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Identification of women at low risk for early severe postpartum anaemia

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ABSTRACT

This study was carried out to identify risk factors for early severe postpartum anaemia (ESPA) and also subgroup of patients at low risk for whom interventions such as routine haemoglobin concentration (Hb) estimation may not be necessary. All women with pre-delivery Hb ≥10 g/dl who underwent vaginal delivery at 28 weeks or greater; from January 2007 through December 2012 at Ladoke Akintola University of Technology (LAUTECH) Teaching Hospital, Osogbo, Nigeria, were included. Cases were women with ESPA, defined as Hb <8 g/dl within 1-3 days postpartum; and control group with Hb ≥ 8 g/dl. With univariate analysis, risk factors associated with ESPA were identified and the effects of confounding factors were eliminated on multivariate analysis. Independent risk factors from the analysis were then used to eliminate high risk groups. Estimated blood loss (EBL) >500 ml was the most significant risk factor [odds ratio (OR) 5.10, 95% CI 3.54, 7.35] for ESPA. Abruptio placenta, instrumental vaginal delivery, preeclampsia, perineal and cervical lacerations and active phase arrest were also found to be significant, with associated OR greater than 2.0. If Hb is obtained only in response to EBL >500 ml, only 2.5% of the remaining population will have ESPA. If all risk factors found to be significant are eliminated, only 0.8% of the population will have ESPA. Interventions such as delaying discharge because haemoglobin estimation is being awaited; will be unnecessary in 99.2% of low risk cases (that is, women without the above risk factors); and in 97.5% of women who did not suffer postpartum haemorrhage.

INTRODUCTION

Anaemia due to iron deficiency is prevalent in pregnancy (WHO, 2008; Bergholt et al.,1999; Bergmann et al, 2001), and postpartum period, although the latter is characterized by physiologically low iron requirement from contraction of a previously expanded red cell mass, resulting in release of iron that can be re-utilized and stored (Institute of Medicine, 1990). Iron supplementation during and after delivery has been demonstrated to enhance recovery of iron stores that has become depleted as a result of pregnancy and delivery (Eskeland et al., 1997; Taylor and Lind, 1981; Krafft et al., 2005; Khan et al., 2006). However, supplementation will not compensate for loss due to postpartum haemorrhage, a major cause of maternal mortality in developing countries

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(Khan et al., 2006; Henrich et al., 2008) and occasionally in developed countries (James et al., 2008; Roberts et al., 2008; De Simoes et al., 2004). Therefore, every effort is often made to optimize the haematocrit level before the onset of labor.

The major morbidity associated with postpartum blood loss is from anaemia. Most mothers recover from postpartum anaemia during the weeks or sometimes months after delivery, but when recovery takes a long time, for example, with an unfavorable baseline haemoglobin concentration around delivery, functional consequences of iron deficiency and anaemia may appear or worsen (Bergmann et al., 2010). These include: depressive symptoms, deficits in cognitive function, fatigue, lower work performance, impaired immune function, poorer functioning of mother–child interaction and even delayed infant development (Corwin et al., 2003; Bodnar, 2005). In view of these consequences, it is important to monitor the prevalence and trends of postpartum anaemia in any setting, and to evaluate the most important risk factors for low hemoglobin values after delivery (Bergmann et al., 2010). However, haemoglobin concentration estimation has delayed postpartum discharge in many instances, and the question is can we identify a subgroup of women for whom routine determination of haemoglobin is not necessary?

The objective of this study was to identify risk factors associated with low postpartum haemoglobin concentrations after delivery and to define lower risk categories of patients for whom target interventions, particularly haematological investigations, may be unnecessary.

MATERIALS AND METHODS

For the study, a perinatal database was created at Ladoke Akintola University of Technology (LAUTECH) Teaching Hospital, Osogbo and data prospectively were collected over a period of 6 years (January 2007 through December 2012). Ethical approval for this study was obtained from the ethical committee of the Hospital. Antepartum and intrapartum variables were recorded at the time of delivery, and all maternal and neonatal charts were then reviewed to obtain postpartum and neonatal data. For the purposes of this study, the perinatal database was used to identify women who:

i. had a vaginal delivery at a gestational age greater than or equal to 28 weeks;
ii. were not anemic at presentation for delivery (haemoglobin concentration greater than or equal to 10 g/dl) and;
iii. had admission and early (1-3 days) postpartum haemoglobin concentration information available.

