A THESIS

# Does gestational anemia affect maternal morbidity during delivery?

By

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CERTIFICATE OF APPROVAL

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This is to certify that the Master's thesis of

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**LIST OF ABBREVIATIONS**

ICD-9…….....……International Classification of Disease Codes (9th edition)

LOS……..Length of Stay

Hct……...Hematocrit

hgb……....Hemoglobin

PPH……....Postpartum Hemorrhage

STORC…… State Obstetric and Pediatric Research Collaboration

WHO……...World Health Organization

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**ABSTRACT**

***Objective:*** To describe the association between gestational anemia and maternal morbidity and requirements for aggressive treatment of postpartum hemorrhage.

***Background****:* Surgical literature has shown perioperative complications with hemoglobin levels below 8g/dL, yet little is known about the impact of moderate or severe anemia on perinatal maternal morbidity. Research suggests that anemia may be a risk factor for severe obstetric hemorrhage, which is the leading cause for pregnancy related deaths in the United States. Despite this research, the specific association between prenatal anemia and maternal morbidity is not well understood.

***Methods:*** We conducted a cross-sectional study on data extracted from the State Obstetric and Pediatric Research Collaboration (STORC) obstetric electronic health record. All single, term (≥37 weeks) deliveries that occurred between 1/1/2006 and 6/1/2009 with a recorded hemoglobin level within 50 days of delivery were eligible for inclusion in this study. Odds of receiving medical, surgical or other (blood transfusion or IV iron) interventions for treatment of postpartum hemorrhage among women with mild, moderate, and severe prenatal anemia was compared to women with no prenatal anemia. Smoking, maternal age, parity, infant birth weight, and high-risk pregnancy were evaluated as potential confounders of this relationship via logistic regression models. We also evaluated the association between anemia and length of stay (as a proxy for complications) among women with and without a postpartum hemorrhage by comparing mean length of stay to women without anemia.

***Results:*** Women with anemia did not have a higher level of morbidity at the time of delivery than women without anemia. The odds of receiving treatment for postpartum hemorrhage among women with mild anemia was 1.28 (95% CI: 0.79 – 2.06) times the odds of receiving treatment in women without anemia after adjusting for advanced maternal age, high risk pregnancy and delivery mode. This was similar to moderate

anemia, where the odds of receiving treatment for a postpartum hemorrhage among women with moderate anemia were 1.42 (95% CI: 0.55-2.78) times the odds for those with no anemia. The mean length of stay for women who delivered vaginally with no anemia was 1.85 (95% CI: 1.83-1.99) days, which was not significantly different from women with mild or moderate anemia (mild 1.84 days [95% CI: 1.64-2.04]; moderate 1.85 days [95% CI: 1.53-2.17]) after adjusting for advanced maternal age and high-risk pregnancy. The mean length of stay for women who delivered via cesarean section with no anemia was 4.05 (95% CI: 3.44 – 4.65) days, which was not significantly different from women with mild or moderate anemia (mild 4.01 days [95% CI: 3.66-4.43]; moderate 3.76 days [95% CI: 3.19-4.33]) after adjusting for advanced maternal age, high-risk pregnancy and diagnosis of a postpartum hemorrhage.

***Conclusion:*** Prenatal anemia was not associated with a more severe postpartum hemorrhage requiring more aggressive management. Having prenatal anemia also did not put women at a higher risk of increased length of stay compared to women without prenatal anemia.

## CHAPTER ONE: INTRODUCTION

Although childbirth is hallowed as a natural and safe experience, the reality is that internationally a half a million women die annually from causes related to childbirth and nearly a quarter of these deaths are caused by a postpartum hemorrhage.(1) Despite improved understanding of risk factors during pregnancy, maternal mortality in the United States has increased nearly 1.7 times over the last decade.(2) In the United States, postpartum hemorrhage ranks among the top three causes of maternal death, along with embolism and hypertension.(3) Postpartum hemorrhage often develops unexpectedly, but early diagnosis and treatment can prevent the morbidity and possible mortality associated with this condition.(4) Early recognition of the risk factors for developing morbidity from a postpartum hemorrhage, prior to the time of delivery, may help to prevent these events from occurring.

Postpartum hemorrhage is the most common maternal morbidity in developed countries.(5) The WHO defined postpartum hemorrhage as an estimated blood loss of greater than 500mL in vaginal deliveries and greater than 1000mL in cesarean deliveries.(6) Clinicians diagnose postpartum hemorrhage by making a visual approximation of blood loss.(5) Unfortunately, the estimation of blood loss by practitioners is often inaccurate, with underreporting being more common.(7) Therefore, it is thought that the rate of postpartum hemorrhage is underestimated. Other more objective measures of a postpartum hemorrhage, such as a 10% decrease in hemoglobin after delivery (8, 9), do not effectively identify women who are actively hemorrhaging during delivery. Therefore, the diagnosis of postpartum hemorrhage continues to be a clinical judgment of the provider based on the observed amount of blood loss.

Appropriate management of postpartum hemorrhage can significantly reduce mortality.(4) Management of postpartum hemorrhage consists of a balance between

conservative techniques and more invasive methods to control the bleeding, which is an individual clinical decision based on the medical characteristics and future fertility desires of the patient.(10) The first-line treatment of excessive bleeding is the administration of one or more of the following uterotonics: oxytocin, methergine, hemabate, and misoprostol.(10) If a combination of uterotonics drugs fails to control the bleeding, tamponade of the uterus can decrease the hemorrhage.(10) When these more conservative methods fail to control the bleeding, practitioners use one of several surgical methods available including bilaterally uterine artery ligation (O'Leary sutures), B-lynch sutures, and finally hysterectomy.(10) In addition, blood transfusions and IV iron can be used to treat hemodynamic instability as a result of a hemorrhage.(11)

Postpartum hemorrhage has been associated with serious morbidity such as: anterior pituitary ischemia (Sheehan's syndrome), myocardial ischemia, dilutional cardiomyopathy and possibly death.(11) Most cases of postpartum hemorrhage develop unexpectedly. Because postpartum bleeding is a risk factor for maternal morbidity and mortality,(5, 11) many studies have attempted to describe risk factors for postpartum hemorrhage. Studies have show that antenatal factors such as maternal age,(12) multiple pregnancies,(12) and maternal diseases such as cardiac disease and hemolytic anemia, elevated liver enzymes and low platelet count syndrome (HELLP),(12) and maternal obesity(5) are risk factors for delivery. Other risk factors for increased bleeding after delivery include infant birth weight >4.5 kg and twin pregnancies.(12) One study used the Medical Birth Registry of Norway to identify the prevalence of risk factors among women with severe obstetric hemorrhage and found a higher odds of women with anemia (hgb <9.0g/dL).(12) This finding suggests that there may be an association between prenatal anemia and increased morbidity from a postpartum hemorrhage.

