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Research Article

Differences in Maternal Morbidity Concerning Risk Factors for Obstetric Hemorrhage

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Abstract

A retrospective study was performed to see differences in morbidity concerning risk factors for obstetrical hemorrhage. Mothers receiving any blood transfusion for obstetrical hemorrhage were enrolled. Patients were divided into subgroups according to risk factors for obstetrical hemorrhage. Outcomes of interest included massive blood loss ≥ 3000 ml, massive blood transfusion ≥ 10 units, and invasive procedures for hemostasis, DIC, and maternal death. 153 cases were received blood transfusion. Abruption (n=35, 23%), birth canal tears (n=31, 20%), atonic bleeding (n=23, 15%), and abnormal placental adherence (APA; n=23, 15%) were the four major factors. APA was the highest condition for invasive procedures (78.3%) with a higher incidence of massive blood loss (65.0%) and massive blood transfusion (73.9%). Abruption was the highest condition for DIC (71.4%) with a higher incidence of massive blood transfusion (51.4%). 48.0% of birth canal tears and 39.0% of atonic bleeding were complicated with massive blood loss. Uterine inversion (n=5) included one maternal death. Except for uterine inversion, the ICU admission rate of the remaining conditions was 13~26%. The observed differences in morbidity concerning risk factors for obstetrical hemorrhage may represent important maternal health phenomena in our region. An identification of differences in morbidity concerning risk factors is essential to provide an effective treatment strategy for obstetrical hemorrhage.

Keywords: Blood transfusion; Maternal morbidity; Risk factor; Obstetrical hemorrhage

Introduction

An autopsy registry study in Japan indicated that amniotic fluid embolism (24%), DIC related to pregnancy-induced hypertension (21%), birth canal tears (11%), and pulmonary thromboembolism (13%) are the four leading risk factors for maternal death [1]. The majority of maternal deaths are therefore due to obstetric hemorrhage such as amniotic fluid embolism or DIC related to pregnancy-induced hypertension. According to recent survey for causes of maternal death worldwide, hemorrhage was the leading cause of maternal death [2]. Thus, it is important to understand causes of obstetrical hemorrhage and re-recognize the severity of obstetric hemorrhage.

During the parturition process, a portion of pregnant patients who have risk factors for obstetric hemorrhage may develop life-threatening conditions. However, the range of illness (i.e., differences in morbidity) concerning each risk factor is still relatively unclear. Blood transfusion, uterine arterial ligation, uterine arterial embolization, hysterectomy, and intensive care unit (ICU) admission are critical components of obstetrical hemorrhage management, and these aspects are also indicators for clinical illness. In general, a small number of pregnant patients require blood transfusion (0.02~0.07%of planned deliveries) or ICU admissions (0.24% of all deliveries in the Netherlands) [3,4]. Rates of severe maternal morbidity, such as those for cases requiring massive blood transfusion or ICU admission, must be higher among pregnant patients who have risk factors for obstetric hemorrhage. In order to determine differences in morbidity concerning risk factors for obstetric hemorrhage, it is important to establish an institutional or regional management protocol for massive hemorrhage to prevent maternal death.

The current study was conducted in the setting of one tertiary and three perinatal centers with standardized care. In this study, we reviewed medical records of pregnant patients receiving blood transfusion for obstetric hemorrhage. We then determined the correlation between risk factors for obstetric hemorrhage and risk-related maternal outcomes that included massive blood loss ≥ 3000 ml, massive blood transfusion ≥ 10 units, invasive procedures for hemostasis, disseminated intravascular coagulation syndrome (DIC), ICU admission, and maternal death. In addition, we compared the risk profile of obstetric hemorrhage between tertiary and secondary centers.

