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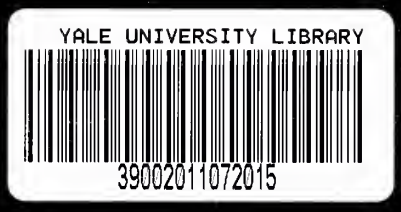

RISK FACTORS ASSOCIATED WITH THE DEVELOPMENT OF PREECLAMPSIA IN ADOLESCENTS

AMY LINK WINKELSTEIN

YALE UNIVERSITY

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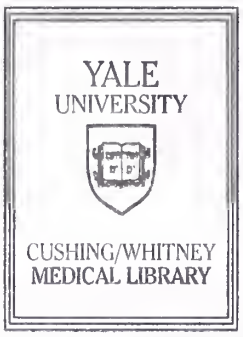
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RISK FACTORS ASSOCIATED WITH THE DEVELOPMENT OF PREECLAMPSIA IN ADOLESCENTS

A Thesis Submitted to the
Yale University School of Medicine
In Partial Fulfillment of the Requirements for the
Degree of Doctor of Medicine

by

Amy Link Winkelstein

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ABSTRACT

RISK FACTORS ASSOCIATED WITH THE DEVELOPMENT OF PREECLAMPSIA IN ADOLESCENT PREGNANCY. Amy L. Winkelstein, Sara J. Marder and Chaur-Dong Hsu. Department of Obstetrics/Gynecology, Yale University, School of Medicine, New Haven, CT.

This study aimed to identify risk factors associated with the development of preeclampsia during adolescent pregnancy. We performed a retrospective cohort study of 435 pregnant adolescent women, age ≤ 18 years, between January 1, 1994 and April 26, 1997. Demographic data, gynecologic age (GA) (years between menarche and conception), chronologic age (CA), prepregnancy body mass index (PBMI), weight gain, medical, surgical, obstetric, gynecologic, social and family history were abstracted from records. Preeclampsia (PE) was defined as hypertensive proteinuria. PBMI was defined as weight/height (kg/m^2). Data were analyzed using contingency table, simple and multiple logistic regression analyses. Data were expressed as odds ratios with 95% confidence intervals (OR, 95% CI). Fifty-six out of 435 pregnant adolescent women (12.9%) developed PE. Simple logistic regression analysis revealed that GA (OR:0.82, 95% CI: 0.69–0.96, p=0.02) and CA (OR:0.81, 95% CI: 0.67-0.99, p=0.04) were negatively correlated with PE. PBMI (OR: 1.11, 95% CI: 1.05-1.17, p=0.0003), prepregnancy weight (OR: 1.01, 95% CI: 1.01-1.02, p=0.0008), total weight gain (OR: 1.046, 95% CI: 1.02-1.07, p=0.0001), weight gain per week (OR: 2.40, 95% CI:1.42-4.06, p=0.001) and urinary tract infection (OR: 2.00, 95% CI:1.03-3.89,p=0.04) were positively correlated with PE. When GA< 4 years (OR: 2.12, 95%CI: 1.20-3.75, p=0.01), CA< 17 years (OR: 1.99, 95% CI: 1.10-3.62, p=0.02) or PBMI ≥30 obese adolescents were at significantly increased risk for PE. After adjustment for significant factors, the risk for PE with GA <4 years (OR:2.22, 95% CI:1.121-4.407, p=0.02), CA< 17 years (OR:2.85, 95%CI: 1.374-5.889, p=0.005), GA <4 years and CA<17 years (OR: 3.27, 95% CI: 1.627-6.552, p=0.0009) or PBMI ≥30 (OR:4.54, 95% CI:1.46-14.14, p=0.009) remained significant. The incidence of PE is higher in pregnant adolescent women than in the general population. Low gynecologic and chronologic age and obesity prior to pregnancy are strong risk factors for PE in adolescent pregnancy.

ACKNOWLEDGEMENTS

I would like to thank Chaur-Dong Hsu, M.D., M.P.H. for his guidance, support and patience. I would also like to thank Sara Marder, M.D. and Ellen Amy Komisaruk, M.D. for their assistance. Additionally, I received financial support through a Yale Medical School Summer Research Fellowship. I would also like to thank Aaron Milstone and my family for their continued love, support, and endless patience.

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Introduction:

Preeclampsia is a leading cause of maternal and neonatal morbidity and mortality worldwide (1). Second only to embolism, it is an important cause of maternal death (2). Preeclampsia places both the mother and the fetus at increased risk for life threatening complications during the antepartum, intrapartum and postpartum periods. The HELLP syndrome, (hemolysis, elevated liver enzymes, low platelets), a severe complication of preeclampsia, can compromise the health of both the mother and the fetus (3). Additionally, preeclampsia is a major cause of preterm delivery, fetal growth restriction and perinatal mortality (4).

Preeclampsia has a reported incidence of 2.6 % to 22.3 % (5, 6). This wide range in incidence is largely due to differences in definition of preeclampsia and study design, e.g. different selection criteria for a study population and differing methods of statistical analysis of data. Despite the high incidence of preeclampsia and the potentially severe consequences of the disease for both mother and child, the etiology of the disease still remains unknown. Although preeclampsia has been studied extensively and many hypotheses regarding etiology exist, the specific etiology of the disease and the risk factors associated with the disease remain poorly understood.

Over the years, researchers have explored many different hypotheses regarding the pathophysiology of preeclampsia. Currently, five major hypotheses exist: 1) placental ischemia, 2) very low-density lipoprotein versus toxicity- preventing activity, 3) immune maladaptation, 4) genetic imprinting and finally, 5) a systemic inflammatory response (7, 8). Six decades ago, Page proposed that the placental component of preeclampsia is mediated by reduced placental perfusion (9). Norwitz et al. also hypothesized that the

primary event in the development of preeclampsia is a failure of the second wave of trophoblast invasion from 16-20 weeks' gestation (10). This failure of trophoblast invasion may be responsible for the destruction of the muscularis layer of the spiral arteries. Norwitz et al. further assert that as the pregnancy progresses and the metabolic demand of the fetoplacental unit increases, the incompletely remodeled spiral arteries are unable to accommodate the needed increase in blood flow. This failure of accommodation and resulting ischemia may lead to further placental dysfunction and what is recognized as preeclampsia clinically (10). Building on this hypothesis, Roberts et al. assert that this abnormal placental perfusion results in the production of circulating factor(s) that alter endothelial cell function (11). The injured endothelium then activates the coagulation cascade resulting in the loss of the ability of the endothelial cells to act as a barrier. Consequently, extravasation of extravascular fluid follows, and the endothelial cells are unable to buffer the effect of the normally circulating pressors. This final breakdown in endothelial cell function leads to what is clinically known as preeclampsia (11). Additionally, Krauss et al. showed that elevated soluble intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule- 1 (VCAM-1) are associated with preeclampsia (12). These findings of increased levels of ICAM-1 and VCAM-1 further support the concept of endothelial cell involvement in the pathogenesis of preeclampsia.

The second major hypothesis currently being evaluated is the very low-density lipoprotein versus toxicity-preventing activity theory (7). This hypothesis is built on the premise that the body mobilizes nonesterified fatty acids in an attempt to compensate for the increased energy demand during pregnancy. It is hypothesized that the mobilization

of nonesterified fatty acids reduces the antitoxic activity of albumin to a point at which very- low density lipoprotein toxicity is expressed and can then cause damage.