The association of anemia with severe obstetric hemorrhage described in Norway is of particular interest because there is little evidence on whether maternal

morbidity is associated with anemia.(12) While gestational anemia has been well investigated for its association with infant outcomes such as low birth weight and pre-term delivery, the impact of anemia on maternal health is not well understood.(13) Anemia is a common condition of pregnancy, therefore understanding the association anemia has with maternal morbidity could greatly improve our perinatal management to prevent poor outcomes. The CDC found that in Oregon 27.4% of pregnant women had prenatal anemia during their third trimester, which was lower than the national prevalence of 33.8%.(14) Most forms of anemia during pregnancy are easily reversible, therefore understanding this association could lead to an obvious preventive intervention.

Anemia is an extremely common condition in pregnancy. The global prevalence of anemia in pregnant women is 41.8%, which is 56 million pregnant women.(15) The World Health Organization defines anemia as hemoglobin of less than 11g/dL. They further divide levels of anemia into mild (hgb 10-10.9 g/dL), moderate (hgb 7-9.9 g/dL) and severe anemia (hgb<7g/dL). During pregnancy hemodilution is a normal physiologic process, which puts women at a higher risk of developing anemia. Blood volume progressively increases through mid-pregnancy and then plateaus in the third trimester. This increase occurs in both red blood cell mass and plasma volume, with a greater increase in the plasma volume compared to red cell mass leading to a hemodilution. There is disagreement about whether this drop in hemoglobin is physiologic or a pathologic change. We do know from the surgical literature that people with hemoglobin at 7-8g/dL have more perioperative complications than individuals without anemia.(16)

Iron deficiency anemia is the most common form of prenatal anemia(17), and is easily treatable. Several studies have shown that iron supplementation during pregnancy will reduce women's risk of anemia in late pregnancy.(2) In contrast, prospective studies in China and Mexico have shown that high maternal hemoglobin

concentrations increase the risk of premature delivery and low birth weight infants.(5, 6) These studies have created controversy over universal treatment of pregnant women with oral iron supplementation. Recently, the Institute of Medicine established an upper limit of iron supplementation at 45 mg/day to reduce gastrointestinal side effects.(7) This is much lower than international recommendations, which start at 60mg/day of oral iron. Despite concerns of iron overload, gestational anemia continues to be a significant health burden in the United States.

Understanding the relationship between anemia and maternal morbidity is an important public health topic because changed medical practices have favored greater tolerance of prenatal iron deficiency anemia, which is a common condition during pregnancy. Additionally, with the emergence of new therapies such as IV iron, which are better tolerated by patients,(4) anemia may be a preventable cause of maternal morbidity. The objective of this study was to quantify the affect of gestational anemia on maternal morbidity and the odds of treatment for postpartum hemorrhage. We evaluated whether women with gestational anemia were at an increased odds of receiving a treatment for postpartum hemorrhage. We also analyzed whether all women with gestational anemia had an longer post-delivery hospital stay than those without anemia, which we used as a proxy for complications at the time of delivery, including infection, more severe bleeds and other poor outcomes.

## CHAPTER TWO: METHODS

### *Background*

The institutional review board at Oregon Health & Science University (IRB00006847) approved our study protocol. This was a cross-sectional study of data that was extracted from the State Obstetric and Pediatric Research Collaboration (STORC) obstetric electronic health record. STORC was an integrated inpatient and outpatient obstetric medical record used at OHSU from February 2005 to June 2009. The record was designed to capture variables used in major perinatal research studies through structured data fields. This record and database was used for both research and clinical purposes. The data was captured using drop down menus, check boxes, auto-population of lab data and free text. Data entered from previous visits or lab draws were pulled forward to notes and providers were given the option to enter data to correct or supplement these auto-populated fields. Additionally, we supplemented the STORC database with information from EPIC for billing and laboratory values to help ensure complete ascertainment of accurate data.

### *Study Population*

All single, live, term gestation (≥ 37 weeks) deliveries to adult women (age ≥18) that occurred at Oregon Health and Science University (OHSU) between 1/1/2006 and 6/1/2009, with a recorded admit date and a hemoglobin or hematocrit recorded within 50 days of delivery were eligible for inclusion in this study. We excluded women with known thalassemia or sickle cell disease or trait, poly or multiple gestation, abruption, uterine rupture, bleeding dyscrasias, placenta previa, thrombocytopenia (<50,000 platelets),(18) and those on blood thinning medications (warfarin, lovenox or heparin). These conditions were associated with either anemia prior to pregnancy or increased likelihood of hemorrhage; therefore their management may differ from routine management of hemorrhage.

***Exposure***

**Maternal Anemia**

We defined maternal gestational anemia as maternal hemoglobin (hgb) <11.0 g/dL as defined by the World Health Organization.(19) We categorized maternal anemia according to WHO definition: none (hgb≥11 g/dl), mild (hgb=10-10.9 g/dl), moderate (hgb=7-9.9 g/dl) and severe (hgb<7 g/dl) based on their pre-delivery hemoglobin (Table 1).(19) We condensed the moderate and severe anemia categories into one category in logistic regression models, as there were only two individuals with severe anemia. In addition to a pre-delivery hemoglobin level we also extracted post-delivery hemoglobin levels for our analysis. When an individual had multiple hemoglobin levels measured either before or after delivery we always used the pre-delivery and post-delivery hemoglobin that was drawn closest to the time of delivery. If a hemoglobin level was not available we utilized hematocrit (HCt) measurements, and converted them to hemoglobin (Hgb) using the following equation:

$$Hgb = \frac{HCt}{3}$$

Table 1: Data extraction method for exposure variable

| Measure | Definition | Variable Location in STORC | Type of variable | How data was collapsed for analysis |
|---|---|---|---|---|
| Pre-Delivery Anemia | None: hgb ≥ 11g/dL<br>Mild: hgb = 10-10.9g/dL<br>Moderate:<br>hgb = 7-9.9g/dL<br>Severe: hgb <7g/dL | Admission Note<br>Clinic Note<br>OB discharge note<br>EPIC laboratory | Auto-populated from lab data with physician entry | Continuous variable will be grouped based on hemoglobin level into none, mild, moderate, severe as previously defined. |

### *Primary Outcomes*

#### Treatments for hemorrhage

Treatments for hemorrhage, the primary outcome, were used as an indicator of severity of hemorrhage. Based on common clinical practice we divided potential treatments into three categories: surgical, medical and other non-pharmaceutical therapies. Surgical treatments included: hysterectomy, b-lynch stitch, uterine artery ligation, balloon tamponade and embolization. Medical treatments included misoprostol, methergine and hemabate. We did not include oxytocin because it is commonly used in obstetrics for multiple purposes including prevention and treatment of hemorrhage, and we were unable to determine the clinical indication for which this treatment was used. The other non-pharmaceutical therapies that were of particular interest included transfusion and IV iron therapy (Table 2). We supplemented the data from STORC on medical treatments with patient treatment from EPIC hospital billing, to ensure that any treatments given were captured.

