release of glucose from muscle and liver. In addition, increased adipocyte mass and TNF-α in insulin resistance also suppresses the production and concentration of circulating adiponectin. Adiponectin is an important insulin sensitizer. So, as adiponectin is reduced, insulin resistance increases. As a consequence, it could lead to hypertension by vasoconstriction, increased renal tubular sodium re-absorption, and sodium retention. Moreover, adipocytes release hormones; angiotensinogen lead to increase in blood pressure through vasoconstriction and fluid retention, and ultimately resulting in manifestation of hypertensive disorders.

This recent study supported the previous studies which hypothesized that gestational diabetes mellitus could precipitate the risk of hypertensive disorder during pregnancy (Feig et al., 2013; Moussa & Sibai, 2015). Hossein-Nezhad et al.(2011) also found that gestational diabetes mellitus could predict the risk of hypertensive disorders independent of age, body mass index and parity (OR 3.18, 95% CI 1.13-8.94, $p=0.03$).

Contrastingly, the research finding revealed that extreme age could not predict the risk of developing hypertensive disorders (Table 4.3). The partial correlation of extreme age and the development of hypertensive disorders were lower

than other risk factors (Appendix F). Furthermore, the fact that Myanmar cultural value could attribute to delay in age of marriage and first birth (UNFPA, 2010). The majority of women in this study were greater than 20 years (Table 4.2). Thus, as a recent study revealed, extreme age seemed to have no effect on the development of hypertensive disorders. In addition, this result reflects the fact that the impact of age on the risk of hypertensive disorders was complex and difficult to predict due to the effect of confounding factors. For example, younger women were more likely to be primiparous and particularly vulnerable to developing preeclampsia and eclampsia. On the other hand, older women were more likely to have chronic hypertension with superimposed preeclampsia as a consequence of increased insulin resistant and metabolic syndrome in increased age (Abalos et al., 2014; Cunningham et al., 2014; Lisonkova & Joseph, 2013, Morikawa et al., 2012). Other previous studies could support this study. A case-control study of Dalmáz, Santos, Botton, & Roisenberg (2011) which described extreme maternal age could not be demonstrated as a risk factor of hypertensive disorders. Savitz et al. (2014) also evidenced that advanced maternal age was strongly associated with chronic hypertension but not any forms of hypertensive disorders in pregnancy. Likewise, a systematic review of Trogstad (2011), it was also concluded that young maternal age was not associated with an increased risk of hypertensive disorders at any cut off point.

Limitations of the Study

Glucose Tolerance Test

In the United Kingdom, screening by risk factors and random glucose measurement was the most frequently used method to screen for gestational diabetes mellitus (Hanna, Peters, Harlow, & Jones, 2008). A national survey from the UK showed that 52% of the respondents used random glucose measurement as a preliminary test for glucose tolerance (van Leeuwen et al., 2011). In Myanmar, the use of combination of risk factors assessment and random blood glucose measurement is the most convenient and economical method of initial screening for diabetes mellitus because fewer women would require an OGTT. However, there was difference in

preliminary test of glucose tolerance between two settings of recent study. In one setting, all pregnant women were underwent preliminary test of glucose tolerance by random plasma glucose measurement but the same was done only in high risk women at another setting. It may lead to underestimation of the prevalence of gestational diabetes mellitus in low risk pregnant women. Therefore, the absence of objective measurements of glucose tolerance may also be considered as limitation of this study. In previous studies of glucose tolerance in Myanmar pregnant women, it was found that blood glucose concentration 2 hour after 75g glucose load was higher in risk group than normal pregnancies (Cho Cho, 1994; Htay Htay, K-Bathike, May Thazin, & Nan Oo, 1992). Thus, based on the findings of previous studies, the pregnant women in the low risk group were assumed to be correctly defined as normal glucose tolerance.

Summary

Hypertensive disorders of pregnancy were the second leading cause of maternal mortality and morbidity in Myanmar with 21% of all maternal death. Therefore, this study was aimed at identifying the significant risk factors that contribute to hypertensive disorders in Myanmar pregnant women depending on extreme age, nulliparity, body mass index ≥ 23 kg/m^2, family history of hypertension and gestational diabetes mellitus. The conceptual framework was based on patho-physiologic concept of hypertensive disorders by Two-stage model. The hypertensive disorders of this study included gestational hypertension, preeclampsia-eclampsia and chronic hypertension with superimposed preeclampsia. Three hundred and eighty eight pregnant women who met the inclusion criteria were recruited from two tertiary teaching hospitals in Yangon by using convenient sampling method. Binary logistic regression analysis with enter method was applied to calculate adjusted odds ratio for the effect of other variables, simultaneously. The findings revealed that four variables could explain 56.1% of the variance in the presence of hypertensive disorders of pregnancy. They were nulliparity (OR 2.55, 95%CI: 1.10-5.93, p=0 .030), body mass index ≥ 23 kg/m^2 (OR 14.83, 95% CI: 3.38-65.18, p= 0.000), family history of

hypertension (OR 3.34, 95% CI: 1.40-8.00, p=.007), and gestational diabetes mellitus (OR 24.60, 95% CI: 8.35-72.45, p= 0.000). The overall rate of correct classification was 92.5%. The risk factors identified in this study is useful for nursing and midwifery practice in screening and monitoring of hypertensive disorders among those who are at risk of hypertensive disorders such as nulliparity, body mass index $\geq$ 23 kg/m^2, family history of hypertension, and gestational diabetes mellitus. Pregnant women who are at risk of hypertensive disorders should be advised to adjust their lifestyle and to control their body weight with diet and physical activity.

CHAPTER VI
CONCLUSION

This chapter presents a summary of the study 'Risk Factors for Hypertensive Disorders in Myanmar Pregnant Women' followed by implications for nursing and midwifery practice and recommendations for future research.

Summary of the Study

This study was a predictive study design aimed to identify the significant risk factors that contribute to hypertensive disorders in Myanmar pregnant women depending on extreme age, nulliparity, body mass index ≥ 23kg/m^2, family history of hypertension and gestational diabetes mellitus. Pathophysiological concept of hypertensive disorders by Two-stage model was used as the conceptual framework for this study.

Data collection was done at Antenatal Clinic of two tertiary teaching hospitals; Central Women's Hospital and North Okkalapa General Hospital, Yangon, Myanmar from 9th March to 31st March, 2016. Three hundred and eighty-eight pregnant women were recruited in the study by using convenient sampling method with the following criteria; singleton pregnancy, gestational age between 36 weeks and 42 weeks, age ≥18 years, Burma language literacy and able to read and write Burma language, well-oriented and able to communicate.

Of three hundred and eighty-eight pregnant women, 52 women (13.4%) were diagnosed with hypertensive disorders of pregnancy. The subjects with hypertensive disorders were followed by telephone at six weeks after delivery to rule out the possibility of chronic hypertension. The blood pressure of these women had returned to normal which lower than 140/90 mmHg. It indicated that these 52 pregnant women were correctly diagnosed with hypertensive disorders of pregnancy defined by this study. No participants dropped out from participating in this study.

The instruments used to collect data consisted of socio-demographic characteristics such as age, race, education, occupation, family income, gravidity, parity, complications in previous pregnancy, medical history, family history of hypertension, family history of diabetes mellitus, family history of hypertensive disorders during pregnancy, body mass index and pregnancy complications.

Binary logistic regression with enter method was used to examine the predictive power of extreme age, nulliparity, body mass index $\geq$ 23kg/m^2, family history of hypertension, and gestational diabetes mellitus on the development of hypertensive disorders during pregnancy.

The result showed that these risk factors except age could predict the risk of developing hypertensive disorders ($p<.05$). Nulliparous women have 2.6 times greater risk for developing hypertensive disorders compared to multiparous women (95% CI: 1.10-5.93, p=0 .030). Women who had body mass index $\geq$ 23 kg/m^2 have 14.8 times higher risk for developing HDP compared to those who had pre-pregnancy BMI $\leq$ 23 kg/m^2 (95% CI: 3.38-65.18, p= 0.000). Women who had family history of hypertension have 3.34-fold increased risk for developing HDP compared to those who had no family history of hypertension (95% CI: 1.40-8.00, p=.007). Women diagnosed with gestational diabetes mellitus have 24.6 times higher risk for developing hypertensive disorders compared to those without gestational diabetes mellitus (95% CI: 8.35-72.45, p= 0.000). These four variables could explain 56.1% of the variance in the development of hypertensive disorders with 92.5% overall rate of correct classification.

Recommendations and Implications

The findings of this study have implications for nursing and midwifery practice. Recommendations for future research are also presented.

Implications for Nursing and Midwifery Practice

Since 80% maternal deaths were occurred at home and HDP was responsible for 5.6% of these maternal deaths (Myanmar Country Report, 2008), it is

critical that the nurses-midwives working in primary health care are needed to pay attention on the risk factors which were related to the development of hypertensive disorders to provide antenatal care efficiently and effectively, and to screen and monitor the blood pressure of pregnant women who are at risk. Thus, the nurses-midwives should be provided the updated knowledge of risk factors confirmed by this study. In addition, the nurses-midwives can help the pregnant women who are at risk of developing hypertensive disorders such as nulliparity, body mass index ≥ 23 kg/m^2, family history of hypertension and gestational diabetes mellitus to examine and adjust their lifestyles, to control their body weight with diet and physical activity and to develop appropriated individualized intervention strategies. Since gestational diabetes mellitus was a significant risk factor of hypertensive disorders, the nurses-midwives should also do standardized correct measurement of random plasma glucose to all pregnant women to screening and monitoring hypertensive disorders. Moreover, the conditions and blood pressure of high risk women should be carefully monitored throughout pregnancy till 6 weeks after delivery to prevent further complications.

Recommendations for Future Research

Screening the high risk pregnancies using these risk factors and examining their lifestyles would identify the unhealthy lifestyle behaviors associated with the development of hypertensive disorders which can be solved by nursing interventions. Further research on appropriate nursing intervention strategies which can reduce the development of hypertensive disorders in high risk pregnancies is recommended. In addition, this research should be replicated in a large group of different ethnic backgrounds to increase representativeness of the study. Lastly, universal consensus for classification of BMI for Asian populations is needed to resolve the controversies regarding body mass index. Therefore, in further studies, it is crucial to find the impact of different BMI categories on the risk of developing hypertensive disorders in Myanmar pregnant women.

REFERENCES

Abalos, E., Cuesta, C., Carroli, G., Qureshi, Z., Widmer, M., Vogel, J. P., et al. (2014). Pre-eclampsia, eclampsia and adverse maternal and perinatal outcomes: A secondary analysis of the World Health Organization Multicountry Survey on maternal and newborn health. *BJOG, 121(Suppl.1)*, 14-24.

Abbassi-Ghanavati, M., Greer, L. G., & Cunningham, F. G. (2009). Pregnancy and laboratory studies: A reference table for clinicians. *Obstet Gynecol, 114*(6), 1326-1331.

Abu-Saad, K., & Fraser, D. (2010). Maternal nutrition and birth outcomes. *Epidemiol Rev, 32*(1), 5-25.

Alexander, J. M., & Cunningham, F. G. (2015). Clinical management. In R. N. Taylor, J. M. Roberts, F. G. Cunningham, & M. D. Lindheimer (Eds.), *Chesley's Hypertensive Disorders in Pregnancy* (4th ed.) (pp. 439-464). San Diego: Academic Press.

Alfadhli, E. M. (2015). Gestational diabetes mellitus. *Saudi Medical Journal, 36*(4), 399-406.

Aliyu, M. H., Luke, S., Kristensen, S., Alio, A. P., & Salihu, H. M. (2010). Joint effect of obesity and teenage pregnancy on the risk of preeclampsia: A population-based study. *J Adolesc Health, 46*(1), 77-82.

Alves, E., Azevedo, A., Rodrigues, T., Santos, A. C., & Barros, H. (2013). Impact of risk factors on hypertensive disorders in pregnancy, in primiparae and multiparae. *Annals of Human Biology, 40*(5), 377-384.

American College of Obstetericians and Gynecologists. (2013). Report of the American College of Obstetricians and Gynecologists' Task Force on hypertension in pregnancy. *Obstetrics & Gynecology, 122*(5), 1122-1131.

American Diabete Association. (2015). Classification and diagnosis of diabetes. *Diabetes Care, 38*(Supplement 1), S8-S16.

American Diabetes Association. (2016). Standards of medical care in diabetes-2016: A bridged for primary care providers. *Clinical Diabetes, 34*(1), 3-21.

Amiel, S. A., Sherwin, R. S., Simonson, D. C., Lauritano, A. A., & Tamborlane, W. V. (1986). Impaired insulin action in puberty: A contributing factor to poor glycemic control in adolescents with diabetes. *N Engl J Med, 315*(4), 215-219.

Arslanian, S. A., & Kalhan, S. C. (1994). Correlations between fatty acid and glucose metabolism: Potential explanation of insulin resistance of puberty. *Diabetes, 43*(7), 908-914.

Ascherio, A., Hennekens, C., Willett, W. C., Sacks, F., Rosner, B., Manson, J., et al. (1996). Prospective study of nutritional factors, blood pressure and hypertension among US women. *Hypertension, 27*, 1065-1072.