Materials and Methods

This study was undertaken retrospectively and obtained approval (#2013-135) from a suitably constituted Ethics Committee at our institution. We retrospectively reviewed the medical charts of pregnant women that received any blood transfusion and were admitted to the Perinatal Center of the University of Miyazaki, the Miyazaki Medical Association Hospital, the Fujimoto General Hospital, or the Nichinan Prefectural Hospital from January 2007 to December 2011. The Perinatal Center of the University of Miyazaki is a tertiary center, whereas the other aforementioned institutions are secondary centers. In our area, 80% of pregnant women give birth at a private clinic, and a risk-allocated system for obstetric care has been

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established [5]. At first, private clinics referred a patient to secondary centers and next referred a patient to the tertiary center, if necessary. Subsequently, all centers dealt mainly with referral cases and the total number of deliveries was 6691 during the period investigated. Emergency trans-arterial embolization for hemostasis is available in the University of Miyazaki perinatal center and Fujimoto General Hospital. The University of Miyazaki has sufficient blood products for emergency cases. Furthermore, access to blood products is ensured within 60 minutes after a request by any of the centers.

We checked risk factors for obstetrical hemorrhage requiring blood transfusion in each case. Risk factors for obstetrical hemorrhage included placental abruption, birth canal tears, atonic bleeding, placenta previa, placenta increta, and uterine inversion. Pregnant women that received a blood transfusion and had other risk factors were classified in the 'other' category. In this study, we regarded birth canal tears to include any traumas related to vaginal or cesarean birth. Then, birth canal tears included cervical laceration, vaginal wall laceration included hematoma, uterine rupture, extensions of cesarean incisions into the tissue nearby uterus. Abnormal placental adherence included placenta accreta, increta, and percreta. Suspected cases of abnormal placental adherence were subjected to pathological examination. If the placenta implanted directly on the myometrium without an intervening endometrium, we diagnosed the case as representing abnormal placental adherence. Abnormal placental adherence with placenta previa was excluded from the placenta previa category. Placenta previa included a low-lying placenta, which was close to an internal uterine os less than 2.0cm. Atonic bleeding was defined as bleeding due to lack of effective contraction of the uterus after delivery in the absence of the above known risk factors. Cases of retained tissue and known myoma were excluded from atonic bleeding and were classified in the 'other' category. If massive bleeding related to amniotic fluid embolism was highly suspected, a blood sample was obtained for serological examination to determine zinc coproporphyrin I (ZnCP-I) and serum sialyl-Tn antigen levels. If the concentrations of ZnCP-I (normal: <1.6 pmol/ml) and/or sialyl-Tn antigen (normal: <45 U/ml) were elevated, we classified the case as representing amniotic fluid embolism [6,7].

The following clinical characteristics were collected: maternal age, parity (primipara), gestational age at delivery (weeks), cesarean delivery, and referral cases from private clinics. Maternal outcomes of interest included estimated blood loss ≥ 3000 ml (massive bleeding) at the hemorrhagic event, disseminated intravascular coagulation syndrome (DIC), massive blood transfusion (≥ 10 units of packed red blood cells (RBC) and/or ≥ 10 units of fresh frozen plasma (FFP), and invasive procedures for hemostasis, ICU admission, and maternal death. Invasive procedures for hemostasis included hysterectomy, uterine arterial ligation by laparotomy, and transcatheter uterine arterial embolization. DIC was diagnosed when the obstetrical DIC score reached 8 points or more in this study. The obstetrical DIC score is given by clinical parameters used to make a prompt diagnosis [8]. Practically, restoration of circulating blood volume, recognition of DIC, and prevention of further blood loss are important milestones for management. We therfore used these outcomes of interest as morbidity assessment for obstetrical hemorrhage.

We then determined the correlation between each risk factor for obstetrical hemorrhage and maternal outcomes. Specifically, we identified the incidence of massive bleeding and DIC, massive blood transfusion, and invasive procedures for hemostasis, ICU admission, and maternal death for each risk factor. In addition, we compared the risk profile for obstetrical hemorrhage between tertiary and secondary centers. Comparison of the risk profile for obstetrical hemorrhage between centers was made using the χ^2 test. Data are expressed as number, incidence (%), or mean ± SD. Probability values < 0.05 were considered statistically significant.

Table 1: Demographic data of women receiving blood transfusion for obstetrical hemorrhage during pregnancy.