#### Length of stay

We included length of stay as an outcome and proxy indicator for increased maternal morbidity. The entire length of hospital stay at the time of delivery was included. Length of hospital stay was measured as a continuous variable in days (Table 2). Current federal law prohibits the restriction of mothers' benefits for hospital length of stay for childbirth less than 48 hours for vaginal delivery and 96 hours for cesarean section.(20) Conceptually, we assumed that a longer length of stay was likely indicative of medical complications during or after childbirth.

Table 2: Data extraction method for primary outcome variables

| Measure | Definition | Variable Location in STORC | Forms of variable entry | How data was collapsed for analysis |
|---|---|---|---|---|
| Surgical Treatment | Hysterectomy<br>b-lynch stitch<br>uterine artery ligation (O'Leary)<br>Embolization<br>Balloon tamponade | Delivery note<br>EPIC billing | Free text:<br>*"embolization"*<br>Check box:<br>*"hysterectomy", "b-lynch", "O'Leary" "balloon"* | YES or NO<br>Yes, if any of defined surgical treatments are documented, will be collapsed into one outcome |
| Medical Treatment | Misoprostol<br>Hemabate<br>Methergine | Delivery note<br>EPIC billing | Free text:<br>*"hemabate", "methergine"*<br>Check box:<br>*"misoprostol"* | YES or NO<br>Yes, if any of defined medical treatments are documented, will be collapsed into one outcome |
| Additional Therapies | Blood Transfusion<br>IV iron | Delivery note<br>OB discharger note<br>EPIC billing | Free text: *"IV iron"*<br>Check box:<br>*"transfusion"* | YES or NO<br>Yes, if any of defined additional therapies are documented, will be collapsed into one outcome |
| Length of stay (LOS) | Continuous variable | Admission note<br>Discharge note<br>EPIC billing | Calculated as:<br>*Time and date discharge is signed - Time and date admission note is opened* | Continuous variable measured in fraction of days. |

***Additional Variable***

**Postpartum Hemorrhage within 24 hours of delivery**

Postpartum hemorrhage is clinically defined as blood loss of >500mL (vaginal delivery) and >1000mL (cesarean delivery) after completion of the third stage of labor (accepted standards for blood loss by delivery type).(6) Since the diagnosis of postpartum hemorrhage is a clinical diagnosis, for our study we defined a postpartum hemorrhage as either a clinical diagnosis recorded in the medical record or a recorded estimated blood loss of >500mL (vaginal delivery) and >1000ml (cesarean delivery) (Table 3).

Table 3: Data extraction method for classification of postpartum hemorrhage

| Measure | Definition | Variable Location in STORC | Forms of variable entry | How data was be collapsed for analysis |
|---|---|---|---|---|
| Postpartum Hemorrhage | Blood loss after completion of the third stage of labor:<br>Vaginal Delivery >500mL<br>Cesarean Delivery >1000mL<br>*Or* clinical diagnosis recorded in the chart | Delivery note<br>OB discharge note | Free text: EBL (cc)<br>Check box: "*postpartum hemorrhage"* | YES or NO<br>Yes if *"postpartum hemorrhage"* is checked or EBL is defined as postpartum hemorrhage given definition. |

***Potential Confounders***

Five variables were evaluated as potential confounders of the relationship between anemia and postpartum hemorrhage: smoking during pregnancy (any smoking during pregnancy), infant macrosomia (>4000g), advanced maternal age (>35 years), parity (nuliparous, multiparous, or grandmaltiparous), race (Caucasian, Hispanic, other or unknown) and high-risk pregnancy (by ICD-9 code). The specific conditions included in high-risk pregnancy were previously classified by Gregory et al. and Korst et al. by ICD-9 codes.(21, 22) This data was extracted from the medical history reported to the clinician by the patient with the exception of infant weight, which was objectively measure by providers at the time of delivery. See Table 4 below for specific location within the medical chart.

Table 4: Data extraction method for potential confounders

| Measure | Definition | Variable Location in STORC | Forms of variable entry | How data was collapsed for analysis |
|---|---|---|---|---|
| Smoking status in pregnancy | Yes or no | Admission note | Check box | YES or NO<br>Yes if box is checked |
| Infant weight at birth | Macrosomia: weight >4000g<br>No Macrosomia: weight ≤ 4000g | Delivery note | Free text: *"infant weight (g)"* | YES or NO<br>Yes if infant weight is recorded as greater than 4000g |
| Maternal age | Advanced maternal age: age >35<br>Normal maternal age: 18 <age ≤ 35 | Admission note<br>Delivery note | Calculated as: *"date of delivery – date of birth"* | YES or NO<br>Yes if calculated age is greater than 35 |
| Parity | Grand multiparous: ≥5 prior deliveries<br>Multiparous: 1-4 prior deliveries<br>Nulliparous: 0 prior deliveries | Admission note | Free text *"gravida, term, preterm, abortions, live births"* | NULLIPAROUS, MULTIPAROUS, or GRAND MULTIPAROUS<br>Categorized as defined using GTPAL recorded at time of admission |
| Race | Caucasian, Hispanic, other or unknown | Admission note | Check box | Categorized using data recorded be provider |
| High Risk | High Risk: one or more maternal high risk condition | Admission note | ICD-9 code in problem list | YES or NO<br>Yes if following conditions are documented:<br>Soft tissue disorder 654.0, 1, 4, 5, 6, 7<br>Severe Hypertension 642.5, 6<br>Other Hypertension 642 except 643.5, 6<br>Antepartum Bleeding 641<br>Liver disorders 646.7<br>Substance abuse 648.3<br>Mental illness 648.4<br>Herpes 054, 647.6<br>Kidney disorder 646.2<br>Thyroid disorder 648.1<br>Asthma 493<br>Diabetes 250, 648.0,8<br>Heart disease 648.5,6 |

**Data Coordination**

Demographic, health care, and health outcome information were obtained from the STORC electronic health record. Specific data including hemoglobin and hematocrit, treatments and diagnoses at the time of discharge were supplemented by EPIC laboratory and billing data respectably. The data from STORC and EPIC billing that were entered as free text were searched for key words using the Microsoft office "find" function. Each entry was then individually reviewed by the researcher and coded for specific diagnoses or interventions written as free text.

All relevant data were extracted by the STORC research team and was provided in an Excel worksheet that was imported into STATA® (version 11.1; StataCorp, College Station Texas), the statistical software package that was used to conduct data analyses for this project. The data from each of the data sources were then merged in STATA using a unique patient ID and admit date, which was important since some patients delivered more than once at OHSU during our study period. Therefore individuals without an admit date were excluded prior to merging the data. The data were then cleaned by individually checking 10% of the total study population for errors in data coding and/or merging.

