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**THE EFFECTS OF PRENATAL CARE, PRENATAL EDUCATION, AND WEIGHT ON PRE-ECLAMPSIA AND ECLAMPSIA IN HAITI**

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# THE EFFECTS OF PRENATAL CARE, PRENATAL EDUCATION, AND WEIGHT ON PRE-ECLAMPSIA AND ECLAMPSIA IN HAITI

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2012

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An abstract of

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## Abstract

### THE EFFECTS OF PRENATAL CARE, PRENATAL EDUCATION, AND WEIGHT ON PRE-ECLAMPSIA AND ECLAMPSIA IN HAITI

By Ahlia Sekkarie

*Purpose:* The research aims of this study were to determine the prevalence and trends of eclampsia and pre-eclampsia, defined as hypertension along with proteinuria, among women at Maison de Naissance (MN), a rural maternal health center in Torbeck, Haiti. The patient data from MN were analyzed to determine the extent to which prenatal care and education and maternal weight explain the risk of pre-eclampsia in the MN population.

*Methods:* A case-control study design was used with cases defined as pregnant women who presented at MN with a pregnancy induced hypertension (PIH), pre-eclampsia or eclampsia diagnosis and controls defined as those women who delivered babies at MN and were not diagnosed with a hypertensive disorder. The cohort included women, age 15 and above, who conceived between April 22, 2010 and October 11, 2012. The original cohort size was 899 and the number of cases was 80. However, 210 subjects were dropped from the analysis because they were duplicates, were missing case status, or were missing demographic information which was required for linking to other characteristics. Odds ratios were calculated using multivariate logistic regression.

*Results:* The incidence of pre-eclampsia and eclampsia was 7.0%. Prenatal care and education were not significantly associated with pre-eclampsia/eclampsia. Older maternal age at delivery (OR=3.18; 95%CI: 1.31, 7.76) and heavier maternal weight (OR=3.24; 95%CI: 1.76, 5.98) measured during prenatal care were both significantly associated with PIH/pre-eclampsia/eclampsia.

*Conclusions:* The prevalence of preeclampsia/eclampsia in this cohort was high, relative to rates in other developing countries. Although MN does a good job of providing prenatal care, more is required to reduce the rate of preeclampsia perhaps by targeting older and heavier women for further interventions.



**Key Words:**
Haiti, Pregnancy Induced Hypertension, Pre-eclampsia, Eclampsia, Maternal Health, Prenatal Care

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**List of Abbreviations**

BMI - Body Mass Index

BR - Birth Registry

eMR - Electronic medical record

HIV - Human Immunodeficiency Virus

MMR – Maternal Mortality Ratio

MN - Maison de Naissance

OR - Odds Ratio

PIH – Pregnancy-Induced Hypertension

PNC - Prenatal Care

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# CHAPTER I: Background & Literature Review

## Background

According to the National High Blood Pressure Education Program, pre-eclampsia is a pregnancy-specific disease occurring at a gestational age greater than 20 weeks with systolic blood pressure of ≥140 mm Hg or diastolic blood pressure of ≥ 90 mm Hg accompanied by proteinuria (urinary excretion of ≥ 0.3 g protein in a 24-h specimen) (1). It is distinguished from gestational hypertension by the absence of proteinuria (2). Pre-eclampsia is often asymptomatic (3, 4). When symptoms occur, however, they include headaches, visual imparity, upper abdominal pain, oliguria, elevated serum creatinine, fetal growth retardation, thrombocytopenia, increased liver enzymes, and pulmonary edema (5). If the condition progresses to seizures that cannot be attributed to any other cause, it is called eclampsia (2). Pre-eclampsia is best treated by early detection which is often difficult in low-resource settings because women do not come in for prenatal care due to various barriers, staff is not trained in identifying the symptoms of pre-eclampsia, or they do not have the necessary screening supplies such as urine dipsticks to test for proteinuria (6-10). Once detected, the most common medication for pre-eclampsia is magnesium sulfate or other anti-hypertensive drugs (7). Other effective treatments include calcium supplementation in high risk cases, aspirin and antioxidants as preventative measures, or immediate delivery if gestational age is 36 weeks or greater (7, 10, 11). However, one study found that low-dose aspirin did not reduce the incidence of pre-eclampsia among high risk women and Osungbade et al. recommend that prophylactic measures like low-dose aspirin need further evidence before recommendation in developing countries (9, 12).

**Pre-eclampsia and Maternal Morbidity and Mortality**

*In Developing Nations*

When grouped, pre-eclampsia and eclampsia comprise one of the leading causes of maternal morbidity and mortality worldwide (10, 11, 13, 14). Pre-eclampsia occurs in 2 to 10% of all pregnancies worldwide, and is seven times higher in developing countries (15; See Appendix A). Pregnancy induced hypertension (including pre-eclampsia and eclampsia) was the leading cause of maternal deaths at 26% between 1997 - 2007 based on regional estimates for Latin America and the Caribbean (14). Women in low and middle income countries are more likely to experience complications associated with pre-eclampsia than women in high income countries due to delays in identifying cases and delays in seeking care (4). Payne et al. developed and validated a model using a prospective cohort study in five low to middle income countries to identify women at higher risk of complications from pregnancy related hypertensive disorders in resource constrained settings. Their final model included gestational age on admission, parity, and the following clinical risk factors: systolic blood pressure, dipstick proteinuria, chest pain/dyspnea, vaginal bleeding along with abdominal pain, and headaches/visual disturbances (4).

*In Haiti*

Haiti has one of the highest maternal mortality ratios (MMR, deaths in women during pregnancy or within 42 days postpartum associated with pregnancy per 100,000 live births) in the Caribbean (16). In 2010, the MMR in Haiti was 350 deaths per 100,000, down from 620 in 1990, but still not at the MDG5 (*Millennium Development Goal 5)* target goal 155 per 100,000 by 2015 (14). Targets for improving maternal health

include reducing maternal mortality and achieving universal access to reproductive health (15). At 42% (n=216), eclampsia was the leading cause of registered maternal deaths in Haiti in 2000 (17). There is little literature on the prevalence and risk factors of pre-eclampsia and eclampsia in Haiti. In one hospital in Haiti, renal failure was the leading cause of death for pre-eclamptic or eclamptic patients (18). A retrospective cohort of pre-eclampsia related maternal mortality in Hôpital Albert Schweitzer in rural Haiti, using abstracted medical records of patients, found that pre-eclampsia affected 18% of deliveries and resulted in 19 deaths during a three year period (19). At the same hospital after the February 2004 coup d'état, Small et al. found that baseline eclampsia rates rose from 0.5% to 14% (p=0.06) because hospital closures limited access to care (20). An unpublished article from 1992 found that the rate of eclampsia was twice as high among pregnant teens 15-19 years compared to older pregnant women (21).

*In Maison de Naissance (MN)*

Maison de Naissance (MN) located in rural Torbeck, Haiti is a modern, culturally appropriate maternity center supporting healthy mothers and babies with free, high quality medical care and ongoing community-oriented support. Founded in 2004, MN is a small private institution supported by the Episcopal Church and the Global Birthing Home Foundation (www.globalbirthinghomefoundation.org). One of the primary goals of MN is to prevent maternal and infant deaths in Haiti. A study conducted by Collet in 2012 found that although 90.2% of women who attended antenatal visits at MN wished to obtain an institutional delivery, over 40% still deliver at home. The study concluded that these women delayed to seek institutional delivery because of lack of knowledge of the signs of labor, family objections, and patient/provider communication issues (22). This is

in concurrence with the "Three Delays" model which proposes that maternal mortality is primarily due to delays in: 1) seeking medical care for an obstetric emergency; 2) access to a facility; and 3) receiving adequate care at the facility (16, 23). MN founders sought to eliminate these delays in their catchment area, a radius of roughly one hour's walk from the clinic. Since its establishment in 2004, MN has only had one maternal death (occurring in a home delivery) compared with an expected 17 given an MMR of 350/100,000 (24).

**Associations: Pre-eclampsia and Eclampsia Risk Factors**

Established risk factors for pre-eclampsia are nulliparity and primiparity (i.e., giving birth to a first child or being pregnant for the first time), higher maternal pre-pregnancy body mass index (BMI; i.e., body mass divided by height squared), underlying medical conditions such as hypertension (i.e., blood pressure exceeding 140/90 mmHG) or diabetes, twin pregnancies, advanced maternal age, and a history of pre-eclampsia both in a previous pregnancy and within one's family (25-35). When comparing a large cohort study of pregnant women in Latin America and the Caribbean to pregnant women in North America and Europe, similar risk factors for pre-eclampsia were revealed (36). The risk factors they identified included nulliparity, history or chronic hypertension, gestational diabetes, advanced maternal age, long inter-birth intervals, and obesity (36). See Appendix B for a chart of risk factors for pre-eclampsia/eclampsia and their corresponding reported magnitudes.