Data	n=153
Maternal age (years)	31.0 ± 5.3
Primipara	69 (45.1%)
Gestational age at delivery	34.3 ± 6.3
Cesarean delivery	87 (56.9%)
Referral case	88 (57.5%)
Maternal death	2

Data are expressed as number, incidence (%), or mean ± SD.

Results

During study period, 153 received blood transfusion for obstetrical hemorrhage. Our records indicated that the average maternal age was 31.0 years, 45% of pregnancies were primiparous, the average gestational age at delivery was 34.4 weeks, 56.9% of pregnancies resulted in cesarean delivery, and 57.5% of pregnancies were referral cases from private clinics during either the intrapartum or postpartum period (Table 1).

Figure 1 shows that the identified risk factors for obstetrical hemorrhage requiring any blood transfusion were placental abruption (35;22.9%), birth canal tears (31;20.3%), atonic bleeding (23;15.0%), abnormal placental adherence (23; 15.0%), placenta previa (16;10.5%), uterine inversion (5;3.3%), and 'other' risk factors (20;13.1%). 2 of abruption, 24 of birth canal tears, 11 of atonic bleeding, 3 of abnormal placental adherence, 1 of placenta previa, and all of uterine inversion were referred to the secondary or tertiary hospitals after developing severe hemorrhage.

Figure 2 indicates that the incidence of massive bleeding (estimated blood loss ≥ 3000 ml) at the hemorrhagic event was 17.0%

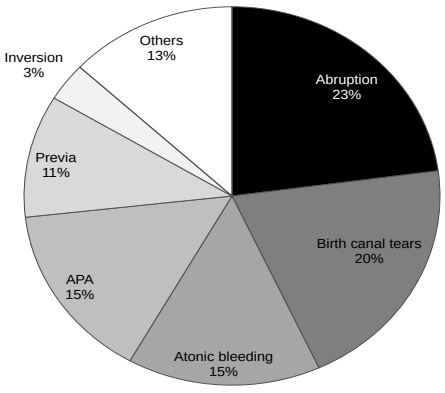

Figure 1: The incidence of each risk factor in the study group.
Abruption: Placental abruption. Tears: Birth canal tears. APA: Abnormal Placental Adherence. Previa: Placenta previa. Inversion: Uterine inversion.

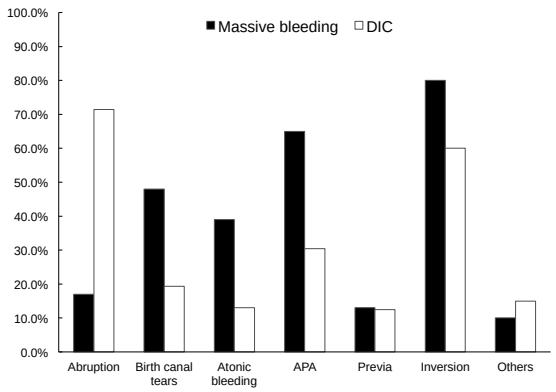

Figure 2: The incidences of massive bleeding and DIC in women with each risk factor. Massive bleeding was defined as estimated blood loss ≥ 3000 ml at the hemorrhagic event. DIC was diagnosed when the obstetrical DIC score reached 8 points or more in this study.
Abruption: Placental abruption. APA: Abnormal Placental Adherence. Previa: Placenta previa. Inversion: Uterine inversion.

for placental abruption, 48.0% for birth canal tears, 39.0% for atonic bleeding, 65.0% for abnormal placental adherence, 13.0% for placenta previa, and 80.0% for uterine inversion. The incidence of DIC was 71.4% for placental abruption, 19.4% for birth canal tears, 13.0% for atonic bleeding, 30.4% for abnormal placental adherence, 12.5% for placenta previa, and 60.0% for uterine inversion.

Figure 3 reveals that the incidence of massive blood transfusion with either ≥ 10 units of packed RBC or 10 units of FFP was 51.4% for placental abruption, 38.7% for birth canal tears, 30.4% for atonic bleeding, 73.9% for abnormal placental adherence, 25.0% for placenta previa, and 80.0% for uterine inversion.