Ball, G. D., Huang, T. T., Gower, B. A., Cruz, M. L., Shaibi, G. Q., Weigensberg, M. J., & Goran, M. I. (2006). Longitudinal changes in insulin sensitivity, insulin secretion, and beta-cell function during puberty. *J Pediatr, 148*(1), 16-22.

Barbieri, M., Rizzo, M. R., Manzella, D., & Paolisso, G. (2001). Age-related insulin resistance: Is it an obligatory finding? The lesson from healthy centenarians. *Diabetes Metab Res Rev, 17*(1), 19-26.

Barger, M. K. (2010). Maternal nutrition and perinatal outcomes. *J Midwifery Womens Health, 55*(6), 502-511.

Barzilai, N., & Ferrucci, L. (2012). Insulin resistance and aging: A cause or a protective Response? *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 67*(12), 1329-1331.

Bdolah, Y., Elchalal, U., Natanson-Yaron, S., Yechiam, H., Bdolah-Abram, T., Greenfield, C., et al. (2014). Relationship between nulliparity and preeclampsia may be explained by altered circulating soluble fms-like tyrosine kinase 1. *Hypertens Pregnancy, 33*(2), 250-259.

Beck, P., & Daughaday, W. H. (1967). Human placental lactogen: Studies of its acute metabolic effects and disposition in normal man. *Journal of Clinical Investigation, 46*(1), 103-110.

Belizan, J. M., & Villar, J. (1980). The relationship between calcium intake and edema, proteinuria, and hypertension-gestosis: An hypothesis. *American Journal of Clinical Nutrition, 33*(10), 2202-2210.

Bentley-Lewis, R., Powe, C., Ankers, E., Wenger, J., Ecker, J., & Thadhani, R. (2014). Effect of race/ ethnicity on hypertension risk subsequent to gestational diabetes mellitus. *Am J Cardiol, 113*, 1364-1370.

Bernstein, I. M., Meyer, M. C., Osol, G., & Ward, K. (1998). Intolerance to volume expansion: A theorized mechanism for the development of preeclampsia. *Obstet Gynecol, 92*(2), 306-308.

Bezerra, P. C., Leao, M. D., Queiroz, J. W., Melo, E. M., Pereira, F. V., Nobrega, M. H., et al. (2010). Family history of hypertension as an important risk factor for the development of severe preeclampsia. *Acta Obstet Gynecol Scand, 89*(5), 612-617.

Bodnar, L. M., Ness, R. B., Markovic, N., & Roberts, J. M. (2005). The risk of preeclampsia rises with increasing prepregnancy body mass index. *Ann Epidemiol, 15*(7), 475-482.

Brantsaeter, A. L., Haugen, M., Samuelsen, S. O., Torjusen, H., Trogstad, L., Alexander, J., et al. (2009). A dietary pattern characterized by high intake of vegetables, fruits, and vegetable oils is associated with reduced risk of preeclampsia in nulliparous pregnant Norwegian women. *J Nutr, 139*(6), 1162-1168.

Bucher, H. C., Guyatt, G. H., Cook, R. J., Hatala, R., Cook, D. J., Lang, J. D., & Hunt, D. (1996). Effect of calcium supplementation on pregnancy induced hypertension and preeclampsia: A meta-analysis of randomized controlled trials. *JAMA, 275*, 1113-1117.

Caliskan, E., Kayikcioglu, F., Ozturk, N., Koc, S., & Haberal, A. (2004). A population-based risk factor scoring will decrease unnecessary testing for the diagnosis of gestational diabetes mellitus. *Acta Obstet Gynecol Scand, 83*(6), 524-530.

Callaway, L. K., O'Callaghan, M., & McIntyre, H. D. (2009). Obesity and the hypertensive disorders of pregnancy. *Hypertens Pregnancy, 28*(4), 473-493.

Campbell, S. K., Lynch, J., Esterman, A., & McDermott, R. (2013). Pre-pregnancy predictors of hypertension in pregnancy among Aboriginal and Torres Strait Islander women in north Queensland, Australia; a prospective cohort study. *BMC Public Health, 13*, 138.

Carson, M. P. (2015). Hypertension and pregnancy. Retrieved October 28, 2015, from http:// emedicine.medscape.com/article/261435-overview

Catalano, P. M., & Hauguel-De, M. S. (2011). Is it time to revisit the Pedersen hypothesis in the face of the obesity epidemic? *Am J Obstet Gynecol, 204*(479-87).

Central Women's Hospital. (2014). *Unpublished data for incidence of hypertensive disorders of pregnancy.* Yangon.

Central Women's Hospital. (2015). *Unpublished data for incidence of hypertensive disorders of pregnancy.* Yangon.

Cho Cho. (1994). *Oral glucose tolerance in normal pregnancy and pregnancy with antecedent macrosomia*. Unpublished master degree thesis, University of Medicine (1), Yangon, Myanmar

Clausen, T., Slott, M., Solvoll, K., Drevon, C. A., Vollset, S. E., & Henriksen, T. (2001). High intake of energy, sucrose, and polyun-saturated fatty acids is associated with increased risk of preeclampsia. *Am J Obstet Gynecol, 185*, 451-458.

Cnossen, J., Leeflang, M., De Haan, E., Mol, B., Van der Post, J., Khan, K., & Ter Riet, G. (2007). Accuracy of body mass index in predicting pre-eclampsia: Bivariate meta-analysis. *BJOG: An International Journal of Obstetrics & Gynaecology, 114*(12), 1477-1485.

Coghill, A. E., Hansen, S., & Littman, A. J. (2011). Risk factors for eclampsia: A population-based study in Washington State, 1987-2007. *Am J Obstet Gynecol, 205*(6), 553 e551-557.

Crete, J. E., & Anasti, J. N. (2013). Diagnosis of gestational diabetes mellitus: Can we avoid the glucose challenge test? *J Am Assoc Nurse Pract, 25*(6), 329-333.

Cudihy, D., & Lee, R. V. (2009). The pathophysiology of pre-eclampsia: Current clinical concepts. *J Obstet Gynaecol, 29*(7), 576-582.

Cunningham, F. G. (2005). Severe preeclampsia and eclampsia: Systolic hypertension is also important. *Obstet Gynecol, 105*(2), 237-238.

Cunningham, F. G., Leveno, K. J., Bloom, S. L., Spong, C. Y., Dashe, J. S., Hoffman, B. L., et al. (2014). *Williams Obstetrics* (24th ed.). Landon: Mc Graw Hill Education.

Cuschieri, S., Craus, J., & Savona-Ventura, C. (2016). The role of untimed blood glucose in screening for gestational diabetes mellitus in a high prevalent diabetic population. *Scientifica, 2016*, 6.

Dalmáz, C. A., Santos, K. G. d., Botton, M. R., & Roisenberg, I. (2011). Risk factors for hypertensive disorders of pregnancy in southern Brazil. *Rev Assoc Med Bras, 57*, 692-696.

Danso, K. A., & Opare-Addo, H. S. (2010). Challenges associated with hypertensive disease during pregnancy in low-income countries. *Int J Gynaecol Obstet, 110*(1), 78-81.

David, A. S., & Valery, A. D. (2014). Descriptive epidemiology of chronic hypertension, gestational hypertension, and preeclampsia in New York State, 1995-2004. *Matern Child Health J, 18*, 829-838.

Davis, E. F., Lewandowski, A. J., Aye, C., Williamson, W., Boardman, H., Huang, R.-C., et al. (2015). Clinical cardiovascular risk during young adulthood in offspring of hypertensive pregnancies: Insights from a 20-year prospective follow-up birth cohort. *BMJ Open, 5*(6), e008136.

Deborah, B. E., Claudine, J., Matthew, H., Xiaozhang, J., & William, S. W. (2011). Prepregnancy body mass index as an independent risk factor for pregnancy-induced hypertension. *J Womens Health (Larchmt), 20*(1).

Department of Health. (1991). *Dietary reference values for food energy and nutrients in the United Kingdom* (Vol. 41). London: HMSO.

DerSimonian, R., & Levine, R. J. (1999). Resolving discrepancies between a meta-analysis and a subsequent large controlled trial. *JAMA, 282*(7).

Douketis, J. D., Paradis, G., Keller, H., & Martineau, C. (2005). Canadian guidelines for body weight classification in adults: Application in clinical practice to screen for overweight and obesity and to assess disease risk. *CMAJ, 172*(8), 995-998.

Dreisbach, A. W. (2015). Pathophysiology of hypertension. Retrieved April 20, 2016, from http:// emedicine. medscape.com/article/1937383-overview

Duley, L., Matar, H. E., Almerie, M. Q., & Hall, D. R. (2010). Alternative magnesium sulphate regimens for women with pre-eclampsia and eclampsia. *Cochrane Database Syst Rev*(8), CD007388.

Ehrenthal, D. B., Jurkovitz, C., Hoffman, M., Jiang, X., & Weintraub, W. S. (2011). Prepregnancy body mass index as an independent risk factor for pregnancy-induced hypertension. *J Womens Health (Larchmt), 20*(1), 67-72.

Esther Tin Htet. (1980). *A prospective study of hypertensive disorders in pregnancy in the Central Women Hospital*. Unpublished master degree thesis, University of Medicine (1), Yangon.

Fattah, C., Farah, N., O'Toole, F., Barry, S., Stuart, B., & Turner, M. J. (2009). Body Mass Index (BMI) in women booking for antenatal care: Comparison between selfreported and digital measurements. *Eur J Obstet Gynecol Reprod Biol, 144*(1), 32-34.

Faul, F., Erdfelder, E., Buchner, A., & Lang, A.-G. (2009). Statistical power analyses using G* Power 3.1: Tests for correlation and regression analyses. *Behavior research methods, 41*(4), 1149-1160.

Faupel-Badger, J. M., Staff, A. C., Thadhani, R., Powe, C. E., Potischman, N., Hoover, R. N., & Troisi, R. (2011). Maternal angiogenic profile in pregnancies that remain normotensive. *Eur J Obstet Gynecol Reprod Biol, 158*(2), 189-193.

Favilli, A., Pericoli, S., Acanfora, M. M., Bini, V., Di Renzo, G. C., & Gerli, S. (2012). Pregnancy outcome in women aged 40 years or more. *J Matern Fetal Neonatal Med, 25*(8), 1260-1263.

Feig, D. S., Shah, B. R., Lipscombe, L. L., Wu, C. F., Ray, J. G., Lowe, J., et al. (2013). Preeclampsia as a risk factor for diabetes: A population-based cohort study. *PLoS Med, 10*(4), e1001425.

Fink, R. I., Kolterman, O. G., Griffin, J., & Olefsky, J. M. (1983). Mechanisms of insulin resistance in aging. *J Clin Invest, 71*(6), 1523-1535.

Foo, J. Y., Mangos, G. J., & Brown, M. A. (2013). Characteristics of hypertensive disorders in twin versus singleton pregnancies. *Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health, 3*(1), 3-9.

Food and Agriculture Organization. (1985). *Energy and protein requirements; report of a joint FAO/WHO/UNU consultation.* Retrieved August 7, 2015, from http://www.fao.org/do CReP/003/aa040e/ AA040E00.htm

Frederick, I. O., Williams, M. A., Dashow, E., Kestin, M., Zhang, C., & Leisenring, W. M. (2005). Dietary fiber, potassium, magnesium and calcium in relation to the risk of preeclampsia. *J Reprod Med., 50*, 332-344.

Gaillard, R., Steegers, E. A., Hofman, A., & Jaddoe, V. W. (2011). Associations of maternal obesity with blood pressure and the risks of gestational hypertensive disorders: The generation R study. *J Hypertens, 29*(5), 937-944.

Ghulmiyyah, L., & Sibai, B. (2012). Maternal mortality from preeclampsia/eclampsia. *Semin Perinatol, 36*(1), 56-59.

Gold, R. A., Gold, K. R., Schilling, M. F., & Modilevsky, T. (2014). Effect of age, parity, and race on the incidence of pregnancy associated hypertension and eclampsia in the United States. *An International Journal of Women's Cardiovascular Health, 4*, 46-53.

Goldberg, G. R., Prentice, A. M., Coward, W. A., Davies, H. L., Murgatroyd, P. R., Wensing, C., et al. (1993). Longitudinal assessment of energy expenditure in pregnancy by the doubly labelled water method. *Am J Clin Nutr 57*, 949-505.

Gong, J., Savitz, D. A., Stein, C. R., & Engel, S. M. (2012). Maternal ethnicity and pre-eclampsia in New York City, 1995–2003. *Paediatr Perinat Epidemiol, 26*(1), 45-52.

Hale, S., Choate, M., Schonberg, A., Shapiro, R., Badger, G., & Bernstein, I. M. (2010). Pulse pressure and arterial compliance prior to pregnancy and the development of complicated hypertension during pregnancy. *Reprod Sci, 17*(9), 871-877.

Hamlin, R. H. J. (1962). Prevention of pre-eclampsia. *Lancet, 1*, 864-865.

Handwerger, S., & Freemark, M. (2000). The roles of placental growth hormone and placental lactogen in the regulation of human fetal growth and development. *J Pediatr Endocrinol Metab, 13*(4), 343-356.

Hanna, F. W. F., & Peters, J. R. (2002). Screening for gestational diabetes; past, present and future. *Diabetic medicine, 19*(5), 351-358.