The population was limited by a number of exclusion criteria. Each patient required a hemoglobin or hematocrit recorded within 50 days of delivery (either at admission or in clinic) since this variable was necessary for categorization of the independent variable (anemia in the third trimester). Missing data for other variables was coded as such, but these subjects were retained in analysis for variables for which they did have data. Subjects were also excluded if they had a personal history (i.e. not family history) of thalassemia, sickle cell disease, or other bleeding dyscrasias, or if the current pregnancy was complicated by abruption, poly or multiple gestation, placenta

previa, blood thinning medications (warfarin, lovenox or heparin) or thrombocytopenia (<50,000 platelets).

***Statistical Analysis***

We used multivariable logistic regression to assess the relationship between prenatal maternal anemia and receiving a treatment for postpartum hemorrhage controlling for potentially confounding maternal characteristics (advanced maternal age, high risk pregnancy, and mode of delivery). We did not analyze individual treatments because they were very rare. We used multivariable linear regression to assess the relationship between prenatal maternal anemia and length of stay after delivery for both vaginal and cesarean delivery controlling for potentially confounding maternal and clinical characteristics (advanced maternal age, high-risk pregnancy and post-partum hemorrhage). We grouped all the treatment outcomes into a dichotomous variable: treatment or no treatment. We created categorical variables for our exposure variable of anemia (none, mild, moderate/severe). We selected those without anemia as the reference population.

To evaluate whether women with gestational anemia were at an increased odds of receiving a treatment for postpartum hemorrhage we limited the population to only women who had a diagnosed postpartum hemorrhage. We assessed difference between levels of anemia (none, mild and moderate) in demographic characteristics, age, advanced maternal age, race, parity, smoking, macrosomia, and high-risk pregnancy, using the chi-squared test for all comparisons except age, for which we used ANOVA. We did not stratify the population by mode of delivery, but did evaluate this variable as a potential confounder since the outcomes were not limited by the mode of delivery. Estimates of unadjusted odds ratios for receiving treatment (medical, surgical or other therapy) for women with mild and moderate anemia compared to those individuals with no anemia (control group), and corresponding 95% confidence intervals

were calculated. We entered potential confounders and anemia into logistic regression models to calculate adjusted odds ratios for the outcome of treatment. We reported the odds ratios and corresponding 95% confidence intervals, with statistical significance considered a confidence interval that did not cross one. The following variables were examined as potential confounders for the association between gestational anemia and each outcome (surgical and medical treatment for postpartum hemorrhage, and other therapies): (1) smoking status (2) macrosomia (3) maternal age and (4) parity (5) high risk (Table 3) and (6) mode of delivery. For each potential confounder we evaluated whether it was associated with the independent variable (anemia) and outcome (treatment), with a *P* value <0.20. Variables that were associated with both the independent variable (anemia) and the outcome were entered simultaneously into the logistic regression equation. Variables that were not associated with either the outcome or independent variable, but were conceptually considered a confounder, were retained and further evaluated in the model. We did this by adding them in a forward stepwise fashion to evaluate whether they significantly changed (>10%) the odds ratio in the final model.

To analyze whether women with gestational anemia had an increased length of hospital stay we included all women in the study population. In this model, length of stay was the outcome of interest as measured in days. For these analyses, the population was stratified by mode of delivery since this changes the expected number of days a woman would spend in the hospital for a normal delivery. We assessed differences between levels of anemia (none, mild and moderate) in demographic characteristics, age, advanced maternal age, race, parity, smoking, macrosomia, and high-risk pregnancy, using the chi-squared test for all comparisons except age for which we used ANOVA. Mean length of stay for women with mild and moderate anemia were compared to those individuals with no anemia (control group), and corresponding 95%

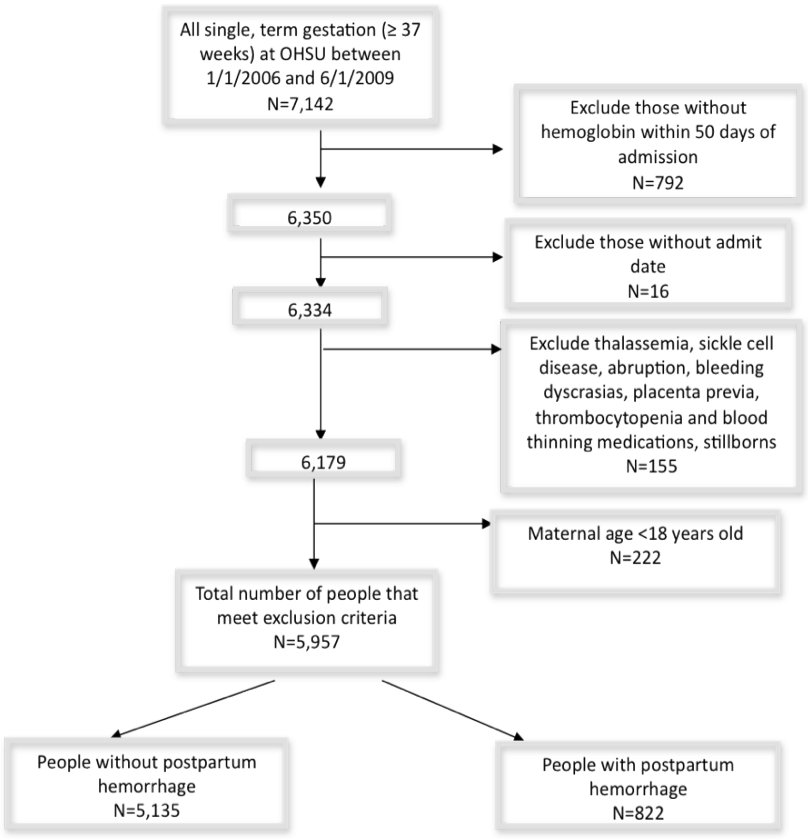
confidence intervals were calculated for each mode of delivery. We then calculated the adjusted mean length of stay and the 95% confidence intervals via linear regression. Statistically significant differences in the length of stay were considered when 95% confidence intervals did not overlap between the control (no anemia) and exposure group (mild or moderate/severe anemia). The following variables were examined as potential confounders for the association between gestational anemia and each outcome (surgical and medical treatment for postpartum hemorrhage, and other therapies): (1) smoking status (2) macrosomia (3) maternal age (4) parity (5) high risk (see Table 3 for details) and (6) postpartum hemorrhage. These characteristics were then evaluated as potential confounders for the linear regression model using the same methods as previously described for logistic regression.

