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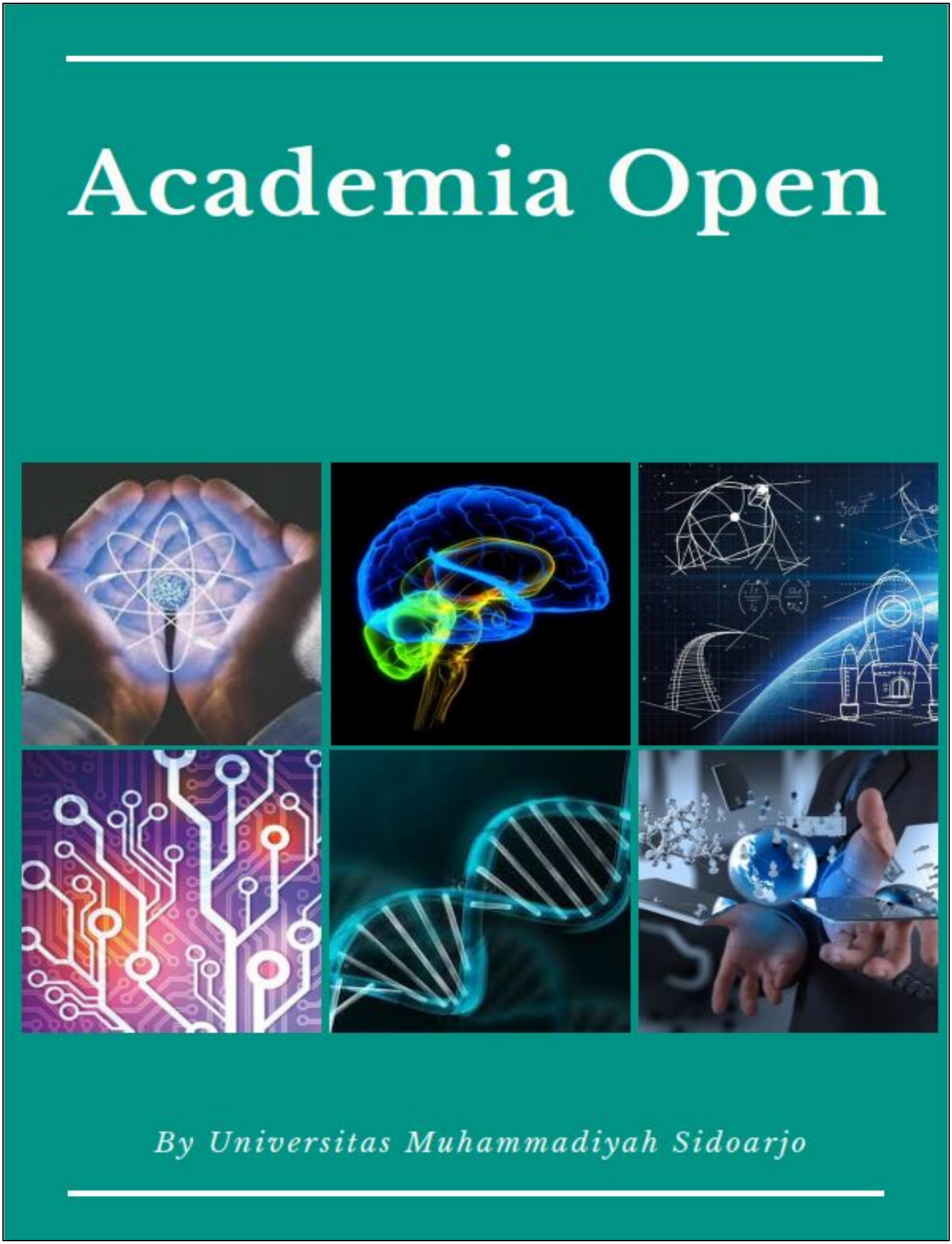

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Revolutionizing Postpartum Hemorrhage Prediction with Insights from Iraq