Another possible basis for the pathophysiology of preeclampsia is the immune maladaptation hypothesis (7). This hypothesis suggests that immune maladaptation in the body causes abnormal placentation with only shallow invasion of spiral arteries by the endovascular cytotrophoblast cells. The trophoblast subsequently fails to induce the physiologic dilation and remodeling of spiral arteries (7). Additionally, an increased decidual release of cytokines, proteolytic enzymes, and free radicals may mediate endothelial cell dysfunction (7, 13). Many examples in the literature support the role of the immune system in the etiology of preeclampsia. Dekker suggests that the increased incidence of urinary tract infection associated with preeclampsia could be due to this immune maladaptation (14). Dekker further proposes that not only urinary tract infections but any type of infection may result in an increased production of inflammatory products including certain cytokines, free radical species and proteolytic enzymes (14). Additionally, Klonoff- Cohen et al. conducted a case- control study comparing the contraceptive and reproductive histories of primiparous women with and without preeclampsia (15). In this study there was a 2.37 fold increased risk of preeclampsia for users of barrier contraceptives that prevent exposure to sperm (95% CI: 1.01-5.58) (15). These findings suggest that there is a protective role of repeated sperm exposure in decreasing the risk of preeclampsia. This protective role implicates a possible role of the immune system in the development of preeclampsia. Robillard et al. also show that in primigravidae and multigravidae women the length of sexual cohabitation before conception was inversely related to incidence of preeclampsia

($p<0.0001$) lending additional support to the immune maladaptation hypothesis (16). Smith et al. reported that there is an increased incidence of preeclampsia in pregnancies that are the result of donor insemination (relative risk: 1.85, 95% CI: 1.20-2.85) (17). Each of these findings reveals that repeated sperm exposure and subsequent immune system desensitization might be protective against the development of preeclampsia.

The genetic imprinting hypothesis suggests that the development of preeclampsia-eclampsia is based on either a single recessive gene or a dominant gene with incomplete penetrance (7). After studying the incidences of preeclampsia and eclampsia in 147 sisters, 248 daughters, 74 granddaughters and 131 daughters-in-law of women with preeclampsia, Chesley and Cooper concluded that preeclampsia is likely determined by a single recessive gene acting in the affected women instead of in their fetuses (18). They determined that the frequency of this gene is 0.25. Additionally, Lie et al found that a woman who was pregnant by a partner who has already fathered a preeclamptic pregnancy in another woman was at twice the risk of developing preeclampsia in her own pregnancy (19). Lie et al further assert that paternal genes, as expressed by the fetus, may contribute to the mother's risk of preeclampsia. They also state that it is unlikely that purely maternal inheritance, specifically by mitochondrial DNA, is involved in preeclampsia (19).

A fifth main hypothesis, newly presented by Redman et al., suggests that the endothelial cell dysfunction and preeclampsia are part of a more generalized intravascular inflammatory reaction (8). This study argues that preeclampsia is the result of the decompensation of a universal maternal intravascular inflammatory response to pregnancy. This decompensation may be the result of either a very strong stimulus or a

very strong maternal response to a stimulus. Redman et al consider preeclampsia as the extreme end in the range of maternal maladaptation to pregnancy.

Many other hypotheses exist pertaining to the pathophysiology of preeclampsia. After finding that in a group of 101 patients with history of severe early-onset preeclampsia 24.7% had a protein S deficiency, 16.0% had activated protein C resistance, 17.7% had hyperhomocysteinemia and 29.4% had the presence of anticardiolipin antibodies, Dekker et al suggested a role of coagulopathies in preeclampsia (20). It appears that preeclampsia likely comprises a group of heterogeneous causes of maternal, fetal, and placental derivation (21).

Despite the absence of a clear understanding regarding the etiology of preeclampsia, extensive research studies have identified many risk factors for the development of the disease. Risk factors include nulliparity, which increases the risk of preeclampsia by 3.8 -5.4 times, (16, 22-26), multiple gestations (risk ratio: 4:1)(22, 27), advanced maternal age (22, 28), preeclampsia in a previous pregnancy (OR: 10.8, 95% CI: 1.2- 29.1) (25), family history of pregnancy-induced hypertension (risk ratio of 5:1) (18), urinary tract infections (OR: 5.3, 95% CI: 2.9-9.7) (23), high pre-pregnancy body mass index (23, 25, 29, 30), in utero exposure to DES (23,30), a family history of hypertension (25), use of a barrier contraceptive (15), length of sexual cohabitation(16), donor intrauterine insemination (17), chronic hypertension (risk ratio: 10:1) (31), diabetes mellitus (risk ratio: 2:1) (24), chronic renal disease (risk ratio: 20:1) (32), antiphospholipid syndrome (risk ratio: 10:1) (33) and angiotensinogen gene T235: homozygous (risk ratio 20:1) and heterozygous (risk ratio 4:1) (34). Those who live at high altitudes also have an increased incidence of preeclampsia when compared to those

living at sea level (35). Palmer et al believe that this finding is secondary to the interference of the high altitude with the normal vascular adjustments needed during pregnancy. They assert that this may be analogous to other conditions that also decrease uteroplacental oxygen delivery such as preeclampsia (35). Asthma during pregnancy has also been shown to increase the risk of preeclampsia suggesting that both preeclampsia and asthma might be caused by a third factor affecting vascular smooth muscle reactivity (OR: 2.52, 95% CI: 1.47-4.35, p=0.0008) (36). Additionally, clinically normal patients with elevated mid-trimester levels of urine beta-core fragment of human chorionic gonadotropin are at increased risk for the subsequent development of preeclampsia (37).

Controversy exists regarding the finding that African American race is a risk factor. Mittendorf et al established in a nested, case-control study that black race was positively associated with preeclampsia (OR: 1.5, 95% CI; 1.1-1.9) while Savitz and Zhang found that in their study population, blacks and whites had similar risks of disease (22, 23).

Other behaviors and factors are protective against the development of preeclampsia. Cigarette smoking appears to have a protective effect in the development of preeclampsia (22, 23, 38, 39). Klonoff- Cohen et al. conducted a case-control study comparing the smoking histories of 110 nulliparous preeclamptic women and 115 healthy nulliparous women aged 15-35 years delivering at North Carolina Memorial Hospital (39). They found that after adjustment for work during pregnancy, alcohol use, medication use, contraceptive choices and family history of preeclampsia there was a negative association between cigarette smoking during pregnancy and preeclampsia (OR: 0.71, 95% CI: 0.33-1.50) (39). In another case- control study, Mittendorf et al also found

a negative association between cigarette use and preeclampsia after multiple logistic regression analysis (OR: 0.6, 95% CI: 0.5-0.8) (23). A history of spontaneous abortions also appears to be protective in multiparous women (OR: 0.09, 95% CI: 0.02-0.48) (25).

Just as there are contradictory findings regarding the risk factors for preeclampsia, even greater disagreement exists regarding the finding that adolescents are at an increased risk for the development of preeclampsia. Many studies have found that mothers with a young maternal age are at increased risk for developing preeclampsia (6, 40-44). Other studies, however, report that there is no increase in the risk of preeclampsia associated with young maternal age, and there may even be an increase in risk as the maternal age increases (45-52). Despite this controversy surrounding the specific risk of developing preeclampsia for adolescents, there are very few studies focusing only on the adolescent population and any unique qualities that may predispose this group to develop preeclampsia. Since approximately one million teenagers become pregnant in the United States each year, it is important to gain a better understanding of the specific risk factors associated with the development of preeclampsia in an adolescent population in order to improve our ability to predict who is at risk for developing preeclampsia and provide better preventive strategies (53). The following retrospective cohort study, therefore, aims to evaluate risk factors associated with the subsequent development of preeclampsia in adolescents.