## CHAPTER THREE: RESULTS

### *Population Characteristics*

There were a total of 7,142 women who delivered single, term gestation deliveries at OHSU between January 1, 2006 and June 1, 2009. After excluding women who did not have a pre-delivery hemoglobin or hematrocrit measured within 50 days of delivery, age greater than 18 and with known bleeding disorders, there were a total of 5,957 deliveries included in this study (See Figure 1). We limited the analytic population to 822 women (16%) with a postpartum hemorrhage to evaluate whether women who had a postpartum hemorrhage and gestational anemia had an increased odds of receiving treatment for postpartum hemorrhage as compared to women who had a postpartum hemorrhage and were not diagnosed with gestational anemia. Within this population 121 (14.7%) had some level of pre-delivery anemia (hemoglobin ≤11.0 g/dL). Among those with anemia, 94 (77.7%) had mild anemia (hemoglobin 10-10.9 g/dL), and 27 (22.3%) had moderate anemia (hemoglobin 7-9.9 g/dL). There were no women with severe pre-natal anemia who had a postpartum hemorrhage.

**Figure 1: Exclusion Criteria**




***Postpartum Hemorrhage Treatment***

Demographic characteristics for the 822 women with a postpartum hemorrhage by level of anemia are provided in Table 5. The test of difference comparing any anemia (mild or moderate) to no anemia demonstrated that the two groups are only statistically different with regards to parity. We found that women with anemia were significantly more likely to be multiparous (p=0.01). All of these characteristics (age, race, parity, tobacco use, macrosomia and high risk pregnancy) were evaluated as potential confounders in our model.

**Table 5: Demographic Characteristics for women with postpartum hemorrhage based on level of anemia, OHSU, 1/1/2006-6/1/2009**

| | Overall Total | No Anemia | Mild Anemia | Moderate Anemia | P-value |
|---|---|---|---|---|---|
| Variable | Mean (%) | Mean (%) | Mean (%) | Mean (%) | |
| N | 822 | 701 (85.3%) | 94 (11.4%) | 27 (3.3%) | |
| Age | 27.6 (±5.9) | 27.8 (±6.0) | 26.7 (±5.9) | 26.6 (±5.0) | |
| Age >35 | 101 (12.3%) | 89 (12.7%) | 11 (11.7%) | 1 (3.7%) | 0.37 |
| Race | | | | | 0.51 |
| White | 195 (23.7%) | 171 (24.4%) | 19 (20.2%) | 5 (18.5%) | |
| Hispanic | 41 (5.0%) | 34 (4.9%) | 7 (7.5%) | 0 | |
| Other | 64 (7.8%) | 54 (7.7%) | 9 (9.6%) | 1 (3.7%) | |
| Unknown | 522 (63.5%) | 442 (63.0%) | 59 (62.8%) | 21 (77.8%) | |
| Parity | | | | | 0.01* |
| Nulliparous | 758 (92.2%) | 653 (93.2%) | 82 (87.2%) | 23 (85.2%) | |
| Multiparous | 54 (6.6%) | 38 (5.4%) | 12 (12.8%) | 4 (14.8%) | |
| Unknown | 10 (1.2%) | 10 (1.4%) | 0 | 0 | |
| Tobacco | | | | | 0.30 |
| None | 562 (68.4%) | 482 (68.8%) | 61 (64.9%) | 19 (70.4%) | |
| Any | 121 (14.7%) | 101 (14.4%) | 18 (19.2%) | 2 (7.4%) | |
| Unknown | 139 (16.9%) | 118 (16.8%) | 15 (16.0%) | 6 (22.2%) | |
| Macrosomia | 142 (17.3%) | 123 (17.6%) | 15 (16.0%) | 4 (14.8%) | 0.88 |
| High Risk Pregnancy | 248 (30.2%) | 209 (29.8%) | 32 (34.0%) | 7 (25.9%) | 0.62 |

The primary outcome of interest was whether women with a postpartum hemorrhage and anemia had higher odds of receiving treatment for a postpartum hemorrhage than women who had a postpartum hemorrhage, but did not have pre-natal anemia. Of the 822 women in our study 521 women (63.5%) had at least one type of intervention (medical, surgical or other) for postpartum hemorrhage, with only 70 women (8.5%) having two interventions and 18 women (2.2%) having all three forms of intervention. Among the 433 women who received only one form of intervention, a majority (93.1%) received only a medical intervention. Women who received two types of intervention were most likely to receive either medical and other therapy (74.3%) or medical and surgical therapy (21.4%).

The odds of receiving treatment for postpartum hemorrhage among women with mild anemia was 1.28 time the odds of receiving treatment in women without anemia (95% CI: 0.79 – 2.06) after adjusting for advanced maternal age, high risk pregnancy

and delivery mode. This was similar to moderate anemia, where the odds of receiving treatment for a postpartum hemorrhage among women with moderate anemia were 1.24 times the odds for those with no anemia (95% CI: 0.55-2.78) (Table 6). We also evaluated tobacco use, parity, race and fetal macrosomia as potential confounders, but they were not associated with either anemia or the treatment outcome.

**Table 6: The odds of receiving treatment for their postpartum hemorrhage among women with anemia compared to women without anemia**

| Women with PPH (n=822) | Women who received treatment (n=521) | Women who did not receive treatment (n=301) | Crude OR (CI 95% ) | Adjusted OR (CI 95% )** |
|---|---|---|---|---|
| No anemia | 440 | 261 | 1.0 | 1.0 |
| Mild anemia | 64 | 30 | 1.27 (0.80, 2.00) | 1.28 (0.79, 2.06) |
| Moderate anemia | 17 | 10 | 1.01 (0.45, 2.24) | 1.24 (0.55, 2.78) |

**Adjusted for: advanced maternal age (>35 years), high risk pregnancy (defined by ICD-9), delivery mode (vaginal vs. caesarean)

### *Length of Stay*

In addition, we measured length of stay as an indicator of morbidity for women with anemia. We stratified on mode of delivery (vaginal vs. cesarean) since by definition the mode of delivery directly influences the length of stay. Demographic characteristics of all women (n=5,957) by level of anemia (none, mild, or moderate/severe) and stratified by route of delivery is provided in Table 7. The test differences comparing women with any form of anemia and a vaginal delivery, with regards to women without anemia and a vaginal delivery, are statistically significantly different with regards to race ($p<0.01$) and parity ($p<0.01$). We found that women who delivered vaginally and had prenatal anemia were more likely to be non-white and multiparous compared to women without anemia who delivered vaginally. Among women who delivered via cesarean section, those with prenatal anemia were more likely to be smokers than women who did not have prenatal anemia ($p<0.01$). All of these variables were evaluated as potential confounders in the final model.

