

POSTPARTUM HAEMORRHAGE: MINIMUM ALLOWABLE HAEMOGLOBIN LEVEL

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Abstract

Despite defining the acceptable postpartum haemoglobin levels, there is neither consensus, nor a strong statistically proven analysis of its minimum safe level and its influence on systemic haemodynamic and oxygen metabolism in particular.

The aim. Therefore, this study aimed to determine statistically minimal allowable haemoglobin levels in postpartum women in case of postpartum haemorrhage which allows the cardiac functional status and oxygen metabolism to be maintained on the lower margin of the physiological range.

Materials and methods: Clinical research was on 113 postpartum women who had received blood transfusions for postpartum haemorrhages were selected for this study. The following circulation parameters were assessed: heart rate (HR), systolic blood pressure (BPs), diastolic blood pressure (BPD), mean arterial pressure (MAP), central venous pressure (CVP), cardiac index (CI), contractility index (ΔS), systemic vascular resistance index (SVRI), systemic oxygen delivery index (IDO_2), systemic oxygen consumption index (IVO_2), tissue oxygen extraction ratio (O_2ER).

Results: Through a comparison of hemodynamic parameters depending on haematocrit and haemoglobin levels in patients with postpartum blood loss it was discovered that in case of blood loss and consequent intensive therapy aimed at TBV (total blood volume) restoration statistically significant changes of BPs, MAP, CI and SVRI were observed. Also, during this study linear high-degree correlations between CI, ΔS and Hb levels were found.

Analysis of systemic oxygen transport dependence on haematocrit and haemoglobin levels for patients during the early postpartum period demonstrates significant differences in cardiac indexes with a strong positive statistically significant correlation between these parameters and haemoglobin levels.

Conclusion. From the calculation of the minimum allowable haemoglobin level in postpartum women in case of blood loss using linear regression with coefficients calculated through the method of least squares the $Hb = 82.5$ g/L value was obtained, which can be considered the minimum allowable level in postpartum women in case of postpartum blood loss which allows the cardiac functional status and oxygen metabolism to be on safety physiological range.

Keywords: minimum level of haemoglobin, haematocrit, correlation, postpartum haemorrhage, systemic transport of oxygen.

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1. Introduction

According to reports in 2015, 8.7 million cases of obstetric haemorrhages (OH) were reported with 83,000 lethal cases related to this complication [1]. Despite the WHO defining the acceptable postpartum haemoglobin levels as 100–109 g/l [2], there is neither consensus nor strong statistically proven analysis of its minimum safe level and its influence on systemic hemodynamic and oxygen metabolism in particular [3].

Currently, there are several national guidelines for the management of OH that highlight the tactics of intensive therapy for these life-threatening conditions. So, for example, Shaylor R. et al. in their review of national guidelines, emphasize the importance of fibrinogen replacement therapy (threshold value: 2 g/l), describe in detail replacement therapy with blood products and pay special attention to haemostasis monitoring [4]. Guidelines for the management of postpartum haemorrhage have been published by several obstetric societies, including the American College of Obstetricians and Gynaecologists (ACOG), the Royal College of Obstetricians and Gynaecologists (RCOG) of the United Kingdom, the Royal College of Obstetricians and Gynaecologists of Australia and New Zealand (RANZCOG), the Society of Obstetricians and Gynaecologists of Canada (SOGC), which include algorithms with certain actions, and specific recommendations for the management of patients with OH [4]. However, all these guidelines have important differences in their recommendations for the transfusion of blood components. At the same time, it is important to note that the system of delivery and consumption of oxygen is a key link around which the pathogenesis of almost any critical condition and the pathological process is formed, and the degree of adequacy of blood circulation is determined, first of all, by how fully the oxygen needs of the body's cellular systems are met [5]. This provision largely refers to disorders that occur against the background of a significant decrease in the level of haemoglobin (Hb) and haematocrit (Ht), as a result of massive blood loss. However, in the presented guidelines, there are no substantiated indications on the minimum acceptable level of haemoglobin, at which the minimum acceptable delivery of oxygen is ensured.

