Effects of the Massive Blood Transfusion in Obstetrics

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Abstract

Background: Massive blood transfusion is a rare condition with rates ranging from 2.3 to 10.0 per 10,000 maternities. Massive transfusion, historically defined as the replacement by transfusion of 10 units of red cells in 24 hours.

Objectives: Evaluate the effects of MBT in obstetrics and its complications, and assess early and late complications.

Patients and methods: This 38-patients cohort study at Qena University Hospital ran from May 2022 through April 2023. MBT occurred when 10 red cells were transfused in 24 hours. MBT = 3 RBCs/1h. Parameters assessed included CBC, coagulation profile, liver and renal function, blood sugar, vital signs, CVP, blood loss, and BMI. Resuscitation targets were Hb 7-9 g/dL, INR <1.5, platelets >50,000/mL, pH 7.35-7.45, CVP 8-12 mmHg. Post-operative monitoring included vital signs and lab tests.

Results: 85% of 38 patients (average age: 31.26 years) had placenta previa (57.89% centralis, 15.79%/21.05% G2/G3). Avg. BMI: 26.79 kg/m^2, GA: 34.37 weeks, blood loss: 2757.59 ml, transferred units: Pre-operative: SBP rose to 105.26 mmHg, DBP to 68.42, pulse rate steady at 86.21 bpm, K to 3.35 mmol/L, Hgb to 10.11 g/dL, and CVP to 9.37 mmHg. 10.53% hypothermia, 52.63% NICU hospitalization, 5.26% renal impairment, and 15.79% disseminated coagulopathy were complications. Post-operative DBP, CVP, and MBT negative associations were found.

Conclusion: Monitoring and managing MBT in placenta previa patients is crucial to reduce complications. Factors influencing transfusion needs include intraoperative blood loss, gestational age, diastolic blood pressure, hemoglobin, AST levels, pulse rate, pH, and CVP.

Keywords: Massive; Blood Transfusion; Obstetrics.

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Introduction

Obstetric hemorrhage is a significant global health concern and remains the leading cause of maternal mortality worldwide. In addition to various interventions such as uterine contractions reinforcement, drug hemostasis, and surgical techniques, massive blood transfusion **(MBT)** plays a critical role in the management of obstetric hemorrhage **(Bazirete et al., 2022; Owen et al., 2021).**

The incidence of MBT in relation to delivery or postpartum hemorrhage **(PPH)** has been reported in high-resource countries, with rates ranging from 2.3 to 10.0 per 10,000 maternities. Additionally, there have been reports of an increasing trend in the rate of MBT following childbirth. These statistics highlight the importance of studying the effects and complications associated with MBT in obstetrics to improve maternal outcomes and refine clinical practices **(Owen et al., 2021).**

MBT carries various potential complications and risks. Excessive blood loss and subsequent MBT can contribute to complications such as disseminated intravascular coagulation **(DIC)**, renal impairment, and dilutional coagulopathy. In addition to these specific complications, MBT can result in early and late-onset complications. Early complications may include transfusion reactions, transfusion-associated circulatory overload, and transfusion-related acute lung injury **(Ajmani, 2020; Ajmani and Ajmani, 2020).**

The main aim of the study was to evaluate the effects of massive blood transfusion in obstetrics, particularly in relation to complications and to evaluate early and late onset complication of massive transfusion.

Patients and methods

This was a cohort study that was conducted in the Obstetrics and Gynecology Department of Qena University Hospital between May, 2022 and April, 2023.

The inclusion criteria for our study encompassed various conditions that were observed in the past. These criteria consisted of patients who had experienced ante-partum hemorrhage, post-partum hemorrhage, and internal hemorrhage due to factors such as disturbed ectopic pregnancy, ruptured uterus, or abdominal trauma. We also included all obstetrical cases where massive obstetric hemorrhage occurred both as antepartum hemorrhage and postpartum hemorrhage. For the purposes of our research, we defined massive blood transfusion as the transfusion of 3 units of packed red blood cells (RBCs) over the course of 1 hour.