Hanna, F. W. F., Peters, J. R., Harlow, J., & Jones, P. W. (2008). Gestational diabetes screening and glycaemic management; national survey on behalf of the Association of British Clinical Diabetologists. *Qjm, 101*(10), 777-784.

Hannon, T. S., Janosky, J., & Arslanian, S. A. (2006). Longitudinal study of physiologic insulin resistance and metabolic changes of puberty. *Pediatr Res, 60*(6), 759-763.

Hays, P. M., Cruikshank, D. P., & Dunn, L. J. (1985). Plasma volume determination in normal and preeclamptic pregnancies. *Am J Obstet Gynecol, 151*(7), 958966.

Heslehurst, N., Rankin, J., Wilkinson, J., & Summerbell, C. (2010). A nationally representative study of maternal obesity in England, UK: Trends in incidence and demographic inequalities in 619 323 births, 1989–2007. *International journal of obesity, 34*(3), 420-428.

Hofmeyr, G. J., Lawrie, T. A., Atallah, A. N., Duley, L., & Torloni, M. R. (2014). Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. *Cochrane Database Syst Rev*(6), Cd001059.

Hogan, J. L., Anglim, B., O'Dwyer, V., Farah, N., Stuart, B., & Turner, M. J. (2012). Body mass index and hypertensive disorders of pregnancy. *An International Journal of Women's Cardiovascular Health, 2*, 28-31.

Holland, E., Moore Simas, T. A., Doyle Curiale, D. K., Liao, X., & Waring, M. E. (2013). Self-reported pre-pregnancy weight versus weight measured at first prenatal visit: Effects on categorization of pre-pregnancy body mass index. *Matern Child Health J, 17*(10), 1872-1878.

Hossein-nezhad, A., Khadijeh, M., Ahmadi, S., Maghbooli, Z., & Karimi, F. (2011). Comparison of incidence of pregnancy induced hypertension in gestational

diabetes mellitus and healthy pregnant women. *Iranian Journal of Diabetes and Lipid Disorders, 10*, 1-9.

Hutcheon, J. A., Lisonkova, S., & Joseph, K. S. (2011). Epidemiology of pre-eclampsia and the other hypertensive disorders of pregnancy. *Best Pract Res Clin Obstet Gynaecol, 25*(4), 391-403.

Imdad, A., Jabeen, A., & Bhutta, Z. A. (2011). Role of calcium supplementation during pregnancy in reducing risk of developing gestational hypertensive disorders: A meta-analysis of studies from developing countries. *BMC Public Health, 11*, S18.

Institute of Medicine. (2005). *Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids (macronutrients)*. Washington, DC: The National Academies Press.

Institute of Medicine. (2009). *Weight gain during pregnancy: Reexamination the guidelines*. Washington, DC: The National Academies Press.

International Diabetes Federation. (2015). Risk Factors. Retrieved May 29, 2016, from http://www.idf.org/about-diabetes/risk-factors

Jansen, P. W., Tiemeier, H., Verhulst, F. C., Burdorf, A., Jaddoe, V. W., Hofman, A., et al. (2010). Employment status and the risk of pregnancy complications: The generation R study. *Occup Environ Med, 67*(6), 387-394.

Jeyabalan, A., Hubel, C. A., & Roberts, J. M. (2015). Metabolic syndrome and preeclampsia. In R. N. Taylor, J. M. Roberts, F. G. Cunningham, & M. D. Lindheimer (Eds.), *Chesley's Hypertensive Disorders in Pregnancy* (4th ed.) (pp. 133-160). San Diego: Academic Press.

Jwa, S. C., Fujiwara, T., Hata, A., Arata, N., Sago, H., & Ohya, Y. (2013). BMI mediates the association between low educational level and higher blood pressure during pregnancy in Japan. *BMC Public Health, 13*(1), 389.

Kaaja, R. (1998). Insulin resistance syndrome in preeclampsia. *Semin Reprod Endocrinol, 16*(1), 41-46.

Kaiser, L., & Allen, L. H. (2008). Position of the American Dietetic Association: Nutrition and lifestyle for a healthy pregnancy outcome. *J Am Diet Assoc, 108*(3), 553-561.

Karumanchi, S. A., Rana, S., & Taylor, R. N. (2015). Angiogenesis and preeclampsia. In R. N. Taylor, J. M. Roberts, F. G. Cunningham, & M. D. Lindheimer (Eds.), *Chesley's Hypertensive Disorders in Pregnancy (4th ed.)* (pp. 113-132). San Diego: Academic Press.

Kelsey, M. M., & Zeitler, P. S. (2016). Insulin Resistance of Puberty. *Curr Diab Rep, 16*(7).

Kenny, L. C., Black, M. A., Poston, L., Taylor, R., Myers, J. E., Baker, P. N., et al. (2014). Early pregnancy prediction of preeclampsia in nulliparous women, combining clinical risk and biomarkers: The Screening for Pregnancy Endpoints (SCOPE) International Cohort Study. *Hypertension, 64*(3), 644-652.

Khalil, A., Jauniaux, E., & Harrington, K. (2009). Antihypertensive therapy and central hemodynamics in women with hypertensive disorders in pregnancy. *Obstetrics & Gynecology, 113*(3), 646-654.

Khalil, A., Syngelaki, A., Maiz, N., Zinevich, Y., & Nicolaides, K. H. (2013). Maternal age and adverse pregnancy outcome: A cohort study. *Ultrasound Obstet Gynecol, 42*(6), 634-643.

Khin May Htwe. (1999). *Effects of maternal pre-pregnancy weight, body mass index and gestational weight gain on pregnancy outcome in Central Women's Hospital*. Unpublished master degree thesis, University of Medicine (1), Yangon.

Khin Ohn Chit. (1983). *A pilot comparative study of the effects of hypertensive disorders in pregnancy on fetal birthweight and perinatal mortality in West Rangoon General Hospital*. Unpublished master degree thesis, University of Medicine (1), Yangon.

Kolasa, K. M., & Weismiller, D. G. (2014). *Nutrition durnig pregnancy and lactation* (Third ed.). Boca Raton: Taylor & Francis Group.

Koleilat, M., Vargas, N., Bell, S., & Whaley, S. (2015). Self-reported pre-pregnancy weight versus weight measured in the first trimester among participants of the special supplemental nutrition program for women, infants and children (WIC). *The FASEB Journal, 29*(Supple 1), 381-388.

Kühl, C. (1991). Insulin secretion and insulin resistance in pregnancy and GDM: Implications for diagnosis and management. *Diabetes, 40*(Supplement 2), 18-24.

Lawn, J. E., Blencowe, H., Pattinson, R., Cousens, S., Kumar, R., Ibiebele, I., et al. (2011). Stillbirths: Where? When? Why? How to make the data count? *THE LANCET, 377*(9775), 1448-1463.

Lee, H., Yoon, C.-H., Park, H.-Y., Lee, H. Y., Choi, D.-J., & Cho, M. C. (2014). Family history of cardiovascular disease is an independent predictor of gestational hypertensive disease and diabetes: The Korean nurses' survey. *Circulation, 130*(Suppl 2), A16725-A16725.

Leffert, L. R., Clancy, C. R., Bateman, B. T., Bryant, A. S., & Kuklina, E. V. (2015). Hypertensive disorders and pregnancy related stroke: Frequency, trends, risk factors, and outcomes. *Obstetrics & Gynecology, 125*(1), 124-131.

Leung, C., Saaid, R., Pedersen, L., Park, F., Poon, L., & Hyett, J. (2015). Demographic factors that can be used to predict early-onset pre-eclampsia. *J Matern Fetal Neonatal Med, 28*(5), 535-539.

Levine, R. J., Hauth, J. C., Curet, L. B., Sibai, B. M., Catalano, P. M., Morris, C. D., et al. (1997). Trial of calcium to prevent preeclampsia. *N Engl J Med, 337*, 69-76.

Levine, R. J., & Karumanchi, S. A. (2005). Circulating angiogenic factors in preeclampsia. *Clin Obstet Gynecol, 48*(2), 372-386.

Levine, R. J., Maynard, S. E., Qian, C., Lim, K. H., England, L. J., Yu, K. F., et al. (2004). Circulating angiogenic factors and the risk of preeclampsia. *N Engl J Med, 350*(7), 672-683.

Lisonkova, S., & Joseph, K. S. (2013). Incidence of preeclampsia: Risk factors and outcomes associated with early- versus late-onset disease. *Am J Obstet Gynecol, 209*(6), 544.e541-544.e512.

Liu, X., Ruan, Y., Liu, Y., & Zhang, W. (2015). Relationship between maternal age and hypertensive disorders in pregnancy. *Zhonghua Yi Xue Za Zhi, 95*(1), 19-22.

Liu, X., Zou, L., Chen, Y., Ruan, Y., Liu, Y., & Zhang, W. (2014). Effects of maternal age on pregnancy: A retrospective cohort study. *Zhonghua Yi Xue Za Zhi, 94*(25), 1984-1988.

Ludwig, D. S. (2002). The glycemic index: Physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. *JAMA, 287*, 2414-2423.

Luo, Z.-C., An, N., Xu, H.-R., Larante, A., Audibert, F., & Fraser, W. D. (2007). The effects and mechanisms of primiparity on the risk of pre-eclampsia: A systematic review. *Paediatr Perinat Epidemiol, 21*, 36-45.

Lynch, A. M., Eckel, R. H., Murphy, J. R., Gibbs, R. S., West, N. A., Giclas, P. C., et al. (2012). Prepregnancy obesity and complement system activation in early pregnancy and the subsequent development of preeclampsia. *Am J Obstet Gynecol, 206*(5), 428 e421-428.

Magee, L. A., Pels, A., Helewa, M., Rey, E., & Von Dadelszen, P. (2014). Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy. *An International Journal of Women's Cardiovascular Health, 4*(2), 105-145.

Magee, L. A., Pels, A., Helewa, M., Rey, E., von Dadelszen, P., Audibert, F., et al. (2015). The hypertensive disorders of pregnancy. *Best Practice & Research Clinical Obstetrics & Gynaecology, 29*(5), 643-657.

Marcoux, S., Brisson, J., & Fabia, J. (1991). Calcium intake from dairy products and supplements and the risks of preeclampsia and gestational hypertension. *Am J Epidemiol, 133*(12), 1266-1272.

Mastrogiannis, D. S., Spiliopoulos, M., Mulla, W., & Homko, C. J. (2009). Insulin resistance: The possible link between gestational diabetes mellitus and hypertensive disorders of pregnancy. *Curr Diab Rep, 9*(4), 296-302.

Maternal and Reproductive Health Division. (2013). *Maternal Death Review (MDR) in Myanmar*. Nay Pyi Taw.

Maton, A. (1993). *Human biology and health*. USA: Prentice Hall.

Mayret-Mesquiti, M., Perez-Mendez, O., & Rodriguez, M. E., et al. (2007). Hypertriglyceridemia is linked to reduced nitric oxide synthesis in women with hypertensive disorders of pregnancy. *Hypertens Pregnancy, 26*, 423-431.

McBride, C. A., Hale, S. A., Subramanian, M., Badger, G. J., & Bernstein, I. M. (2014). The relationship of a family history for hypertension, myocardial infarction, or stroke with cardiovascular physiology in young women. *Reprod Sci, 21*(4), 509-516.

McCarthy, F., & Kenny, L. C. (2015). Hypertension in pregnancy. *Obstetrics, Gynaecology & Reproductive Medicine, 25*(8), 229-235.

McCowan, L. M. E., Roberts, C. T., Dekker, G. A., Taylor, R. S., Chan, E. H. Y., Kenny, L. C., et al. (2010). Risk factors for small-for-gestational-age infants by customised birthweight centiles: Data from an international prospective cohort study. *BJOG: An International Journal of Obstetrics & Gynaecology, 117*(13), 1599-1607.

Meek, C. L., Murphy, H. R., & Simmons, D. (2016). Random plasma glucose in early pregnancy is a better predictor of gestational diabetes diagnosis than maternal obesity. *Diabetologia, 59*(3), 445-452.

Mehta, B., Kumar, V., Chawla, S., Sachdeva, S., & Mahopatra, D. (2015). Hypertension in pregnancy: A community based study. *Indian J Community Med., 40*(4), 273-278.

Metzger, B. E., Buchanan, T. A., Coustan, D. R., De Leiva, A., Dunger, D. B., Hadden, D. R., et al. (2007). Summary and recommendations of the fifth international workshop-conference on gestational diabetes mellitus. *Diabetes Care, 30*(Supplement 2), S251-S260.

Metzger, B. E., Coustan, D. R., & Committee, O. (1998). Summary and recommendations of the fourth international workshop-conference on gestational diabetes mellitus. *Diabetes Care, 21,* B161.

Mijal, R. S., Holzman, C. B., Rana, S., Karumanchi, S. A., Wang, J., & Sikorskii, A. (2011). Midpregnancy levels of angiogenic markers in relation to maternal characteristics. *Am J Obstet Gynecol, 204*(3), 244.e241-244.e212.

Ministry of Health. (2008). *Myanmar country report to the 6th ASEAN & Japan high level officials meeting on caring societies: "Healthy Next Generation" under the tight collaboration between health and social welfare*. Retrieved June 6, 2016, from http://www.mhlw.go.jp/ bunya/kokusaigyomu/asean/ asean/kokusai/ siryou/dl/h20_myanmar.pdf

Misra, A. (2015). Ethnic specific criteria for classification of body mass index: A perspective for Asian Indians and American Diabetes Association position statement. *Diabetes Technol Ther, 17*(9), 667-671.