Revolusi Prediksi Perdarahan Pascapersalinan dengan Wawasan dari Irak

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Abstract

Background: Postpartum hemorrhage (PPH) is a severe complication affecting women with gestational hypertension or preeclampsia, yet predictive models for PPH in this population remain underdeveloped. **Specific Background:** Existing studies have not adequately addressed the combined influence of antepartum and intrapartum factors on the predictability of PPH. **Knowledge Gap:** There is a lack of comprehensive models integrating both antepartum and intrapartum variables to predict PPH risk in women with gestational hypertension or mild preeclampsia. **Aims:** The study investigates the predictability of preeclampsia (PPH) in women with gestational hypertension or preeclampsia at term using logistic regression models incorporating both antepartum and intrapartum factors. **Methods:** The study, conducted in Karbala, Iraq, involved 1252 women with hypertension or preeclampsia, developed two logistic regression models, and assessed their predictive efficacy using receiver operating characteristic analysis and calibration techniques. **Results:** A study found that 168 participants (10.4%) experienced preterm pregnancies, with antepartum predictors including maternal age, pre-pregnancy BMI, and preeclampsia, and intrapartum factors like gestational age and labor duration. **Novelty:** The study introduces a novel predictive model for Pregnancy-Positive Hypertension (PPH) that integrates antepartum and intrapartum variables for risk assessment in high-risk populations. **Implications:** The study suggests that combining antepartum and intrapartum variables can improve risk stratification and preventive measures, requiring further refinement for improved maternal care outcomes.

Highlights:

1. Antepartum and intrapartum variables enhance PPH prediction accuracy.
2. Model B outperforms antepartum-only model in predicting PPH.
3. Results stress need for improved risk stratification and prevention strategies.

Keywords: postpartum hemorrhage, gestational hypertension, preeclampsia, predictive modeling, logistic regression

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Introduction

Hypertensive disorders occurring during pregnancy have been linked to significant levels of maternal morbidity and mortality, as documented in various studies [1], [2] . It has been observed that women experiencing hypertensive disorders are at a heightened risk of developing postpartum hemorrhage (PPH), as indicated by multiple sources [3] , [4] . Instances of severe PPH may lead to critical maternal health complications including adult, coagulopathy, shock, Sheehan syndrome, infertility ,respiratory distress syndrome and ultimately, maternal death [5] . Our research team conducted a randomized controlled trial known as the Hypertension and Preeclampsia Intervention Trial At Term (HYPITAT) trial, where we discovered that inducing labor was associated with superior result for mothers compared to expectant monitoring, all without causing a rise in the rate of cesarean section deliveries [6] . This trial's findings predominantly stemmed from the variance in the progression towards severe conditions, such as systolic blood pressure equal to or exceeding 170 mmHg, diastolic blood pressure equal to or exceeding 110 mmHg, or proteinuria equal to or exceeding 5 g/24 h, between the groups undergoing labor induction and expectant monitoring. Because postpartum hemorrhage (PPH) was identified to have a connection with hypertensive disorders during pregnancy, we made sure to incorporate PPH into the combined primary outcome of our research study [3], [4] . Despite the fact that the induction of labor did not lead to an increase in the occurrence of PPH, the overall prevalence of PPH documented in our study stood at 10%, a figure significantly higher than the 0.4–1.3% risk of PPH seen in populations with low risk factors [3] , [7] . This correlation was also highlighted in the LEMMoN study, which pointed out an occurrence rate of PPH at 4.0 per 1000 deliveries in the Netherlands, with 11.2% of instances of PPH being accompanied by preeclampsia. [8]. Due to the elevated prevalence of postpartum hemorrhage (PPH) in individuals with a pregnancy-induced hypertensive condition, the identification of those at an escalated risk of experiencing PPH holds significant importance. The primary objective was to analyze the feasibility of predicting the occurrence of PPH in individuals diagnosed with pregnancy induced hypertension or mild preeclampsia at full term based on both antepartum and ante- or intrapartum prognostic factors. The underlying hypothesis posited that it could be plausible to pinpoint individuals with an increased likelihood of developing PPH compared to those solely affected by preeclampsia. Consequently, such identified patients would necessitate specific vigilance during the initial postnatal period to mitigate the likelihood of PPH incidence. This study aimed to contribute to the existing body of knowledge on the risk assessment and management of PPH in individuals with pregnancy-related hypertensive disorders, potentially offering insights into tailored interventions for this at-risk population. By exploring the predictive value of various clinical indicators in anticipating PPH development in this specific cohort, the research sought to enhance clinical decision-making and optimize postpartum care strategies for improved maternal health outcomes

Methods

study that unfolded within the premises of Al Hasan AL Mujtaba teaching hospital, Iraq. and in Alfalluja teaching hospital. Alfalluja. Iraq from January 2011to July 2013 .