In contrast, the exclusion criteria applied to patients with cardiac diseases, renal failure, or a history of hypersensitivity reactions following blood transfusions. These criteria were used to determine the eligibility of participants for our study, looking back at the parameters that guided our selection process.

Massive blood transfusion is defined as the transfusion of 3 units of packed red blood cells (RBCs) over 1 hour or any blood components in 30 minutes **(Meyer et al., 2018; Savage et al., 2015).**

We employed various tools and procedures for different laboratory testing, which included a complete blood count, coagulation profile, liver function tests (ALT and AST), kidney function tests, and random blood sugar measurements. We measured vital signs such as pulse, blood pressure, oxygen saturation, ECG, and respiratory rate. Intravenous access and central venous lines were established when required for medical interventions. The quantification of blood loss was achieved by considering the cumulative values of soaked towels (each equivalent

to 100-150 ml/towel), the quantity in the suction drain container, and the amount collected on waterproof drapes.

Targets for resuscitation in the context of massive transfusion were defined, including maintaining hemoglobin levels between 7 to 9 g/dL, INR below 1.5, platelet counts exceeding 50,000/mL, pH within the range of 7.35 to 7.45, and central venous pressure (CVP) readings between 8 to 12 mmHg.

Each patient underwent a detailed medical history assessment, focusing on maternal information such as name, age, and parity, along with comorbidities.

Clinical examinations were conducted, with an emphasis on arterial blood pressure measurement and the calculation of body mass index (BMI) by dividing weight in kilograms by height in meters. Vital signs were measured regularly.

Laboratory investigations covered liver enzymes, including aspartate aminotransferase (AST), alanine transaminase (ALT), and albumin levels. Kidney function tests, including urea and creatinine levels, were performed, along with a coagulation study, which included prothrombin time (PT), prothrombin concentration (PC), and the international normalized Ratio (INR). Complete urine analysis, random blood sugar measurement, complete blood count, arterial blood gas (ABG) analysis, and electrolyte level assessments were also part of the laboratory investigations.

Postoperatively, clinical data were collected six hours after the patients' recovery from surgery. This included monitoring vital signs such as pulse, blood pressure, respiratory rate, and temperature. Laboratory data, including CBC, liver function tests, kidney function (serum creatinine), coagulation profiles, ABG analysis, and electrolyte levels, were also assessed six hours postoperatively.

Research outcomes: Primary research outcome was to monitor effect of massive blood transfusion. Secondary research outcome was to evaluate and determine which obstetric cases would benefit from massive blood transfusion and to deal with complications of massive blood transfusion.

Ethical Code: SVU-MED-OBG024-1-22-4-386

Statistical analysis

Data is depicted through either the utilization of mean and standard deviation (qualitative data representation) or numerical values and percentages (quantitative data representation). Group comparisons were conducted using the Chi-Square test or Ficher exact test for quantitative data, the Mann-Whitney U test for continuous data that did not adhere to normal distribution, and the Student's t-test for continuous data that adhered to normal distribution. Statistical significance was established at a significance level of less than 0.05. Pearson correlation was used for association between different parameters.

Results

In the study, 38 participants were included. Their average age was 31.26 years, with a standard deviation of 4.63. Regarding conception conditions, the majority of participants had placenta previa, accounting for 34 participants or 89.47% of the total. Placenta previa centralis was observed in 22 participants, representing 57.89% of the total, while placenta previa ant G2 and G3 were present in 6 (15.79%) and 8 (21.05%) participants, respectively. Additionally, a small percentage of participants had experienced incomplete abortion (2, 5.26%) and post-abortion bleeding (2, 5.26%). The participants' body mass index (BMI) averaged at 26.79 Kg/m^2, with a standard deviation of 1.87. The gestational age (GA) at the time of

measurement was 34.37 weeks on average, with a standard deviation of 4.69. In terms of blood loss, the participants had an average blood loss of 2757.59 ml, with a standard deviation of 277.52. Lastly, the mean number of Transferred Units was 11.05, with a standard deviation of 1.84 (**Table .1, Fig.1).**