Statement of Purpose:

The present retrospective cohort study seeks to identify the risk factors associated with the development of preeclampsia in adolescents. The aim is to use this information to improve the current understanding of the etiology and pathogenesis of this disorder

and facilitate identification of adolescent patients at risk for the development of preeclampsia.

Materials and Methods:

Subjects were selected from all patients who delivered a live singleton at Yale–New Haven Hospital during the time period between January 1, 1994 and April 26, 1997. Patients with pre-existing renal disease, chronic hypertension, diabetes mellitus, a pregnancy facilitated by in vitro fertilization, a multiple gestation or age over eighteen years were excluded from our study. Only patients receiving prenatal care in the Yale University Women's Center, the Hill Health Center and Community Health Care Plan were included.

A standard form devised by the investigators was used to abstract information from the 435 charts that fit the criteria specified above (Appendix A). The Human Investigation Committee of the Yale University School of Medicine authorized the review of charts (Protocol # 9052; Appendix B). Maternal demographic information included age, race, marital status, employment status, type of insurance, clinic service and whether level of education was age appropriate. Information on personal habits included cigarette use, alcohol use and use of illicit drugs. Data abstracted regarding past and present medical and obstetric history included gravidity, parity, age at menarche, gynecologic age, pre-pregnancy height and weight, pre-pregnancy body mass index, weight gain during pregnancy, gestational age at first visit, number of prenatal visits, gestational age at delivery, gestational diabetes during pregnancy, one hour GCT test results, HIV status if known, positive culture for Group B Streptococcus during pregnancy, hyperemesis gravidarum during this pregnancy, sexually transmitted diseases

diagnosed during this and prior pregnancies, history of induced or spontaneous abortions, urinary tract infections during this pregnancy, maximum blood pressure recorded during each trimester of this pregnancy and presence of preeclampsia during prior or current pregnancy. Neonatal data included birth weight, gestational age at delivery, incidence of low birth weight and preterm births, and neonatal morbidity and mortality.

Pre-pregnancy body mass index was calculated using the Quetelet index (weight (kg)/ meters^2) incorporating the pre-pregnancy weight reported by the patient during the first prenatal visit and the height measured and recorded at the first prenatal visit. Gynecologic age was defined as chronological age at conception minus the patient's age at menarche (54). A diagnosis of preeclampsia was given if patients had two blood pressure measurements taken after twenty weeks gestational age and obtained at least six hours apart that were ≥ 140 mmHg systolic or ≥ 90 mmHg diastolic. Additionally, in order to receive the diagnosis of preeclampsia patients had to have at least two urine dipstick measurements obtained at least six hours apart with greater than or equal to 2+ protein. Patients were further classified as having severe preeclampsia if they met any of the following criteria: systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥110 mmHg, proteinuria > 5g/ 24 hours, elevated serum creatinine, grand mal seizures, pulmonary edema, oliguria < 500ml/24 hours, microangiopathic hemolysis, thrombocytopenia, hepatocellular dysfunction, intrauterine growth retardation or oligohydramnios, or headache, visual disturbances, epigastric or right-upper quadrant pain (55).

In the univariate analysis, categorical variables were tested with the chi square or Fisher exact test and continuous variables with two-tailed Student *t* test. Statistical

significance was defined as a P value < 0.05. Multiple logistic regression analysis was then used to determine whether the factors found to be statistically significant by univariate analysis remained significant after controlling for potentially confounding variables. Data was expressed as odds ratios with 95% confidence intervals. All statistical analyses were performed using StatView 5.0 for Power Macintosh.

Results:

Part I:

During the time period between January 1, 1994 and April 26, 1997, 435 women eighteen years or younger who fit the above specified criteria delivered at Yale-New Haven Hospital. Table 1 presents the maternal demographic characteristics of these women.

The average chronologic age of the population was 16.2 years with a standard deviation of 1.4 and a standard error of 0.07. Our study population was 60.2% African American, 20.5% Hispanic and 19.3% Caucasian. Ninety-seven percent of this population was unmarried while the remaining three percent were married. 70.8% of these adolescents were unemployed. 80.7% of these young mothers received Medicaid as their insurance. 87.4% of the population who delivered at Yale-New Haven Hospital during this time period also received their prenatal care in the Women's Center. The remaining 9.2% and 1.8% of our population received their prenatal care at the Hill Health Center and Community Health Care Plan respectively. Information regarding where the subject received her prenatal care was not available for eleven of the four hundred and thirty-five charts (1.6 %). 55.6% of this study population had an age appropriate education level.

Table 1 Maternal Demographic Characteristics

Maternal Demographic Characteristics	Number	Percent (%)
Average Chronologic Age	16.2 years	Not applicable
Race		
African American	262/435	60.2
Hispanic	89/435	20.5
Caucasian	84/435	19.3
Marital Status		
Single	422/435	97
Married	13/435	3
Employment Status		
Unemployed	308/435	70.8
Medicaid	351/435	80.7
Prenatal Clinic Site		
Yale University Women's Center	380/435	87.4
Hill Health Center	40/435	9.2
CHCP	8/435	1.8
Level of Education Age Appropriate	242/435	55.6

CHCP-Community Health Care Plan

Table 2 presents the pertinent medical history data from our population. The average pre-pregnancy height of our population was 64.0 inches with a standard deviation of 2.5 and a standard error of 0.1. Information on pre-pregnancy height for forty-four of the 435 subjects was not found in the corresponding charts. The average

pre-pregnancy weight of the subjects was 134.4 pounds with a standard deviation of 29.0 and a standard error of 1.5. Information on pre-pregnancy weight was not available for fifty-three subjects. The average pre-pregnancy body mass index (BMI) was calculated to be 23 kg/m^2 with a standard deviation of 4.63. The pre-pregnancy BMI was not calculated for sixty-four subjects given the corresponding lack of either pre-pregnancy height or pre-pregnancy weight.

Table 2 Selected Maternal Medical Characteristics

Medical Characteristic	**Value**	**Standard Deviation**	**Standard Error**
Average Pre-Pregnancy Height	64.0[A]	2.5	0.1
Average Pre-Pregnancy Weight	134.4[B]	29.0	1.5
Average Pre-Pregnancy BMI	23[C]	4.63	

BMI- Body Mass Index
[A]expressed in inches
[B]expressed in pounds
[C]expressed in kg/m^2

The information regarding past and present obstetric history is shown in Table 3. 69.9% of the population was nulliparous. The average age at menarche of the study group was 11.8 years with a standard deviation of 1.47 and a standard error of 0.07. The minimum age at menarche was eight years old and the maximum age was seventeen years old. The average gynecologic age (GA) was 4.39 years with a standard deviation of 1.79 and a standard error of 0.09 with a maximum age of 9 years. The average weight gain during pregnancy was 27.05 pounds with a standard deviation of 13.48 and a

standard error of 0.71. The average weight gain per week was 1.18 pounds with a standard deviation of 0.53 and a standard error of 0.03. The average gestational age at the first prenatal visit was 14.49 weeks with a standard deviation of 7.17 and standard error of 0.36. The average number of prenatal visits was 9.70 with a standard deviation of 4.0 and a standard error of 0.20.