Prior to the commencement of the randomization process, it was imperative that written informed consent be procured from 1253 patient involved in the study, ensuring that all participants were fully aware of the implications and procedures of the trial. The population selected for this clinical trial consisted exclusively of women who were experiencing a singleton pregnancy, with the fetus positioned in a cephalic presentation, and who were at a gestational age ranging from 36 weeks and 0 days to 41 weeks and 0 days, provided that their pregnancy was complicated by the presence of gestational hypertension or mild preeclampsia, thereby making them eligible to participate in the research study. The condition known as gestational hypertension was specifically characterized by a diastolic blood pressure reading of 95 mmHg or higher, which had to be measured on two separate occasions with a minimum interval of 6 hours between assessments to confirm the diagnosis. Furthermore, mild preeclampsia was delineated by an occurrence of diastolic blood pressure at or exceeding 90 mmHg, which again required two measurements taken at least 6 hours apart, and this diagnosis was additionally coupled with the presence of proteinuria. The definition of proteinuria utilized in this clinical context was established by local protocols, which included criteria such as the presence of ≥2+ protein detected on a dipstick test, a total protein excretion of greater than 300 mg within a 24-hour period of urine collection, or a protein-to-creatinine ratio surpassing 30 mg/mmol. In total, a cohort of 806 women provided their informed consent to participate in the study, from which 402 women were subsequently randomly assigned to undergo induction of labor while the remaining 404 women were assigned to be monitored expectantly. An additional cohort of 397 women chose not to provide consent for the randomization process; however, they did grant permission for the utilization of their medical data, and as such, they were managed in accordance with local protocols at the discretion of the attending obstetrician overseeing their care. For those women who were allocated to the induction of labor group, the procedure was initiated within a time frame of 24 hours following the randomization process, thereby ensuring that the necessary interventions were conducted in a timely manner to optimize maternal and fetal outcomes. Women who were part of the expectant group were carefully monitored and observed continuously until either the spontaneous commencement of the delivery process occurred or until a specific medical indication arose that necessitated the initiation of the delivery procedure. The comprehensive monitoring regimen included not only frequent measurements of maternal blood pressure, which are essential for understanding the cardiovascular status of the mother, but also involved thorough assessments of proteinuria, a laboratory test that helps in evaluating kidney function and potential

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complications during pregnancy, as well as examinations of the overall fetal condition to ensure the well-being of the unborn child. For those interested in acquiring further detailed information regarding the study's methodology and findings, we strongly encourage a thorough review of the HYPITAT trial [6] , which provides a wealth of relevant data and insights into this area of research.

In the context of the present study, we undertook the significant endeavor of combining and analyzing data from both randomized and nonrandomized women, thereby creating a single, comprehensive cohort that allowed for a more robust examination of the relevant factors at play. The endpoint of primary postpartum hemorrhage (PPH), which was meticulously considered in this study, was explicitly defined as a blood loss exceeding 1000 mL within a 24-hour period following the delivery, [5] , [9] as supported by previous literature and established guidelines. To ensure adherence to the local protocol, the estimation of blood loss was conducted through either visual assessment techniques or by employing weighing methods, both of which are critical for accurately gauging the volume of blood lost during and after childbirth. In order to substantiate and further validate the findings derived from our initial analysis, we undertook a repetition of our analytical procedures based on an alternative endpoint, which was specifically the determination of the need for blood transfusion, thereby enhancing the reliability and applicability of our results. In an effort to systematically analyze the potential predictability of a particular clinical outcome, we meticulously developed two distinct models tailored for this purpose. Initially, we constructed an antepartum model, designated as model A, wherein we methodically investigated the extent to which postpartum hemorrhage (PPH) could be anticipated based on a variety of clinical characteristics, including but not limited to parity, maternal age, smoking behaviors, pre pregnancy body mass index (BMI), ethnicity, levels of education, and history of previous abortions, along with both diastolic and systolic blood pressure readings, as well as an array of laboratory findings such as proteinuria, hemoglobin levels, hematocrit values, platelet counts, uric acid levels, creatinine concentrations, and the activities of aspartate aminotransferase, alanine aminotransferase, and lactate dehydrogenase, in addition to identifying women who have been diagnosed with either preeclampsia or gestational hypertension. Subsequently, we embarked on the formulation of the second model, referred to as model B, which encompassed all the aforementioned antepartum variables while also integrating a range of intrapartum variables that included critical factors such as gestational age at the time of delivery, methods of pain relief administered, the duration of both the dilatation and bearing down stages of labor, the utilization of pharmacological agents such as prostaglandins, oxytocin, or magnesium sulfate, the onset of labor, the chosen mode of delivery, instances of perineal rupture, and the performance of episiotomies. It is crucial to note that the calculation of gestational age within the context of these models was conducted utilizing either ultrasound measurements or by referencing the first day of the last menstrual period, thereby ensuring a comprehensive approach to assessing the variables at play in relation to the outcomes of interest. Through this rigorous methodological framework, we aimed to elucidate the multifaceted interactions among these diverse factors and their implications for predicting postpartum hemorrhage, ultimately contributing to the broader field of obstetric research. The integration of both antepartum and intrapartum variables into our models signifies a holistic approach to understanding the complexities of labor and delivery, thereby laying the groundwork for future inquiries into the predictive capacity and clinical management of postpartum complications.