Table 1. Participant Characteristics and Conception Conditions

Variables	Value (N = 38)
Age	31.26 ± 4.63
Conception	
• **Placenta previa**	34(89.47%)
• **Placenta previa centralis**	22(57.89%)
• **placenta previa ant G2**	6(15.79%)
• **placenta previa ant G3**	8(21.05%)
• **Incomplete abortion**	2(5.26%)
• **Post abortion bleeding**	2(5.26%)
BMI (Kg/m^2)	26.79 ± 1.87
G.A (Weeks)	34.37 ± 4.69
Blood loss (ml)	2757.59 ± 277.52
Number of Transferred Unites	11.05 ± 1.84

BMI: Body Mass Index, BMI: Body Mass Index, GA: Gestational Age

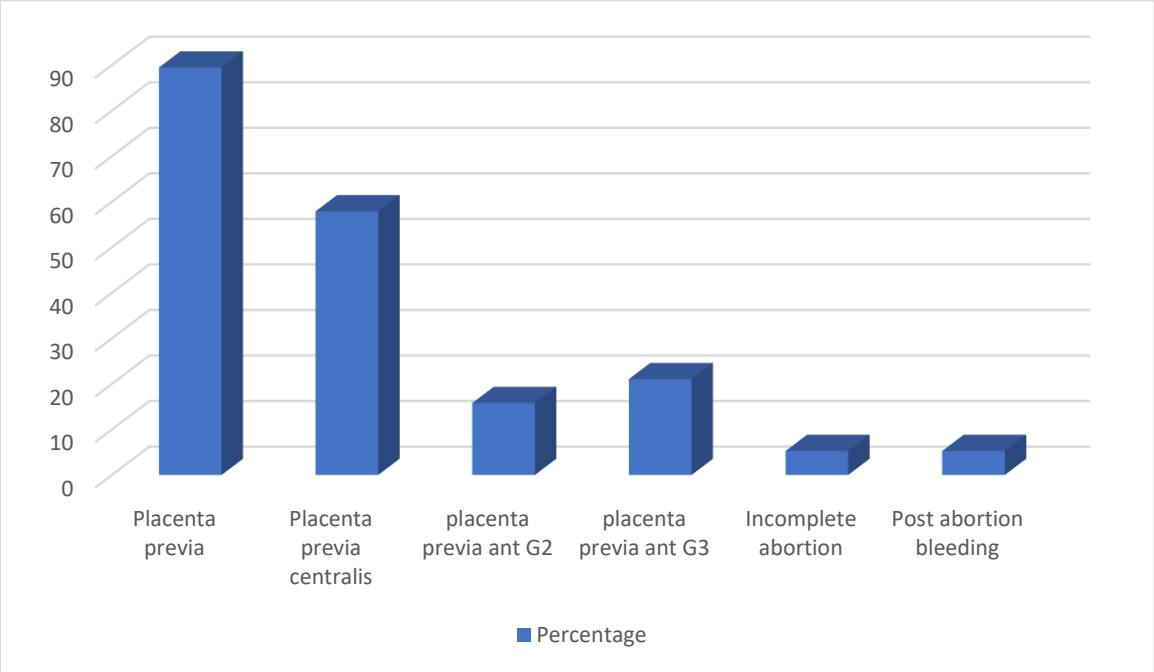

Fig.1. Conception among included subjects

Regarding blood pressure, Systolic Blood Pressure (SBP) increased from 103.16 to 105.26 mmHg ($p = 0.31$, non-significant), while Diastolic Blood Pressure (DBP) increased from 66.32 to 68.42 mmHg ($p = 0.186$, non-significant). Pulse rate decreased from 87.26 to 86.21 bpm ($p = 0.492$, non-significant). TMP (temperature) showed minimal variation, decreasing from 36.89 to 36.88°C ($p = 0.851$, non-significant). ALT decreased significantly from 38.45 to 21.47 U/L ($p < 0.0001$, significant), whereas AST increased from 22.79 to 27.74 U/L ($p = 0.037$,