Table 3 Selected Maternal Obstetric Characteristics

Obstetric Characteristic	**Value**	**Standard Deviation**	**Standard Error**
Nulliparous	69.9%	Not applicable	Not applicable
Average age at Menarche (years)	11.80	1.47	0.07
Average GA (years)	4.39	1.79	0.09
Average weight gain during pregnancy (lbs)	27.05	13.48	0.71
Average weight gain per week (lbs)	1.18	0.53	0.03
Average gestational age at first prenatal visit (weeks)	14 .49	7.17	0.36
Average number of prenatal visits	9.70	4.00	0.20

GA = Gynecologic Age

Many women in our study experienced complications of pregnancy as seen in Table 4. Two women (0.5%) developed gestational diabetes. Twenty-one women (4.8%) had positive cultures for Group B Streptococcus (GBS) during pregnancy. Forty-five women (10.3%) had at least one sexually transmitted disease (STD) diagnosed during this pregnancy. Eighty-one women (18.6%) had and received treatment for a urinary tract infection (UTI) during this pregnancy. Fifty-six women fit the criteria previously cited for preeclampsia during this pregnancy. Our incidence of preeclampsia in this population was 12.9%.

Table 4 Complications During Pregnancy

Complication	Number	Percent (%)
Gestational Diabetes	2/435	0.5
Positive Culture for GBS	21/435	4.8
Sexually Transmitted Disease	45/435	10.3
Urinary Tract Infection	81/435	18.6
Preeclampsia	56/435	12.9

Univariate statistical analysis with contingency table (chi square and Fisher exact tests) or the Student *t* test as appropriate revealed that gynecologic age (GA), chronologic age (CA), pre-pregnancy BMI, UTI, the total weight gain during pregnancy, the pounds gained per week of pregnancy and pre-pregnancy weight were statistically significant risk factors for the development of preeclampsia in adolescents during pregnancy. Gynecologic age and chronologic age have a negative correlation with the development of preeclampsia. Pre-pregnancy BMI, UTI, total weight gain during

pregnancy, weight gain per week of pregnancy and pre-pregnancy weight were all positively correlated with preeclampsia in adolescents. Table 5 reveals the specific Odds Ratio (OR), 95% Confidence Interval (CI) and p value for each variable after analysis by simple logistic regression.

Table 5 Significant Risk Factors after Simple Logistic Regression

Risk Factor	Odds Ratio	95% CI	P value
GA	0.82	0.69-0.96	0.02
CA	0.81	0.67-0.99	0.04
Pre-Pregnancy BMI	1.11	1.05-1.17	0.0003
UTI	2.00	1.03-3.89	0.04
Total Weight Gain During Pregnancy	1.046	1.02-1.07	0.0001
Weight Gain per Week of Pregnancy	2.40	1.42-4.06	0.001
Pre-Pregnancy Weight	1.01	1.01-1.02	0.0008

GA- Gynecologic Age **CA**- Chronologic Age
UTI- Urinary Tract Infection **BMI**- Body Mass Index

After adjustment for significant factors, multiple logistic regression analysis revealed that gynecologic age, pre-pregnancy BMI, weight gain per week of pregnancy and the total weight gain during pregnancy remained significant for the development of preeclampsia. The specific adjusted odds ratio and 95% confidence interval for each variable is expressed in Table 6 below. Chronologic age and incidence of UTI during

pregnancy were no longer significant after adjustment for significant factors with multivariate logistic regression analysis.

Table 6 Statistical Significance after Multivariate Logistic Regression Analysis

Characteristic	Adjusted Odds Ratio	95 % CI	P value
Gynecologic Age	0.81	0.67 - 0.99	0.04
Pre-Pregnancy BMI	1.10	1.03 -1.18	0.01
Pre-Pregnancy Weight	1.01	1.00- 1.02	0.01
Weight gain per week of pregnancy	2.19	1.27 - 3.76	0.004
Total weight gain	1.04	1.02 – 1.06	0.001

Although both the amount of weight gained per week of pregnancy and the total weight gain during pregnancy remained significant after multivariate logistic regression analysis, we feel that the weight gained per week is a more accurate measure than the total weight gain. This increased accuracy is due to the finding that women with preeclampsia will have a higher weight gain during pregnancy than those without preeclampsia. Subsequently, these same individuals with the greater total weight gain will often deliver earlier than normal controls secondary to the complications of preeclampsia, thus making the total weight gain not clinically significant and less reliable.

Part II:

After finding that a high pre-pregnancy BMI was positively associated with an increased risk for the development of preeclampsia in adolescent pregnancies, we attempted to further subcategorize pre-pregnancy BMI in order to determine if a specific pre-pregnancy BMI was either protective against or predisposed an adolescent to the development of preeclampsia. The study population was the same as that described in the materials and methods section above. The sub-categorization of BMI, as defined by Cnattingius et al, divides subjects into four distinct groups based on BMI as seen in Table 7 below.

Table 7 Classification by Pre-Pregnancy Body Mass Index

Classification[A]	Body Mass Index Range[B]
Underweight/Lean	< 20.0
Normal weight[C]	20.0 – 24.9
Overweight	25.0 – 29.9
Obese	≥ 30.0

[A] Cnattingius, S, Bergstrom, R, Lipworth, L, Kramer, MS. Prepregnancy weight and the risk of adverse pregnancy outcomes. N Engl J Med 1998; 338:147-52.
[B] Body mass index is expressed in kg/m^2
[C] This group will be used as the reference group in further analyses.

Simple logistic regression analysis revealed that obese adolescents had a significantly higher risk for the development of preeclampsia when compared to those with a normal pre-pregnancy body mass index (OR: 4.4, 95% CI: 1.8-10.9, p = 0.001). The incidences of preeclampsia in women categorized as underweight, normal weight,

overweight and obese were 9.2%, 11.1%, 19.0% and 35.7%. Table 8 presents the crude odds ratio, 95% confidence interval and p value for each subcategory.

Table 8 Simple logistic regression analysis of pre-pregnancy BMI for underweight, overweight, and obese adolescents when compared to normal weight adolescents for risk of preeclampsia

Category	Number	Percent (%)	Odds Ratio	95% CI	P Value
Normal weight	188	50.0	1.0	Referent	
Underweight	98	26.1	0.81	0.36-1.84	0.61
Overweight	63	16.8	1.88	0.87-4.09	0.11
Obese	27	7.2	4.44	1.81-10.9	0.001

After adjustment for statistically significant factors with multiple logistic regression analysis, the risk of developing preeclampsia with a pre-pregnancy BMI >30 kg/m^2 remained significant (adjusted OR: 4.54, 95% CI: 1.46 - 14.14, p = 0.009) while being underweight or overweight remained insignificant. Adolescents with a pre-pregnancy BMI > 30 kg/m^2 have a four-fold increased risk of developing preeclampsia during pregnancy. Additionally, when the underweight and overweight adolescents were compared to the normal weight adolescents, there was no significant increase in the risk of developing preeclampsia nor was there any protective effect of being underweight. Table 9 below shows the adjusted odds ratio, 95% CI and p value for each subcategory after multiple logistic regression analysis.