**Table 7: Demographics for women with postpartum hemorrhage based on level of anemia**

| | Vaginal Deliveries | | | | | Cesarean Deliveries | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Overall Total** | **No Anemia** | **Mild Anemia** | **Moderate Anemia** | **P-value** | **Overall Total** | **No Anemia** | **Mild Anemia** | **Moderate Anemia** | **P-value** |
| Variable | Mean (%) | Mean (%) | Mean (%) | Mean (%) | | Mean (%) | Mean (%) | Mean (%) | Mean (%) | |
| N | 4,066 | 3,443 (84.7%) | 452 (11.1%) | 171 (4.2%) | | 1,890 | 1,612 (85.3%) | 192 (10.2%) | 86 (4.6%) | |
| Age | 28.0 (±5.8) | 28.2 (±5.8) | 27.1 (±5.9) | 26.5 (±5.3) | | 29.3 (±5.9) | 29.5 (±5.9) | 28.4 (±5.8) | 27.2 (±5.6) | |
| Age >35 | 462 (11.4%) | 403 (11.7%) | 48 (10.6%) | 11 (6.4%) | 0.19 | 316 (16.7%) | 278 (17.3%) | 30 (15.6%) | 8 (9.3%) | 0.27 |
| Race | | | | | <0.01* | | | | | 0.11 |
| White | 968 (23.8%) | 858 (24.9%) | 87 (19.3%) | 23 (13.5%) | | 491 (26.0%) | 433 (26.9%) | 41 (21.4%) | 17 (19.8%) | |
| Hispanic | 211 (5.2%) | 166 (4.8%) | 38 (8.4%) | 7 (4.1%) | | 179 (9.5%) | 150 (9.3%) | 22 (11.5%) | 7 (8.1%) | |
| Other | 313 (7.7%) | 263 (7.6%) | 34 (7.5%) | 16 (9.4%) | | 205 (10.9%) | 165 (10.2%) | 29 (15.1%) | 11 (12.8%) | |
| Unknown | 2,574 (63.3%) | 2,156 (62.6%) | 293 (64.8%) | 125 (73.1%) | | 1,015 (53.7%) | 864 (53.6%) | 100 (52.1%) | 51 (59.3%) | |
| Parity | | | | | <0.01* | | | | | 0.14 |
| Nulliparous | 3,687 (90.7%) | 3,135 (91.1%) | 405 (89.6%) | 147 (86.0%) | | 1,720 (91.0%) | 1,473 (91.4%) | 168 (87.5%) | 79 (91.9%) | |
| Multiparous | 278 (6.8%) | 221 (6.4%) | 37 (8.2%) | 20 (11.7%) | | 146 (7.7%) | 116 (7.2%) | 23 (12.0%) | 7 (8.1%) | |
| Unknown | 101 (2.5%) | 87 (2.5%) | 10 (2.2%) | 4 (2.3%) | | 24 (1.3%) | 23 (1.4%) | 1 (0.5%) | 0 | |
| Tobacco | | | | | 0.71 | | | | | 0.01* |
| None | 2,635 (64.8%) | 2,231 (64.8%) | 299 (66.2%) | 105 (61.4%) | | 1,196 (63.3%) | 1,030 (63.9%) | 115 (59.9%) | 51 (59.3%) | |
| Any | 680 (16.7%) | 569 (16.5%) | 78 (17.3%) | 33 (19.3%) | | 365 (19.3%) | 294 (18.2%) | 53 (27.6%) | 18 (20.9%) | |
| Unknown | 751 (18.5%) | 643 (18.7%) | 75 (16.6%) | 33 (19.3%) | | 329 (17.4%) | 288 (17.9%) | 24 (12.5%) | 17 (19.8%) | |
| Macrosomia | 405 (10.0%) | 325 (9.4%) | 56 (12.4%) | 24 (14.0%) | 0.06 | 319 (16.9%) | 268 (16.6%) | 34 (17.7%) | 17 (19.8%) | 0.82 |
| High Risk Pregnancy | 1,087 (26.7%) | 901 (26.2%) | 137 (30.3%) | 49 (28.7%) | 0.09 | 680 (36.0%) | 568 (35.2%) | 73 (38.0%) | 39 (45.3%) | 0.15 |

Among women who delivered vaginally, the mean length of stay for women without anemia was 1.91 days (95% CI: 1.83-1.99), which was not significantly different from women with mild or moderate anemia (mild 1.84 days [95% CI: 1.64-2.04]; moderate 1.85 days [95% CI: 1.53-2.17]) after adjusting for advanced maternal age and high-risk pregnancy. Among women who delivered via cesarean, the mean length of stay for women with no anemia was 4.05 days (95% CI: 3.44 – 4.65), which was not significantly different from women with mild or moderate anemia (mild 4.01 days [95% CI: 3.66-4.43]; moderate 3.76 days [95% CI: 3.19-4.33]) after adjusting for advanced maternal age, high-risk pregnancy and diagnosis of a postpartum hemorrhage. In each of these models we evaluated age, race, parity, smoking, fetal macrosomia, postpartum hemorrhage and high-risk pregnancy as potential confounders. Those that were not included in the final model were either not associated with anemia or were not associated with length of stay.

***Use of treatments in women without a postpartum hemorrhage***

In total 27.9% (n=1,664) of women with singleton term live deliveries without known bleeding disorders received treatments associated with postpartum hemorrhage. Among this group of women receiving treatment, 68.7% (n=1,143) did not have a diagnosis of postpartum hemorrhage nor an estimated blood loss consistent with postpartum hemorrhage recorded in their chart. We wanted to understand what factors were playing a role in the variation indications for treatment. Factors we examined included medical and demographic characteristics (Table 8) of the populations as well as differences among treatments chosen.

**Table 8: Demographic Characteristics in all women who received a treatment associated with Postpartum Hemorrhage**

| | PPH with Treatment | No PPH with Treatment | p-value |
|---|---|---|---|
| N | 521 | 1,143 | |
| Age (years) | 27.5(±5.9) | 29.1(±6.1) | <0.01* |
| Race | | | 0.07 |
| White | 125 (24.0%) | 280 (24.5%) | |
| Hispanic | 27 (5.2%) | 94 (8.2%) | |
| Other | 40 (7.7%) | 105 (9.2%) | |
| Unknown | 329 (63.2%) | 664 (58.1%) | |
| Parity | | | 0.73 |
| Nulliparous | 480 (92.1%) | 1,056 (92.4%) | |
| Multiparous | 34 (6.5%) | 67 (5.9%) | |
| Unknown | 7 (1.3%) | 20 (1.8%) | |
| Smoking | 80 (15.4%) | 206 (18.0%) | 0.37 |
| Marcrosomia | 82 (15.7%) | 157 (13.7%) | 0.55 |
| High risk pregnancy | 179 (34.4%) | 448 (39.2%) | 0.06 |
| Average pre-delivery hemoglobin (g/dL) | 12.0 (±1.1) | 12.0 (±1.3) | 0.32 |
| Vaginal deliveries | 400 (76.8%) | 612 (53.5%) | <0.01* |

*Statistically significant for p-value<0.05

Women who received treatment with or without the diagnosis of postpartum hemorrhage had a similar distribution of race, parity, smoking during pregnancy, pre-delivery hemoglobin and fetal macrosomia. Women without a postpartum hemorrhage were significantly older (29.1±6.1 years) than women with a diagnosis of postpartum hemorrhage (27.5 ±5.9 years). There was a nearly significant difference (p=0.06) in the proportion of women with a high-risk pregnancy in the group without a postpartum hemorrhage (39.4%) compared to the group with a postpartum hemorrhage (34.4%). In addition, we found that 46.5% of those without a diagnosis of postpartum hemorrhage had a cesarean delivery, while only 23.2% of those with a diagnosis of postpartum hemorrhage had cesarean delivery.