*Nulliparity*

Nulliparity, defined as a woman who has never given birth previously, is an established risk factor for pre-eclampsia and eclampsia (28, 29, 33, 34, 35). In all these

studies, the odds of developing pre-eclampsia for a nulliparous woman range from 3 to 5 times that of a woman who has previously given birth. Primiparity, defined as a woman pregnant for the first time, is also associated with pre-eclampsia and eclampsia. A meta-analysis of 26 studies reported a significant summary OR of 2.4. (26). The cohort and case-control studies ranged across a period of 10 years, the majority were based in the US or other developed countries, and had crude ORs ranging from 1.44 to 5.48 (26). For example, a 2005 retrospective cohort titled, "Risk factors for pre-eclampsia in nulliparous and parous women: the Jerusalem Perinatal Study" by Funai et al. reported an OR of 2.58 adjusted for race, maternal education and social class, paternal age, previous preterm birth, religion, paternal occupation, year of delivery, and season. This study showed that nulliparous women were almost three times as likely to develop pre-eclampsia as their counterparts who had previously given birth, controlling for a range of variables (26).

*High Maternal Body Mass Index (BMI)*

A high maternal BMI is an established risk factor for pre-eclampsia and eclampsia (27, 28, 30, 32, 33, 34, 35). Odds ratios in these studies ranged from 2 to 5. A systematic review of risk factors of preeclampsia at antenatal booking found that a high BMI before pregnancy and during pregnancy were associated with a 2.5 and 1.6 times higher odds of pre-eclampsia, respectively (28). One of the reviewed retrospective cohort studies found that women with a pre-pregnancy BMI over 35 had 4 times the risk of developing pre-eclampsia compared to women with a pre-pregnancy BMI between 19 and 27, but they did not find a significant risk for increased weight gain during pregnancy (37). However, a systematic review of thirteen cohort studies comparing the risk of pre-eclampsia among women with the highest BMI to those with the lowest and adjusting for confounders, did

find that the risk of pre-eclampsia increased with weight gain during pregnancy. The risk of pre-eclampsia doubled with each 5 to 7 kg/m2 increase in pre-pregnancy BMI (27).

*Underlying/Preexisting Medical Conditions*

Several underlying or preexisting medical conditions are established risk factors for pre-eclampsia. Both preexisting diabetes and gestational diabetes as well as chronic hypertension have been shown to be significantly associated with pre-eclampsia and eclampsia (3, 28, 31, 32, 34, 38). Duckitt & Harrington in a systematic review of controlled cohort studies published between 1966 and 2002 found that renal diabetes, chronic autoimmune disease, and antiphospholipid syndrome were all also associated with a higher risk of pre-eclampsia (28). Davies et al. found that women who developed pre-eclampsia had a higher prevalence of chronic hypertension and renal disease compared to women who did not in a population based nested case-control study (38). Antiphospholipid antibody syndrome and factor V Leiden mutation have also been found to be associated with pre-eclampsia (3).

*Twin pregnancies*

Twin pregnancy is an established risk factor for pre-eclampsia (28, 29, 32). The systematic review conducted by Duckitt & Harrington in 2005 included five cohort studies with the risk of pre-eclampsia nearly tripling if a woman is pregnant with twins regardless of chorionicity and zygosity of the pregnancy (28). A case-control study of 38 in-vitro pregnancies found that triplets further tripled the risk of pre-eclampsia compared to twin pregnancies (39).

*High maternal age*

High maternal age is an established risk factor for pre-eclampsia (28, 35). This association holds even for multiparous women (35). Only one study reviewed by Duckitt & Harrington controlled for pre-existing conditions (28). A retrospective cohort study of 1404 women found that women older than age 40 had twice the risk of developing pre-eclampsia regardless of parity (40). According to data from the US National Hospital Discharge Survey from 1979 to 1986, the risk of pre-eclampsia increases by 30% for every additional year past age 34 (41).

*Prenatal care*

A study using data from the Centers for Disease Control and Prevention's Pregnancy Mortality Surveillance System to examine pregnancy-related deaths from pre-eclampsia and eclampsia from 1979 to 1992 found that having no prenatal care was associated with 9.9 times the risk of pre-eclampsia compared to women with any level of care, and that this risk was doubled among women of black race (42). According to UNICEF statistics, 90.3% of Haitian women have at least one antenatal care visit, while only 67.3% have the recommended four antenatal care visits (43). The WHO recommends at least four antenatal care visits so interventions such as tetanus vaccination, infection screening and treatment, and information regarding warning signs to look for during pregnancy can be administered and/or identified (44).

*History of Pre-eclampsia*

A history of pre-eclampsia, either in the family or in a previous pregnancy, is strongly associated with pre-eclampsia (3, 28, 30, 34). A study by Arngrimsson et al. looked at family history of eclampsia and pre-eclampsia through three generations in 94 families in Iceland because of its homogenous populations (45). They found that the risk

of pre-eclampsia nearly tripled if there was a family history of pre-eclampsia (45). However, one of the reviewed case-control studies did not find a significant association between pre-eclampsia and a family history of pre-eclampsia (33). Another systematic review of five cohort studies found that women with a previous history of pre-eclampsia had seven times the risk of pre-eclampsia in a subsequent pregnancy (28). This variable was ultimately not included in the analysis portion of this study because it was not available in the current data.

*Smoking*

An inverse association between smoking and pre-eclampsia has been reported (29, 46). In the systematic review of 29 cohort and case-control studies from 1966 to 1998 by Conde-Agudelo et al., the typical relative risk was 0.68 (95% CI: 0.67, 0.69) and the typical odds ratio was 0.68 (95% CI: 0.57, 0.81) (46). They also reported an inverse dose-response relationship between smoking and pre-eclampsia (46). Odegard et al. only reported this inverse association among those with late onset pre-eclampsia (34). However, some authors have reported a higher risk of hypertensive complications among smokers (35).

*Socioeconomic status & Education*

The effect of socioeconomic factors on pre-eclampsia risk is conflicting (25, 35, 47). A population-based cohort study conducted in the Netherlands of 3,547 pregnant women with low education level reported a 5.12 higher odds of pre-eclampsia compared to women with a high education level (47). A prospectively collected birth cohort of 9,247 singleton pregnancies from Finland also found that low education was associated with higher odds of pre-eclampsia compared to mothers with moderate levels of

education (35). However, a literature review by Trogstad et al. concluded a null relationship between socioeconomic status and pre-eclampsia (25). This variable was ultimately not included in the analysis portion of this study because it was not available in the data.

*Race & Ethnicity*

Two studies looked at Haitian women living in North America as an independent group compared to either white women or African American women. Both studies concluded that pre-eclampsia and related morbidity were more common or potent in Haitian women (48,49). The study by Rey et al. compared the incidence of pre-eclampsia in 208 white Canadian born and 74 Haitian born women with mild chronic hypertension with controls being white and black women who delivered in the same center (48). The retrospective cohort study by Odell et al. looked at all self-identified African American or Haitian women who delivered at a single facility in Massachusetts during a four year time period (49). They concluded that unknown factors make pre-eclampsia much more likely among Haitian women (49). Among nulliparous women, black women have a risk of pre-eclampsia that is twice as high as that of white women (33).

*Season*

According to Trogstad et al. current evidence is insufficient in establishing season as a risk factor for pre-eclampsia (25); however, several studies have reported an association of pre-eclampsia with colder weather (50, 51, 52). There are no significantly cold seasons in Haiti, therefore, this variable was not considered further in the analysis portion of this study.

*Inter-birth Interval (IBI)*

Using the Latin American and Caribbean Perinatal System database, Conde-Agudelo et al. showed that inter-birth intervals longer than 59 months were associated with an increased risk of pre-eclampsia and eclampsia (36). Ultimately, this variable was not included in the analysis portion of the study because it was not collected by or discernable based on MN data. After adjusting for the interval between births, a change of partner is not associated with an increased risk of pre-eclampsia (53).

*Nutrition*

A systematic review of nutrition in pre-eclampsia concluded that the majority of studies investigating this association were poorly designed and underpowered. It has also been concluded that sodium restriction, calcium, fatty-acids, zinc, and magnesium supplements during mid-gestation were all ineffective therapies for pre-eclampsia/eclampsia. Larger studies are needed to determine the effect of antioxidant therapy with vitamins C and E (54). Nutrition-based data were not collected by MN, therefore nutrition not included in the analysis portion of this study.