Result and Discussion

From the initial cohort of 1,253 women who were meticulously selected for inclusion in the HYPITAT trial, we were able to discern a total of 1,232 women who met the stringent eligibility criteria for participation in the current study, thereby forming a significant sample for our analysis. It is noteworthy that 21 women were excluded from this analysis due to the fact that the total volume of blood loss they experienced was unknown, which presents a potential confounding variable that could influence the outcomes of the study. Within the remaining cohort of eligible participants, a total of 168 women, representing approximately 10.4% of the sample, experienced postpartum hemorrhage (PPH), while conversely, 1,064 women, which accounts for 89.6%, did not suffer from this complication. The distribution and comparison of various potential prognostic variables between those women who developed PPH and those who did not is comprehensively illustrated in Table 1. It is important to highlight that during the antepartum phase of pregnancy, there were no statistically significant differences observed in the clinical characteristics of the women in both groups. However, laboratory findings revealed a noteworthy observation where women who went on to develop PPH exhibited a lower count of platelets and a higher prevalence of diagnoses of preeclampsia compared to their counterparts who did not experience PPH. When examining the intrapartum period, it became evident that women who ultimately experienced PPH had a higher gestational age at the time of delivery, which was statistically significant ($p = 0.007$), and they also underwent a longer duration during both the dilatation and bearing down stages of labor ($p = 0.019$ for both metrics), in addition to giving birth to infants with a higher birthweight ($p = 0.009$). Furthermore, this group of women underwent more frequent episiotomies ($p = 0.024$) and had a greater incidence of retained placenta, which necessitated manual removal ($p < 0.001$), indicative of the complexities associated with PPH. It is pertinent to note that the values of p associated with these findings are not displayed in Table 1 for clarity and focus. The factors that were found to have a statistically significant association with PPH during the univariate analysis included gestational age at delivery, which had an odds ratio (OR) of 1.3 for each additional week ($p = 0.003$), the mode of delivery, which showed an odds ratio of 1.7 for vaginal instrumental delivery in contrast to spontaneous delivery ($p = 0.04$), and the duration of the dilatation stage, which had an odds ratio of 1.1 per hour ($p = 0.03$). Additionally, the birthweight of the infants, which presented an odds ratio of 1.6 per kilogram ($p = 0.008$), and the occurrence of episiotomy, which had an odds ratio of 1.6 ($p = 0.04$), were also significantly associated with PPH as demonstrated

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in Table 2. Notably, manual delivery of the placenta was found to have an exceptionally strong association with the occurrence of PPH in the univariate analysis, with an odds ratio of 25.0 when comparing retained placenta to spontaneous placental delivery ($p < 0.001$), underscoring the critical nature of this variable. Due to the evident correlation, this variable was excluded from the multivariable analysis, as it is well understood that the presence of retained placenta already constitutes a substantial factor contributing to the incidence of PPH. Furthermore, the variable of birthweight was also excluded from consideration as a prognostic factor, given that this information is only ascertainable post-delivery, complicating our ability to assess its impact prior to the event. In addition, it is essential to acknowledge that we did not consistently have access to the estimated birthweight data obtained through ultrasound imaging for all of our patients; furthermore, it has been well-documented that ultrasound estimates of fetal birthweight can often be imprecise and unreliable. In order to enhance the likelihood of identifying authentic prognostic variables that are crucial for the development of our predictive model, there has been a strong recommendation to adopt more lenient p-value thresholds; consequently, we decided to incorporate all prognostic variables that exhibited a significance level of $p < 0.157$ during the univariate analysis phase into the model for further evaluation. The findings derived from the multivariable analysis of prognostic model A, which is exclusively based on antepartum prognostic variables, as well as model B, which additionally incorporates variables pertinent to the delivery process alongside the antepartum prognostic variables, are meticulously summarized in Table 2 for comprehensive examination. For both prognostic models under consideration, we performed an averaging of the five imputed predicted risk scores associated with each individual patient, thereby allowing us to culminate in a singular performance estimate that reflects the overall efficacy of the models. Upon assessment, it was determined that both model A and model B exhibited a moderate level of discrimination, as evidenced by the area under the ROC curve measuring 0.59 (with a 95% confidence interval ranging from 0.53 to 0.64) for model A, and a slightly enhanced value of 0.64 (with a 95% confidence interval from 0.59 to 0.70) for and 1b. Furthermore, the calibration of these models was found to be moderate for model A, with a Hosmer–Lemeshow p-value of 0.26, whereas model B demonstrated superior calibration performance with a Hosmer–Lemeshow p-value of 0.36. This observation suggests the potential feasibility of distinguishing between women categorized as having a low risk versus those identified as having a high risk for the subsequent development of PPH. Additionally, the bootstrapping technique applied in our analysis indicated a tendency for some overfitting, as evidenced by the corrected ROC areas under the curve, which were found to range from 0.550 to 0.554 for model A, while for model B, the corrected ROC areas were slightly elevated, ranging from 0.607 to 0.612, thereby highlighting the nuanced differences in the predictive capabilities of these models. In order to thoroughly confirm and substantiate the results derived from our comprehensive analysis, we undertook a meticulous repetition of our investigative procedures, this time specifically focusing on the necessity for blood transfusions as the primary outcome variable of interest. For the purpose of this particular analysis, we retained the same cohort of 1232 women, among whom a notable subset, comprising 52 individuals, which represents approximately 4.6% of the total population, were identified as having required a blood transfusion during their medical care. The independent antepartum prognostic factors associated with postpartum hemorrhage (PPH) were found to include several crucial variables, such as the prepregnancy body mass index (BMI), which exhibited an odds ratio (OR) of 0.94 per kilogram per square meter (kg/m2) with a p-value of 0.06, along with the level of education, for which an odds ratio of 1.7 was noted for individuals possessing a higher education level, yielding a p-value of 0.09, and the hematocrit levels, which demonstrated an odds ratio of 0.19 per unit with a statistically significant p-value of 0.002. The intrapartum variables that were integrated into the analytical model included the gestational age at the time of delivery, which revealed an odds ratio of 1.47 per week with a highly significant p-value of less than 0.002, as well as the administration of oxytocin, which was associated with an odds ratio of 1.57, albeit with a p-value of 0.15 indicating a less robust association. Both Model A and Model B exhibited moderate discriminatory power, as evidenced by the areas under the receiver operating characteristic (ROC) curve, which were calculated to be 0.69 (with a 95% confidence interval ranging from 0.62 to 0.77) for Model A and a more favorable 0.75 (with a 95% confidence interval from 0.68 to 0.81) for Model B, thereby reflecting their respective efficacy in predicting outcomes. Furthermore, the calibration of both models was assessed to be satisfactory, as indicated by the Hosmer–Lemeshow test results, which yielded a p-value of 0.82 for Model A and a p-value of 0.54 for Model B, thus providing additional confidence in the reliability of the models employed, although it should be noted that the specific tables related to these findings are not presented within this document.