Møller, N., Gormsen, L., Fuglsang, J., & Gjedsted, J. (2003). Effects of ageing on insulin secretion and action. *Hormone Research in Paediatrics, 60(suppl 1)*(Suppl. 1), 102-104.

Mongeau, J. G. (1987). Heredity and blood pressure in humans: An overview. *Pediatr Nephrol, 1*(1), 69-75.

Moraes, R. S., Fuchs, F. D., Dalla Costa, F., & Moreira, L. B. (2000). Familial predisposition to hypertension and the association between urinary sodium excretion and blood pressure in a population-based sample of young adults. *Braz J Med Biol Res, 33*(7), 799-803.

Morgan, L., Svyatova, G., Zakhidova, N., & Walker, J. (2015). Clinical features of pre-eclampsia in 2613 Central Asian women and babies recruited for genetic studies. *An International Journal of Women's Cardiovascular Health, 5*(1), 26-27.

Morikawa, M., Cho, K., Yamada, T., Yamada, T., Sato, S., & Minakami, H. (2012). Risk factors for eclampsia in Japan between 2005 and 2009. *Int J Gynaecol Obstet, 117*(1), 66-68.

Moussa, H. N., & Sibai, B. M. (2015). Hypertensive disorders in pregnancy complicated by diabetes. In O. Langer (Ed.), *The diabetes in pregnancy dilemma* (2nd ed.). USA: People's Medical Publishing House.

Moyer, V. A. (2014). Screening for gestational diabetes mellitus: US Preventive Services Task Force recommendation statement. *Annals of internal medicine, 160*(6), 414-420.

Mukhopadhyay, A., Sharma, P., Dasgupta, S., Dasgupta, S., Sharma, P. P., & Ghosh, T. K. (2012). Prediction of pre-eclampsia: Comparative analysis of two screening tests. *J Indian Med Assoc, 110*(8), 546-547.

Myatt, L., Clifton, R. G., Roberts, J., Spong, C. Y., Wapner, R. J., Thorp, J., et al. (2013). Can changes in angiogenic biomarkers between the first and second trimesters of pregnancy predict development of pre-eclampsia in a low-risk

nulliparous patient population? *BJOG: An International Journal of Obstetrics & Gynaecology, 120*(10), 1183-1191.

National Collaborating Centre for Women's and Children's Health. (2010). NICE clinical guideline *Hypertension in Pregnancy: The management of hypertensive disorders during pregnancy*. London: RCOG Press.

National Diabetes Data Group. (1979). Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes, 28*(12), 1039-1057.

National Institute for Health and Clinical Excellence. (2014). Hypertension in pregnancy pathway. Retrieved May 12, 2015, from http:// pathways. nice. org.uk/pathways /hypertension-in-preg nancy.

Naw Mary Paw. (1995). *The study of hypertensive disorders in pregnancy in North Okkalapa General Hospital*. Unpublished master degree thesis, University of Medicine (2),Yangon.

Nerenberg, K., Daskalopoulou, S. S., & Dasgupta, K. (2014). Gestational diabetes and hypertensive disorders of pregnancy as vascular risk signals: An overview and grading of the evidence. *Canadian Journal of Cardiology, 30*(7), 765-773.

Niromanesh, S., Laghaii, S., & Mosavi-Jarrahi, A. (2001). Supplementary calcium in prevention of pre-eclampsia. *International Journal of Gynecology & Obstetrics, 74*, 17-21.

Nolan, C. J. (2011). Controversies in gestational diabetes. *Best Pract Res Clin Obstet Gynaecol, 25*(1), 37-49.

North Okkalapa General Hospital. (2013). *Unpublished data for incidence of hypertensive disorders of pregnancy*. Yangon.

North, R. A., McCowan, L. M. E., Dekker, G. A., Poston, L., Chan, E. H. Y., Stewart, A. W., et al. (2011). Clinical risk prediction for pre-eclampsia in nulliparous women: Development of model in international prospective cohort. *BMJ, 342*.

Ogden, C. L., Carroll, M. D., Kit, B. K., & Flegal, K. M. (2014). Prevalence of childhood and adult obesity in the United States, 2011-2012. *JAMA, 311*(8), 806-814.

Panel, I. C. (2010). International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care, 33*(3), 676-682.

Phaloprakarn, C., Tangjitgamol, S., & Manusirivithaya, S. (2009). A risk score for selective screening for gestational diabetes mellitus. *Eur J Obstet Gynecol Reprod Biol, 145*(1), 71-75.

Poon, L. C. Y., Kametas, N. A., Chelemen, T., Leal, A., & Nicolaides, K. H. (2010). Maternal risk factors for hypertensive disorders in pregnancy: A multivariate approach. *J Hum Hypertens, 24*(2), 104-110.

Póvoa, A. M., Costa, F., Rodrigues, T., Patrício, B., & Cardoso, F. (2008). Prevalence of hypertension during pregnancy in Portugal. *Hypertens Pregnancy, 27*(3), 279-284.

Qiu, C., Coughlin, K. B., Frederick, I. O., Sorensen, T. K., & Williams, M. A. (2008). Dietary fiber intake in early pregnancy and risk of subsequent preeclampsia. *Am J Hypertens., 21*, 903-909.

Raghupathy, R. (2010). A role for the immune system in the etiology of pre-eclampsia. *Kuwait Medical Journal, 42*(4), 270-276.

Redman, C. W., & Sargent, I. L. (2007). Immunological factors and placentation: Implications for pre-eclampsia. In F. Lyall & M. Bellfort (Eds.), *Preeclampsia: Etiology and Clinical practice.* (pp. 103-115). New York: Cambridge University Press.

Redman, C. W. G., Sargent, I. L., & Taylor, R. N. (2015). Immunology of normal pregnancy and preeclampsia. In R. N. Taylor, J. M. Roberts, F. G. Cunningham, & M. D. Lindheimer (Eds.), *Chesley's Hypertensive Disorders in Pregnancy* (4th ed.) (pp. 161-179). San Diego: Academic Press.

Register Nurse Association of Ontario. (2005). Nursing management of hypertension. Retrieved July 10, 2016, from http://rnao.ca/sites/rnao-ca/files/Nursing_Management_of_Hypertension.pdf

Rich-Edwards, J. W., Ness, R. B., & Roberts, J. M. (2015). Epidemiology of pregnancy-related hypertension. In R. N. Taylor, J. M. Roberts, F. G.

Cunningham, & M. D. Lindheimer (Eds.), *Chesley's Hypertensive Disorders in Pregnancy* (4th ed.) (pp. 37-55). San Diego: Academic Press.

Roberts, J. M., & Bodnar, L. M. (2007). Report on the WIC nutrition risk criterion for hypertension in pregnancy. Retrived August 7, 2015, from https://www.cdph.ca.gov/programs/wicworks/Documents/WPM/WIC-PEPB-Expert Report.pdf

Roberts, J. M., Bodnar, L. M., Patrick, T. E., & Powers, R. W. (2011). The role of obesity in preeclampsia. *Pregnancy Hypertens, 1*(1), 6-16.

Roberts, J. M., Cunningham, F. G., & Lindheimer, M. D. (2015). *Chesley's Hypertensive Disorders in Pregnancy* (4th ed.). San Diego: Academic Press.

Roberts, J. M., & Hubel, C. A. (1999). Is oxidative stress the link in the two-stage model of pre-eclampsia? *Lancet Glob Health, 354*, 788-789.

Roberts, J. M., & Hubel, C. A. (2009). The two stage model of preeclampsia: Variations on the theme. *Placenta* (Suppl A), S32-37.

Roes, E. M., Sieben, R., Raijmakers, M. T., Peters, W. H., & Steegers, E. A. (2005). Severe preeclampsia is associated with a positive family history of hypertension and hypercholesterolemia. *Hypertens Pregnancy, 24*(3), 259-271.

Sacks, F. M., & Kass, E. H. (1988). Low blood pressure in vegetarians: Effects of specefic foods and nutrients. *Am J Clin Nuir, 48*, 795-800.

Savica, V., Bellinghieri, G., & Kopple, J. D. (2010). The effect of nutrition on blood pre-ssure. *Annu Rev Nutr, 30*, 365-401.

Savitz, D. A., Danilack, V. A., Engel, S. M., Elston, B., & Lipkind, H. S. (2014). Descriptive epidemiology of chronic hypertension, gestational hypertension, and preeclampsia in New York State, 1995-2004. *Matern Child Health J, 18*(4), 829-838.

Saw-Lwin, Mary-Krasu, & Win-Pe. (2002). *A study on hypertensive disorders of pregnancy in Mandalay General Hospital for the year 1993*. Paper presented at the Myanmar Health Research Congress, Yangon.

Say, L., Chou, D., Gemmill, A., Tuncalp, O., Moller, A. B., Daniels, J., et al. (2014). Global causes of maternal death: A WHO systematic analysis. *Lancet Glob Health, 2*(6), e323-333.

Schneider, S., Freerksen, N., Rohrig, S., Hoeft, B., & Maul, H. (2012). Gestational diabetes and preeclampsia-similar risk factor profiles? *Early Hum Dev, 88*(3), 179-184.

Scott-Pillai, R., Spence, D., Cardwell, C. R., Hunter, A., & Holmes, V. A. (2013). The impact of body mass index on maternal and neonatal outcomes: A retrospective study in a UK obstetric population, 2004-2011. *BJOG, 120*(8), 932-939.

Shankar, S. S., & Steinberg, H. O. (2013). Insulin resistance and hypertension. In A. C. Koch & P. G. Chrousos (Eds.), *Endocrine Hypertension: Underlying Mechanisms and Therapy* (pp. 239-250). Totowa: Humana Press.

Shin, D., & Song, W. O. (2015). Prepregnancy body mass index is an independent risk factor for gestational hypertension, gestational diabetes, preterm labor, and small- and large-for-gestational-age infants. *J Matern Fetal Neonatal Med, 28*(14), 1679-1686.

Singh, M., Pathak, M. S., & Paul, A. (2015). A study on atherogenic indices of pregnancy induced hypertension patients as compared to normal pregnant women. *Journal of clinical and diagnostic research: JCDR, 9*(7), BC05.

Singh, R. (2013). Hypertensive disorders in pregnancy. *Clinical Queries: Nephrology, 2*(2), 47-55.

Singh, S. K., & Rastogi, A. (2008). Gestational diabetes mellitus. *Clinical Researh & Reviews, 2,* 227-234.

Skajaa, K., Dorup, I., & Sandstrom, B. M. (1991). Magnesium intake and status and pregnancy outcome in a Danish population. *Br J Obstet Gynaecol., 98,* 919-928.

Stella, M. Y., & Nagey, D. A. (1992). Validity of self-reported pregravid weight. *Ann Epidemiol, 2*(5), 715-721.

Stuebe, A. M., Landon, M. B., Lai, Y., Spong, C. Y., Carpenter, M. W., Ramin, S. M., et al. (2012). Maternal BMI, glucose tolerance, and adverse pregnancy outcomes. *Am J Obstet Gynecol, 207*(1), 62.e61-67.

Susser, M. (1981). Review of dietary behavior during pregnancy. In J. Dobbing (Ed.), *Maternal Nutrition in Pregnancy: Eating for Two?* (pp. 64-65). Landon: Academic Press.

Swe Swe Hlaing. (2001). *Pregnancy outcome among nulliparous and multiparous women with pre-eclampsia*. Unplished master degree thesis, University of Medicine (1), Yangon.

Syngelaki, A., Pastides, A., Kotecha, R., Wright, A., Akolekar, R., & Nicolaides, K. H. (2015). First trimester screening for gestational diabetes mellitus based on maternal characteristics and history. *Fetal Diagn Ther, 38*(1), 14-21.

Tebeu, P. M., Foumane, P., Mbu, R., Fosso, G., Biyaga, P. T., & Fomulu, J. N. (2011). Risk factors for hypertensive disorders in pregnancy: A report from the Maroua Regional Hospital, Cameroon. *J Reprod Infertil, 12*(3), 227-234.

Thadhani, R., Mutter, W. P., Wolf, M., Levine, R. J., Taylor, R. N., Sukhatme, V. P., et al. (2004). First trimester placental growth factor and soluble fms-like tyrosine kinase 1 and risk for preeclampsia. *J Clin Endocrinol Metab, 89*(2), 770-775.

Than Than Oo. (2001). *Determinants of hypertensive disorders of pregnancy in Mandalay General Hospital*. Unpublished master degree thesis, University of Medicine, Mandalay.

Tihtonen, K. M., Koobi, T., & Uotila, J. T. (2006). Arterial stiffness in preeclamptic and chronic hypertensive pregnancies. *Eur J Obstet Gynecol Reprod Biol, 128*(1-2), 180-186.

Tilg, H., & Moschen, A. R. (2006). Adipocytokines: Mediators linking adipose tissue, inflammation and immunity. *Nat Rev Immunol, 6*, 772-783.

Tranquilli, A. L., Dekker, G., Magee, L., Roberts, J., Sibai, B. M., Steyn, W., et al. (2014). The classification, diagnosis and management of the hypertensive disorders of pregnancy: A revised statement from the ISSHP. *Pregnancy Hypertens, 4*(2), 97-104.