Examining treatment differences, both groups more commonly received medical (pharmaceutical) treatments over surgical treatment or other interventions associated with postpartum hemorrhage. Regardless of whether or not they had a postpartum hemorrhage, over 90% of people who received a treatment received a medical form of treatment. When looking at the whole population that received a medical treatment,

there were differences in the numbers of medical treatments given to women with a postpartum hemorrhage compared to those without a postpartum hemorrhage ($p<0.01$). A larger proportion of women without a diagnosis of postpartum hemorrhage (72.5%) received monotherapy (a medication other than Pitocin) than those with a diagnosis of postpartum hemorrhage (56.2%). Among the group receiving monotherapy, those with a postpartum hemorrhage were more likely to receive methergine ($p<0.01$), and women without a diagnosis of postpartum hemorrhage were more likely to receive misoprostol ($p=0.01$).

Sixty-eight (6.4%) of the women who received medical treatment without the diagnosis of postpartum hemorrhage, received all three additional medications, methergine, hemabate and misoprostol, around delivery. We looked at this group in more depth since they had received a substantial amount of treatment. Within the group of women without a postpartum hemorrhage, there was not a significant difference in the proportion of high-risk pregnancies between the group that received one form of medical treatment (61.2%) and the group that received all three medical treatments (57.4%). There was also no difference in the in the mean pre-delivery hemoglobin levels between the group who received one treatment (12.0 ±1.2 g/dL) and the group that received three treatments (12.1±1.3 g/dL). Overall, the only measureable difference between the women who received one treatment and those who received three treatments among women who did not have a postpartum hemorrhage was mean age of women who received only one additional treatment was 28.9 years, while the mean age of women who received all three treatments was 30.6 years.

In addition to exploring medical treatment choices for women without a postpartum hemorrhage, we looked at the surgical treatments that were performed on women without a postpartum hemorrhage. There were 65 (5.7%) women without a postpartum hemorrhage that received a surgical form of treatment. This was a

significantly smaller proportion of women receiving surgical intervention (p=0.04) than the 8.5% (n=44) of women with a postpartum hemorrhage who received surgical treatment. All of the women without a postpartum hemorrhage who received a surgical intervention delivered via cesarean section. Sixty-two of the 62 women received a uterine artery ligation, and the other three were given a b-lynch stitch intra-operatively.

The final interventions that we explored in the population of women without a postpartum hemorrhage were other forms of non-medical and non-surgical treatment associated with postpartum hemorrhage including IV iron and blood transfusion. Among the group receiving a treatment, 18.2% of those with a postpartum hemorrhage received either iv iron or a blood transfusion, compared with 7.8% in the population that did not have postpartum hemorrhage ($p<0.01$). We then looked at the treatments individually and found that women who were diagnosed with postpartum hemorrhage were significantly more likely to receive a blood transfusion ($p<0.01$) than the group that did not have postpartum hemorrhage, but there was not a significant difference in the proportion receiving IV iron between the two groups (p=0.09).

## CHAPTER FOUR: DISCUSSION

In this study there was not a significant association between gestational anemia and maternal morbidity. To measure morbidity in the general population we used the proxy of difference in length of hospitalization between women with anemia and those without. In this population mild (hgb=10-10.9g/dL) and moderate (hgb=7-9.9g/dL) anemia was associated with multiparity, but not with other maternal characteristics such as age, tobacco use or high-risk pregnancy. Since federal law prohibits the restriction of mothers' benefits for hospital length of stay for childbirth less than 48 hours for vaginal delivery and 96 hours for cesarean section, we assumed a prolonged length of stay within the same delivery method would be indicative of a medical complication.(20) While this assumption may have been accurate for large or medically significant morbidity, it is possible that length of stay may have been too coarse a measure to capture subtle differences in maternal outcomes.(23) By using length of stay as a proxy for measurement of medical complications and by categorizing it as a continuous variable we may have created bias, preventing the ability to truly detect a difference in morbidity.

Although we did not find that anemia was an independent risk factor for maternal morbidity in this population, previous studies have shown that anemia is associated with poorer outcomes in women who have a postpartum hemorrhage.(12) In a Norwegian population, anemia (hgb <9g/dL) was associated with an increased odds (OR: 2.20, 95% CI: 1.63 – 3.15) of severe postpartum hemorrhage compared to women without severe hemorrhage.(12) In this study, investigators defined severe postpartum hemorrhage as estimated blood loss >1500mL or blood transfusion.(12) Understanding the risk factors for morbidity from postpartum hemorrhage is important because postpartum hemorrhage continues to be leading cause of mortality worldwide and one of the leading causes of maternal morbidity in the United States.(9) In our investigation, we did not observe a

statistically significant increase in the odds of receiving treatment for postpartum hemorrhage among women with mild (hgb=10-10.9g/dL) and moderate (hgb=7-9.9g/dL) anemia compared to women without anemia (OR=1.28 [95% CI: 0.79-2.06], OR=1.24 [95% CI: 0.55-2.78], respectively).

In our study, we limited the study population to women who had hemoglobin or hematocrit recorded in the EPIC laboratory data or STORC database within 50 days of delivery, which limits the ability to generalize these findings. Almost 10% of the original population was excluded because of they did not have this data recorded in EPIC or STORC. This is likely due to the fact that many of these women did not receive their prenatal care at OHSU, so their pre-delivery information was unavailable. Although, in practice, most women who did not have a known hemoglobin should have had their blood drawn upon admission. However, it is possible that these women did have a recent hemoglobin measurement documented in outside records that were not specifically documented in the OHSU records.