significant). S. Creatinine concentration exhibited minor variation, increasing from 0.67 to 0.68 mg/dL (p = 0.781, non-significant), and pH levels decreased slightly from 7.36 to 7.35 (p = 0.432, non-significant). Hemoglobin (Hgb) increased from 9.3 to 10.11 g/dL (p = 0.011, non-significant), while platelet count (Plt) showed slight variation from 185.42 to 166 × 10^3/µL (p = 0.197, non-significant). Potassium (K) concentration significantly decreased from 3.5 to 3.35 mmol/L (p < 0.0001, significant), as did calcium (Ca) from 1.38 to 1.16 mmol/L (p < 0.0001, significant). Sodium (Na) exhibited minor variation, decreasing from 137.26 to 136 mmol/L (p = 0.057, non-significant). Conversely, Central Venous Pressure (CVP) significantly increased from 3.89 to 9.37 mmHg (p < 0.0001, significant), **(Table, 2).**

Table 2. Comparison between Pre-Operative and Post-operative data among included subjects

Variables	Pre-Operative (N = 38)	Postoperative (N = 38)	P. Value
Blood pressure (mmHg)			
SBP	103.16 ± 10.57	105.26 ± 6.97	0.31
DBP	66.32 ± 8.31	68.42 ± 5.01	0.186
Pulse (Beat/min)	87.26 ± 7.79	86.21 ± 5.21	0.492
TMP (C)	36.89 ± 0.13	36.88 ± 0.3	0.851
ALT (U/L)	38.45 ± 9.17	21.47 ± 8.1	<0.0001*
AST (U/L)	22.79 ± 10.58	27.74 ± 9.77	0.037*
S. Create (mg/dL)	0.67 ± 0.07	0.68 ± 0.21	0.781
PH	7.36 ± 0.06	7.35 ± 0.05	0.432
Hgb (g/dL)	9.3 ± 1.66	10.11 ± 0.94	0.011*
Plt (× 10^3/µL)	185.42 ± 64.41	166 ± 65.53	0.197
K (mmol/L)	3.5 ± 0.17	3.35 ± 0.15	<0.0001*
Ca (mmol/L)	1.38 ± 0.1	1.16 ± 0.06	<0.0001*
Na (mmol/L)	137.26 ± 3.11	136 ± 2.54	0.057
CVP (mmHg)	3.89 ± 3.03	9.37 ± 1.33	<0.0001*

Among the reported complications, all participants required admission to the intensive care unit (ICU), with an average of 3.3 ± 1.66 days. There was no decrease in their conscious level as Glasgow comma scale was 15 in all participants. About 52.63% required admission to the neonatal intensive care unit (NICU). There were no reported cases of disseminated intravascular coagulation (DIC) or electrolyte disturbances. Renal impairment was observed in 2(5.26%) participants, while hypothermia affected 4(10.53%) patients. Additionally, 6(15.79%) participants experienced disseminated coagulopathy (D. Coagulopathy). (**Table,3, Fig.2).**

Table 3. ICU Admission, Conscious level and Complications

Variables	Value (%) (N = 38)
ICU Admission (Days)	3.3 ± 1.66
Conscious level	15 ± 0
NICU admission	20(52.63%)
DIC	0(0%)
Renal impairment	2(5.26%)
Electrolyte disturbance	0(0%)
Hypothermia	4(10.53%)
D. Coagulopathy	6(15.79%)