Table 9 Multiple Logistic Regression Analysis of pre-pregnancy BMI for underweight, overweight, and obese adolescents when compared to normal weight adolescents for risk of preeclampsia

Category	Number	Percent (%)	Adjusted Odds Ratio	95% CI	P Value
Normal Weight	188	50.0	1.0	Referent	
Underweight	98	26.1	0.83	0.35-1.96	0.67
Overweight	63	16.8	1.83	0.78-4.29	0.16
Obese	27	7.2	4.54	1.46-14.14	0.009

Part III:

Since simple logistic regression analysis revealed that gynecologic and chronologic age were statistically significant risk factors for preeclampsia in adolescent pregnancy, we attempted to determine which specific gynecologic and chronologic ages put an adolescent at greater risk for the development of preeclampsia. Our initial findings revealed that only gynecologic age remained statistically significant after analysis with multivariate logistic regression. It was felt that the wide range of ages in the chronologic age category, with fewer subjects at the lower end of the range, was confounding to make the entire group less statistically significant. We, therefore, aimed to isolate which age groups were at a higher risk for the development of preeclampsia.

The same study group as previously mentioned in the materials and methods section was used. The information was abstracted from the appropriate charts using the questionnaire in Appendix A.

Groups of individuals with a gynecologic age and chronologic age below specific cutoff values were analyzed using simple logistic regression analysis. A gynecologic age less than 5 or 4 years was found to be a more specific cutoff value for identifying individuals with a statistically significant risk of developing preeclampsia (OR: 1.83, 95% CI 1.02-3.31, p = 0.04). Additionally, individuals with a chronologic age less than 17 or 16 years was a statistically significant cutoff value for the development of preeclampsia in adolescents (OR: 1.99, 95% CI: 1.10-3.62, p = 0.02). Table 10 shows these results.

Table 10 Statistical Significance of Selected Gynecologic and Chronologic Ages by Simple Logistic Regression Analysis

Variable[A]	Odds Ratio	95% CI	P value
GA < 5	1.84	1.02 - 3.31	0.04
GA < 4	2.12	1.20 - 3.75	0.01
CA < 17	1.99	1.10 - 3.62	0.02
CA < 16	1.93	1.08 - 3.47	0.03

[A] Gynecologic Age (GA) and Chronologic Age (CA) are expressed in years

After adjustment for significant factors, analysis with multiple logistic regression revealed that a gynecologic age less than four years, chronologic age less than seventeen years and a chronologic age less than sixteen years all remained significant risk factors for developing preeclampsia during adolescent pregnancy. Furthermore, the cumulative effect of analyzing gynecologic age with chronologic age increased the strength of the association and the risk for developing preeclampsia. Those individuals with a gynecologic age less than four years and a chronologic age less than seventeen years appear to be at the greatest risk for developing preeclampsia, (adjusted OR: 3.27, 95%

CI: 1.627 – 6.552, p= 0.0009) as shown in table 11 below. Although an individual with a chronologic age less than seventeen years or less than sixteen years appears to be at increased risk for the development of preeclampsia, chronologic age less than seventeen years was felt to be a more accurate predictor of preeclampsia as it is more inclusive.

Table 11 Statistical Significance of Gynecologic and Chronologic Ages by Multiple Logistic Regression Analysis

Variable[A]	Adjusted Odds Ratio	95 % CI	P Value
GA < 4	2.22	1.121 - 4.407	0.02
CA < 17	2.85	1.374 - 5.889	0.005
CA < 16	2.06	1.039 – 4.074	0.039
GA < 5 and CA < 16	2.60	1.294 – 5.203	0.007
GA < 4 and CA < 16	2.72	1.287 – 5.741	0.009
GA < 5 and CA < 17	2.86	1.452 - 5.638	0.002
GA< 4 and CA < 17	3.27	1.627 - 6.552	0.0009

[A]Gynecologic Age (GA) and Chronologic Age (CA) are expressed as years

In summary, our study found that individuals with a pre-pregnancy body mass index greater than 30kg/m^2, the individual's pre-pregnancy weight, the amount of weight one gains per week during pregnancy, a chronologic age less than seventeen years, a gynecologic age less than four years, a gynecologic age less than five years in addition to a chronologic age less than sixteen or seventeen years, and a gynecologic age less than

four years in addition to a chronologic age less than sixteen or seventeen years are each significant risk factors for developing preeclampsia during pregnancy.

Discussion:

Our retrospective cohort study found that adolescents with a pre-pregnancy body mass index > 30 kg/m^2 were 4.5 times more likely to develop preeclampsia during pregnancy than those adolescents with a pre-pregnancy body mass index in the "normal" range of 20.0 kg/m^2 – 24.9 kg/m^2. This finding confirms prior studies that showed an association between elevated body mass index and preeclampsia (23, 25, 29,56-59). In these investigations, body mass index is used as a measure of relative obesity.

Obesity is characterized by expanded blood volume and increased cardiac output (60). Additionally, excess weight increases the body's oxygen consumption, leading to an increase in stroke volume and cardiac output in an effort to meet the increased metabolic demands. Hypertension likely results when the systemic vascular resistance fails to decrease as cardiac output increases (60). In the context of this pre-existing physiology in obese individuals, pregnancy increases cardiac output above this already elevated baseline (56). Stone et al postulate that obese individuals may already be maximally vasodilated early in pregnancy and are unable to compensate for the additional increase in cardiac output resulting from pregnancy (56). While the body attempts to sustain the increased blood flow, hypertension may develop and exacerbate the endothelial injury and lead to the clinical sequela of preeclampsia (56).

Potter et al offer another explanation for the association between obesity and preeclampsia (61). Their research showed that patients who develop preeclampsia have increased levels of triglycerides when compared with controls (61). Endersen et al. also

revealed that the sera of preeclamptic patients have a higher ratio of free fatty acids to albumin and increased lipolytic activity when compared with the sera from uncomplicated pregnancies (62). Additionally, the sera from these preeclamptic women induced triglyceride accumulation in cultured endothelial cells with a reduction in prostacyclin release. Wang J et al further showed that hyperlipidemic sera enhances endothelial lipid peroxide production (63). Wang Y et al described the endothelial cell damage that results from endothelial lipid peroxides and the subsequent vasoconstriction and platelet aggregation the lipid peroxides promote (64). Stone et al postulated that obesity-associated hyperlipidemia may directly or indirectly, through lipid peroxides, damage maternal endothelial cells (56). Endothelial cell damage may contribute to the severity of the preeclamptic process, thus explaining the association between obesity and preeclampsia (56).

Prior studies have also subcategorized BMI in order to determine which individuals are at the greatest risk of developing preeclampsia. Sibai et al examined a cohort of healthy nulliparous women and found that the incidence of preeclampsia in this population was 7.6% (58). The investigators divided the population into four groups: BMI < 19.8 kg/m^2, BMI 19.8 kg/m^2 – 25.9 kg/m^2, BMI 26 kg/m^2 - 34.9 kg/m^2 and BMI > 35.0 kg/m^2. An increased incidence of preeclampsia was associated with an increase in BMI as evidenced by an incidence of 4.3% in the group with BMI <19.8 kg/m^2 and an incidence of 12.6% in the group with a BMI of > 35 kg/m^2. When these two extreme groups were compared, the odds ratio was 3.22 for those with BMI > 35 kg/m^2 versus those with BMI < 19.8 kg/m^2, suggesting that individuals with a BMI > 35 were at least three times more likely to develop preeclampsia than those with a BMI < 19.8 (58). Von

Stallie et al also conducted a retrospective case-control study of severe preeclampsia (65). They defined severe obesity as a BMI > 32.3 kg/m^2 and found that a BMI > 32.3 kg/m^2 was positively associated with preeclampsia, (OR: 3.5, 95% CI: 1.68 - 7.46). Individuals considered to have severe obesity by this definition were three times more likely to develop preeclampsia than those with a BMI < 32.3 kg/m^2 (65).