## CHAPTER II: Manuscript

# THE EFFECTS OF PRENATAL CARE, PRENATAL EDUCATION, AND WEIGHT ON PRE-ECLAMPSIA AND ECLAMPSIA IN HAITI

Ahlia Sekkarie

## Introduction

Haiti has the highest maternal mortality ratio in the Western hemisphere (16). The most recent estimate of 350 deaths per 100,000 live births in 2010 represents a 22% decrease from the previous ratio of 450 deaths per 100,000 live births in 2010 (14). However, the Millennium Development Goal 5 target in Haiti of 155 deaths per 100,000 live births by 2015 has still not been realized (14). In 2000, eclampsia was the most common cause of maternal death in Haiti at 42% (17). Eclampsia and its precursor, pre-eclampsia, are treatable, but often occur where there is no prenatal care or symptoms are not recognized by healthcare professionals. In Haiti, less than 36 percent of births take place in health facilities (55).

Pre-eclampsia most commonly occurs in the 20$^{th}$ week of pregnancy or later. It is clinically identified by: 1) blood pressure greater than 140/90 mm HG or two consecutive measures of blood pressure increase; and 2) proteinuria which is damage to the kidney "filter" that allows for protein in the urine (1). Proteinuria can be identified using a dipstick test. Pre-eclampsia can progress to eclampsia if seizures develop in the pregnant woman (2). Symptoms of pre-eclampsia include abnormal swelling (edema), sudden weight gain, “late” nausea/vomiting, stomach and/or shoulder pain, migraine-like headaches, and/or changes in vision. Associated risk factors of pre-eclampsia include: maternal age over 39 years or under 18 years, nulliparity (i.e., first birth), mothers

carrying multiple babies, toxemia, having a baby by a different father, obesity, a personal or family history of pre-eclampsia, and chronic health conditions such as high blood pressure, diabetes, and kidney disease (56, 57).

According to UNICEF statistics, while 90.3% of Haitian women have at least one antenatal care visit, only 67.3% have the recommended four antenatal care visits (43). Maison de Naissance (MN) located in Torbeck, Haiti is a modern, culturally appropriate maternity center supporting healthy mothers and babies with free, high quality medical care and ongoing community-oriented support. One of the primary goals of MN is to prevent maternal and infant deaths through improved prenatal, delivery, and family planning services. It is not known how to prevent pre-eclampsia; however, early prenatal care and education may prevent many cases of eclampsia through early detection of pregnancy-induced hypertension, monitoring for symptoms of pre-eclampsia, and treatment of pre-eclampsia when it does occur (17). Since its opening in 2004 through 2013, the clinic has recorded 39,253 prenatal visits and 4,716 deliveries (Carol Hogue, Personal Communication, April 9, 2014). During this time period, applying an expected maternal Mortality ratio (MMR) of 350 per 100,000 births, 17 maternal deaths were expected. During that period, however, there was only one maternal death of a woman who received prenatal care at MN, but who delivered at home (24).

The research aims of this current study were to determine: 1) the incidence and trends of eclampsia and pre-eclampsia among women at MN; 2) whether a greater number of prenatal care visits and prenatal education were associated with lower rates of pre-eclampsia among women at MN; 3) the extent to which known risk factors for eclampsia/pre-eclampsia can explain the risk of pre-eclampsia in the MN population; and

4) the difference in utilization of prenatal care and risk factors between those patients who present with gestational hypertension and those who go on to develop pre-eclampsia/eclampsia, using a case-control study design. Answers to these questions may further explain the low maternal mortality rate at MN, may identify areas for further improvement in prenatal care at MN, and may be used as a resource for other health facilities in Haiti attempting to decrease maternal mortality.

The data collected and analyzed for this study were obtained from prenatal, birth, and referral registries used at MN. In addition, data from several other eMR databases were linked with these registries to obtain demographic and other variables of interest. The primary explanatory variables were prenatal care and prenatal education. Common risk factors of pre-eclampsia such as maternal age, blood pressure, parity, and maternal weight were identified and controlled for statistically.

*Hypotheses*

1.) Pre-eclampsia and eclampsia will be prevalent in the population of women attending prenatal care at MN.
2.) The prenatal care and prenatal education offered to pregnant women will not be protective against pre-eclampsia or eclampsia in the study population.
3.) Known risk factors such as increased/higher weight will explain some of the excess risk of pre-eclampsia and eclampsia in this population.

## Methods

*Data collection and entry*

Some of the patient data collected at Maison de Naisance (MN) in Torbeck, Haiti were in the form of electronic medical records (eMR), while some data were extracted

from ledger registries hand-written in French by MN medical staff. Four of MN's primary registries were of particular interest to the current research study: the prenatal, birth, patient education, and referral registries. The prenatal registry was in the form of an eMR and included demographic information. The original eMR system was created in 2004 when the clinic began operation to provide a big picture of care from pregnancy through birth for research purposes. However, the data are not consistent from database to database and do not create a historical profile of care. For example, a woman may have been logged into the birth registry, but not in the prenatal care registry because she presented at MN only to deliver her baby and vice-versa. For example, a previous study found that only 75% of women who planned to deliver at a facility ultimately did so (22). Therefore, the prenatal registry was not used to determine the cohort because many pregnant women who visit MN for prenatal care do not return to MN to give birth. The birth and referral registries were in ledgers hand-written in French. The birth registry had two formats: birth registry 1 (BR1) collected before July, 2012 and birth registry 2 (BR2) collected on or after July, 2012. BR2 included many of the same variables as BR1, but with some additions including baby HIV status and whether a HIV prophylaxis was given at birth. In BR2, women were also asked whether they had received prenatal care. The patient education registry was used to determine whether patients had received prenatal education about the potential danger signs during pregnancy in addition to other important prenatal care information. When possible, missing data from any of the four primary registries was found in other available databases included in the eMR.

During a week-long trip in fall 2013, researchers from Emory University Rollins School of Public Heath, Department of Epidemiology, collected the hand written patient

registries from MN. Due to the short duration of the trip, they took images using the TurboScan smart phone application by Piksoft, 2013. These scanned images were uploaded to a secure storage site at Emory University, and subsequently, data were manually entered into a MS Excel spreadsheet by trained and certified Emory University MPH graduate students. If information in the registries was not entered (i.e., blank), it was assumed to be missing and not a negative response because usually "Yes" or "No" was indicated.

For this analysis, the date of conception was used to identify those women who conceived between April 22, 2010 to October 11, 2012, and who gave birth at MN or who were referred at the time of birth to another facility due to complications. To obtain the sample, we used encounter data from the birth and referral registries from July 1, 2011 to March 31, 2013. This time frame was chosen because it was feasible to enter this amount of data during the time frame of the project, and women who conceived after that time frame may not have given birth yet at the time of data collection.

The delivery date in conjunction with the gestational age was used to estimate the date of conception. Of 322 (47%) observations missing the delivery date itself, the filename inside two of the three birth registry data files was used to estimate the delivery date for 190. These filenames placed the baby's delivery date within a two week period, on average. The mid-point date of the delivery within a particular date range was used as an estimate of the baby's date of delivery. For instance, if the filename of the birth registry file was January 01, 2012-January 14, 2012, the baby's delivery date was estimated to be January 7, 2012. This estimation is sufficiently accurate for the purposes

of the study since the estimate is within such a short time period. Of the remaining 132 with missing delivery date, 67 were found in other databases and 65 remained missing.

For the 14 observations with gestational age missing, mean age for cases and controls were independently substituted. For the controls, the mean substituted value for missing gestational age was 39.1 weeks. For the cases, the mean substituted value was 34.9 weeks. The gestational age was indicated as 'Term' or 'Full Term' in the registries for 78 observations. For these observations a substitution of 40 weeks was used.

All patient information available for the sample based on the birth and referral registries was linked to the information from the prenatal registry within the larger eMR using the unique key, Demographic ID.

*Data management and IRB*

Prior to the start of this study, the protocol was submitted to and approved by the Emory University Institutional Review Board using the expedited procedure. To ensure data confidentiality, data were stored on a secure, private drive at the Emory University Rollins School of Public Health, IT Department server system, and were accessible only by the researchers. In these Haiti datasets, Personal Health Information (PHI) included dates (such as birth dates, and visit dates to the clinic for prenatal care), residence location, names, and medical record numbers. PHI was only used to aid in the data linking process.