Figure 4 shows that the incidence of invasive procedures for hemostasis was 0% for placental abruption, 19.4% for birth canal tears, 8.7% for atonic bleeding, 78.3% for abnormal placental adherence, 0% for placenta previa, and 0% for uterine inversion. The incidence of ICU admission was 22.9% for placental abruption, 16.1% for birth canal tears, 13.0% for atonic bleeding, 26.1% for abnormal placental adherence, 12.5% for placenta previa, and 60.0% for uterine inversion. Uterine inversion included one case of maternal death.

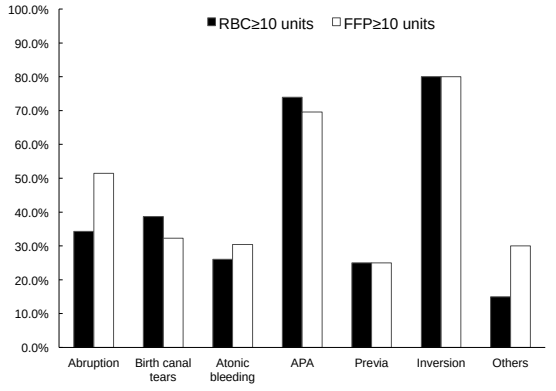

Figure 3: The incidence of massive blood transfusion in women with each risk factor. Massive blood transfusion was defined as ≥ 10 units of packed red blood cells (RBC) and/or ≥ 10 units of fresh frozen plasma (FFP). **Abruption:** Placental abruption. APA: Abnormal Placental Adherence. Previa: Placenta previa. Inversion: Uterine inversion.

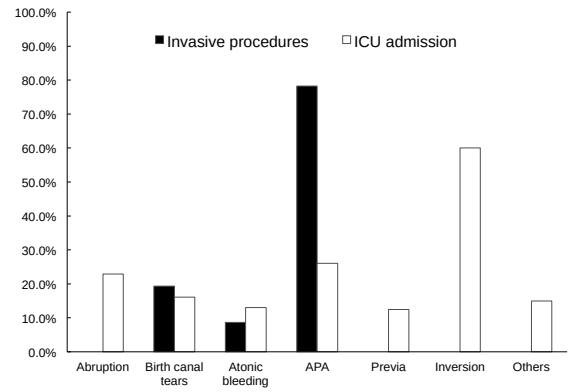

Figure 4: The incidences of invasive procedures for hemostasis and ICU admission in women with each risk factor. Invasive procedures for hemostasis included hysterectomy, uterine arterial ligation by laparotomy, and transcatheter uterine arterial embolization.
Abruption: Placental abruption; APA: Abnormal Placental Adherence; Previa: Placenta previa; Inversion: Uterine inversion.

Other risk factors are summarized in Table 2. A case of deep venous thromboembolism had a sudden and complete blockage of the main bilateral pulmonary arteries. The patient died shortly after admission in spite of resuscitation. There were no cases of amniotic fluid embolism based on serum examination in the study period.

Comparison of the risk profile for obstetrical hemorrhage between tertiary and secondary centers is shown in Figure 5. There was an increased incidence of placental abruption and birth canal tears in secondary centers, whereas abnormal placental adherence was frequently observed for cases in the tertiary center (p=0.03).

Discussion

There is an insufficient of published data regarding the risk of obstetrical hemorrhage and risk-related differences in morbidity in arural obstetric setting. Our study attempted to address this issue and showed that placental abruption (23%), birth canal tears (20%), atonic bleeding (15%), and abnormal placental adherence (15%) were the four major leading risk factors for obstetrical hemorrhage requiring blood transfusion. Additionally, mothers showing a high risk factor such as abnormal placental adherence or placental abruption had

Table 2: Medical and obstetrical risk factors in the 'other' group.

Risk factor	n=20
Acute fatty liver	2
HELLP syndrome	2
Ectopic pregnancy	2
Septic abortion or Hemorrhage after abortion	2
Retained tissue	3
Hematoma after cesarean section	1
Myoma uteri	1
Ovarian vein rupture	1
Deep venous thrombosis	2
Sepsis after urinary tract infection	1
Anemia of unknown cause or Iron deficiency anemia	2
Anaphylactic shock	1

Data are expressed as number.