Wolfe et al also found that a maternal body mass index greater than the 90th percentile for the individual was predictive of preeclampsia (OR: 2.26, 95% CI: 1.71-2.99) (59). Interestingly, they noted that pre-pregnancy maternal weight was as predictive of preeclampsia as pre-pregnancy BMI. This finding led this research group to assert that there is no additional advantage to calculating maternal BMI instead of simply weighing the patient. Our study confirms this finding since both pre-pregnancy weight and pre-pregnancy BMI were both positively associated with preeclampsia (OR 1.01, 95% CI 1.00-1.02 and OR: 4.44, CI: 1.03-1.18 respectively). Sibai et al also agreed with this finding in their study that evaluated 2947 healthy women with a single fetus (57). These women were prospectively followed from randomization at 13-27 weeks gestation through delivery. Half of these women were given low dose aspirin while the remainder received placebo. These investigators measured the relative pre-pregnancy weight, calculated as a percentage of desired weight for height, of these subjects. The relative pre-pregnancy weight was predictive of preeclampsia with a p value of <0.01 (57).

Mittendorf also reported that a pre-pregnancy BMI > 30 kg/m^2 was associated with preeclampsia (OR: 2.7, 95% CI: 1.6-4.4) (23). Chesley et al also found that severe obesity is a risk factor for the development of preeclampsia; yet, he stated that this

finding was present secondary to the confounding presence of chronic hypertension in his population (66). Since our study excluded all patients with pre-existing chronic hypertension, chronic hypertension is not a confounding factor in our study. Cnattingius et al reported that the rate of preeclampsia among nulliparous women increased as body mass index increased: the incidence of preeclampsia was 2.8% in lean women and 10.2% in obese women (67). In this study, it appears that being in the underweight category was actually protective against the development of preeclampsia. Although our study used the same categories and values for underweight and obese women as Cnattingius et al., we did not find that women in the underweight category were protected against preeclampsia.

Our current study differs from previous studies since we evaluated the risk of increased pre-pregnancy BMI in women eighteen years old or younger. These previously mentioned studies evaluated the influence of pre-pregnancy BMI on the risk of preeclampsia in the general population, thus making no distinction between adolescents and adults in the analysis. Additionally, previous studies have examined BMI as a risk factor for adverse pregnancy outcomes such as early and late fetal death, preterm delivery, and growth retardation instead of preeclampsia alone (67). Our study, however, does have several limitations associated to our finding that high BMI is positively associated with preeclampsia. For example, pre-pregnancy weight was abstracted from the charts where it was initially obtained by patient report at the first prenatal visit. The patients self reported their pre-pregnancy weight and so it is subject to recall bias. Pre-pregnancy weight was used as an individual variable as well as part of the calculation for pre-pregnancy BMI, therefore subjecting pre-pregnancy BMI to this same recall bias.

Additionally, our subjects were not divided into nulliparous and multiparous groups for purposes of analysis nor were they analyzed within racial groups.

In addition to finding an association between elevated pre-pregnancy BMI and preeclampsia in adolescents, this study also found a strong association between low gynecologic and/or low chronologic age and the risk of developing preeclampsia. As mentioned previously, this finding confirms many existing studies (40-44). Leppert et al looked at the effect of maternal age on various birth outcomes (41). They noted that in a group of 529 women aged 13-19 years there was a 6.6% incidence of preeclampsia while there was an incidence of 2.6% in the 20-36 year old age group. Teenagers, therefore, appear to be twice as likely to experience preeclampsia than women older than twenty years of age (41). In a retrospective study comparing the pregnancy performance of 471 primigravid patients less than 15 years old with a control group of 471 primigravids between 19-25 years old, Duenhoelter et al found that 34.2 % of the women less than 15 years of age developed preeclampsia whereas only 25.3% of the women in the older age group did ($p<0.01$) (40). This study further supports the finding that younger mothers, more specifically adolescents, are at increased risk for preeclampsia. Using information from the National Hospital Discharge survey conducted by the National Center for Health Statistics from 1979-1986, Saflas et al also noted that women less than 15 years old had a 2.8 fold higher risk of developing preeclampsia than women between 30 – 40 years of age (5). In another retrospective case-control study, 9.9 % of the adolescents developed preeclampsia while only 4% of the women aged 20-30 years did giving a p value of <0.001 (42). Clark et al also looked at preeclampsia in adolescents and noted that 22.3%, developed preeclampsia (6). They then found that although prenatal care helped decrease

the incidence of preeclampsia from 22.3% to 11-13 % the incidence still remained high (6). Satin et al. established that pregnant adolescents, younger than 17 years, had an increased incidence of medical complications for both the mother and the fetus when compared with older mothers (43). Additionally, the risks may be the greatest for the youngest teenagers.

Although our study and the previously mentioned studies have shown evidence that adolescents are at higher risk for preeclampsia than the general population, many studies contradict this finding. For example, Berenson et al showed that there was not a significant difference between the development of preeclampsia in pregnant women 12-15 years old (9%) when compared to 16-17 year olds (9%) and 20-22 year olds (10%) (45). They therefore eoncluded that young maternal age was not a risk factor for preeclampsia (45). In this study, there were 147 nulliparous women in the group of 12-15 year olds and nearly twice as many in the 16-17 year old group (45). This discrepancy in the number of subjects in each group is most likely secondary to the smaller number of women who deliver babies at an age less than 15 years. Given the small sample size in the study population there may not have been adequate statistical power to detect a true statistical difference in this population when compared to those aged 16-17 and those 20-22 years old. Additionally, the patients in this study participated in specialized adolescent programs that may have improved their prenatal care and thus helped decrease the risk of preeclampsia.

Poma et al also did not find a significant difference in the incidence of preeclampsia between primigravids <16 years old (14.6%) and primigravids greater than 20 years old (11.3%) (46). Hoff et al compared women 12-16.99 years old with women

17-31 years old by race and found that there was not a significant difference between adolescents and adults when compared within the same race (47). Other studies have also shown that there is not a significant difference between the incidence of preeclampsia in adolescents when compared to adults (48, 50-52). In the study conducted by Osbourne et al, the investigators did not attempt to differentiate between preeclampsia and other forms of hypertension (52). Felice et al. examined the correlation between both the chronologic and gynecologic age and the frequency of preeclampsia and did not find that those with a lower chronologic or gynecologic age were at increased risk (49).

These discrepancies regarding whether adolescents are at increased risk of preeclampsia likely results from differences in patient population, clinical care, or methodologies. For example, these studies do not all use the same criteria for diagnosis of preeclampsia. Felice et al define preeclampsia as a blood pressure greater than 140/90 or an increase in either systolic pressure by 20 mmHg or diastolic pressure by 15 mmHg (49). Bozkaya et al define preeclampsia as two blood pressure readings greater than 90 mmHg measured twenty-four hours apart (42). Still other studies do not specify the criteria they used for defining preeclampsia (6, 40, 46).