*Study Population*

A case-control study design was employed in this study. The control group was defined as those women who conceived between April 22, 2010 and October 11, 2012 who gave birth at MN, but who were not diagnosed with a pregnancy-related

hypertensive disorder. Cases were defined as pregnant women who presented at MN with pregnancy induced hypertension (PIH), pre-eclampsia, or eclampsia. The original cohort size was 899, 80 of whom were cases. However, patients without a Demographic ID (n=205) were excluded from the analysis since they could not be linked to any demographic information or the prenatal registry and thus, had no information on maternal weight and pre-existing conditions that were important for the analysis. Thirteen cases and 192 controls were missing Demographic ID, accounting for 22.8% of the initial sample. In addition, four duplicate maternal entries and one observation with unknown case or control status were removed from the sample leaving a final sample size of 689 pregnant women. Among those that were removed from the dataset there were fewer cases (6.2%) compared to the prevalence of cases in the final dataset (9.7%). It is unknown why the patients were missing the Demographic ID. If the reason they are missing is not random, such as they all only presented at MN to deliver, and a Demographic ID was not assigned, this could bias the results of the study as all of these mothers would not have had prenatal care.

*Outcome Variable*

The outcome or dependent variable, a case, was indicted by a binary variable where '0' indicated no pregnancy-induced hypertension (PIH), pre-eclampsia or eclampsia and '1' indicated PIH, pre-eclampsia or eclampsia. A woman was identified as having pre-eclampsia if she was marked in the referral registry as having pre-eclampsia (PES), mild pre-eclampsia (PEL), or if she was treated for pre-eclampsia with anti-hypertensive drugs such as Magnesium Sulfate (MgSO4) or Apresoline.

*Exposure Variables*

The two primary exposure variables were number of prenatal care visits and receipt of prenatal education about potential danger signs a woman could experience during pregnancy. These two were chosen as the primary exposure variables because they are easily modifiable, i.e., clinic staff could educate patients about prenatal care and pre-eclampsia to decrease incidence. In addition, these variables were almost fully populated in the dataset, did not have many missing observations, and they have not been studied in this context previously.

The number of prenatal care visits was categorized as: no prenatal care visits, one to three prenatal care visits, and four or more prenatal care visits. These categorizations were chosen because the WHO provides statistics for at least one antenatal care visit and four or more antenatal care visits. At least four antenatal care visits are recommended by the WHO (44). The "No prenatal care visits" category was designated as the reference category for this variable.

MN provided prenatal education to their clients on 17 topics such as diet, hygiene, breastfeeding, drug use, infant care, and potential danger signs of pregnancy. Education about the potential danger signs during pregnancy was chosen as a proxy for prenatal education about pre-eclampsia or eclampsia. Any pregnant woman who received education about danger signs regardless of receiving education in other areas was assigned a value of '1' for this exposure variable and a '0' if she did not receive prenatal education about danger signs during pregnancy.

*Control Variables*

The control variables included in this study were those maternal risk factors shown to be associated with pre-eclampsia/eclampsia in the literature that were available

in the MN databases. These were maternal age older than 40 years, nulliparity, being overweight or obese, smoking, and having a history of diabetes. Other risk factors such as chronic hypertension, renal disease, inter-birth-interval, and socioeconomic status were not available in the MN data. Not all chosen control variables such as parity were indicated as confounders in a Directed Acyclic Graph (DAG); however, they were still included because of their strong association with pre-eclampsia in the literature (Figure 1).

*Maternal age*

Maternal age was categorized as '0' if the mother's age at delivery was less than 40 years and a '1' if the mother was 40 years or older. Delivering before the age of 40 years has been identified in the literature as an age cut-off for pre-eclampsia risk (28). This variable was determined by subtracting the baby's date of birth from the mother's date of birth. If the mother's age was known, but the mother's actual DOB variable was missing, the mother's year of birth was calculated based on the baby's DOB from the registry. For example, if the baby was born in 2012, then 2012 minus the mother's age equals the mother's year of birth. If both the mother's age and birth date were missing (n=73) her age was categorized as under 40 years since the mean age was 27.6 years.

*Nulliparity*

Nulliparity (i.e., having had no previous births, sometimes called primiparity, i.e., having had no previous pregnancies) has been shown to be associated with an increased risk of pre-eclampsia in the literature (26). Parity was categorized dichotomously. Women who were giving birth for the first time were assigned a value of '1' for the parity variable, and women with previous deliveries were assigned '0'. Ten observations

were missing parity. The mode for parity was '0' so missing parity information was substituted with 0.

*High maternal weight*

Height was not collected by the medical staff at MN, and therefore, BMI could not be calculated to determine obesity status. In addition, pre-pregnancy weight was not available. Only maternal weight during prenatal care was available. Fifty-eight pregnant women in the sample were missing weight observations; for them, the overall mean was assigned. Based on data from previous literature which used a maternal weight cut-off of 80 kg (176 lbs.) to indicate high maternal weight (34), a new dichotomous variable was created in which women at or above 176 lbs. were assigned a value of '1' and women less than 176 lbs. were assigned a value of '0'.

*Smoking*

Smoking status, determined at the pregnant woman's first prenatal care visit (PNC) visit, was available in the dataset with no missing values, and it was classified as a dichotomous variable with a '1' indicating that the pregnant woman was smoking and '0' indicating she was not smoking during her pregnancy.

*Diabetes*

Previous history of diabetes was available in the dataset with no missing values as a dichotomous variable with '1' indicating a diagnosis of diabetes, and a '0' indicating no diabetes.

*Gestational age*

Gestational age in weeks as a continuous variable was only included in the model comparing women who presented to MN with PIH and those who presented with pre-

eclampsia/eclampsia. Gestational age is a risk factor for adverse outcomes of pregnancy related hypertensive disorders (4). Fourteen observations were missing gestational age and were mean substituted as indicated above.

**Data analysis**

Data analysis was conducted using SAS software, version 9.3 for Windows. Frequencies for all categorical variables, stratified by case or non-case were computed. Means and standard deviations for continuous variables were also calculated. Two sample pooled T-tests were conducted to determine whether there were significant differences between the means of cases and controls. For the bivariate analysis, chi-square was used to test the differences characteristics of pre-eclamptic/eclamptic patients and patients without pre-eclampsia/eclampsia. Correlations between continuous variables were also assessed. Crude ORs were computed, and two separate multivariate logistic regression models were tested assessing the association between cases, control variables, and each primary exposure variable: prenatal visits and prenatal education about the potential danger signs during pregnancy, respectively. Prenatal care visits had 3 categories, with no prenatal care visits (PNC) as the reference category. Pooled t-tests and logistic regression were used to compare PNC utilization and risk factors between women who presented to MN with PIH and those who presented with pre-eclampsia/eclampsia.

**Results**

*Univariate and Bivariate Analysis*

There were 67 cases in the sample (9.7%). Of those, 18 had PIH (2.6% of entire sample). Seven percent (7%) had pre-eclampsia/eclampsia. The average maternal age at delivery was 27.7 years (SD = 6.67), and maternal age at delivery ranged from 15 to 46 years (Table 1). In the sample, 4.2% of the mothers were 40 years of age or older, while among cases, 10.5% of mothers were 40 years or older ($p< 0.0074$) (Table 2). The mean maternal weight was 146.2 pounds (Table 1). Cases had a significantly higher weight than controls ($p< 0.001$) (Table 1). Among cases, 25.4% of mothers had a high maternal weight (greater than or equal to 176 pounds), while in the entire sample only 11% of mothers had a high maternal weight (Table 2). In Haiti, 21% of women are obese (58). These two statistics are not directly comparable, however, because one is referring to pre-pregnancy weight, while the other is referring to maternal weight. There were only two cases of diabetes, and none among the PIH/pre-eclampsia/eclampsia cases; therefore, diabetes was not included in the model. Only maternal age and weight had significant chi-square values indicating a significant difference between cases and non-cases (Table 2). Maternal weight was positively correlated with maternal age, number of prenatal visits, and parity ($p < 0.0001$). Parity and maternal age were also positively correlated ($p = 0.0148$).

The average parity among the sample was 1.2 (Table 1). Being nulliparous accounted for 44.6% of the overall sample (Table 2). There was no significant difference in parity between cases and controls. A little over 2% (2.2%) of mothers smoked (Table 2).

The number of PNC visits ranged from zero to nine with a mean of 3.18 PNC visits and a mode of four. Three visits and four visits were the 33% and 66% tertile

cutoffs, respectively. Cases had 3.6 PNC visits on average, while controls had slightly fewer visits, 3.12 on average ($p = 0.0356$), and this difference was statistically significant (Table 1). However, when categorized as zero visits, 1 to 3 visits, or 4 or more visits, there was no significant difference ($p = 0.612$) (Table 2). Only 6.4% mothers had no PNC visits (Table 2). In the sample, 87.7% of mothers received some sort of prenatal education, and 77.4% received prenatal education specifically about the potential danger signs during pregnancy (Table 2). In Haiti, as a whole, 65% of mothers were informed of signs of pregnancy complications from 2007 to 2012 (55). There was no significant difference between cases and controls in regards to prenatal education, whether it was any prenatal education received or prenatal education specific to the potential danger signs during pregnancy (Table 2).