Prognostic variables	Women with postpartumhemorrhage (n = 168)	Women without postpartumhemorrhage (n = 1064)
Nulliparous	76%	72%
Maternal age (years)	30.0 (23.0–39.0)	30.0 (22.0–38.0)
Maternal smoking	13%	12%
Prepregnancy BMI (kg/m2)	24.5	25.4
Systolic	(125–160)	124–162
Diastolic	(90–105	88–105
Duration of dilatation stage (min)	45.7–671	40.0–640
Duration of bearing down stage (min)	4.0–118	3.0–106
Use of prostaglandins	39%	41%
Use of oxytocin	60%	59%

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Use of intravenous antihypertensives 11 (10%) 65 (7%)		
Induction of labor	66%	66%
Mode of deliverySpontaneous	60%	70%
Vaginal instrumental delivery	21%	15%
Cesarean delivery	19%	15%
Use of magnesium sulfate	10%	8%

Table 1. *Distribution of prognostic variables among women with and women without postpartum hemorrhage at term*

Discussion

In the framework of this comprehensive cohort study, we meticulously assessed various prognostic variables that may influence the occurrence of postpartum hemorrhage (PPH) in a specific population of women who have been diagnosed with either gestational hypertension or mild preeclampsia and who are beyond the threshold of 36 weeks of gestation. It is important to note that while the prediction of such outcomes in the antepartum phase is often fraught with inaccuracies and uncertainties, it has been established that during the actual delivery process, it is indeed possible to identify women who are at an increased risk of experiencing PPH by synthesizing prognostic variables derived from both the antepartum period and those pertinent to the delivery itself. The antepartum variables that were incorporated into our analytical model consisted of key factors such as maternal age, body mass index prior to pregnancy, and the occurrence of a preeclampsia diagnosis in the women under study; conversely, the intrapartum variables that were taken into account included the gestational age at the time of delivery, the duration of the dilation stage during labor, as well as instances of perineal rupture or the performance of an episiotomy.