A case control study was performed on this population to determine risk factors associated with a low early postpartum haemoglobin concentration.

Our perinatal database used standard definitions which are therefore applicable to the present study. Thus for purposes of this study, grand multiparity was defined as five or more prior deliveries. Preterm delivery was defined as less than 37 completed weeks of gestation, postdates as greater than 40 completed weeks. Active phase arrest was defined as progress of labour touching the 4 h action-line of the World Health Organization (WHO) partograph; patients in this category, who were augmented and proceeded to deliver vaginally, were included in the study. Prolonged second stage was defined as greater than 1 h in parous patients and greater than 2 h in nulliparas, with an additional 1 h allowed for the presence of conduction anesthesia. Prolonged third stage was defined as greater than 30 min following passive management, or failure to deliver the placenta by controlled cord traction during active third stage management. Macrosomia was defined as a birth weight greater than 4 kg. Patients with marginal placenta previa who underwent a successful vaginal delivery were counted as having a placenta previa.

Placenta previa was coded based on earlier sonographic diagnosis. Transfusion, as coded in the database, was assumed to mean at least one unit of red blood cells. The outcome variable of interest was early (1-3 days) postpartum haemoglobin concentration less than 8 g/dl. This was chosen for the following reasons: 1) severe anaemia is defined as less than 8.0 g/dl and 2) this represented a range of haemoglobin concentration values above which most clinicians would be comfortable discharging a stable patient without further evaluation.

Cases were defined as patients with an early postpartum haemoglobin concentration less than 8 g/dl or patients receiving a transfusion regardless of discharge haemoglobin concentration. The remainder of the population served as the control groups.

Statistical analyses

Using SPSS, two analyses of individual risk factors by early postpartum haemoglobin concentration were performed to produce odds ratios (ORs) and 95% confidence intervals (CIs) for each risk factor. Because several risk factors are interrelated, individual risk factors were chosen for further analysis on the basis of greater statistical significance ($P<0.05$). A logistic regression model was then used to determine which variables were most highly associated with an early postpartum haemoglobin concentration less than 8 g/dl. The patient data were then reanalyzed using the risk factors derived from the logistic regression analysis.

Table 1. Demographic and pre-labour characteristics.

Risk factor	Cases (haemoglobin concentration <8 g/dl)	Controls (haemoglobin concentration ≥8 g/dl)	P-value
Age <20 years	19(13.3)	216(15.2)	0.667
Age >35 years	31(21.7)	326(23.0)	0.872
Nullipara	88(62.1)	704(49.6)	<0.005
Grandmultipara	18(12.7)	140(9.9)	0.346
Prior caesarean	12(8.4)	62(4.4)	0.046
Prior postpartum haemorrhage	8(5.8)	28(2.0)	0.013
Multiple pregnancy	5(3.4)	24(1.7)	0.219
Preterm	19(13.2)	149(10.5)	0.345
Postdate	15(10.7)	129(9.1)	0.531

Note: Values in parenthesis are percentages of each demographic/pre-labour characteristics.

Four sub-groups with successively lower risk for lower haemoglobin less than 10 and 8 g/dl were identified by excluding risk factors in order of decreasing statistical significance of the odds ratio. The first sub-group was defined by excluding all patients with estimated blood loss greater than 500 ml, as this was the single greatest risk factor for low postpartum haemoglobin concentration. The second sub-group was identified by excluding those patients with risk factors associated with an OR of greater than 2.0 for low early postpartum haemoglobin concentration. The third sub-group comprised those patients without risk factors associated with ORs greater than 1.5, and the fourth sub-group excluded all patients with any risk factor identified from the multivariate analysis. These lower-risk groups were analyzed for the percentage of patients with low early postpartum haemoglobin concentration. As there is no well-defined abnormal cut off for the postpartum haemoglobin, percentages of the population with early postpartum haemoglobin concentration less than 10 g/dl and less than 8 g/dl are given for each sub-group.