Trogstad, L., Magnus, P., & Stoltenberg, C. (2011). Pre-eclampsia: Risk factors and causal models. *Best Practice & Research Clinical Obstetrics & Gynaecology, 25*(3), 329-342.

Trumbo, P. R., & Ellwood, K. C. (2007). Supplemental calcium and risk reduction of hypertension, pregnancy-induced hypertension, and preeclampsia: An evidence-based review by the US Food and Drug Administration. *Nutr Rev, 65*, 78-87.

UNFPA. (2010). *Report on situation analysis of population and development, reproductive health and gender in Myanmar*. Retrieved June 11, 2015, from http://yangon.sites.unicnetwork.org/files/2013/05/july-2010-Report-on-Situation-Analysis-UNFPA.pdf

Vadachkoria, S., Woelk, G. B., & Mahomed, K. (2006). Elevated soluble vascular cell adhesion molecule-1, elevated homocystinemia, and hypertriglyceridemia in relation to preeclampsia risk. *Am J Hypertens., 19*, 235-242.

Van Gaal, L. F., Mertens, I. L., & De Block, C. E. (2006). Mechanisms linking obesity with cardiovascular disease. *Nature, 444*, 875–880.

van Leeuwen, M., Opmeer, B. C., Yilmaz, Y., Limpens, J., Serlie, M. J., & Mol, B. W. J. (2011). Accuracy of the random glucose test as screening test for gestational diabetes mellitus: A systematic review. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 154*(2), 130-135.

van Leeuwen, M., Opmeer, B. C., Zweers, E. J., van Ballegooie, E., ter Brugge, H. G., de Valk, H. W., et al. (2010). Estimating the risk of gestational diabetes mellitus: A clinical prediction model based on patient characteristics and medical history. *BJOG, 117*(1), 69-75.

Van Oostwaard, M., Langenveld, J., Bijloo, R., Wong, K., Scholten, I., Loix, S., et al. (2012). Prediction of recurrence of hypertensive disorders of pregnnacy between 34 and 37 weeks of gestation: Retrospective cohort study. *BJOG, 119*, 840-847.

Vest, A. R., & Cho, L. S. (2014). Hypertension in pregnancy. *Curr Atheroscler Rep, 16*(3), 395.

Villar, J., Abdel-Aleem, H., Merialdi, M., Mathai, M., Ali, M. M., Zavaleta, N., et al. (2006). World Health Organization randomized trial of calcium supplementation among low calcium intake pregnant women. *Am J Obstet Gynecol, 194*(3), 639-649.

Villar, J., Repke, J., Belizan, J. M., & Pareja, G. (1987). Calcium supplementation reduces blood pressure during pregnancy: Results of a randomized controlled clinical trial. *Obstet Gynecol, 70*(3 Pt 1), 317-322.

Vintzileos, A. M., & Ananth, C. V. (2014). First trimester prediction of ischemic placental disease. *Semin Perinatol, 38*(3), 159-166.

Visser, G. H. A., & de Valk, H. W. (2013). Is the evidence strong enough to change the diagnostic criteria for gestational diabetes now? *American Journal of Obstetrics & Gynecology*, *208*(4), 260-264.

Vogel, J. P., Souza, J. P., Mori, R., Morisaki, N., Lumbiganon, P., Laopaiboon, M., et al. (2014). Maternal complications and perinatal mortality: Findings of the World Health Organization Multicountry Survey on maternal and newborn health. *BJOG, 121 Suppl 1*, 76-88.

Wallis, A. B., & Saftlas, A. F. (2008). A gram of prevention: A modest increase in fiber consumption may reduce risk of preeclampsia. *American Journal of Hypertension, 21*(8), 849-850.

Werner, E. F., Pettker, C. M., Zuckerwise, L., Reel, M., Funai, E. F., Henderson, J., & Thung, S. F. (2012). Screening for gestational diabetes mellitus: Are the criteria proposed by the International Association of the Diabetes and Pregnancy Study Groups cost-effective? *Diabetes Care, 35*(3), 529-535.

Whelton, S. P., Hyre, A. D., Pedersen, B., Yi, Y., Whelton, P. K., & He, J. (2005). Effect of dietary fiber intake on blood pressure: A meta-analysis of randomized, controlled clinical trials. *J Hypertens, 23*, 475-481.

Wolf, M., Sandler, L., Munoz, K., Hsu, K., Ecker, J. L., & Thadhani, R. (2002). First trimester insulin resistance and subsequent preeclampsia: A prospective study. *J Clin Endocrinol Metab, 87*, 1563-1568.

Wolf, M., Shah, A., Lam, C., Martinez, A., Smirnakis, K. V., Epstein, F. H., et al. (2005). Circulating levels of the antiangiogenic marker sFLT-1 are increased in first versus second pregnancies. *Am J Obstet Gynecol, 193*(1), 16-22.

World Health Organization. (2004). Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies: WHO expert consultation. *Lancet, 363*(9403), 157-163.

World Health Organization. (2009). *STEPwise approach to chronic disease risk factor surveillance*. Retrieved August 14, 2015, from http://www. who.int/ chp/ steps/ myanmar/en/

World Health Organization. (2010). *Package of interventions for family planning, safe abortion care, maternal, newborn and child health*. Retrieved June 16, 2015, from http://www.clacaidigital.info:8080/xmlui/handle/123456789/ 307

World Health Organization. (2011). *WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia*. Retrieved June 7, 2015, from http:// www.ncbi.nlm.nih.gov/books/NBK140561/

World Health Organization. (2013). *Diagnostic criteria and classification of hyperglycemia first detected in pregnancy*. Retrieved January 1, 2015, fromhttp://apps.who.int/iris/bitstream/10665/85975/1/WHO_NMH_MND_ 13.2_eng.pdf

World Health Organization. (2014). *WHO country cooperation strategy, Myanmar, 2014-2018*. Retrieved June 11, 2015, from http://www.searo. who.int/ myanmar/ CCS_Myanmar.pdf?ua=1

World Health Organization. (2015). Obesity and overweight. Retrieved August 7, 2015, from http //www.who.int/mediacentre/ factsheets/ fs311/en/ index. html

World Health Organization. (2016). Global Health Observatory (GHO) data: Overweight and obesity. Retrieved June 14, 2016, from http://www. who. int/gho/ncd/ risk_factors/ overweight/en/

Wright, D., Syngelaki, A., Akolekar, R., Poon, L. C., & Nicolaides, K. H. (2015). Competing risks model in screening for preeclampsia by maternal characteristics and medical history. *Am J Obstet Gynecol, 213*, 62.e61-10.

Yang, J. J., Lee, S., Choi, J., Song, M., Han, S., Yoon, H., et al. (2015). Subsequent risk of metabolic syndrome in women with a history of preeclampsia: Data from the Health Examinees Study. *J Epidemiol, 25*(4), 281-288.

Ye, C., Ruan, Y., Zou, L., Li, G., Li, C., Chen, Y., et al. (2014). The 2011 survey on hypertensive disorders of pregnancy in China: Prevalence, risk factors, omplications, pregnancy and perinatal outcomes. *PLoS One, 9*(6), e100180.

APPENDICES

APPENDIX A
PARTICIPANT INFORMATION SHEET

In this document, there may be some statements that you do not understand. Please ask the researcher or her representative to give you explanations until you are well understood.

Title of Research Project: Risk Factors of Hypertensive Disorders in Myanmar Pregnant Women

Researcher : Miss Ei Wah Phyu Thet

Research Site 1) Antenatal Clinic of Central Women Hospital, Yangon, Myanmar.Tel. 951 222804, 951 222805

2) Antenatal Clinic of North Okkalapa General Hospital, Yangon, Myanmar. Tel. 959 690295, 959 699422

Work Address : Nursing Related Field Practice Training School, Dagon (East) Township, Yangon Division, Myanmar

: Faculty of Nursing, Mahidol University, 2 Wang Lang Rd, Bangkoknoi District, Bangkok, Thailand

Source of Fund : Self-funding

This research project aims to identify the significant risk factors that contribute to hypertensive disorders in Myanmar pregnant women depending on extreme age, nulliparity, high body mass index $\geq$ 23kg/m^2, family history of hypertension and gestational diabetes mellitus.

The expected benefits are as follows: it is likely to yield general knowledge for pregnant women regarding hypertensive disorders. It will be useful in recognizing risk factors for hypertensive disorders in pregnant women.

The risks resulting from participating in the study are not greater than minimal. The foreseeable risks are as follows; it will consume the times of

participants, and you may feel discomfort to answer the questionnaire. In addition, you may miss an opportunity for the routine antenatal care services.

You are assured that you can stop the completing questionnaire and withdraw from participating in the study at anytime of data collection. The data will be collected in the private room with adequate facilities such as chair, water, fan and toileting facilities. To prevent from missing an opportunity for routine antenatal care services, the data collection will be commenced after you have received all antenatal care procedure. To prevent the development of serious complications, you are observed by the researcher and the research assistant while collecting the data. If you are suffering headache, blurred vision, faint, discomfort, or other unusual symptoms from your current hypertension, complain to the researcher immediately. The researcher will check your blood pressure, and notify the obstetrician and medical team immediately.

You are invited to participate in this research project because you are the pregnant women who meet the criteria of the study such as singleton pregnancy with gestational age between 36 to 42 weeks. An estimated 388 pregnancy will be participated in this study. The time of participating will approximately be about 45 minutes.

Participation of the study is voluntary. You have the right to withdraw from the project at anytime without prior notice. If you do not participate in this research project, you will receive a standard assessment and treatment.

The participant is not responsible for any expense to participate in this research.

If you decide to participate in the research project, you will go through the following procedure, you have to complete personal data questionnaire, and it will take your time about 15 to 20 minutes. When responding to questions, you can answer freely and sincerely based on your actual experiences. You can ask the researcher for any unclear questions at any time when filling out the experiences.

The participant’s private information will be kept confidential, it will not be subject to an individual disclosure, but will be included in the research report as part of the overall results. Individual information may be examined by the researcher, the supervisor, and the members of ethics committees.

If you have any questions about this research please feel free to contact the following person; the researcher- Miss Ei Wah Phyu Thet, Telephone: 959 73100735, 669 84428950, Email: eiwah.phy@student.mahidol.ac.th

The research project is approved by The Institutional Review Boards, Faculty of Nursing (IRB-NS) at the office of IRB-NS room 503 5th floor, Faculty of Nursing, Mahidol University, 999 Phuttamonthon 4 Road, Salaya, Nakhon Pathom 73170 Thailand. Tel: 66 2 441 5333 ext.2531, 2532. Fax: 66 2 441 5333 ext 2531. Email: nsirbnursing@mahidol.ac.th, ns.irbnursing@gmail.com

Also, the research project is approved by Ethical and Research Committee, University of Nursing, Yangon. Address: No.677/709, Bogyoke Aung San Road, Lanmadaw Township, Yangon, The Republic of the Union of Myanmar Tel: 01-222 883, 222 884. Fax: 227449 Email: ionygn@mptmail.net.mm

On the condition that I am not treated as indicated in the information sheet distributed to the subjects, I can contact the Chair, or the representative of the IRB-NS, Bangkok and ERC-UON, Yangon at the contact address presenting above.

I thoroughly read the details in this document.

Signature……..……. Participant

Name……..……..

Date ……/……/……..

PARTICIPANT INFORMATION SHEET (MYANMAR VERSION)

သုတေသနစီမံချက်နှင့်ပတ်သက်သောအကြောင်းအရာအချက်အလက်များ

မရှင်းလင်းသည့် အကြောင်းအရာအချက်အလက်များရှိပါက သုတေသနပြုသူ (သို့) ကိုယ်စားလှယ်အား မေးမြန်းနိုင်ပါသည်။

သုတေသနခေါင်းစဉ် - မြန်မာလူမျိုးကိုယ်ဝန်ဆောင်မိခင်များတွင် ကိုယ်ဝန်ဆောင်စဉ် သွေးတိုးခြင်းနှင့် ပတ်သက်သောနောက်ဆက်တွဲရောဂါ အန္တရာယ် ဖြစ်စေနိုင်သော အချက်များ

သုတေသနပြုသူ - ဒေါ်အိဝါဖြူသက်

သုတေသနပြုလုပ်မည့်နေရာ ၁။ ကိုယ်ဝန်ဆောင်စောင့်ရှောက်မှုပြင်ပလူနာဌာန၊ ဗဟိုအမျိုးသမီးဆေးရုံကြီး၊ ရန်ကုန်တိုင်းဒေသကြီး။
တယ်လီဖုန်း- ၉၅၁၂၂၈၀၄၊ ၉၅၁ ၂၂၈၀၅

၂။ ကိုယ်ဝန်ဆောင်စောင့်ရှောက်မှုပြင်ပလူနာဌာန၊ မြောက်ဥက္ကလာပ အထွေထွေရောဂါကုဆေးရုံကြီး ရန်ကုန်တိုင်းဒေသကြီး။
တယ်လီဖုန်း- ၉၅၉ ၆၉၀၂၉၅၊ ၉၅၉ ၆၉၉၄၂၂

အလုပ်တည်နေရာ ၁။ သူနာပြုနှိုးနွယ်ကွင်းဆင်းလေ့ကျင့်သင်တန်းကျောင်း၊ ဒဂုံမြို့သစ်အရှေ့ပိုင်းမြို့နယ်၊ ရန်ကုန်တိုင်းဒေသကြီး