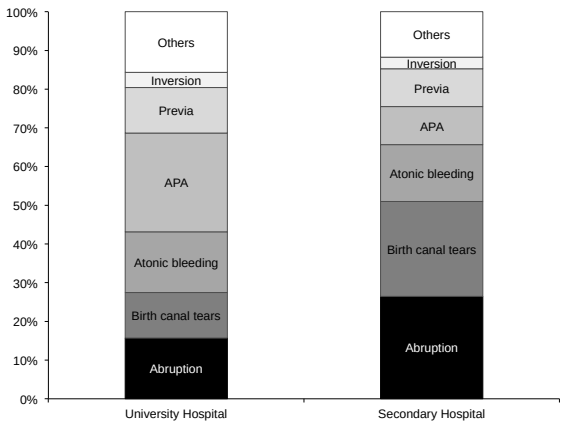

Figure 5: Comparison of the risk profile for obstetrical hemorrhage between tertiary and secondary centers. In our area, 80% of pregnant women give birth at a private clinic, and a risk-allocated system for obstetric care has been established. At first, private clinics referred a patient to secondary centers and next referred a patient to the tertiary center (University hospital), if necessary. A significant difference of the risk profile for obstetrical hemorrhage was found between tertiary (University hospital) and secondary centers according to the X^2 test (p=0.03).
Abruption: Placental abruption; APA: Abnormal Placental Adherence; Previa: Placenta previa; Inversion: Uterine inversion

a high possibility of developing life-threatening conditions at the hemorrhagic event. The observed differences of morbidity in relation to risk factors for obstetrical hemorrhage may represent important maternal health phenomena in our region.

Placental abruption was the most common risk factor in our study and is also associated with severe morbidity. Placental abruption was the highest condition for DIC (71%) with a higher incidence of massive blood transfusion (51%). With the exception of placental abruption, the incidences of DIC for the remaining conditions were proportional to the degrees of hemorrhage, and all incidences were less than 30% (Figure 2). The reason for a higher DIC score in placental abruptions was partially due to a methodological problem because the score increased when a serious etiology such as placental abruption was noted [8]. Nevertheless, it has been reported that placental abruption is the most frequent antecedent cause for DIC in an obstetric setting based on the International Society of Thrombosis and Hemostasis scoring system for overt DIC [9]. There were no cases of invasive procedures for mothers with placental abruption in spite of the high incidence of DIC. This might be a result of the massive administration of FFP followed by minimizing hemostasis procedures. In fact, the dosage of FFP was much higher than the dose of RBC in mothers with placental abruption (Figure 3). It has also been reported that the increased fresh frozen plasma: red blood cell (FFP:RBC) ratio was helpful in reducing the need for advanced interventional procedures in cases involving postpartum hemorrhage [10]. Thus, we should pay attention to placental abruption as the most common risk factor for obstetrical hemorrhage requiring blood transfusion, and concern ourselves with the manner of blood product administration to minimize morbidity.

Abnormal placental adherence was the third common risk factor in our study. 78% of mothers with abnormal placental adherence required invasive procedures for hemostasis, and 65% of mothers with abnormal placental adherence suffered from blood loss ≥ 3000 ml with a higher incidence of massive blood transfusion (74%). In addition, the incidence of ICU admission (26%) was as high as that of placental abruption (23%). Similar reports have shown that morbidities associated with abnormal placental adherence included transfusion of >10 units (23~40%), blood loss ≥ 2500 ml (44~69%), ICU admission (30~39%), and hysterectomy for hemostasis (57~66%) [11,12,13,14]. Therefore, we must recognize that abnormal placental adherence produced a greater risk for severe maternal morbidity, and that more needs to be done to minimize morbidities. In our study, the rate of massive transfusion for mothers (74%) was somewhat higher than that of others (23~40%). This discrepancy concerning the incidence of massive blood transfusion might be a result of the difference in management. In terms of the timing of delivery, for example, twelve of the 23 cases involving abnormal placental adherence sunder went cesarean section at 37–39 weeks and all suffered a massive blood loss greater than 2400 ml (data not shown). Recently, a planned delivery for placenta accreta at around 34 weeks following steroid administration was introduced [15]. This reduced the frequency of blood transfusion and ICU admission [11]. Morbidities associated with abnormal placental adherence will be reduced with multidisciplinary care that includes planned delivery and improvement of operative procedures.