RESULTS

From the period, beginning January 2007 and ending December 2012, there were 3,616 deliveries entered into the perinatal database with gestational ages of 28 weeks or greater. Among these, 832 (23%) were excluded from analysis either because they had no available data regarding haemoglobin concentration (n=144), had only an admission haemoglobin concentration (n=97), or had only a postpartum haemoglobin determination available (n=591). Thus only 2784 (78%) had complete admission and discharge haemoglobin concentration information available in the database. Among these, 2010 (72.2%) were vaginal deliveries, including operative and breech vaginal deliveries. The mean haemoglobin concentration at admission was 12.1±1.4 g/dl with a slight skewing toward higher values. Of the population delivering vaginally, 1560 (79.6%) had admission with haemoglobin concentration of 10 g/dl or greater, qualifying them for inclusion into the study group. In this population, the average postpartum haemoglobin concentration was 12.8±1.6 g/dl.

There were 141 women (9.0% of the study population) who had an early postpartum haemoglobin concentration less than 8 g/dl or who received a transfusion and therefore qualified as cases. Table 1 presents the demographic data, including age, gestational age at delivery, and parity for the cases and controls. Table 2 shows labor and delivery characteristics for the cases and controls. All variables shown in Tables 1 and 2 were analyzed individually for their relationship to early postpartum haemoglobin concentration less than 8 g/dl. Table 3 presents the unadjusted and adjusted ORs and associated 95% CIs for each risk factor found to be statistically significant in relation to early postpartum haemoglobin concentration less than 8 g/dl. The single greatest risk factor for postpartum anaemia was found to be a clinical estimate of blood loss greater than 500 ml. This was associated with an OR of 6.21 (95% CI 4.32, 8.93). The results of the logistic regression on the risk factors found to be statistically significant at univariate analysis are presented in the fourth column of Table 3. Estimated blood loss was still the most significant risk factor (OR 5.10, 95% CI 3.54, 7.35). Abruptio placenta, instrumental vaginal delivery, preeclampsia, perineal/ cervical lacerations and active phase arrest were also found to be significant, with associated ORs greater than 2.0. Several risk factors found to be significant in unadjusted analysis did not maintain statistical significance following adjustment. These included prolonged second stage, chorioamnionitis and fetal macrosomia. Some factors considered to be clinically interrelated were found to be independent risk factors, for

Table 2. Labour and delivery characteristics.

Characteristics	Haemoglobin concentration <8 g/dl		Haemoglobin concentration ≥8 g/dl		P
	n	Percentage	n	Percentage	
Postdate	15	10.7	129	9.1	0.531
Induction	27	19.3	148	10.4	0.001
Augmentation	51	36	302	21.3	<0.001
Preeclampsia	16	11.1	55	3.9	<0.001
Active phase arrest	17	11.9	71	5	<0.001
Prolonged second stage	27	19.4	173	12.2	0.015
Chorioamnionitis	11	7.5	65	4.6	0.128
Abruptio placenta	5	3.6	16	1.1	0.013
Fetal macrosomia	16	11.7	109	7.7	0.096
Forceps/vacuum	62	43.8	253	17.8	<0.001
Episiotomy	68	48.5	595	41.9	0.131
Perineal laceration	39	28	165	11.6	<0.001
Cervical laceration	7	5.2	33	2.3	0.038
Prolonged 3rd stage	14	9.9	95	6.7	0.155
PPH	69	49	190	13.4	<0.001

Table 3. Unadjusted and adjusted odds ratios for early postpartum haemoglobin concentration <8 g/dl.