Table 3 presents crude ORs and 95% CI for the risk of PIH/pre-eclampsia/eclampsia for each independent variable. Only maternal age and maternal weight revealed significant ORs. Mothers who delivered at 40 years or older had a 3.18 odds of developing PIH/pre-eclampsia/eclampsia compared to mothers who were younger than 40 years old when they delivered (95% CI: 1.31, 7.76). Mothers with a maternal weight at or over 176 pounds had 3.24 odds of developing PIH/pre-eclampsia/eclampsia compared to mothers who weighed under 176 pounds (95% CI: 1.76, 5.98). The ORs for four or more PNC visits and prenatal education about potential danger signs during pregnancy were both slightly above 1.00 suggesting that these variables were not protective against a hypertensive disorder, but since these were not significant, this is inconclusive.

A pooled t-test comparing the average number of PNC visits between patients with PIH and patients who developed pre-eclampsia/eclampsia was not significant. PIH patients had a significantly higher maternal weight (173.8 lbs.) compared to pre-eclampsia/eclampsia patients (154.6 lbs.) (p=0.0333). The difference in maternal age was also significant (p=0.0221). PIH patients were older at 33.3 years compared to pre-eclampsia/eclampsia patients at 28.9 years. Differences in parity and gestational age were not significant.

*Modeling*

Two separate models, one for each exposure variable of interest, were used to assess the relationship between: 1) PNC visits and pregnancy-related hypertensive disorders; and 2) prenatal education about potential danger signs during pregnancy and pregnancy-related hypertensive disorders. Prenatal care visits had 3 categories, with no visits as the reference. In both initial models, age, weight, parity, and smoking status were controlled. Age and weight were included because they were shown to be significant in the earlier univariate and bivariate analysis. Parity and smoking were not significant, but were included because of their importance in the literature. Collinearity was not apparent in these models.

*Model 1- Prenatal care (PNC) visits as primary exposure variable*

*The initial logistic regression model:*

$$\text{Logit P (Case)} = \alpha + \beta_1 \text{ (Number PNC visits)} + \beta_2 \text{ (Age)} + \beta_3 \text{ (Weight)} + \beta_4 \text{ (Parity)} + \beta_5 \text{ (Smoking)}$$

An all possible-subsets approach was used to determine the best model. Parity and smoking were dropped from the model since they were not significant and after dropping them from the model, the results did not change by greater than 10%.

*Final model:*

$$\text{Logit P (Case)} = \alpha + \beta_1 \text{ (Number PNC visits)} + \beta_2 \text{ (Age)} + \beta_3 \text{ (Weight)}$$

The final multivariate logistic regression model indicated significant odds ratios for age and weight, but the OR for 1 to 3, or 4 or more PNC visits was not significant (Table 4). Mothers at or over 40 years old at delivery had 3.05 odds of developing pre-eclampsia/eclampsia compared to mothers who were less than 40 years old when they delivered while controlling for weight and number of PNC visits (95% CI: 1.22, 7.63) (Table 4). Mothers over 176 pounds had 3.06 odds of developing pre-eclampsia/eclampsia compared to mothers less than 176 pounds after controlling for age and PNC visits (95% CI: 1.63, 5.75) (Table 4).

*Model 2 - Prenatal education about danger signs as primary exposure variable*

*The initial logistic regression model:*

$$\text{Logit P (Case)} = \alpha + \beta_1 \text{ (Danger signs educ.)} + \beta_2 \text{ (Age)} + \beta_3 \text{ (Weight)} + \beta_4 \text{ (Parity)} + \beta_5 \text{ (Smoking)}$$

An all possible-subsets approach was used to determine the best model. Parity and smoking were dropped from the model since they were not significant and after dropping the model did not change by greater than 10%.

*Final model:*

$$\text{Logit P (Case)} = \alpha + \beta_1 \text{ (Danger signs educ.)} + \beta_2 \text{ (Age)} + \beta_3 \text{ (Weight)}$$

As with the previous model, only age and weight had significant odds ratios (Table 5). The ORs for these two variables were also similar to the previous model. Mothers at or

over 40 years old at delivery had a 3.18 odds of developing pre-eclampsia/eclampsia compared to mothers who were less than 40 years old at delivery, while controlling for weight and prenatal education about potential danger signs during pregnancy (95% CI: 1.26, 7.99) (Table 5). Mothers over 176 pounds had 3.02 odds of developing pre-eclampsia/eclampsia compared to mothers less than 176 pounds after controlling for age and prenatal education about dangers signs during pregnancy (95% CI: 1.62, 5.63) (Table 5). Smoking had a protective effect on pre-eclampsia and eclampsia in both initial models, but it was not significant (Tables 4, 5).

Logistic regression was used to model PNC utilization and risk factors between women who presented to MN with PIH and those who presented with pre-eclampsia/eclampsia. None of the covariates in the model were significant (Table 6):

$$\text{Logit P (PES)} = \alpha + \beta_1 (\text{Number PNC visits}) + \beta_2 (\text{Age}) + \beta_3 (\text{Weight}) + \beta_4 (\text{Parity}) + \beta_5 (\text{Gestational age}).$$

**Discussion**

The results indicate that the women in this sample who are most likely to become hypertensive in pregnancy including those who go on to develop pre-eclampsia/eclampsia are older when they deliver and have a higher maternal weight. This is corroborated by previous literature worldwide and in Haiti (21). Although smoking was not significantly associated with hypertensive disorders in this study, the OR was below one suggesting a protective effect as previous studies have shown (29, 46).

Prenatal education about potential danger signs during pregnancy and the number of PNC visits had odds ratios slightly over one, but they were not significant. If they were significant, the ORs would indicate that perhaps women with more health issues may

visit the clinic more often because of pregnancy complications such as pre-eclampsia and eclampsia. In fact, the t-test between average number of PNC visits for cases and non-cases indicated a significant difference between the two, with cases having had more PNC visits.

A major limitation of this study may explain why these ORs were not significant, and slightly positive. Of the original sample of 899, 205 (almost 25%) of the observations were excluded because they were missing a Demographic ID and thus could not be linked to demographic factors and other covariates such as weight and smoking status. Of these, 192 were controls. It is unknown why these patients were missing the Demographic ID, but it is possible the majority only presented themselves to MN to deliver and a Demographic ID was not assigned. This could bias the results of the study as all of these mothers did not have PNC or prenatal education from MN.

In the sample, the average number of PNC visits was 3.2 with only 6.6% of mothers never having had a PNC visit. In Haiti as a whole, 10% of mothers have no prenatal visits (55). It is encouraging that MN is able to reach a greater proportion of women for antenatal care. However, among those who received PNC, the incidence of pregnancy-related hypertensive disorders in this sample was high at 9.9%. (64 of 645). The incidence of pre-eclampsia alone was 7.0%. This is at the higher end of the 2 to 10% pre-eclampsia incidence worldwide (15, 59, 60), but lower than at another Haitian hospital where pre-eclampsia affected 18% of deliveries and resulted in 19 deaths (19). It is possible the incidence was lower at this hospital because hypertension was identified early on, and thus, pre-eclampsia rates were lower. MN has had no maternal deaths. In addition, accurate estimates of the incidence of pre-eclampsia are often difficult to obtain

because diagnostic criteria are not standardized (57). This may be true for MN as well. There are several theories as to why MN has had such low maternal mortality. A common cause for maternal mortality in Haiti is the high rate of home deliveries. A previous study at MN looking at the barriers to on-site delivery at the clinic indicated approximately 60% of women who received PNC at MN gave birth in a medical facility compared to less than 36% of Haitian women in general (55).

The bivariate analysis comparing women who presented with PIH to those who presented with pre-eclampsia/eclampsia indicated that women presenting with PIH were significantly older and heavier. However, none of the covariates in the regression model were significant. Payne et al. found that women who developed adverse outcomes from pre-eclampsia were significantly younger in age (4). Pregnancy-induced hypertension (PIH) can't be prevented, but it can be screened for during prenatal care and treated. Early treatment prevents its progression to pre-eclampsia or eclampsia. Women presenting with PIH had slightly more PNC visits (mean = 4.39) compared to women presenting with pre-eclampsia/eclampsia (mean = 3.31), suggesting that more intensive monitoring may have prevented some cases. However, the difference in average number of visits was not significant ($p=0.0609$). It is not clear why younger women were more likely to present with pre-eclampsia especially since there was not a significant difference in PNC visits or parity between the two age groups.