၂။ သူနာပြုဌာနကြီး၊ မဟီဒေါတက္ကသိုလ်၊ အမှတ် ၂ ၊ ဝန်းလန်လမ်း၊ ဘန်ကောက်နွိုင်း၊ ဘန်ကောက်မြို့၊ ထိုင်းနိုင်ငံ။

တယ်လီဖုန်း- ၀၆၆ ၉ ၈၄၄၂၈၉၅၀ ၊ ၀၉၅ ၉ ၇၃၁၀၀၇၃၅

အထောက်အပံ - သုတေသနပြုသူ

ဤသုတေသနစာတမ်းသည် မြန်မာလူမျိုး ကိုယ်ဝန်ဆောင်မိခင်များတွင် သွေးတိုးခြင်းနှင့်ပတ်သက်သော နောက်ဆက်တွဲရောဂါအန္တရာယ် ဖြစ်စေနိုင်မည့် အချက်များ (ကိုယ်အလေးချိန်အညွှန်းကိန်း၊ အသက်၊ သားဦးရေ၊ ကိုယ်ဝန်ဆောင်စဉ် ဆီးချိုရောဂါဖြစ်ခြင်း၊ နှင့် မိသားစုတွင်သွေးတိုးရောဂါ ဖြစ်ခြင်း) ကိုလေ့လာဆန်းစစ်ရန် ရည်ရွယ် ပါသည်။

ဤသုတေသနမှ ရရှိလာမည့် သတင်း အချက်အလက်များသည် မြန်မာနိုင်ငံရှိ ကိုယ်ဝန်ဆောင်မိခင်များတွင် သွေးတိုးခြင်းနှင့်ပတ်သက်သော နောက်ဆက်တွဲရောဂါများ နှင့်ပတ်သက်၍ ဗဟုသုတများရရှိရန် ရည်ရွယ်ပါသည်။ ကိုယ်ဝန်ဆောင်စဉ်သွေးတိုးခြင်းနှင့် ပတ်သက်သော နောက်ဆက်တွဲ ရောဂါများ ဖြစ်ပေါ်စေနိုင်သော အန္တရာယ်အချက် အလက်များ ကိုသတိပြုမိစေရန် ဖြစ်ပါသည်။

လူကြီးမင်းအနေဖြင့် မေးခွန်းများအားဆက်လက်ဖြေဆိုရန် ရပ်ဆိုင်းခြင်း နှင့် သုတေသနမှ နှုတ်ထွက်ခြင်းအား မည်သည့်အချိန်တွင်မဆို ပြုလုပ်နိုင်ပါသည်။ သုတေသန အချက်အလက်များ ကောက်ယူခြင်းအား ကိုယ်ဝန်ဆောင်စောင့်ရှောက်မှု ခံယူပြီးချိန်မှသာ အခြားသီးသန့်ခန်းတွင် ပြုလုပ်မည်ဖြစ်ပါသည်။ သုတေသနအချက်အလက်များ ကောက်ယူနေစဉ်အတွင်း ခေါင်းကိုက်ခြင်း၊ မူးဝေခြင်း၊ မသက်သာဖြစ်ခြင်းနှင့် ပုံမှန်မဟုတ်သော ရောဂါလက္ခဏာများဖြစ်ပေါ်လာပါက တာဝန်ကျန်းမာရေးဝန်ထမ်းများထံ သတင်းပို့၍ လိုအပ်သောစစ်ဆေးကုသမှုများအား ချက်ချင်း ပြုလုပ်ပေးမည် ဖြစ်ပါသည်။

လူကြီးမင်းသည် သုတသနတွင်ပါဝင်ရန် သတ်မှတ်ထားသော စံချိန်စံညွှန်းများ (ကိုယ်ဝန်သက် ၃၆ ပတ်မှ ၄၂ ပတ်အတွင်း၊ သန္ဓေသားတဦးတည်း ကိုယ်ဝန်ဆောင်ဖြစ်ခြင်း အစရှိသည်) နှင့် ကိုက်ညီသူဖြစ်ပါသည်။ ဤသုတေသနတွင် စုစုပေါင်းကိုယ်ဝန်ဆောင် ၃၈၈ ဦးပါဝင်မည်ဖြစ်ပါသည်။ သုတေသနတွင် ပါဝင်ရမည့် ကြာမြင့်ချိန်မှာ ၄၅ မိနစ်ခန့် ဖြစ်ပါသည်။

ဤသုတေသနတွင်ပါဝင်ရန် လူကြီးမင်း၏ သဘောဆန္ဒအရသာ ဖြစ်၍ အချိန်မရွေး နုတ်ထွက်နိုင်ပါသည်၊ သုတေသနတွင် ပါဝင်ရန် ငြင်းဆို/နုတ်ထွက် ပါကလည်း ကိုယ်ဝန်ဆောင် စောင့်ရှောက်မှုအား စံချိန်စံညွှန်းနှင့် အညီရရှိမည် ဖြစ်ပါသည်။

လူကြီးမင်းအနေဖြင့် ဤသုတေသနနှင့်ပတ်သက်သော ကုန်ကျစရိတ်များ ကျခံရန် မလိုအပ်ပါ။

ဤသုတေသနစီမံချက်တွင် လူကြီးမင်းအနေဖြင့် ပါဝင်ရန်သဘောတူပါက မေးခွန်းလွှာပေးဝေ၍ မေးခွန်းများကို ၁၅ မိနစ်မှ မိနစ် ၂၀ ခန့် ဖြေကြားပေးရမည် ဖြစ်ပါသည်။ မေးခွန်းများကို ဖြေဆိုရာတွင် မိမိ၏အမှန်တကယ် အချက်အလက်များကို အခြေခံ၍ လွတ်လပ်ပွင့်လင်းစွာ ဖြေဆိုနိုင်ပါသည်။ မေးခွန်းများကို ဖြေဆိုစဉ် မရှင်းလင်းသည့် အချက်အလက်များ ရှိပါကလည်း သုတေသနပြုသူအား အချိန်မရွေး မေးမြန်းနိုင်ပါသည်။

ကောက်ယူရရှိသည့် သတင်းအချက်အလက်များကိုလည်း လျှို့ဝှက်စွာ ထိန်းသိမ်း ထားရှိမည် ဖြစ်ပါသည်။ ဤစီမံချက်တွင်ပါဝင်သော သုတေသနပြုသူနှင့် ကြီးကြပ်သူ ဆရာများ မှအပ မည်သူတစ်ဦးတစ်ယောက်ကိုမျှ ဖတ်ရှု့စေမည်မဟုတ်ပါ။ ဤသုတေသန စီမံချက်မှလေ့လာတွေ့ရှိချက်များကို စာတမ်းရေးသားပြုစုပြီး ဆေးဘက်နှင့် သူနာပြုဆိုင်ရာ ညီလာခံများ၌ စာတမ်းတင်သွင်းခြင်း၊ ဆွေးနွေးတင်ပြခြင်း၊ ကျန်းမာရေးနှင့်နီးနွယ်သောဂျာနယ်များ၌ ရေးသားဖော်ပြခြင်းတို့ကို ပြုလုပ်သွားမည် ဖြစ်ပါသည်။ သို့ရာတွင် လူကြီးမင်း၏ အမည်နှင့် နေရပ်လိပ်စာတို့ကို လုံးဝ (လုံးဝ) ထုတ်ဖော် ရေးသားမည် မဟုတ်ပါ။

ဤသုတေသနပြုလုပ်ရန်အတွက် ထိုင်းနိုင်ငံ မဟီဒေါတက္ကသိုလ်၏ သုတေသန နှင့်ကျင့်ဝတ်ဆိုင်ရာ ကော်မတီ (အခန်း ၅၀၃၊ ၅ လွှာ၊ သူနာပြုဌာနကြီး၊

မဟီဒေါတက္ကသိုလ်၊ ဘန်ကောက်မြို့၊ ထိုင်းနိုင်ငံ၊ တယ်လီဖုန်းအမှတ် ၀၆၆ ၂ ၄၄၁ ၅၃၃၊ လိုင်းခွဲ-၂၅၃၁/ ၂၅၃၂၊ Email: nsirbnursing@mahidol.ac.th/ns.irbnursing @gmail.com) နှင့် ရန်ကုန် သူနာပြု တက္ကသိုလ်၏ သုတေသန နှင့်ကျင့်ဝတ်ဆိုင်ရာ ကော်မတီ (အမှတ် ၆၇၇/၇၀၉၊ ဗိုလ်ချုပ်အောင်ဆန်းလမ်း၊ လမ်းမတော်မြို့နယ်၊ ရန်ကုန်တိုင်းဒေသကြီး၊ တယ်လီဖုန်းအမှတ် ၀၁ ၂၂၂ ၈၈၃/ ၂၂၂၈၈၄၊ Email: ionygn@mptmail.net.mm) ထံမှ သဘောတူခွင့်ပြုမိန့် ရရှိခဲ့ပြီး ဖြစ်ပါသည်။

ဖော်ပြထားသည့် သုတေသနစီမံချက်နှင့် ပတ်သက်သော အကြောင်းအရာ အချက်အလက်များ အတိုင်း လိုက်နာဆောင်ရွက်ခြင်းမရှိပါက သုတေသနနှင့် ကျင့်ဝတ်ဆိုင်ရာ ကော်မတီသို့ အထက်ဖော်ပြပါ လိပ်စာများအတိုင်း ဆက်သွယ် နိုင်ပါသည်။

သေချာစွာ ဖတ်ရှုပြီး၍ နားလည်သဘောတူပါသည်။

သုတေသနတွင် ပါဝင်သူ၏ လက်မှတ် ----------

အမည် ----------

ရက်စွဲ ----------

APPENDIX B
CONSENT FORM FOR INFORMED AND VOLUNTARY PARTICIPATION IN RESEARCH

Date ……../……/……

My name is ---------- aged ---------- years old, now living at the address; No.---------- Road/ street ---------- Sub-district---------- District ---------- Province ---------- Postal code ---------- Contact no. ----------

I give my voluntary consent to participate as a subject in the research project entitled 'Hypertensive Disorders of Pregnancy in Myanmar Pregnant Women".

In doing so, I am informed of the background and purpose of research project; its procedural details to carry out or to be carried out; its expected benefits and foreseeable risks that may occur to the subjects, including methods to prevent and handle harmful consequences. I thoroughly read the detailed statements in the information sheet given to the research participants. I was also given explanations and my questions were answered by the researcher/ her representative of the research project.

I am aware of my right to further information concerning benefits and risks from the participation in the research project. I have the right to stop the answering questionnaire or withdraw from participating at anytime without prior notices. I have the right to receive a standard assessment and treatment although I stop the answering questionnaire or withdraw from participating in the research project. I have the right to complain the researcher or her representative if the symptoms of complications such as headache, faint or unusual symptoms that occurred during collecting the data. I have the right to receive standard assessment and treatment for these complications immediately. I consent to the researcher's use of my private information obtained in this research, but do not consent to an individual disclosure of private information. The information must be presented as part of the research results as a whole.

On the condition that I have any questions about the research procedures, or on the condition that I suffer from an undesirable side effect from this research, I can contact the Researcher- Miss Ei Wah Phyu Thet, Tutor, Nursing Related Field Practice Training School, East Dagon Township, Yangon. Tel: 959 73100735, 669 84428950, Email: eiwahphyuthet@gmail.com

On the condition that I am not treated as indicated in the information sheet distributed to the subject, I can contact the following addresses;

1) Chair of The Institutional Reviews Boards, Faculty of Nursing (IRB-NS) at the office of IRB-NS room 503 5th floor, Faculty of Nursing, Mahidol University, 999 Phuttamonthon 4 Road, Salaya, Nakhon Pathom 73170 Thailand Tel 66 2 441 5333 ext 2531, 2532 Fax 66 2 441 5333 ext 2531, Email: nsirbnursing@mahidol.ac.th, ns.irbnursing@gmail.com

2) Chair of Ethical and Research Committee, University of Nursing, Yangon. Address: No.677/709, Bogyoke Aung San Road, Lanmadaw Township, Yangon, The Republic of the Union of Myanmar Tel: 01-222 883, 222 884. Fax: 227449 Email: ionygn@mptmail.net.mm

I thoroughly understand the statement in the information sheet for the research subjects and in this consent form. I consent to participate in this research project voluntarily. I thereby give my consent.

Signature ……. (Participant)
Name ……..……..
Date...…../……/……..

In case that the participant is not literate, the reader of all the statements for the participants is (Mr./Mrs./Ms…….), who gives his/her signature as a witness.

Signature ……. (Participant)
Name ……..
Date ……../……/……..