***Defining Postpartum Hemorrhage***

The prevalence of postpartum hemorrhage in our study group was 13.8%, which is substantially higher than the national prevalence of postpartum hemorrhage of 5%.(24) A portion of this higher prevalence of postpartum hemorrhage in our study population is likely related to the fact that we defined postpartum hemorrhage as either the clinical diagnosis or a recorded blood loss of >500mL or >1000mL (vaginal or cesarean delivery respectively) on discharge paperwork. There have been a number of studies describing the difficulty in defining postpartum hemorrhage due to the lack of objective measurements.(25) In addition, the estimated blood loss in our study was taken from the OB delivery note or in a few cases, the discharge summary when estimated blood loss was not included in the delivery note. There were only 3 individuals in our study that had an estimated blood loss of >500mL or >1000mL (vaginal

or cesarean delivery respectively) consistent with the definition of a postpartum hemorrhage recorded in the discharge note and not the delivery note, who did not receive a clinical diagnosis of postpartum hemorrhage.

The inclusion of estimated blood loss from the entire hospitalization may explain why a high proportion of women in our study with a postpartum hemorrhage, 36.6% (n=301) did not receive a treatment for a postpartum hemorrhage. It is possible that clinicians did not recognize these women as having a postpartum hemorrhage and therefore did not initiate intervention for their bleeding. Delay in diagnosis and treatment of postpartum hemorrhage has been recognized as one of the major problems in reducing risk from a postpartum hemorrhage.(8) Even with optimal management, up to 3% of vaginal deliveries will progress to severe postpartum hemorrhage (>1500mL estimated blood loss).(11) Since we considered estimated blood loss from to define postpartum hemorrhage, some of these women may not have received treatment because their clinicians did not feel they had a postpartum hemorrhage. Therefore, it is possible that we created a selection bias by increasing the number of women in our study who did not have the outcome of interest (treatment). Including a larger proportion of women who did not have the outcome into our study group could have made it more difficult to see any differences in the odds of receiving treatment between those with and without anemia.

Another surprising finding in our study was that 19.2% (n=1,143) of the total population was treated with a medication, surgery or other therapy associated with postpartum hemorrhage, without receiving the diagnosis of a postpartum hemorrhage. This large population of women who received some form of treatment without a diagnosis of postpartum hemorrhage was of particular interest in this study, because it suggests a level of variation in practice of management; the providers in our study were using these interventions for indications other than a postpartum hemorrhage. Prior

studies by Wennberg and colleagues in the 1970's showed significant variation in incidence of common surgeries in areas of Maine and Vermont that were more reflective of differences in physician judgment about indications for procedures than differences in surgical indication.(26)

After exploring the differences in demographic characteristics and therapeutic choices for women without a diagnosis of postpartum hemorrhage compared to women with a postpartum hemorrhage, we believe that clinicians in our study were using these interventions as prophylaxis for women without a postpartum hemorrhage. The only demographic characteristic difference between these two groups was a slightly higher mean age in women without a postpartum hemorrhage, but the therapeutic behaviors in this population were different, and generally less invasive. Women without a diagnosis of postpartum hemorrhage were more likely to receive only one type of medical therapy, in addition to oxytocin, instead of receiving multiple medications.

Women without a diagnosis of postpartum hemorrhage who received some form of treatment were less likely to receive blood transfusions than women who did have a diagnosis of postpartum hemorrhage, and 95.4% of the women without a postpartum hemorrhage who received a surgical intervention were given a uterine artery ligation. Uterine artery ligation is also indicated if the uterine artery is nicked during a cesarean section. We did not individually review each chart, but we assume that many of these procedures were secondary to surgical laceration rather than uterine atony or other signs bleeding. Much of the current research has evaluated variation specifically in surgical practices. In the area of gynecology, it has been shown that the practice of hysterectomy varies by patient and physician characteristics rather than evidence based medical need.(27) Few studies have been done on medical decision making in obstetrics, and how that varies based on clinical training. Unfortunately, in this study we

did not have data on providers or their level of training, which may influence their clinical judgment.

It is important to understand that the actual diagnosis of postpartum hemorrhage is clinical. Therefore decisions about therapeutic interventions are being made simultaneously with the clinicians' decisions to diagnosis a postpartum hemorrhage. It has been shown in many studies that clinicians do a poor job of estimating blood loss during delivery.(8, 28) This suggests that there may not be a clear line or diagnosis at which clinicians begin treating a postpartum hemorrhage, but instead a more blurred approach to diagnosis and treatment. Using medications or other interventions without a clear indication should be carefully explored because these therapies carry their own risk of complications. By understanding clinician decision making about treatment for postpartum hemorrhage we may be able to improve outcomes by improving the precision of both diagnosis and treatment.

***Strengths***

The data from this study was collected from a large clinical database at Oregon Health Sciences University, which serves a diverse population in Portland and high-risk pregnancies from around the state. Therefore, the results of this study are a reflection of the higher-risk population in Oregon. Using a clinical database prevents recall bias since the data was being recorded at the bedside. One of the most significant strengths of this study is that we were able to use supplemental databases (laboratory and billing data) to verify the independent variable and outcomes of interest. This strengthens the validity of the data that we were using.

***Limitations***

While using a clinical database provides strength, there are also limitations to not being able to develop the questions specifically for the research question of interest. We were limited in the number of variables that we could control for in this study.

Specifically, we did not have data on socioeconomic status or body mass index prior to pregnancy. There is evidence that obesity is a risk factor for more severe postpartum hemorrhage, and should be included in future studies. The other limitation of a clinical database is that there were a number of variables that had a significant amount of missing data (such as race). Since this sample is reflective of the population in Oregon, a majority of the sample population is likely white, but having this data missing may have changed our ability to control appropriately for race.

As a cross-sectional study we were unable to track changes in hemoglobin levels over an entire pregnancy. There is some question of whether prolonged anemia is worse than anemia for a short period of time during pregnancy. For this study, our hypothesis was that women with anemia would not have the same iron reserves at the time of delivery as women without anemia putting them at higher odds of receiving intervention. Therefore a hemoglobin level at or near the time of delivery was most appropriate for reflecting their status at the physiologic time of interest.

## CHAPTER FIVE: CONCLUSION

In this study we did not find an association between prenatal anemia and increased maternal morbidity in women with a postpartum hemorrhage or the population as a whole. Overall our population had relatively few individuals with moderate or severe anemia, which may have prevented us from seeing significant differences in outcomes between those with and without anemia. Therefore these findings may not be applicable to a larger, more diverse population that has a higher prevalence of moderate and severe prenatal anemia.

The discovery that such a large percentage of our population was receiving treatment for a postpartum hemorrhage without the diagnosis of this condition was surprising, and is important to understand. It appears that providers were intervening with treatments, before the bleeding was significant enough to meet the clinical definition of an obstetric hemorrhage. Although prevention of bleeding is important to reduce morbidity, these interventions pose their own risks to the patient and their use must be carefully considered. Streamlining the indications for use of these interventions based on evidence of effectiveness may help improve outcomes and reduce unnecessary adverse effects from the treatments. Further studies on the clinical uses of interventions for postpartum hemorrhage are necessary to clarify current uses of treatment methods.

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