One of the strengths of the study was the large amount of data collected by MN. Unfortunately, much data were missing in our sample. In developing countries, there is usually a lack of reliable data on maternal conditions (7). Missing and unreliable data was a challenge that we encountered, but it was overcome using mean substitution techniques

and further sleuthing into other MN databases to capture valid data values. For example, almost one-quarter of the sample was missing a Demographic ID which would have allowed them to be linked to other MN registries. As another example, the data indicated that only 2 of the original 899 pregnant women had prenatal diabetes. Perhaps, this sample is exceptionally healthy compared to other studies that have reported diabetes among 8.9% of the Haitian women in Port-au-Prince (61). There were also variables not collected at MN such as information on chronic hypertension, history of pre-eclampsia, and inter-birth interval that were important to control for because they are strongly associated with pre-eclampsia in the literature. Matching the birth and referral registries to the prior eMR by unique identifiers like name and dates of birth in order to capture the correct Demographic ID for the individual also presented a significant challenge. From the hand-written log-books in French, one hundred and twenty ((120) commission errors in patient names including spelling errors and transposition errors which switched the person's first and last names were identified and corrected.

Another issue with the data was that the final date range of our cohort changed from that which was originally planned. The final cohort had conception dates ranging from April 22, 2010 to October 11, 2012. This extension in time came about due to missing data that were identified from other registries and reconciled. Data errors of commission and omission during data entry occurred due to difficulties in accurately identifying what was hand-written and in French. It was a challenge to enter data from hand-written ledgers in French because of the large amount of time required to translate and abstract, and because sometimes the handwriting was illegible. Technical errors also were experienced especially with the date fields since date formatting was prone to

transposition errors, e.g., the US commonly uses mm/dd/yyyy while Haiti follows dd/mm/yyyy. Ultimately, any discrepancies in conception date should not bias study outcomes since transcription date errors were at most within a year of the original date, and date was not used as a predictor in the model. However, the use of the scanning smart phone application, TurboScan, greatly aided this process and allowed researchers to have high quality images of the hand-written ledgers and maximize their time while visiting MN in Haiti to collect data. Smart phone applications like this have great potential in situations which require the collection of a large amount of data in a short time-period.

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## TABLES

**Table 1.** Descriptive Statistics for Continuous Variables

| | All (N=689) | | | Cases (N=67) | | Controls (N=622) | | T-test |
|---|---|---|---|---|---|---|---|---|
| **Variable** | **N** | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** | **P-value** |
| Number prenatal visits | 689 | 3.2 | 1.81 | 3.6 | 2.01 | 3.12 | 1.79 | 0.0356 |
| Maternal age (yrs) | 616 | 27.7 | 6.67 | 30.1 | 6.63 | 27.5 | 6.62 | 0.0027 |
| Parity | 679 | 1.2 | 1.66 | 1.4 | 1.92 | 1.2 | 1.63 | 0.3019 |
| Maternal weight (lbs.) | 631 | 146.2 | 23.9 | 159.7 | 32.51 | 144.7 | 22.33 | <.0001 |
| Gestational age (wks.) | 686 | 38.8 | 2.84 | 34.8 | 5.36 | 39.2 | 1.99 | <.0001 |

**Table 2.** Frequencies of Categorical Variables

| | All (N=689) | | Cases (N=67) | | Controls (N=622) | | Chi-square |
|---|---|---|---|---|---|---|---|
| **Variable** | **N** | **Percent** | **N** | **Percent** | **N** | **Percent** | **P-value** |
| **Prenatal visits** | | | | | | | 0.612 |
| 0 | 44 | 6.4 | 3 | 4.5 | 41 | 6.6 | |
| 1-3 | 350 | 50.8 | 32 | 47.8 | 318 | 51.1 | |
| ≥ 4 | 295 | 42.8 | 32 | 47.8 | 263 | 42.3 | |
| **Danger signs education** | | | | | | | 0.2002 |
| Yes | 533 | 77.4 | 56 | 83.6 | 477 | 76.7 | |
| No | 156 | 22.6 | 11 | 16.4 | 145 | 23.3 | |
| **Maternal age (yes)** | | | | | | | 0.0074 |
| < 40 | 660 | 95.8 | 60 | 89.6 | 600 | 96.5 | |
| ≥ 40 | 29 | 4.2 | 7 | 10.5 | 22 | 3.5 | |
| **Weight (lbs)** | | | | | | | <.0001 |
| < 176 | 613 | 89.0 | 50 | 74.6 | 563 | 90.5 | |
| ≥ 176 | 76 | 11.0 | 17 | 25.4 | 59 | 0.5 | |
| **Parity** | | | | | | | 0.7668 |
| Nulliparous | 307 | 44.6 | 31 | 46.3 | 276 | 44.4 | |
| Multiparous | 382 | 55.4 | 36 | 53.7 | 346 | 55.6 | |
| **Diabetes** | | | | | | | 0.6421 |
| Yes | 2 | 0.3 | 0 | 0.0 | 2 | 99.7 | |
| No | 687 | 99.7 | 67 | 100.0 | 620 | 0.3 | |
| **Smoking** | | | | | | | 0.6861 |
| Yes | 674 | 97.8 | 1 | 1.5 | 608 | 97.8 | |
| No | 15 | 2.2 | 66 | 98.5 | 14 | 2.3 | |

**Table 3.** Crude ORs for the Odds of PIH/Pre-eclampsia/Eclampsia

| Variable | Estimate | SE | P-value | OR | 95% CI | |
|---|---|---|---|---|---|---|
| **Prenatal visits** | | | | | | |
| 0 | - | - | - | 1.00 | - | - |
| 1-3 | 0.2158 | 0.22 | 0.3253 | 1.24 | 0.807 | 1.907 |
| ≥ 4 | 0.2158 | 0.22 | 0.3253 | 1.54 | | |
| **Danger signs educ.** | | | | | | |
| No | - | - | - | 1.00 | - | - |
| Yes | 0.4367 | 0.34 | 0.2032 | 1.55 | 0.79 | 3.032 |
| **Maternal age (yrs)** | | | | | | |
| < 40 | - | - | - | 1.00 | - | - |
| ≥ 40 | 1.1575 | 0.45 | 0.0109 | 3.18 | 1.305 | 7.756 |
| **Weight (lbs)** | | | | | | |
| < 176 | - | - | - | 1.00 | | |
| ≥ 176 | 1.1769 | 0.31 | 0.0002 | 3.24 | 1.759 | 5.984 |
| **Parity** | | | | | | |
| Multiparous | - | - | - | 1.00 | - | - |
| Nulliparous | 0.0765 | 0.26 | 0.7668 | 1.08 | 0.651 | 1.79 |
| **Smoking** | | | | | | |
| No | - | - | - | 1.00 | - | - |
| Yes | -0.4185 | 1.04 | 0.6883 | 0.66 | 0.085 | 5.084 |

**Table 4.** Initial and Final Models with Prenatal Care Visits as Primary Exposure

| Parameter | B | SE | OR | 95% CI | |
|---|---|---|---|---|---|
| **Initial model** | | | | | |
| Intercept | -2.7331 | 0.36 | - | - | - |
| 4 + visits[1] | 0.0926 | 0.23 | 1.20 | 0.50 | 2.91 |
| 1 to 3 visits[2] | 0.0926 | 0.23 | 1.10 | 0.71 | 1.71 |
| Advanced age | 1.2203 | 0.48 | **3.39** | **1.32** | **8.70** |
| High weight | 1.1468 | 0.33 | **3.15** | **1.67** | **5.95** |
| Nulliparity | 0.2539 | 0.27 | 1.29 | 0.76 | 2.20 |
| Smoking | -0.3136 | 1.06 | 0.73 | 0.09 | 5.82 |
| **Final model** | | | | | |
| Intercept | -2.639 | 0.34 | - | - | - |
| 4 + visits[1] | 0.1124 | 0.23 | 1.25 | 0.52 | 3.03 |
| 1 to 3 visits[2] | 0.1124 | 0.23 | 1.12 | 0.72 | 1.74 |
| Advanced age | 1.1164 | 0.47 | **3.05** | **1.22** | **7.63** |
| High weight | 1.1179 | 0.32 | **3.06** | **1.63** | **5.75** |

[1]OR = exp (E* - E)B = exp (2-0)B = exp(2B).

[2]OR = exp (E* - E)B = exp (1-0)B = exp(B).