Our study showed the high incidence of massive blood transfusion in cases involving birth canal tears. In fact, the incidence of massive blood transfusion of birth canal tears was close to that of placental abruption and atonic bleeding (Figure 3). According to Mhyreet al., abnormal placentation including placenta accreta, previa, and retained tissue, uterine atony, placental abruption, and postpartum hemorrhage associated with coagulopathy were frequent risk factors for massive blood transfusion in the United States. In contrast, obstetric trauma was a less frequent factor for massive blood transfusion [13]. Delivery in a private clinic may play an important role in the increased incidence of massive blood transfusion. In our area, 80% of pregnant women give birth at a private clinic [5]. In fact, 24 of the 31 cases of birth traumas were transferred from private clinics after deliveries (referral cases for an individual factor not shown in the results). We should keep in mind that differences between medical systems influence maternal morbidities.

Our study showed that cases of uterine inversion included one maternal death. The absolute number of uterine inversions was small (n=5), but the overall prognosis was very poor with a higher incidence of massive blood loss, DIC, massive blood transfusion, and ICU admission. All uterine inversions were transferred from private clinics after deliveries. Therefore, it is postulated that an early attempt was not made to treat the uterus as quickly as possible and this resulted in poor prognosis. There were no cases of amniotic fluid embolism based on clinical and serum examination for the period examined. However, we experienced a rare case of amniotic fluid embolism in which massive platelet aggregations were confirmed in pulmonary capillaries by an autopsy before the study period [16]. It is estimated that 24% of all maternal deaths in Japan are caused by amniotic fluid embolism [1]. We should also keep in mind that uterine inversion and amniotic fluid embolism are rare but serious conditions that occur during labor and delivery.

The risk profile for blood transfusion differed between tertiary and secondary centers (Figure 5). There was an increased incidence of placental abruption and birth canal tears in secondary centers, whereas abnormal placental adherence was frequently observed in the tertiary center (p=0.03). This difference was also due to a regional risk-allocated system, in which cases with known complications such as abnormal placental adherence were forwarded directly to the tertiary center. Furthermore, a new-onset case such as placental abruption was first transferred to the secondary center. Therefore, an institutional preparation for obstetric hemorrhage should be considered based on the institutional risk profile of obstetrical hemorrhage.

The other risk factors can be divided into two groups comprising obstetrical and medical risk factors (Table 2). Obstetrical risk factors included ectopic pregnancy, sepsis related to abortion, acute fatty liver, HELLP syndrome, and retained tissue, and all were related to massive hemorrhage or coagulopathy. Medical risk factors included anemia of unknown causes, deep venous thromboembolism, and sepsis after urinary tract infection. The incidences of certain obstetrical and medical risk factors could be reduced by an improvement of management procedures. Pulmonary embolism is the third leading risk factor of maternal death [1]. Pulmonary embolism is not directly related to obstetrical hemorrhage, although it is a significant cause of morbidity during pregnancy.

A limitation of our study is the paucity of data from private clinics. A risk-allocated system for obstetric care has been established in our region, although it is possible that blood transfusion practices for obstetrical hemorrhage in private clinics might be more frequent in emergency cases. There is therefore a need to expand the survey of mothers receiving blood transfusion for obstetrical hemorrhage.

In conclusion, we demonstrated that the monitoring of mothers receiving any blood transfusion for obstetrical hemorrhage and regarded as strong candidates for maternal death is essential in order to clarify the current differences in maternal morbidity in relation to risk factors, and establish an effective management protocol for obstetrical hemorrhage. Most maternal deaths related to obstetrical hemorrhage are not unavoidable events, and should be reduced by an effective regional risk-allocated system with multidisciplinary care.

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Disclosure

There is no financial or other relationship that might lead to a conflict of interest.

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