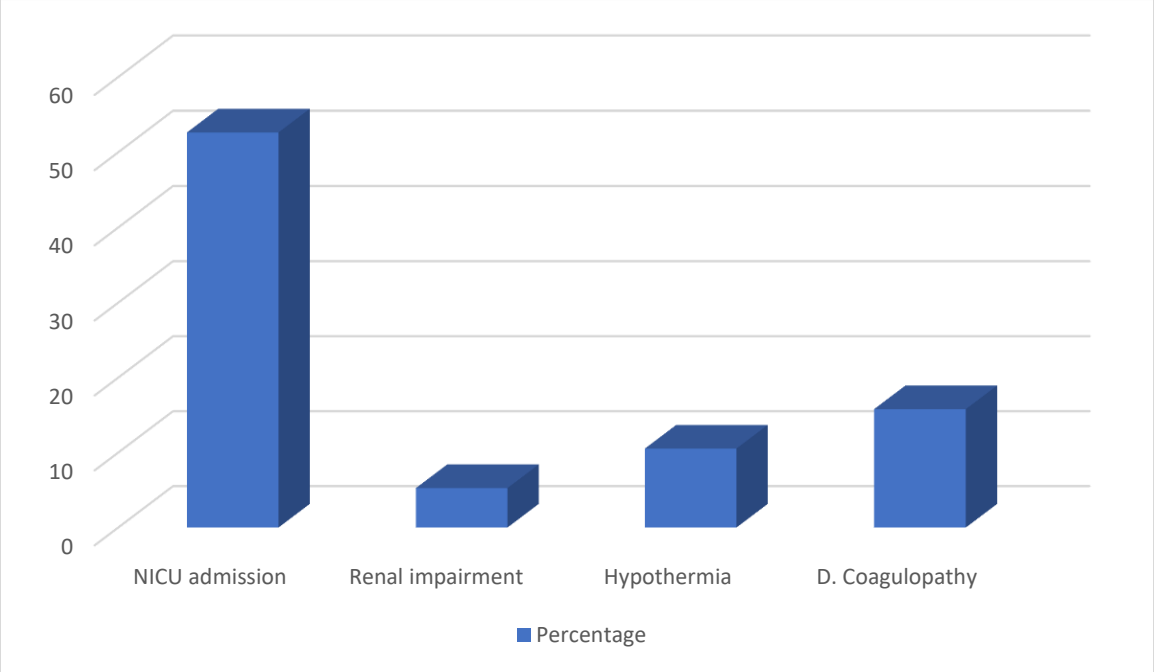

Fig.2. Complications occurrence among included subjects

Regarding pre-operative data, there was significant positive correlation between blood loss and number of units transferred. Placenta previa was significantly associated with number of units transferred. gestational age, DBP, Hgb and AST all showed significant positive correlation with number of units transferred. Both, pulse and Ph showed significant negative correlations, there was no significant correlation between Hgb level and blood loss. Regarding post-operative data, there was negative correlation between DBP and low CVP on one side and need for massive blood transfusion on other side. (**Table .4).**

Table 4. Correlation between different parameters pre and post-operative with intra operative blood loss and number of units transferred

Parameters	Blood loss (ml)		N. Unit	
	r	P. Value	r	P. Value
Pre-operative				
Blood loss (ml)			.690**	0.00108
N. Unit	.690**	0.00108		
Age	0.143169	0.55874	0.34397	0.14931
Conception				
• **Placenta previa**	0.327475	0.17112	.489*	0.03367
• **Placenta previa centralis**	0.320402	0.1811	0.32215	0.1786
• **Placenta previa ant G2**	0.227801	0.34826	0.148454	0.54415
• **Placenta previa ant G3**	-0.34965	0.14227	-0.15934	0.51468
• **Incomplete abortion**	-0.31229	0.38302	-0.40173	0.08821
• **Post abortion bleeding**	-0.13778	0.57379	-0.27013	0.26336
BMI	0.035436	0.88549	0.277398	0.25022
G.A	0.264249	0.2743	.557*	0.01317
SBP	0.389384	0.41315	0.448054	0.05437
DBP	0.29045	0.2277	.522*	0.02181
Pulse	-0.23622	0.33025	-.470*	0.04224
Hgb	0.41491	0.07733	.630**	0.00385
Plt	.456*	0.04952	0.338499	0.18241
ALT	0.303603	0.20637	0.142113	0.56167
AST	.640**	0.00316	.548*	0.01504
PH	-0.2327	0.33772	-.475*	0.03995
S. Create	-0.16486	0.50001	-0.34573	0.1471
CVP	-0.29007	0.22834	-0.28333	0.23981
TMP	0.146243	0.55023	0.254493	0.29306
K	0.372345	0.11644	0.235495	0.33177
Ca	-0.06426	0.79382	0.017917	0.94386
Post operative				
SBP	-0.33876	0.15598	-0.36949	0.13849
DBP	-0.21011	0.38794	-.593**	0.00751
Pulse	0.025668	0.91693	0.270986	0.26179
Hgb	-0.1039	0.67209	-0.41628	0.07626
Plt	-0.02627	0.91498	-0.14605	0.55078
ALT	0.291138	0.22655	-0.05023	0.8382
AST	0.055082	0.82278	0.210855	0.38621
PH	0.030512	0.90132	0.002105	0.99317
S. Create	-0.00984	0.96812	-0.01756	0.94312
CVP	-0.39915	0.09046	-.643**	0.00297
TMP	-0.06796	0.78222	0.041522	0.86597
K	0.276642	0.25157	0.07077	0.77342
Ca	-0.07811	0.7506	0.070685	0.77369