Note: Significant Odds Ratios are bolded

**Table 5.** Initial and Final Models with Prenatal Danger Signs Education as Primary Exposure

| Parameter | B | SE | OR | 95% CI | |
|---|---|---|---|---|---|
| **Initial model** | | | | | |
| Intercept | -2.8993 | 0.35 | - | - | - |
| Danger signs educ. | 0.3809 | 0.35 | 1.46 | 0.73 | 2.92 |
| Advanced age | 1.2572 | 0.49 | **3.52** | **1.36** | **9.10** |
| High weight | 1.1263 | 0.32 | **3.08** | **1.65** | **5.78** |
| Nulliparity | 0.2382 | 0.27 | 1.27 | 0.74 | 2.17 |
| Smoking | -0.4141 | 1.06 | 0.66 | 0.08 | 5.29 |
| **Final model** | | | | | |
| Intercept | -2.7971 | 0.33 | - | - | - |
| Danger signs educ. | 0.392 | 0.35 | 1.48 | 0.74 | 2.94 |
| Advanced age | 1.1555 | 0.47 | **3.18** | **1.26** | **7.99** |
| High weight | 1.1055 | 0.32 | **3.02** | **1.62** | **5.63** |

Note: Significant Odds Ratios are bolded

**Table 6.** Model comparing PIH cases to Pre-eclampsia/eclampsia cases

| Parameter | B | SE | P-value | OR | 95% CI |
|---|---|---|---|---|---|
| **Initial model** | | | | | |
| Intercept | 4.4078 | 2.43 | 0.0702 | - | - |
| 4 + visits[1] | 0.2458 | 0.59 | 0.6778 | 1.64 | 0.16,16.26 |
| 1 to 3 visits[2] | 0.2458 | 0.93 | 0.6778 | 1.28 | 0.40, 4.08 |
| Advanced age | -0.9240 | 0.48 | 0.3223 | 0.397 | 0.06, 2.47 |
| High weight | -1.0821 | 0.67 | 0.1088 | 0.339 | 0.09, 1.27 |
| Nulliparity | -0.2960 | 0.63 | 0.6390 | 0.774 | 0.22, 2.56 |
| Gestational age in wks. | -0.0903 | 0.07 | 0.1898 | 0.914 | 0.80, 1.05 |

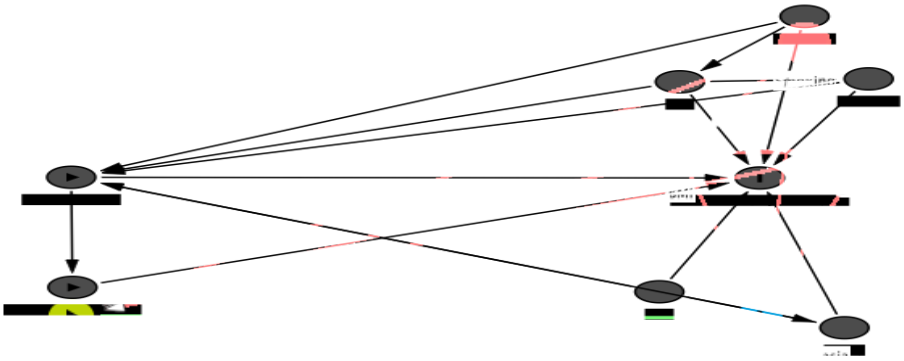
[1]OR = exp (E* - E)B = exp (2-0)B = exp(2B).

[2]OR = exp (E* - E)B = exp (1-0)B = exp(B).

Note: Significant Odds Ratios are bolded

# FIGURES

**Figure 1.** Directed Acyclic Graph



Note. DAG analysis approach from Johannes Textor, Juliane Hardt, Sven Knüppel. DAGitty: A Graphical Tool for Analyzing Causal Diagrams.*Epidemiology*, 5(22):745, 2011.

## CHAPTER III: Public Health Implications & Future Directions

The incidence of pre-eclampsia/eclampsia in this cohort was high at 7.0%, relative to rates in other developing countries. Prenatal care and education were not significantly associated with pregnancy-related hypertensive disorders. This study did not address complications associated with pre-eclampsia and eclampsia although these may be more likely to be affected by prenatal care (PNC) (62). Older maternal age at delivery and heavier maternal weight measured during PNC were both significantly associated with PIH/pre-eclampsia/eclampsia. Although MN does a good job of providing prenatal care, more is required to reduce the rate of pre-eclampsia perhaps by targeting older and heavier women for pre-conception interventions, including nutrition counseling and outreach for family planning services.

The burden of pre-eclampsia/eclampsia is primarily in low income countries. For example, an infant born to a mother with pre-eclampsia in a low income country has a three times higher mortality compared with babies born to women from high income countries (10). Causes of pre-eclampsia, although studied extensively in the past ten years, have not been determined yet (63). Research in developing nations such as Haiti increases understanding of the causes of the disease, aids in identifying the most vulnerable individuals in the population, and contributes to the global movement towards improving maternal and child health, particularly the WHO's *Millennium Development Goal 5*.

Pre-eclampsia continues to be an issue for Haiti. Haiti has one of the highest maternal mortality ratios in the Caribbean (16). In 2010, the MMR in Haiti was 350 deaths per 100,000. Eclampsia was the leading cause registered to maternal deaths (17).

According to Genette Thelusmond, a Haitian midwife, it is important to educate mothers about the symptoms of eclampsia so that they seek timely treatment because many Haitian women believe that the seizures caused by eclampsia mean that she is spiritually possessed or has been cursed (64). In addition, because a large number of births are not attended by skilled birth attendants or in a skilled facility, the risk of maternal mortality from these conditions is elevated in Haiti. While MN staff encourage pregnant women to deliver in facilities, over 40% of women who attended antenatal visits at MN still delivered at home (22). Better community-based education on the benefits of skilled birth attendance is recommended.

The current investigation is particularly important because the majority of prior research on risk factors for pre-eclampsia is based on populations in developed nations. This is partly because in developing countries there is a lack of reliable data on maternal conditions (7). There is little literature available on the incidence or prevalence of pre-eclampsia and eclampsia in Haiti and associated risk factors (18 – 21). The current study corroborates and adds to the small body of literature about the incidence and risk factors of pre-eclampsia in Haiti.

It is also important to increase the knowledge base and skill level of clinic staff to identify women most at risk for pre-eclampsia. This information has the potential to direct prevention and treatment resources towards the most vulnerable women such as those who are overweight or of advanced maternal age. In this sample, older women were at a higher risk of pregnancy-related hypertensive disorders, but they were less likely to seek PNC. The opposite trend was apparent with overweight women. They were likely to have more PNC visits. Two actions MN can take to reduce the risk of hypertensive

disorders are: 1) primary prevention through weight control of overweight women; and 2) more monitoring of older pregnant women.

Researchers have recognized the importance of prevention through early detection of increases in blood pressure or proteinuria to prevent complications from pre-eclampsia (25). For example, the miniPIERS, a clinical risk prediction model for adverse outcomes of hypertensive disorders in pregnancy, could provide the basis for an education program to increase the knowledge of women and clinic staff at MN about the signs and symptoms of pre-eclampsia and other hypertensive disorders (4). The model looks primarily at medical risk factors such as parity, gestational age, head headache/visual disturbances, chest pain/shortness of breath, vaginal bleeding with abdominal pain, systolic blood pressure, and proteinuria detected using a dipstick (4).

Further research should focus on thorough data collection and should look particularly at the severity and screening of pre-eclampsia, and not just incidence. It is the most severe cases that advance to eclampsia, causing maternal death. Clinic staff at MN believe that the clinic prevents more severe cases of pre-eclampsia because of the high rate of PNC visits that local women in the community receive. However, this could not be supported by the current investigation because of a lack of data on the severity of the pre-eclampsia. It is possible that increased PNC visits is contributing to MN's record of no maternal deaths.