Risk factors	Unadjusted OR	95% CI	Adjusted OR	95% CI
PPH	6.21	4.32-8.93	5.10	3.54-7.35
Abruptio placenta	3.36	1.21-9.28	3.01	1.05-8.67
Forceps/vacuum	3.60	2.51-5.16	3.00	2.09-4.32
Preeclampsia	3.08	1.71-5.55	2.73	1.48-5.05
Perineal laceration	2.96	1.98-4.43	2.57	1.70-3.88
Active phase arrest	2.57	1.46-4.51	2.28	1.27-4.09
Cervical laceration	2.33	1.03-5.29	2.09	0.89-4.90
Induction	2.06	1.31-3.24	1.81	1.13-2.89
Augmentation	2.08	1.44-3.00	1.77	1.22-2.58

Table 4. Haemoglobin concentration profiles on four sub-groups.

Sub-groups	% of study population	Mean % ± SD of discharge haemoglobin concentration	% with haemoglobin concentration <10 g/dl	% with haemoglobin concentration <8 g/dl
Total	100	10.1 ± 1.9	29.3	9.0
One	90.1	10.4 ± 1.4	13.3	2.5
Two	83.6	10.9 ± 1.4	10.1	1.9
Three	69.4	11.1 ± 1.2	5.5	0.9
Four	47.0	11.6 ± 1.6	1.7	0.8

example, augmentation and active phase arrest remained statistically significant after multivariate analysis.

When various risk factors were eliminated from the population, a progressively smaller percentage of the population was found to have an early postpartum haemoglobin concentration less than 8 g/dl. Table 4 presents data for sub-groups of the population formed by successively eliminating risk factors for low postpartum

haemoglobin concentration. The mean early postpartum haemoglobin concentration in all four sub-groups is 10.1±1.9. If haemoglobin concentrations are obtained only in response to an estimated blood loss greater than 500 ml, 2.5% of the remaining population will have an early haemoglobin concentration less than 8 g/dl, and 13.3% will have a concentration less than 10 g/dl (Table 4, sub-group one). If all risk factors found to be significant in Table 3 are eliminated, only 0.8% of the population will have a haemoglobin concentration less than 8 g/dl (Table 4, sub-group four). Of this, approximately 0.6% are patients receiving transfusions, who were counted as having a haemoglobin concentration less than 8 g/dl for this calculation.

DISCUSSION

Although it is a standard practice to obtain a postpartum haemoglobin concentration on all deliveries in many institutions, there is little in literature regarding either the normal range or the utility of this value (Bergmann et al., 2010; Corwin et al., 2003; Bodnar, 2005; Dar et al., 2006). A recent literature suggests that routine haemoglobin concentration estimation in low-risk women is not necessary (Bergmann et al., 2010). In the present study, we evaluated the risks of severe anaemia or need for blood transfusion in women after excluding identified risk factors. In the absence of risk factors (Table 4, sub-group 4), our data show that less than 1% of the non-anaemic population delivering vaginally will have a discharge haemoglobin concentration less than 8 g/dl. If routine postpartum haemoglobin concentration determination is reserved only for patients with an estimated blood loss greater than 500 ml, only 2.5% of the remaining patients will have early postpartum haemoglobin concentration less than 8 g/dl (Table 4, sub-group 1). Based on data in Table 4, clinicians can select low-risk sub-groups for which the risk of unrecognized anaemia is reasonable. Furthermore, it is likely that those with lower haemoglobin concentrations will have events, signs, or symptoms, such as late postpartum bleeding, dizziness, or orthostasis, that will prompt the clinician to obtain a haemoglobin concentration determination (Nicol et al., 1997).

We do not have postpartum vital signs or symptoms available in our database to correlate with haemoglobin concentration values, but it seems reasonable to expect that those patients with the lowest haemoglobin concentration values would also display signs or symptoms leading to the diagnosis of a clinically significant anaemia requiring intervention. It is likely, for example, that a significant fraction of those with a low discharge haemoglobin concentration in the absence of risk factors experienced late postpartum hemorrhage (greater than 1 h postpartum), which is not a variable available in the database.