CONSENT FORM FOR INFORMED AND VOLUNTARY PARTICIPATION IN RESEARCH (MYANMAR VERSION)

သုတေသနစီမံချက်တွင် ပါဝင်ရန်သဘောတူခြင်း

အမည် ---------- အသက် ------- နှစ်.....လ၊ နေရပ်လိပ်စာ-

အမှတ် ---------.လမ်း ---------- ရပ်ကွက် ----------

မြို့နယ် ---------- တိုင်းဒေသကြီး ----------

တယ်လီဖုန်းအမှတ် ----------

ကျွန်ုပ်သည် သုတေသနစီမံချက်၏ ရည်ရွယ်ချက်၊ သုတေသနလုပ်ဆောင်မည့် အစီအစဉ်များ၊ ရရှိမည့်အကျိုးကျေးဇူး၊ ဖြစ်ပေါ်နိုင်သောဆိုးကျိုးများ နှင့် ဖြေရှင်းပေးမည့် နည်းလမ်းများ၊ သုတေသနစီမံချက်နှင့်ပတ်သက်သော အကြောင်းအရာအချက်အလက် များကိုဖတ်ရှုပြီးနားလည် သဘောပေါက်ပါသည်။ မရှင်းလင်းသော အချက် များကိုလည်း ကျေနပ်မှုရရှိသည် အထိ မေးမြန်းသိရှိခဲ့ပါသည်။

ကျွန်ုပ်သည် မေးခွန်းများအား ဆက်လက်ဖြေဆိုရန် ရပ်ဆိုင်းခြင်း နှင့် သုတေသနမှ နုတ်ထွက်ခြင်း အားမည်သည့်အချိန်တွင်မဆို ပြုလုပ်နိုင်ပါသည်။ သုတေသနတွင် ပါဝင်ရန်ငြင်းဆို/နုတ်ထွက်ပါကလည်း ကိုယ်ဝန်ဆောင်စောင့်ရှောက်မှုအား စံချိန်စံညွှန်းနှင့်အညီ ရရှိမည် ဖြစ်ပါသည်။ သုတေသနနှင့်ပတ်သက်သောမေးခွန်းများ ဖြေဆိုနေချိန်အတွင်း ရုတ်တရက် ခေါင်းကိုက်ခြင်း၊ မူးဝေခြင်း၊ မသက်သာဖြစ်ခြင်းနှင့် ပုံမှန်မဟုတ်သော ရောဂါလက္ခဏာများ ဖြစ်ပေါ်လာပါက လိုအပ်သော စစ်ဆေးကုသမှုများ အားချက်ချင်းခံယူခွင့် ရှိပါသည်။ ကျွန်ုပ်၏အမည်နှင့် နေရပ်လိပ်စာတို့ကို ထုတ်ဖော် ရေးသားခြင်းမပြုပါက ဤသုတေသနအတွက် ကောက်ယူထားသည့် သတင်း အချက် အလက်များကို သုတေသန စာတမ်းရေးသားပြုစုရန် အတွက်လည်းကောင်း၊ ဆေးဘက်နှင့် သူနာပြုဆိုင်ရာညီလာခံများ၌ တင်ပြဆွေးနွေးရန် အတွက်လည်းကောင်း၊ ကျန်းမာရေးနှင့် နီးနွယ်သော ဂျာနယ်များ၌ ရေးသား ဖော်ပြရန်အတွက် လည်းကောင်း ကျွန်ုပ်သဘောတူ ပါသည်။

ကျွန်ုပ်သည် သုတေသနနှင့်ပတ်သက်၍ မရှင်းလင်းသော အချက်အလက် များ ရှိပါက(သို့) နောက်ဆက်တွဲဆိုးကျိုးများ ပေါ်ပေါက်လာပါက သုတေသနပြုသူ

ဒေါ်အိဝါဖြူသက်၊ နည်းပြ၊ သူနာပြုနှိုးနွယ် ကွင်းဆင်းလေ့ကျင့် သင်တန်း ကျောင်း၊ ဒဂုံမြို့သစ်(အရှေ့ပိုင်း)မြို့နယ်၊ ရန်ကုန်တိုင်းဒေသကြီး၊ တယ်လီဖုန်းအမှတ်-၀၉၅၉ ၇၃၁၀၀၇၃၅၊ ဝဖွ ၉ ၈၄၄၂၈၉၅၀၊ Email: eiwahphyuthet@gmail.com သို့ ဆက်သွယ်နိုင်ပါသည်။

ဖော်ပြထားသည့် သုတေသန စီမံချက်နှင့် ပတ်သက်သော အကြောင်းအရာ အချက်အလက်များအတိုင်းလိုက်နာဆောင်ရွက်ခြင်းမရှိပါက သုတေသနနှင့် ကျင့်ဝတ် ဆိုင်ရာကော်မတီသို့ အောက်ဖော်ပြပါလိပ်စာများအတိုင်းဆက်သွယ်နိုင်ပါသည်။

၁။ သုတေသန နှင့်ကျင့်ဝတ်ဆိုင်ရာ ကော်မတီ၊ အခန်း ၅၀၃၊ ၅ လွှာ၊ သူနာပြုဌာနကြီး၊ မဟီဒေါတက္ကသိုလ်၊ ဘန်ကောက်မြို့၊ ထိုင်းနိုင်ငံ၊ တယ်လီဖုန်းအမှတ် ဝဖွ ၂ ၄၄၁ ၅၃၃၃၊ လိုင်းခွဲ-၂၅၃၁/ ၂၅၃၂၊ Email: nsirbnursing@mahidol.ac.th/ ns.irbnursing@gmail.com

၂။ သုတေသန နှင့်ကျင့်ဝတ်ဆိုင်ရာ ကော်မတီ၊ သူနာပြုတက္ကသိုလ်၊ ရန်ကုန်၊ အမှတ် ၆၇၇/၇၀၉၊ ဗိုလ်ချုပ်အောင်ဆန်းလမ်း၊ လမ်းမတော်မြို့နယ်၊ ရန်ကုန်တိုင်း ဒေသကြီး၊ တယ်လီဖုန်းအမှတ် ၀၁ ၂၂၂ ၈၈၃/ ၂၂၂၈၈၄၊ Email: ionygn@ mptmail.net.mm

ကျွန်ုပ်သည် "ကိုယ်ဝန်ဆောင်စဉ် သွေးတိုးခြင်းနှင့် ပတ်သက်သော နောက်ဆက်တွဲ ရောဂါအန္တရာယ် ဖြစ်စေနိုင်သောအချက်များ" သုတေသန စီမံချက်တွင် ပါဝင်ရန် မိမိ၏ ဆန္ဒအလျောက်သဘောတူပါသည်။

သုတေသနတွင် ပါဝင်သူ၏ လက်မှတ် ----------
အမည် ----------
ရက်စွဲ ----------

အကယ်၍ သုတေသနတွင်ပါဝင်သူသည် စာရေးဖတ်ရန်အခက်အခဲရှိသူဖြစ်ပါက

အသိသက်သေ၏လက်မှတ် ----------
အမည် ----------
ရက်စွဲ ----------

APPENDIX C

THE PERSONAL DATA QUESTIONNAIRE

Code No. ---------- Date----------

PART I

Instruction: Please answer the questions according to your actual information by marking the sign (√) in the corresponding box provided or add answer in the space provided.

1. What is your age? _____ years _____ months

2. What is your race? _____

3. What is the highest level of education you have completed?
   (If currently enrolled, mark the highest degree received)

   ☐ elementary school or below ☐ middle school
   ☐ high school ☐ diploma or vocational training
   ☐ university, or higher

4. What type of job are you doing?

   ☐ homemaker ☐ employed for wages
   ☐ self-employed ☐ student
   ☐ others (specify) _____

5. What is your family income/month? _____ Kyats

6. How many times had you been pregnancy?

☐ never ☐ 1 time
☐ 2 times ☐ 3 times
☐ 4 times or more

7. How many times had you been delivered?

☐ never ☐ 1time
☐ 2 times ☐ 3times
☐ 4 times or more

8. Do you have any of the following complications in previous pregnancy? (you can select more than one item)

☐ no complications ☐ gestational hypertension
☐ preeclampsia ☐ eclampsia
☐ gestational diabetes mellitus ☐ others (specify) _____

9. Do you have any of the following medical problems before pregnancy? (you can select more than one item)

☐ no medical problem ☐ chronic hypertension
☐ diabetes mellitus ☐ renal diseases
☐ cardiovascular diseases ☐ others (specify) _____

10. Is there anyone in your family have chronic hypertension? (you can select more than one item)

☐ no one ☐ father
☐ mother ☐ siblings

11. Is there anyone in your family has diabetes mellitus? (you can select more than one item)

☐ no one ☐ father
☐ mother ☐ siblings

12. Is there anyone in your family has a history of hypertensive disorders during pregnancy?(you can select more than one item)

☐ no one ☐ mother
☐ siblings

THE PERSONAL DATA QUESTIONNAIRE

Code No. ---------- Date----------

PART II

Instruction: The following information regarding with present pregnancy will be collected from the mother's antenatal record sheet, and then mother's BMI will be calculated by the researcher.

1. Gestational age at the time of data collection _____
2. Pre-pregnancy body weight (kg) _____
3. Height (cm) _____
4. Body mass index (BMI) (kg/m^2) _____

   ☐ ≤ 18.49 kg/m^2
   ☐ 18.50-22.99 kg/m^2
   ☐ 23.00-27.49 kg/m^2
   ☐ ≥ 27.50 kg/m^2

5. Pregnancy complications

   ☐ no complications
   ☐ chronic hypertension
   ☐ gestational hypertension
   ☐ preeclampsia
   ☐ superimposed preeclampsia
   ☐ eclampsia
   ☐ gestational diabetes mellitus
   ☐ others (specify) _____

THE PERSONAL DATA QUESTIONNAIRE

(MYANMAR VERSION)

ကိုယ်ရေးအချက်အလက်ဆိုင်ရာ မေးခွန်းများ

ရက်စွဲ။...../...../..... လို့ုဝှက်အမှတ်စဉ်။.....

အပိုင်း (က)

အညွှန်း။ ပေးထားသော လေးထောင့်ကွက်အတွင်း အမှန်ခြစ်(√) ၍လည်းကောင်း၊ ကွက်လပ်ဖြည့်၍လည်းကောင်း ဖြေဆိုပေးပါ။

၁။ အသက် .....နှစ် .....လ

၂။ တိုင်းရင်းသားလူမျိုး .....

၃။ ပညာအရည်အချင်း (အမြင့်ဆုံးရောက်ရှိခဲ့သည့် အဆင့်)

- ☐ မူလတန်း
- ☐ အလယ်တန်း
- ☐ အထက်တန်း
- ☐ ဒီပလိုမာ(သို့)သက်မွေးဝမ်းကျောင်းပညာရပ်
- ☐ တက္ကသိုလ်

၄။ အလုပ်အကိုင်

- ☐ အိမ်မှုကိစ္စ
- ☐ လခစား
- ☐ ကိုယ်ပိုင်အလုပ်အကိုင်
- ☐ ကျောင်းသူ
- ☐ အခြားအလုပ်အကိုင် (အတိအကျဖော်ပြရန်).....

၅။ လစဉ်မိသားစုဝင်ငွေ(ကျပ်) .....

၆။ ကိုယ်ဝန်ဆောင်ခဲ့သည့်အကြိမ်အရေအတွက်

- ☐ မရှိပါ
- ☐ ၁ ကြိမ်
- ☐ ၂ ကြိမ်
- ☐ ၃ကြိမ်
- ☐ ၄ကြိမ် နှင့် အထက်

၇။ကလေးမွေးဖွားခဲ့သည့်အကြိမ်အရေအတွက်

☐ မရှိပါ ☐ ၁ ကြိမ်

☐ ၂ ကြိမ် ☐ ၃ ကြိမ်

☐ ၄ ကြိမ် နှင့် အထက်

၈။ ယခင်ကိုယ်ဝန်ဆောင်စဉ်အတွင်း အောက်ဖော်ပြပါရောဂါပြဿနာများ ဖြစ်ပွားခဲ့ဖူး ပါသလား။

☐ မဖြစ်ပွားခဲ့ပါ ☐ သွေးတိုးရောဂါဖြစ်ခြင်း

☐ ကိုယ်ဝန်ဆိပ်တက်ခြင်း ☐ တက်နာဖြစ်ခြင်း

☐ ဆီးချိုရောဂါဖြစ်ခြင်း ☐ အခြားရောဂါများ (အတိအကျဖော်ပြရန်).....

၉။ ကိုယ်ဝန်မဆောင်မီ အောက်ဖော်ပြပါရောဂါပြဿနာများ ဖြစ်ပွားခဲ့ဖူးပါသလား။

☐ မဖြစ်ပွားခဲ့ပါ ☐ သွေးတိုးရောဂါ

☐ ကျောက်ကပ်ရောဂါ ☐ ဆီးချိုရောဂါ

☐ နှလုံး၊ သွေးကြောရောဂါများ ☐ အခြားရောဂါများ (အတိအကျဖော်ပြရန်).....

၁၀။ မိသားစုဝင်များတွင် သွေးတိုးရောဂါဖြစ်ပွားသူရှိပါသလား။

(တစ်ဦးထက်ပို၍ ရွေးချယ် နိုင်ပါသည်)

☐ မရှိပါ ☐ ဖခင်

☐ မိခင် ☐ ညီအကိုမောင်နမများ

၁၁။ မိသားစုဝင်များတွင် ဆီးချိုရောဂါဖြစ်ပွားသူရှိပါသလား။

(တစ်ဦးထက်ပို၍ ရွေးချယ် နိုင်ပါသည်)

☐ မရှိပါ ☐ ဖခင်

☐ မိခင် ☐ ညီအကိုမောင်နမများ

၁၂။ မိသားစုဝင်များတွင် ကိုယ်ဝန်ဆောင်စဉ် သွေးတိုးခြင်း၊ ကိုယ်ဝန်ဆိပ်တက်ခြင်း၊ တက်နာဖြစ်ခြင်းတို့ ဖြစ်ပွားခဲ့ဖူးပါသလား။

☐ မရှိပါ ☐ မိခင်

☐ ညီအကိုမောင်နမများ

ကိုယ်ရေးအချက်အလက်ဆိုင်ရာ မေးခွန်းများ

ရက်စွဲ။...../...../..... လှို့ဝှက်အမှတ်စဉ်။.....