# APPENDICES

**Appendix A.** Tabulated Prevalence of Pre-eclampsia/Eclampsia

| **Prevalence of Pre-eclampsia/Eclampsia** | | |
|---|---|---|
| **Prevalence (%)** | **Source** | **Comments** |
| 2 – 10 | WHO, 2005 | Pre-eclampsia incidence worldwide; seven (7) times higher in developing countries (2.8% of live births) than in developed countries (0.4%). |
| 5 – 6 | Walker, 2000 | Pre-eclampsia |
| 3 – 5 | Roberts & Cooper, 2001 | Pre-eclampsia |
| 2 – 7 | Sibai et al., 2005 | Pre-eclampsia in healthy nulliparous women |
| 3.6 | Hutcheon, et al. 2011 | Pre-eclampsia in USA. Accurate estimates of the incidence of pre-eclampsia are difficult to obtain because of a lack of standardization of diagnostic criteria in population databases. |

**Appendix B.** Tabulated Magnitude of Pre-eclampsia/Eclampsia Risk Factors

| **Magnitude of the Risk Factors for Pre-eclampsia/Eclampsia** | | | |
|---|---|---|---|
| **Estimate, 95% CI** | **Risk Factors** | **Reference** | **Study Quality / Comments** |
| 5.12 (2.20 – 11.93) | Low education level | Silva et al., 2008 | Population-based cohort study in Netherlands of 3547 pregnant women. Compared to high education level. |
| Null | Socioeconomic status<br><br>Seasonality | Trogstad et al., 2011 | Literature review |
| Risk doubled with each 5–7kg/m2 increase in pre-pregnancy BMI | High maternal BMI | O'Brien et al., 2003 | Systematic review. Two reviewers independently retrieved all relevant English language cohort studies through a systematic search. The risk ratio was calculated by comparing the risk of pre-eclampsia among women with the highest BMI and those with the lowest. 13 studies, 1.4 million women. Adjusted for chronic hypertension, diabetes mellitus or multiple gestations and other confounders. |
| 7.19 (5.85 – 8.83) | Previous history | Duckitt & Harrington, 2005 | Systematic review of controlled studies published 1966-2002. Unadjusted relative risks. Risk is also increased with an interval of 10 years or more since a previous |

| | | | |
|---|---|---|---|
| | | | pregnancy, autoimmune disease, renal disease, and chronic hypertension. |
| 9.72 (4.34 – 21.75) | Antiphospholipids antibodies | - | - |
| 3.56 (2.54 – 4.99) | Pre-existing diabetes | - | - |
| 2.93 (2.04 -4.21) | Twin pregnancy | - | - |
| 2.91 (1.28 – 6.61) | Nulliparity | - | - |
| 2.90 (1.70 – 4.93) | Family history | - | - |
| 1.38 (1.01 – 1.78) | High blood pressure | | At booking, diastolic ≥ 80 mm Hg |
| 1) 2.47 (1.66 – 3.67)<br>2) 1.55 (1.28 – 1.88) | High BMI 1) before pregnancy 2)booking | - | - |
| 1.96 ( 1.34 – 2.87) | Maternal age ≥ 40 | - | For multiparous women |
| 0.68 (0.67 – 0.69) | Cigarette smoking | Conde et al., 1999 | Systematic review. 28 cohort studies and 7 case-control studies, 833,714 women were included. Relative risk |
| 3.5 (3.0 - 4.2) | Twin pregnancy | Coonrod et al., 1995 | Population-based cohort study. Relative risk independent of other factors. |
| 4.0 (3.3 - 4.8) | Nulliparity | - | - |
| 1.8 (1.2 - 2.6) | Black race | - | - |
| 2.42 ( 2.16 - 2.71) | Primiparity | Z. C. Luo et al., 2007 | Meta-analysis, 26 eligible studies, compared to multiparous. Adjusted for confounders. |
| 0: 3.0 (2.1 – 2.4)<br>> 4: 0.5 (0.2 -1.4) | Parity (Ref = 1-4) | Hartikainen et al., 1998 | Prospectively collected birth cohort of 9247 singleton pregnancies from the northernmost provinces of Finland with the expected date of delivery falling between July 1, 1985 and June 30, 1986. |

| | | | |
|---|---|---|---|
| | | | Adjusted OR. |
| < 20: 0.9 (0.4 – 1.9)<br>30-34: 1.3 (0.8 – 2.0)<br>≥ 35: 2.5 (1.5 -4.1) | Age (Ref = 20-29) | - | - |
| < 20: 0.6 (0.4 – 0.9)<br>≥ 27: 1.8 (1.0 – 3.2) | BMI (Ref = 20-27) | - | - |
| 0.5 (0.3 – 0.8) | Smoking (Ref = no) | - | - |
| Low: 2.1 (1.4 – 3.1)<br>High 1.1 (0.7 – 1.7) | Education (Ref = moderate) | - | - |
| 1.6 (1.0 -2.5) | Employment (Ref = no) | - | - |
| 5.4 (2.8 – 10.3) | Nulliparous | Eskenazi et al., 1991 | Case-control study between 1984-85 of women who gave birth at Northern CA KP Medical Centers. 139 cases, 132 controls. Adjusted OR. |
| 10.8 (1.2 – 29.1) | Previous history | - | - |
| 2.7 (1.2 – 6.2) | High BMI | - | - |
| 2.1 (1.1 – 4.4) | Work during preg. | - | - |
| 1.7 (0.92 – 3.2) | Family hx of hypt. | - | - |
| 12.3 (1.6 – 100.8) | Black (only nulliparous) | - | - |
| 3.5 (1.68 – 7.46) | Severe obesity | Stone et al., 1994 | Retrospective case control (n=70). Adjusted OR. USA |
| 7.2 (2.74 – 18.74) | Previous history (in multiparous) | - | - |
| 3.6 (2.6 – 5.0) | Nulliparity | Odegard et al., 2000 | A population-based, nested case-control study from 12,804 deliveries that took place over three years at a birth clinic in Norway. Cases of pre-eclampsia (n = 323) and healthy controls (n = 650). Also has OR by pre-eclampsia |

| | | | |
|---|---|---|---|
| | | | severity. |
| 3.6 (2.0 – 6.6) | Hypertension (systolic ≥130) | - | Was also significant for Systolic 120 -129. But not for diastolic. |
| 3.0 (1.7 – 5.3) | High maternal weight (≥80kg) | - | Associated with mild or moderate, but not severe preeclamsia. |
| 42.4 (11.9 – 151.6) | Previous history | - | For early onset disease |
| 0.6 (0.4 – 0.9) | Smoking | - | But no effect for early onset group and women with repeated pre-eclampsia. |
| 3.72 (1.45 – 9.53) | Gestational diabetes | Duckler et al., 2001 | Retrospective cohort study. N=385 primiparous women with and without pre-eclampsia. Outcome = pre-eclampsia at second pregnancy. |
| 5.58 (2.72 – 11.43) | Type 1 diabetes | Ros et al., 1998 | Population-based cohort study. The Swedish Medical Birth Register - includes all nulliparas age 34 years or less who gave birth at the University Hospital of Uppsala, Sweden, during 1987–1993 - Odds Ratio. |
| 3.11 (1.61 – 6.00) | Gestational diabetes | - | - |
| 4.17 (2.30 – 7.55) | Twin birth | - | - |
| 5.19 (2.35 – 11.48) | Obese (BMI > 29) | - | - |
| 0.66 (0.49 – 0.88) | Smoking (1-9) | - | ≥ 10 was also significant |
| 0.69 (0.54 – 0.88) | Summer birth | - | Compared to winter |
| Null | - | - | Infant sex, maternal age, maternal height, mother's place of birth, maternal education, cohabiting with child's father, history of infertility, |

| | | | |
|---|---|---|---|
| 1.12 (1.11 – 1.13) | Interbirth interval (for each 1 year increase) | Skjaerven et al., 2002 | Medical Birth Registry of Norway, a population-based registry that includes births that occurred between 1967 and 1998. 551,478 women studied who had two or more singleton deliveries and 209,423 women studied who had three or more singleton deliveries. After adjustment for the interval between births, a change of partner is not associated with an increased risk of pre-eclampsia. |
| More superimposed pre-eclampsia compared to white ($p< 0.01$) | Black Haitian | Rey, 1996 | 208 white (born in Canada) and 74 black **(born in Haiti)** women with mild chronic hypertension. Controls included 17,677 white and 2,400 black normotensive women delivered in the same center between 1987 and 1991 |
| Chronic hypert dif ($p=0.006$) Pre-eclampsia dif ($p=0.27$) | Haitian (compared to Af. Am) | Odell et al., 2006 | Retrospective cohort study of all Black women self-identified as African-American (n = 12,258) or Haitian (n = 4320) delivering a singleton infant in Massachusetts between 1996 and 2000. |
| RR, 0.94 (0.78, 1.14) | Scheduled Prenatal Care visits | McDuffie et al., 1996 | Randomized controlled trial. Group-model HMO. A |

| | | | |
|---|---|---|---|
| | | | total of 2764 pregnant women, judged to be at low risk of adverse perinatal outcomes. Only 2.7% fewer pnc visits in control group. |
| RR 9.9 (7.05, 13.84) | No prenatal visits | MacKay et al., 2001 | Data from the Centers for Disease Control and Prevention's Pregnancy Mortality Surveillance System; examined pregnancy-related deaths from pre-eclampsia and eclampsia from 1979 to 1992. |
| 5.3% vs 1.8% | Renal Disease | Davies et al., 1970 | Population-based nested case control study in Jerusalem. |
| 12.1% vs 0.3% | Chronic Hypertension | - | - |
| 1.69 (1.07 – 1.53) | Winter (Ref = summer) | Immink et al., 2008 | Retrospective study of pre-eclampsia patients in South Africa. |