One of the most interesting findings is that, even in a teaching institution in which blood loss is estimated by practitioners of varying levels of experience, the estimated blood loss remains the strongest predictor of a low discharge haemoglobin concentration. Because of the work of Toledo et al. (2010), Zhang et al. (2010), Gharoro et al. 2009 and Sukprasert et al. (2006), studying the actual amount of blood lost at delivery, the clinical estimate of blood loss frequently is regarded as inaccurate (Schorn, 2010; Al Kadri et al., 2010). Indeed, their work suggests that the conventional estimates may be approximately doubled to obtain a truer idea of the actual blood volume lost. Toledo et al. (2010) observed an average pre-delivery haemoglobin concentration of 37.5% and an average blood loss of 505 ml in patients delivering vaginally. Zhang et al. (2010) noted no change in haemoglobin concentration from antepartum to postpartum, despite a well-documented average loss of 600 ml of blood volume in his sample of 75 vaginal deliveries. However, even though the assigned value may be falsely low by established convention, the trend of estimated blood loss has validity; a larger estimate of blood loss effectively predicts a lower discharge haemoglobin concentration.

Other clinical findings remained important as independent risk factors. The most significant are those that contribute to intrapartum bleeding, such as placental abruption. The bleeding caused by this condition often is not included in the estimated blood loss at delivery. Similarly, factors that are related to atony and delayed postpartum hemorrhage, such as preeclampsia, prolonged active phase, and oxytocin use, remain as risk factors after multivariate analysis.

Unlike our findings, Bergmann et al. (2010) reported that vaginal and cervical lacerations, which are known to be associated with peripartum haemorrhage, did not remain independent risk factors in their study. They attributed this to the fact that the bleeding due to a cervical or vaginal laceration is likely to be included in the estimated blood loss. They also stated that for similar reasons, operative vaginal delivery did not prove to be an independent risk factor. On the other hand, perineal laceration, cervical laceration and forceps/vacuum deliveries proved to be independent risk factors in our study. It is possible that there is a tendency to underestimate the amount of bleeding caused by perineal lacerations, whereas cervical and vaginal lacerations are almost always associated with a large clinical estimate of blood loss.

The exact haemoglobin concentration value that represents pathologic anaemia on postpartum days (1-3) is not well defined from prior studies. It has been noted that postpartum haemoglobin concentrations are lowest

in the early postpartum period (0-3 days) and rise toward the antepartum haemoglobin concentration value within 6-7 days. In a previous analysis of 9598 vaginal deliveries, Coombs et al. (2009) noted an average postpartum haemoglobin concentration of 33.7%, with more than one-third of patients showing no change or an increase in haemoglobin concentration from admission. This result was confirmed by Prendiville and Harding (1988) in a study of 1700 vaginal deliveries, showing an average drop in hemoglobin of 0.1 to 0.6 g/dl. However, no study has correlated early postpartum days' haemoglobin concentration data with late postpartum (4-6 weeks) haemoglobin concentrations except in the most general fashion. One Finnish study, Hemminki and Rimpela (1991), looking at routine versus selective iron supplementation in the antenatal period noted that, despite a significant difference in the numbers of patient who were anaemic immediately postpartum with different iron regimens, both groups had l-2% rates of anaemia (defined as haemoglobin concentration less than 11.7 g/dl) at the postpartum checkup. Based on these data, routine determination of the postpartum haematocrit in order to target a population for iron supplementation is not well supported by the literature.

In our data, the vast majority of women, even in high-risk sub-groups, were not significantly anaemic in the immediate postpartum period. In fact, only 9% had a discharge haemoglobin concentration less than 8 g/dl or received a transfusion. In the absence of risk factors, there was more than a 98% likelihood that clinically significant anaemia was not present (here defined somewhat arbitrarily as a haemoglobin concentration below 8 g/dl). Without clear evidence from the literature as to how to manage asymptomatic postpartum anaemia, and considering the ease with which haemoglobin estimation can be obtained if clinically warranted, postpartum haemoglobin concentration determinations should be reserved for clinical indications, eliminating a routine laboratory workup for many low-risk patients. Also good antenatal care with the use of iron supplements during pregnancy should be encouraged by clinicians, particularly in low socioeconomic countries. This will ensure good haemoglobin concentration of women in labour and thereby reduce the occurrence and/or sequelae of ESPA.

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