Prognostic variables	Univariable analysis P value	Multivariable analysis	
		Model A p value	Model B p value
Nulliparity	0.37		
Multiparity (para 4+)	0.81		
Maternal age (years)	0.157	0.13	0.08
Maternal smoking	0.71		
Prepregnancy BMI (kg/m2)	0.07	0.07	0.08
Blood pressure (mmHg) Systolic	0.67		
Diastolic	0.54		
Duration of dilatation stage (h)	0.003		0.08
Duration of bearing down stage (min)	0.21		
Use of prostaglandins	0.63		
Use of oxytocin	0.94		
Use of intravenous antihypertensives	0.23		
Use of magnesium sulfate	0.44		
Induction of labor (vs. spontaneous)	0.96		
Mode of delivery (vs. spontaneous)			
Vaginal instrumental delivery	0.04		
Cesarean delivery	0.19		

Table 2. *prognostic factors associated with postpartum hemorrhage in women with mild hypertensive disorders during term pregnancy through both univariable and multivariable analyses of antepartum (model A) and intrapartum (model B) models*

On a global scale, it is widely recognized that obstetric hemorrhage stands as one of the foremost causes of maternal mortality and severe maternal morbidity, contributing to a staggering 25% of all maternal deaths recorded in various health statistics [10]. In the specific context of the Netherlands, during the period spanning

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from 1993 to 2005, the predominant cause of maternal mortality was attributed to (pre)eclampsia, which was associated with a maternal mortality ratio (MMR)—defined as maternal deaths per 100,000 live-born children—of 3.5. Following this, the second most prevalent cause of maternal mortality was a combination of thromboembolism and cardiovascular diseases, which presented an MMR of 1.6, indicating a significant health concern in this demographic. The fourth leading cause of maternal mortality during this timeframe was classified as sudden death during pregnancy, which had an MMR of 0.8, while obstetric hemorrhage and obstetric sepsis were also noted as contributing factors, each with an MMR of 0.7 [2]. The severe maternal morbidity that arises as a direct consequence of PPH encompasses a range of critical health issues, including but not limited to adult respiratory distress syndrome, coagulopathy, shock, irreversible loss of fertility, and the condition known as Sheehan syndrome [5] . Thus, it becomes evident that hypertensive disorders of pregnancy, in conjunction with PPH, play a pivotal role in significantly elevating the risks associated with maternal mortality and severe morbidity. Furthermore, findings from the HYPITAT trial have indicated that the incidence of PPH is markedly higher among women who are affected by hypertensive disorders during the term of their pregnancy, with an observed rate of 10% as compared to a much lower rate of 0.4–1.3% found in a low-risk population. In stark contrast to these findings, Zwart et al. conducted a study that revealed that major obstetric hemorrhage, which is clinically defined as the necessity for transfusion, presents its own set of challenges and risks that warrant further investigation and analysis. the occurrence of severe obstetric interventions, such as the transfusion of four or more units of red blood cells, the surgical procedure known as hysterectomy, or the medical technique of arterial embolization, was observed to be accompanied by preeclampsia in approximately 11.2% of the documented cases, as indicated by source [8] . Numerous other scholarly studies have similarly identified a notable and significant correlation between the condition of preeclampsia and the incidence of postpartum hemorrhage (PPH) [3], [4]. In particular, a comprehensive investigation focusing on vaginal deliveries revealed that the frequency of PPH was five times more prevalent in pregnancies complicated by preeclampsia [4], while in two additional studies that specifically concentrated on cesarean deliveries, it was discovered that preeclampsia was associated with an approximate two-fold increase in the risk of experiencing PPH [4] , [11]. It is our hypothesis that a disruption or imbalance in the levels of angiogenic and anti-angiogenic factors present in the maternal circulation may serve to elucidate the observed relationship between hypertensive disorders occurring during pregnancy and the incidence of PPH. Moreover, it should be noted that hypertension, in conjunction with a reduction in platelet counts, may adversely influence the total volume of blood loss experienced during and after delivery. Additionally, the potential connection between preeclampsia and coagulopathy has the capacity to exacerbate the severity of PPH. Given the elevated prevalence of PPH among women who are affected by hypertensive disorders related to pregnancy, we posulate that the ability to accurately predict PPH in individuals suffering from gestational hypertension or preeclampsia is of paramount importance and should be prioritized in clinical settings. In addition to this, it is worth noting that research studies that specifically address the predictors associated with PPH in these particular populations of women are relatively scarce and underrepresented in the current literature. The data that has been meticulously collected within the framework of the HYPITAT study presented a promising opportunity to identify various prognostic variables that are potentially predictive of PPH; however, it is essential to acknowledge that certain limitations were also present within this research. The methodological framework underlying the study design is confronted with certain inherent limitations, primarily attributable to the fact that it constitutes a secondary data analysis derived from a post hoc examination of a dataset that was initially gathered for a distinctly different research objective, specifically that of the HYPITAT study. Additionally, it is noteworthy that a multitude of prognostic variables exhibited a range of missing values, which could potentially compromise the integrity of the analysis. In light of this challenge, the missing data pertaining to these predictive variables were subjected to imputation, as the alternative approach of excluding such data points would invariably result in a significant reduction of statistical power in the context of multivariable analysis, as previously noted in reference [12]. Furthermore, it is important to acknowledge that there exists an array of alternative methodologies for the operational definition of postpartum hemorrhage (PPH), each possessing its own merits and drawbacks. While it is widely recognized within the academic community that the estimation of blood loss is frequently subject to considerable underreporting [13], [8] . we opted to adopt a definition of PPH as blood loss exceeding 1000 mL within a 24-hour period following delivery, [5], [9] a criterion that was consistently utilized in the HYPITAT trial and enjoys broad international acceptance. Moreover, it is worth mentioning that other potential definitions of PPH could include the necessity for blood transfusion or a notable decrease in hemoglobin levels. Among these alternatives, the latter option was regarded as the most objective measure; however, it is crucial to recognize that this approach is inherently contingent upon the availability of standardized assessments of both pre- and post-hemorrhage hemoglobin levels, a data set which, regrettably, was not accessible for a considerable number of the women included in the study. Consequently, the interplay of these various factors ultimately underscores the complexities and challenges associated with defining and analyzing postpartum hemorrhage within the context of the existing literature. It is likely that the necessity for a blood transfusion emerged as the most viable option for management in this context; however, it is critical to acknowledge that such a criterion for management is heavily influenced by the specific transfusion policies that are in place locally within the healthcare system. In order to provide a comprehensive understanding of the situation, we undertook a reiteration of our analysis, which focused explicitly on the necessity for transfusion; this subsequent examination revealed an even greater predictability regarding the incidence of postpartum hemorrhage (PPH) in women who were diagnosed with gestational hypertension or exhibited mild preeclampsia, as evidenced by an area under the curve measuring 75% in contrast to a lesser 64%. The overarching risk factors associated with the development of PPH within the general population encompass a range of elements, including but not limited to, advanced maternal age, obesity in mothers, extended duration of labor, the induction and augmentation of labor, an overdistended uterus which may result from conditions such as high birth weight or macrosomia, multiple gestation, and hydramnios, along with complications