In addition to the lack of a uniform definition of preeclampsia in these studies, there is not a consistent definition of young maternal age. Some studies define young maternal age as individuals less than fifteen years old (5, 40, 45) while other studies consider all individuals under nineteen to be of young maternal age (41). Regardless of what age limit researchers choose for their studies, there is no clear definition explaining why each age was chosen as the upper limit of young maternal age.

At this time it is unclear how biologic immaturity may influence the risk of preeclampsia. One possible explanation may be that the uterine vasculature is less well developed in young women conceiving closer to menarche than in those with a higher gynecologic age or further from menarche. Another possibility is that the uterus may need repeated exposure to ovarian hormones, i.e. a specific number of cycles before conception. Until it is clearer how biologic immaturity influences the risk of preeclampsia, gynecologic age may represent a more accurate measure of a woman's biologic readiness for pregnancy than her chronologic age alone.

The results from our study also revealed that there was a positive association between the amount of weight gained per week of pregnancy and the risk of developing preeclampsia. As was previously mentioned, we feel that the weight gain per week of pregnancy is a more sensitive and reliable risk factor to predict the development of preeclampsia. Our finding of an association between the amount of weight gained during pregnancy and the risk of developing preeclampsia confirms other studies (68-72). Over a decade ago here at Yale, Shepard et al studied maternal weight gain as a proportion of prepregnant weight to examine its relationship to complications experienced during pregnancy, labor and delivery for healthy women. Women in this study did not have preexisting chronic disease, were within their normal prepregnant weight for height and delivered single infants without any congenital malformations between 37 to 42 weeks (68). Their population included women aged 14 years and older. 11.6% of their study population was 14-20 years old and the incidence of preeclampsia in their total population was 3.6% (68). Shepard et al found that women with a proportional weight gain greater than 35% had a fourfold risk of becoming preeclamptic when compared to

women with weight gains in the range of 16% - 25% (relative risk =4.01, 95%CI: 1.69-9.51) (68). They recommend that evaluating maternal weight gain in terms of a proportion of prepregnant weight will be a better predictor of preeclampsia and other complications of pregnancy than absolute maternal weight gain.

Building on the findings of Shepard et al and others (68-72) who showed a linear relationship between weight gain and the development of preeclampsia, Theron and Thompson attempted to use centile charts to screen for pregnancy complications. Their goal was to improve the tools available to the clinician when evaluating an individual's risk, based on her weight gain, for developing preeclampsia based (70). Theron and Thompson examined 1003 women with a singleton pregnancy for an association between weight gain and pregnancy complications (70). They measured weight gain as the average weight gain per week over the entire record. Weight gain was then divided into four categories of equal frequency: $\leq$ 0.33kg/week, > 0.33kg/week and $\leq$0.45 kg/week, >0.45kg/week and $\leq$0.56kg/week, >0.56kg/week. The mean age of the women in the study was 25.2 years (range 14-43 years). The incidence of preeclampsia in their population was 7.3% (73/1003) (70). Although the incidence of preeclampsia increased with increasing weight gain, Theron and Thompson found that excessive weight gain is not an effective screening procedure for preeclampsia (70). A previous study by Redman also confirms this finding (71).

A subsequent study by Theron and Thompson, examining the usefulness of adaptive centiles for weight gain and sudden weight gain spurts in identifying those who will develop preeclampsia, confirmed their earlier finding of an association between preeclampsia and increased weight gain (72). In this study, Theron and Thompson

examined the usefulness of a sudden weight gain spurt as a predictor of preeclampsia. They concluded that a sudden weight gain spurt, defined as crossing centile bounds or >0.9kg per week weight gain, is not a reliable sign of impending preeclampsia (72).

Although there appears to be an association between excessive weight gain and preeclampsia, the usefulness of excessive weight gain to identify women who will develop preeclampsia during pregnancy is often questioned. It is unlikely that the weight gain itself causes the preeclampsia. Additionally, it is difficult to determine if the preeclampsia was preceded by sudden or gradual weight gain. Also, it is unclear if the weight gain is actually fluid retention. If the weight gain is a marker of fluid retention then this weight gain would be a result of preeclampsia itself and not a cause of it. In order to be a useful screening tool, weight gain must antedate a rise in diastolic blood pressure or the development of proteinuria. Additionally, as Chesley noted in his earlier work, a sudden weight gain may be obscured unless observed over one or two weekly periods (69). Since many pregnant adolescents have poor attendance in prenatal clinics, leading to greater time periods between appointments, a sudden weight gain may be missed. Currently, an effective means for incorporating weight gain as a screening modality with a reasonable sensitivity and specificity does not exist. Until centiles for weight gain with good sensitivity and specificity are developed, weight gain will remain ineffective as a screening tool.

Although previous studies have found that UTI during pregnancy may place an individual at greater risk for preeclampsia, in our study, UTI did not remain significant after multiple logistic regression analysis (23,73,74). Hsu et al, however, did report that

the women in their study who received magnesium sulfate had urinary catheterization, a known risk factor for UTI, which may have been a possible confounding factor (73).

In summary, our study revealed that obesity prior to pregnancy, the amount of weight gain per week of pregnancy, and biologic youth, as defined by low gynecologic and chronologic age, are strong risk factors for the development of preeclampsia in adolescents. Since it appears that obesity prior to pregnancy is a strong risk factor for the development of preeclampsia in adolescent pregnancy, future research should focus on strategies to normalize BMI before pregnancy in an effort to reduce the frequency of preeclampsia. Future research should also investigate methods to incorporate weight gain per week of pregnancy into a useful clinical tool that can assess the risk of preeclampsia with improved sensitivity, specificity, and positive predictive value. Additionally, continued laboratory research is necessary to help determine the possible relationship between the pathophysiology of preeclampsia and biologic youth. More research is still needed to examine the possible association between urinary tract infections and preeclampsia.

Appendix A: Data Collection Form

Zip Code __ __ __ __ __

Study # __ __ __ __

Age at LMP __ __

Menarche __ __

Gynecologic Age __ __

G__P__ __ __ __

Service: ___ [University Private CHCP/YHP HROB HIll]

Date of admission: __ __/__ __/__ __

Date of delivery: __ __/__ __/__ __

Date of discharge: __ __/__ __/__ __

Prenatal Information

Race: ___ [African-American Caucasian Hispanic ASian

Other _____(list)]

Religion: ___ [None Catholic Protestant Jewish Budhhist Hindu Muslim

Other _____(list)]

LMP: __/__/__

EDD: __/__/__

EDD by LMP date: __Yes __No

Earliest Ultrasound: __ __.__ __ weeks

IVF: __Yes __No

Marital Status: ___ [Single SEparated Married Divorced Widowed] If married, number of years in current marriage: __ __

Last grade completed: ____ [(13) for first year of college, etc.]