အပိုင်း (ခ)

အညွှန်း။ ယခုကိုယ်ဝန်နှင့်ပတ်သက်သော အောက်ဖော်ပြပါ အချက်အလက်များကို ကိုယ်ဝန်ဆောင်မှတ်တမ်းမှ ကောက်ယူမည်ဖြစ်ပြီး ကိုယ်ဝန်ဆောင်မိခင်၏ ကိုယ်အလေးချိန်အညွှန်းကိန်း (BMI) ကို သုတေသနပြုသူမှ တွက်ချက်မည်ဖြစ်ပါသည်။

၁။ ကိုယ်ဝန်ဆောင်သက်တမ်း .....

၂။ ကိုယ်ဝန်မဆောင်မီကိုယ်အလေးချိန်(ကီလိုဂရမ်) .....

၃။ အရပ်အမြင့် (စင်တီမီတာ) .....

၄။ ကိုယ်အလေးချိန် အညွှန်းကိန်း (BMI) .....

- ☐ ၁၈.၄၉ နှင့် အောက်
- ☐ ၁၈.၅၀-၂၂.၉၉
- ☐ ၂၃.၀၀-၂၇.၄၉
- ☐ ၂၇.၅၀ နှင့် အထက်

၅။ ယခုကိုယ်ဝန်ဆောင်စဉ်အတွင်း နောက်ဆက်တွဲရောဂါပြဿနာရှုပ်ထွေးချက်များ

- ☐ မရှိပါ
- ☐ နာတာရှည်သွေးတိုးရောဂါ
- ☐ ကိုယ်ဝန်ဆောင်စဉ် သွေးတိုးရောဂါဖြစ်ခြင်း
- ☐ ကိုယ်ဝန်ဆိပ်တက်ခြင်း
- ☐ နာတာရှည်သွေးတိုးရောဂါရှိခြင်းကြောင့် ကိုယ်ဝန်ဆိပ်တက်ခြင်း
- ☐ တက်နာဖြစ်ခြင်း
- ☐ ကိုယ်ဝန်ဆောင်စဉ် ဆီးချိုရောဂါဖြစ်ခြင်း
- ☐ အခြားရောဂါများ (အတိအကျဖော်ပြရန်) .....

APPENDIX D

LIST OF EXPERTS FOR CONTENT VALIDITY

The Content of a Personal Data Questionnaire

1. Assistant Professor Dr. Chaweewan Yusamran
   Department of Obstetrics and Gynaecological Nursing
   Faculty of Nursing, Mahidol University
2. Assistant Professor Vasana Jitima
   Department of Obstetrics and Gynaecological Nursing
   Faculty of Nursing, Mahidol University
3. Lecturer Dr. Supawadi Wayuhuerd
   Department of Obstetrics and Gynaecological Nursing
   Faculty of Nursing, Mahidol University

APPENDIX E

INSTITUTIONAL REVIEW BOARD APPROVAL DOCUMENT

CERTIFICATE OF APPROVAL
From
Institutional Review Board Faculty of Nursing Mahidol University

COA No.IRB-NS2016/325.1502

Title of Project:	**RISK FACTORS OF HYPERTENSIVE DISORDERS IN MYANMAR PREGNANT WOMEN**
Project Number:	**IRB-NS2016/06.1501**
Principle Investigator:	**Miss Ei Wah Phyu Thet**
Name of Institution:	**Faculty of Nursing Mahidol University**
Approval includes	1) IRB-NS Submission form version received date 9 February 2016 2) Participant Information sheet version date 9 February 2016 3) Consent form version date 9 February 2016 4) Questionnaire version received date 9 February 2016

Institutional Review Board Faculty of Nursing Mahidol University is in full compliance with International Guidelines for Human Research Protection such as Declaration of Helsinki, The Belmont Report, CIOMS Guidelines and the International Conference on Harmonization in Good Clinical Practice (ICH-GCP)

Date of Approval: **15 February 2016**

Date of Expiration: **14 February 2017**

Signature of Chair:

Fongcum Tilokal

(Associate Professor Dr. Fongcum Tilokskulchai)

Chair

Signature of Dean, Faculty of Nursing

Yajai Sitthimongkol

(Associate Professor Dr. Yajai Sitthimongkol)

Dean, Faculty of Nursing

Office of Institutional Review Board Faculty of Nursing Mahidol University Room 503 Faculty of Nursing, Mahidol University
999 Phuttamonthon 4 Road, Salaya, Nakhon Pathom 73170, THAILAND Tel: (662)-441-5333 Ext. 2531, 2532

UNIVERSITY OF NURSING, YANGON

Certificate of Ethical Clearance

THE REPUBLIC OF THE UNION OF MYANMAR
MINISTRY OF HEALTH
DEPARTMENT OF HEALTH PROFESSIONAL RESOURCE
DEVELOPMENT AND MANAGEMENT
UNIVERSITY OF NURSING (YANGON)
Ethical & Research Committee

CERTIFICATE OF ETHICAL CLEARANCE

The Ethical and Research Committee of The University of Nursing, Yangon, approves the following proposed research project. It does not violate rights, well being, and / or endanger human subjects.

Research Project Title : Risk Factors of Hypertensive Disorders in Myanmar Pregnant Women

Principal Investigator : Miss Ei Wah Phyu Thet

Date of approval : March 3, 2016

3/3/16

Professor Dr. Myat Thandar
Rector
Chairperson, Ethical and Research Committee
University of Nursing, Yangon.

APPENDIX F

BINARY LOGISTIC REGRESSION ANALYSIS

Regression

Variables Entered/Removed[b]			
Model	Variables Entered	Variables Removed	Method
1.	Age, Family History of HT, Parity, BMI, GDM[a]		Enter

a. All requested variables entered.
b. Dependent Variable: Hypertensive disorders

Model Summary[b]					
Model	R	R^2	Adjusted R^2	Std. Error of the Estimate	Durbin-Watson
1	.669[a]	.447	.440	.255	2.179

a. Predictors: (Constant), Age, Family History of Hypertension, Parity, BMI, GDM

b. Dependent Variable: Hypertensive disorders

ANOVA[b]						
Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	20.148	5	4.030	61.865	.000[a]
	Residual	24.882	382	.065		
	Total	45.031	387			

a. Predictors: (Constant), Age, Family History of Hypertension, Parity, BMI, GDM

b. Dependent Variable: Hypertensive disorders

Coefficient[a]				
Model		Unstandardized Coefficients		Standardized Coefficients
		B	Std. Error	Beta
1	(Constant)	-.067	.025	
	BMI	.128	.027	.188
	Parity	.063	.026	.092
	Family History of HT	.089	.027	.129
	GDM	.614	.049	.516
	Age	.059	.031	.076

a. Dependent Variable: Hypertensive disorders

Coefficient[a]						
Model		t	Sig.	Correlations		
				Zero-order	Partial	Part
1	(Constant)	-2.712	.007			
	BMI	4.666	.000	.357	.232	.177
	Parity	2.382	.018	.126	.121	.091
	Family History of HT	3.275	.001	.265	.165	.125
	GDM	12.539	.000	.616	.540	.477
	Age	1.915	.056	.224	.098	.073

a. Dependent Variable: Hypertensive disorders

Coefficients[a]			
Model		Collinearity Statistics	
		Tolerance	VIF
1	(Constant)		
	BMI	.895	1.118
	Parity	.974	1.026
	Family History of HT	.939	1.064
	GDM	.853	1.173
	Age	.928	1.077

a. Dependent Variable: Hypertensive disorders

Collinearity Diagnostics[a]						
Model	Dimension		Eigenvalue	Condition	Variance Proportions		
			3.309	Index	(Constant)	BMI	Parity
1	1			1.000	.02	.03	.03
		2	.878	1.942	.02	.00	.10
dimension0	dimension1	3	.648	2.260	.01	.00	.02
		4	.539	2.478	.00	.16	.51
		5	.435	2.760	.02	.44	.00
		6	.192	4.150	.94	.37	.34

a. Dependent Variable: Hypertensive disorders

Collinearity Diagnostics				
Model	Dimension	Variance Proportions		
		Family History of HT	GDM	Age
1	1	.03	.02	.03
	2	.02	.49	.14
	3	.02	.36	.67
	4	.23	.05	.03
	5	.64	.00	.03
	6	.05	.07	.10

Residuals Statistics[a]

	Minimum	Maximum	Mean	Std. Deviation	N
Predicted Value	-.07	.89	.13	.228	388
Residual	-.823	1.008	.000	.254	388
Std. Predicted Value	-.881	3.295	.000	1.000	388
Std. Residual	-3.225	3.948	.000	.994	388

a. Dependent Variable: Hypertensive disorders

Logistic Regression

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	388	100.0
	Missing Cases	0	.0
	Total	388	100.0
Unselected Cases		0	.0
Total		388	100.0

a. If weight is in effect, see classification table for the total number of cases.

Dependent Variable Encoding

Original Value	Internal Value
Without HDP	0
HDP	1

Categorical Variables Codings

		Frequency	Parameter coding (1)
GDM	no	353	1.000
	yes	35	.000
Parity	multipara	211	1.000
	nullipara	177	.000
Family History of HT	no	226	1.000
	family history of hypertension	162	.000
Age	20-34yrs	290	1.000
	extreme of age	98	.000
BMI	<23 kg	191	1.000
	23kg and above	197	.000

Block 0: Beginning Block

Classification Table[a,b]

Observed			Predicted		
			Hypertensive disorders		Percentage Correct
			Without HDP	HDP	
Step 0	Hypertensive disorders	Without HDP	336	0	100.0
		HDP	52	0	.0
	Overall Percentage				86.6

a. Constant is included in the model.

b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	-1.866	.149	156.773	1	.000	.155

Variables not in the Equation

			Score	df	Sig.
Step 0	Variables	BMI	49.477	1	.000
		Parity	6.135	1	.013
		FHT	27.293	1	.000
		Age	19.472	1	.000
		GDM	147.017	1	.000
	Overall Statistics		173.606	5	.000

Block 1: Method = Enter

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	141.805	5	.000
	Block	141.805	5	.000
	Model	141.805	5	.000

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	163.907[a]	.306	.561

a. Estimation terminated at iteration number 7 because parameter estimates changed by less than .001.

Hosmer and Lemeshow Test

Step	Chi-square	df	Sig.
1	12.560	8	.128

Contingency Table for Hosmer and Lemeshow Test

		Without HDP		HDP		
		Observed	Expected	Observed	Expected	Total
Step 1	1	49	48.872	0	.128	49
	2	15	15.911	1	.089	16
	3	50	49.667	0	.333	50
	4	39	38.590	0	.410	39
	5	31	30.345	0	.655	31
	6	46	46.199	2	1.801	48
	7	34	35.860	5	3.140	39
	8	38	36.493	5	6.507	43
	9	29	28.860	11	11.140	40
	10	5	5.202	28	27.798	33

Classification Table[a]

Observed			Predicted		
			Hypertensive disorders		Percentage Correct
			Without HDP	HDP	
Step 1	Hypertensive disorders	Without HDP	331	5	98.5
		HDP	24	28	53.8
	Overall Percentage				92.5

a. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
								Lower	Upper
p 1[a]	BMI	2.697	.755	12.747	1	.000	14.831	3.375	65.180
	Parity	.937	.430	4.736	1	.030	2.552	1.098	5.932
	FHT	1.207	.445	7.353	1	.007	3.344	1.397	8.003
	Age	.756	.451	2.816	1	.093	2.130	.881	5.152
	GDM	3.203	.551	33.758	1	.000	24.595	8.350	72.449
	Constant	-5.941	.828	51.535	1	.000	.003		

a. Variable(s) entered on step 1: BMIBinary, ParityBinary, FHTBinary, AgeBinary, GDM.

BIOGRAPHY

NAME	Ei Wah Phyu Thet
DATE OF BIRTH	26 August 1984
PLACE OF BIRTH	Yangon, Myanmar
INSTITUTIONS ATTENDED	Yangon Nursing Training School, 2002-2005 DIP. In Nursing Science Dagon University, 2005-2009 Bachelor of Law (L.L.B) Yangon University of Nursing, 2010-2011 Bachelor of Nursing Science Mahidol University, 2014-2015 Master of Nursing Science (Midwifery)
SCHOLARSHIP RECEIVED	Norwegian Scholarship for Capacity Building for Institutions in Myanmar
RESEARCH GRANTS	Self-Funding
HOME ADDRESS	15/58, VIP (3) Quarter, Shwe Pyi Thar Township, Yangon Division, Myanmar 11411 Tel. 09784693859, 0973100735, 01636102 E-mail: eiwahphyuthet@gmail.com eiwahphyuthet@outlook.com
POSITION & OFFICE	Tutor Nursing Related Field Practice Training School No (2) Highway Road, East-Dagon Township, Yangon Division, Myanmar 11421 Tel. 01585138