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such as abruptio placenta, placenta previa, preeclampsia, and HELLP syndrome, which is characterized by hemolysis, elevated liver enzymes, and low platelet counts, as well as a history of prior cesarean deliveries, previous experiences of PPH, episiotomies, operative deliveries—especially those classified as emergency cesarean sections—and instances of anemia, as cited in references [3], [4], [5], [14]. A significant number of the aforementioned variables were also identified as independent prognostic indicators of PPH within the scope of our study, particularly those factors such as increased maternal age, the condition of preeclampsia, prolonged labor, and the practice of episiotomy. Furthermore, in our univariate analysis, we established a strong correlation between high birth weight and the retention of placenta, both of which were notably associated with an increased risk of PPH. The decision to exclude certain variables from our multivariable analysis was made primarily due to their significant association with the occurrence of postpartum hemorrhage (PPH), in addition to the fact that these variables are only ascertainable following the delivery process itself. Specifically, the variables of decreased platelet count, labor induction, and augmentation of labor through the administration of oxytocin were omitted from the final analytical model that we employed in this research. However, it is worth noting that augmentation with oxytocin was, in fact, incorporated into our validated analytical model, thereby allowing us to explore its potential effects. Furthermore, certain conditions such as multiple pregnancies, placenta previa, and a history of previous cesarean deliveries were explicitly identified as exclusion criteria within the framework of the HYPITAT trial, and as a direct consequence, these conditions were not evaluated in the context of the present study. Additionally, it is important to highlight that placental abruption did not manifest as a complication within the HYPITAT trial, which consequently precluded any investigation into this particular condition in our analysis. In a somewhat surprising revelation, it has been found that multiparity, specifically in women classified as para 4 or greater, did not show a significant association with the incidence of postpartum hemorrhage, challenging some widely held beliefs in obstetrical practice. Recent empirical studies have illustrated a notable increase in severe maternal morbidity that is attributable to major obstetrical hemorrhage in various Western nations, as evidenced by a series of references [15] , [16]. Several plausible explanations have been proposed to account for these concerning trends, including factors such as the rising age of women at the time of childbirth, an increased rate of cesarean deliveries, and the prevalence of high birthweight infants, commonly referred to as macrosomia, all of which are findings that resonate with the results obtained in our own study. Moreover, the issue of maternal obesity has emerged as an increasingly prevalent lifestyle concern that necessitates urgent public health interventions, particularly given its established connections with conditions like diabetes mellitus and the occurrence of macrosomia [17] . Intriguingly, our study revealed that a higher pre pregnancy body mass index (BMI) was associated with a reduced likelihood of experiencing postpartum hemorrhage, a finding that was consistent across both univariable and multivariable analyses conducted. The perplexing nature of this contradictory outcome in our study population remains unexplained; however, it is conceivable that the relatively elevated pre pregnancy BMI values observed among the women who were affected by a pregnancy-related hypertensive disorder may have contributed to this unexpected result. The majority of instances of postpartum hemorrhage (PPH) can be attributed predominantly to uterine atony, which refers to the lack of muscle tone in the uterus, as well as the retention of placental tissue following childbirth [5] . In light of this understanding, we reached a consensus that it would be unnecessary and potentially misleading to incorporate uterine atony or retained placenta as variables within our prognostic model, given the established recognition of these factors as fundamental contributors to the occurrence of PPH; furthermore, the critical phase during which proactive and effective prophylactic postpartum management could be implemented has already elapsed. Additionally, it is pertinent to note that the identification of uterine atony necessitates clinical recognition, which inherently introduces a degree of subjectivity into the variable in question. The evaluation of the efficacy of our prediction model was conducted through a meticulous assessment of both discrimination and calibration metrics. The Receiver Operating Characteristic (ROC) curve analysis revealed that the discriminative capacity of both models was moderate, suggesting an adequate ability to differentiate between outcomes. However, it is crucial to emphasize that in the context of performance assessment for a predictive model, the aspect of calibration is of greater significance than that of discriminative capacity alone. Consequently, the overarching clinical objective of our model is to effectively differentiate between women who are categorized as being at low risk and those who present with a higher risk for the development of PPH. Furthermore, the results stemming from our calibration assessments and internal validation processes suggest that Model B possesses the capability to accurately distinguish between women identified as being at a low risk for PPH and those who are classified as being at a heightened risk for developing this serious condition. In summary, the intricate interplay between these variables and the predictive capabilities of our model underscores the importance of a nuanced understanding of risk factors associated with PPH in clinical practice.