Education age -appropriate: ___Yes ___No

Employed: ____Yes __No ___Unknown

Insurance: _____(name)

Contraceptive method as of LMP: ___ [None BCPs DepoProvera/Norplant

Diaphragm Condoms IUD]

Gestational age at first prenatal visit: __ __ weeks

Prenatal Visit Number: __ __

Prepregnancy weight: __ __ __lbs/kg (circle)

1st visit height: __ __ __in/cm (circle) weight: __ __ __lbs/kg (circle) BMI: _____

Weight at delivery: __ ___ ___lbs/kg (circle)

Weight gain over pregnancy: __ __lbs/kg (circle) over __ __weeks

Smoker during pregnancy: __Yes __No ___Unknown

If yes, number of cigarettes per day: __ __ If quit, at what gestation: __ __ wks

Alcohol " " : __Yes __No Amount: _____

Drugs " " :___ [None IV Heroin IV cocaine Powder cocaine

Crack cocaine Marijuana Other List:_____]

Urine toxicology positive during this pregnancy: __Yes __No __Unknown

[List:_____]

Caffeine use during pregnancy: __Yes __No __Unknown Amount ___ oz/d

Depression during pregnancy: __Yes __No

Exercise during pregnancy: __Yes __No __Unknown Amount ___min/d

Meds in pregnancy: _____

_____

_____

_____

Prenatal Hct: 1st_____(__/__ /__) last_____(__/__/__)

One-hour GCT: _____(__/__/__)

Blood Type: _____ [A B AB O]

Rh: _____ [Negative Positive]

PPD: _____[Negative Positive Unknown]

Triple Screen (leave blank if not available): __ __.__ __ MOM (AFP)

__ __.__ __ MOM (hCG)

__ __.__ __MOM (Estriol)

Screen positive for: ___ Down Syndrome ___NTD

HepBsAg: ___ [Negative Positive]

Rubella: ___ [Nonimmune Immune]

RPR: ___ [Nonreactive Reactive]

Blood pressures: __ __ __/__ __ __ (first visit) __ __ weeks

__ __ __/__ __ __ (1st trimester, highest) Highest SBP: __ __ __

__ __ __/__ __ __ (2nd trimester, highest) Highest SBP: __ __ __

__ __ __/__ __ __ (3rd trimester, highest) Highest SBP: __ __ __

Bleeding during this pregnancy: ___None First tri Second tri Third tri

Hyperemsis gravidarum: __Yes __No

Gestational Diabetes: __Yes __No

Ultrasound EFW <10th%ile: __Yes __No __Unknown

STD during pregnancy (Circle any): Gonorrhea Chlamydia Trichomonas

cOndyloma Herpes Syphilis]

Bacterial vaginosis during pregnancy: __Yes __No

Group B strep culture positive any time during current pregnancy or delivery: __Yes __No

HIV: ___ [Negative Positive not Tested]

UTI: __Yes __No

Multiple gestation: __Yes(number of fetuses___) __No

Other antepartum complications: _____

_____

_____

Number of antepartum admissions: ____

Reasons: _____

_____

_____

Past Obstetric History

Number of previous induced/elective terminations of pregnancy: _____

Number of previous first trimester miscarriages: _____

Number of previous second trimester miscarriages: _____

Years since last pregnancy: __ __

Breastfed: __Yes -__ __months __No

Years of each birth (>24 weeks): 19__ __

19__ __

19__ __

19__ __

19__ __

History of previous pregnancy with: _____ [LBW PTD Stillbirth

pReeclampsia/eclampsia Congenital anomaly Other List:

_____ _____]

Past Medical History

Preexisting diabetes: __Yes __No

Preexisting or hypertension on 2 separate occasions less than 20 weeks: __Yes __No

Asthma: __Yes __No

HIV: __Yes __No __Unknown

Sickle Cell Disease: __Yes __No

Hyperthyroidism: __Yes __No

Renal disease: __Yes __No

SLE: __Yes __No

Antiphospholipid Syndrome: __Yes __No

Operations: __Yes __No List:_____

_____

History of Depression: __Yes __No

Other Medical history: __Yes __No List: _____

_____

_____

_____

_____

Medications: _____

_____

_____

_____

Family History/Relationship: _____/_____

_____/_____

_____/_____

_____/_____

Labor & Delivery

Gestational Age at delivery: _ _._ _ (1d=_ _.14, 2d=_ _.29, 3d=_ _.43, 4d=_ _.57, 5d=_ _.71, 6d=_ _.86)

Neonatal number: ____

PIH: ___None ___Mild ___Severe

Superimposed on chronic hypertension: __Yes __No

Antepartum B/Ps:

Highest SBP: _ _ _ Highest DBP:_ _ _

Lowest SBP: _ _ _ Lowest DBP: _ _ _

Proteinuria:

Highest Dipstick: __Zero-trace __+1 __+2 __+3 __+4

Highest 24hr protein: _ _._ _gm

Criteria for Severe PIH:

SBP ≥160 mmHg: ___Yes ___No

DBP≥110 mmHg: ___Yes ___No

Proteinuria ≥5g/24hr: ___Yes ___No

Elevated serum Cr: ___Yes ___No

Eclampsia: ___Yes ___No

Pulmonary edema: ___Yes ___No

Oliguria ≤500ml/24hr: ___Yes ___No

Thrombocytopenia (<100K): ___Yes ___No

Elevated LFTs: ___Yes ___No

HELLP: ___Yes ___No

IUGR: ___Yes ___No

Oligohydramnios: ___Yes ___No

Cerebral disturbances: ___Yes ___No

Visual disturbances: ___Yes ___No

Epigastric/RUQ pain: ___Yes ___No

Therapy for preeclampsia: ___MgSO4 ___Dilantin ___Phenobarbital ___Hydralazine ___Labetalol ___Nifedipine ___Aldomet ___Other

Days from diagnosis to delivery: ___ days

Highest blood pressure in labor: _ _ _/_ _ _ Highest SBP: _ _ _

Induction: __Yes __No Augmentation: __Yes __No

If yes, reason: ____ [Infection Tracing abnormality Preeclampsia prolonged Rupture of membranes Other List: _____ None given(5)]

Method(s) (circle any): PG gel Misoprostol Cervidil Laminaria Pitocin

Epidural: __Yes __No

Cesarean section: __Yes __No

If yes, indication (circle any): ___ [nonreassuring fetal Testing (tracing or pH) labor Arrest failed Instrument Elective Other List:_____]

Vaginal delivery: ____ Spontaneous Forceps Vacuum

Tracing Abnormalities: ___ [None persistent nonReactive persistent Late decelerations Bradycardia]

Chorioamnionitis (fever/antibiotics/positive tap): __Yes __No

Abruption (retroplacental clot at delivery): __Yes __No

Confirmed by placental pathology: __Yes __No

Stillbirth: __Yes __No

Maternal mortality: __Yes __No

Other complications in labor: _____ _____

Apgars: ___(1 min) ___(5 min) ___(10 min)

Cord pH: __.__ __ (a) __.__ __ (v) __not obtained (0)

Postpartum Course

Highest blood pressure: __ __ __/__ __ __ Highest SBP: __ __ __

Postpartum complication (circle any): [None Hemorrhage Fever Endometritis

Depression Preeclampsia eClampsia Other List:_____]

Contraceptive choice(circle any): [None DepoProvera OCPs Progesterone-only pill

NorpLant IUD Foam/condoms DiAphragm Other List:_____]

Neonatal Course

Sex: ___ [Male Female]

Birth weight: _____gm or __ __lbs __ __oz

Circle: AGA SGA LGA

Positive blood cultures: __Yes __No Organism: _____

Morbidity: ___ [Pneumonia RDS BPD NEC IVH

Hyperbilirubinemia Other List: _____]

Mortality: __Yes __No

Congenital anomaly: __Yes __No List: _____

Length of hospital stay: ___days

Blood Type: ___ [A B AB O]

Rh: ___ [Negative Positive

Breastfeeding: __Yes __No

SIDS: __Yes __No

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