Discussion

In our study, regarding demographic data, the average age was 31.26 years, with 89.47% having placenta previa (57.89% centralis). A small number experienced incomplete abortion or post-abortion hemorrhage. Most had a high BMI, and the mean gestational age was 34.37 weeks (20–37 weeks).

Obesity and high BMI are linked to increased obstetric risks, including gestational diabetes, hypertension, and placental abnormalities, raising bleeding risk during pregnancy and delivery **(Degez et al., 2021; Polic et al., 2020).**

Our study and **Mwanamsangu et al. (2020)** found that maternal overweight and obesity are risk factors for postpartum hemorrhage (PPH), with obese women more likely to have cesarean births. **Davey et al. (2020)** supported this, reporting a 1.40 adjusted odds ratio (95% CI: 1.3-1.5) for severe PPH in overweight and obese women compared to normal-weight women.

Contrarily, **Ovesen et al. (2011)** found no BMI-PPH association in their Danish cohort study, suggesting variations in demographics, methods, and sample sizes.

Placenta previa, especially the centralis subtype, leads to severe pregnancy and labor bleeding, necessitating significant blood transfusions. It occurs when the placenta attaches low in the uterus, obstructing the cervix, and increasing the risk of separation and bleeding **(Park and Cho 2020).** Our findings align with **Zhou et al. (2021),** who observed substantial blood transfusions in 95.8% of cesarean sections due to placenta previa. **Liu et al. (2021)** also reported similar results, attributing 55.83% of severe postpartum hemorrhages to abnormal placentation.

In our study Pre-operative medical assessments revealed normal coagulation function and blood volume. However, obstetric procedures resulted in substantial blood loss and transfusions. While calcium and temperature remained stable, potassium and central venous pressure showed slight decreases. The augmentation and inhibition of coagulation and fibrinolytic systems during pregnancy can lead to coagulation factor consumption, increasing bleeding risk and potentially causing DIC **(Vermeulen and Van de Velde 2022; Wasserloos et al., 2021).**

Our investigation also confirmed normal pre-operative coagulation. However, genetic and acquired coagulation abnormalities can elevate the risk of postpartum hemorrhage (PPH) and blood transfusions. **Hews-Girard et al. (2023)** highlighted the connection between inherited bleeding disorders (IBDs) and PPH, reporting an adjusted relative risk (aRR) of 1.26 and a 95% CI of 1.08 to 1.46, indicating a higher PPH risk in IBD patients. Genetic bleeding disorders can impede blood clotting and hemostasis, leading to prolonged bleeding and clot formation issues.

Our study data revealed that obstetric blood transfusions had various effects on physiological parameters. Transfusions were associated with increased SBP, DBP, hemoglobin, ALT, AST, serum creatinine, and CVP. Conversely, pulse rate, platelet count, pH, temperature, potassium, and calcium decreased after transfusion. These findings suggest that blood transfusions can impact vital signs and biochemical indicators.