While it is widely acknowledged that maternal mortality rates are exceedingly low in the Netherlands, it is imperative to highlight that the complications associated with postpartum hemorrhage (PPH) continue to pose a significant challenge within the realm of maternal healthcare, and thus, it is our sincere hope that this comprehensive study will serve as a catalyst, inspiring a greater number of researchers and practitioners to delve into the intricate intersection of PPH and hypertensive disorders that manifest during pregnancy. The findings derived from our research strongly suggest that postpartum hemorrhage can indeed function as an auxiliary indicator, providing valuable insights into the overall quality and efficacy of obstetric care provided to patients. Additionally, several of the prognostic factors that were identified throughout our investigation were closely linked to specific aspects of obstetric management and various medical interventions, which are inherently preventable with the right strategies in place. By incorporating these critical factors into the established flow charts utilized in local clinical protocols, healthcare providers may significantly enhance their ability to recognize cases of PPH promptly, thereby facilitating timely and effective treatment responses that could potentially save lives. In

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instances where there exists an elevated risk for developing postpartum hemorrhage, it is crucial that heightened vigilance is exercised during the early postpartum phase, during which targeted prophylactic measures or therapeutic interventions should be employed to mitigate potential complications. Moreover, the modeling results we obtained from our study lay a foundational framework for the subsequent advancement of the proposed model, which would necessitate operationalization efforts such as the precise definition of threshold values for continuous clinical parameters. This endeavor aims to culminate in the creation of a model that is not only clinically applicable but also requires external validation to ensure its robustness and reliability in real-world settings. Ultimately, the implications of our research underscore the importance of addressing both the prevention and management of postpartum hemorrhage, which remains a critical area of focus within maternal health discourse. As we continue to explore and refine our understanding of these complex medical phenomena, it is essential that we foster collaborative efforts across various disciplines to enhance the overall quality of care provided to expectant mothers. By doing so, we can work towards ensuring that maternal health outcomes are optimized, thereby contributing to the overall well-being of both mothers and their newborns

Conclusion

In conclusion, our comprehensive analysis underscores several critical insights into the predictors of postpartum hemorrhage (PPH) in women diagnosed with gestational hypertension or mild preeclampsia. Notably, both antepartum and intrapartum variables, such as gestational age, mode of delivery, and the duration of labor, emerged as significant predictors of PPH, with the strongest associations found with retained placenta and high birthweight. The multivariable models demonstrated moderate discriminatory and calibration capabilities, particularly Model B, which included intrapartum factors. These findings highlight the potential for targeted preventive measures and interventions, emphasizing the need for enhanced vigilance and tailored management strategies to mitigate PPH risk. Future research should focus on refining predictive models with larger, diverse cohorts and exploring the integration of additional variables, such as detailed birthweight estimations and comprehensive antenatal care metrics. Such advancements are crucial for improving risk stratification and optimizing maternal care outcomes.

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