In line with our results, **Zhou et al. (2021)** reported statistically significant changes in hemoglobin levels before and after blood transfusions, with post-surgery hemoglobin levels showing a slight increase.

A substantial portion of our participants required admission to the intensive care unit (ICU) after extensive blood transfusions due to the complexity of their cases and the need for specialized care.

However, the absence of disseminated intravascular coagulation (DIC) and electrolyte abnormalities indicated the safety of the transfusion process, as participants maintained normal consciousness, confirming the safety of blood transfusions.

These complex cases often required expert neonatal care and it was given in our study, as evidenced by the high rate of neonatal intensive care unit (NICU) admissions 20 (52.63%). Instances of renal impairment (5.26%), hypothermia (10.53%), and coagulopathy (15.79%) underscored the importance of vigilant monitoring and appropriate treatment.

Furthermore, increased massive blood transfusion (MBT) may reduce pregnancy complications, as demonstrated by **Xie et al. (2021),** who reported significant reductions in hysterectomy incidence and maternal mortality rate among MBT patients. Similarly, **Ochiai et al. (2021)** noted that a Massive Blood Transfusion Protocol (MTP) for postpartum hemorrhage (PPH) effectively addressed severe DIC, highlighting the potential for improved maternal outcomes through early blood product availability.

Our research established a significant positive correlation between intraoperative blood loss and transfusions. Gestational age, diastolic blood pressure, hemoglobin levels, and AST showed positive correlations with the number of units transferred, indicating their influence on transfusion volume. Conversely, post-operative transfusion units were negatively correlated with diastolic blood pressure and central venous pressure, suggesting that lower values of these parameters were associated with larger transfusion volumes. Platelet count exhibited an adverse link with intraoperative blood loss, and the number of units transferred showed negative correlations with blood pressure, hemoglobin, and platelets. Pulse rate had a positive association with transfused units, implying higher blood transfusion rates.

Consistent with our findings, **Kang et al. (2020)** reported that placenta previa increased the likelihood of requiring a five-unit PRBC transfusion after surgery. However, gestational age did not impact blood transfusion requirements. Differences in study populations, methodologies, and factors may explain variations in our findings compared to Kang et al.'s. Obstetric blood transfusion depends on several factors, including the severity of the condition and maternal health.

Our results also aligned with **Matsunaga et al. (2012),** revealing a negative correlation between RCC transfusion volume and Hb levels before transfusion in all obstetric conditions except placenta previa. Some placenta previa patients had short intervals between bleeding and blood tests, making it difficult to accurately represent blood loss, with transfusion volumes determined primarily by intraoperative blood loss counts. Notably, a majority of our patients had placenta previa.

Several pre-operative factors correlated with maternal and neonatal ICU admissions. Maternal ICU hospitalization was positively linked to NICU admission, indicating an interconnection. A significant negative correlation was observed between pre- and post-operative AST level differences and NICU admission, suggesting that a greater decrease in AST levels post-transfusion increased NICU hospitalization rates.

Consistent with our findings, **Manjavidze et al. (2020)** reported a strong association between ANC and maternal ICU hospitalization with NICU admissions. Adequate prenatal care and potential maternal ICU-related complications may impact infant health, necessitating NICU care.

This research on large blood transfusion in obstetrics has significant drawbacks. The limited sample size may restrict the generalizability of the results. The research focused on placenta previa patients; hence the findings may not apply to other obstetric patients with various diseases or risk profiles. Therefore, extending these results to other patient groups requires care.

Conclusion

Study findings emphasize monitoring and managing massive blood transfusions in placenta previa patients, reducing complications like renal issues, hypothermia, and coagulopathy. Factors influencing transfusion needs include intraoperative blood loss, gestational age, diastolic blood pressure, hemoglobin, and AST levels. High pulse rate and low pH correlate with reduced transfusion needs. Low diastolic blood pressure and CVP correlate with increased need for massive blood transfusion. High AST and low platelet count correlate with ICU admission pre-operatively.

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