Therefore, this study aimed to determine statistically minimal allowable haemoglobin level in postpartum women in case of postpartum haemorrhage which allows the cardiac functional status and oxygen metabolism to be maintained on the lower margin of the physiological range.

2. Materials and methods

This retrospective observational study was conducted and performed in the «Lviv Regional Clinical Perinatal Center» (Lviv, Ukraine). Clinical research was performed on 113 postpartum women who had received blood transfusions for the postpartum haemorrhage and were selected for this study. The age of participants fell between 19 and 38 years (mean 27.5 ± 5.2 years), and the average weight – was between 74 and 91 kg (mean 84.8 ± 5.2 kg). All patients were divided into 4 groups based on their haematocrit and haemoglobin levels. In group I these parameters fell between $Ht = 20.0\text{--}22.9\%$, $Hb = 45.1\text{--}50.4$ g/L ($n = 29$), in group II – $Ht = 23.0\text{--}25.9\%$, $Hb = 52.3\text{--}60.2$ g/L ($n = 30$), in group III – $Ht = 26.0\text{--}28.9\%$, $Hb = 63.4\text{--}68.9$ g/L ($n = 26$) and in group IV – $Ht = 29.0\text{--}30.0\%$, $Hb = 70.1\text{--}79.9$ g/L ($n = 28$).

Patient population

We recruited non-labouring parturients, who had a caesarean section under spinal anaesthesia if they fulfilled the following inclusion criteria: > 18 years of age, American Society of Anaesthesiologists (ASA) Class II, and category 3 or 4 caesarean section. Exclusion criteria included: patient refusal, < 18 years of age, previous neurosurgery, ASA Class III and IV, presence of skin tattoos within the thermal imaging area, any contraindication to neuraxial technique, active infections, chronic bleeding, maternal core temperature > 38 °C, and inability to comply with standard positioning and conduct of anaesthesia.

Bioethics statements were approved by the Ethics Committee of Shupik National Healthcare University of Ukraine, Kyiv, (protocol code No. 9 and date of approval 22/10/2018). Informed consent was obtained from all study participants.

Women with comorbidities that could contribute to the increased lactic acid levels (sepsis, liver disorders, diabetic ketoacidosis, congenital and acquired heart defects, cardiac insufficiency, respiratory failure, and significant electrolyte imbalances) were excluded from the study.

All patients received intensive care and surgical interventions according to the obstetric haemorrhages' urgent management protocols aimed at the restoration of total blood volume (TBV), termination of the bleeding and haemostatic dysfunctions as well as correction of discovered disruptions of homeostasis [6].

Data sources/ measurements

Systemic circulation parameters were monitored to clinically assess hemodynamic status in the observed group (monitoring systems «IntellsVue MP50», Netherlands). The following

parameters were assessed: heart rate (HR), systolic blood pressure (BPs), diastolic blood pressure (BPD), mean arterial pressure (MAP), central venous pressure (CVP), cardiac index (CI), contractility index (ΔS), systemic vascular resistance index (SVRI), systemic oxygen delivery index (IDO₂), systemic oxygen consumption index (IVO₂), tissue oxygen extraction ratio (O₂ER).

Gas composition of arterial and mixed venous blood, acid-base status and determination of the level of haemoglobin, haematocrit, electrolytes (K⁺, Ca⁺⁺, Na⁺) and lactate were performed immediately after blood sampling using the blood gas analyzer «ABL800 Flex Series 835» («Radiometer», Denmark).

Statistical methods

Obtained parameters were compared between every two groups using Wilcoxon rank-sum test for numerical variables and Pearson's χ^2 -test for categorical variables. Logistic regression was used in this paper to calculate the odds ratio and their 95 % confidence intervals (CI) of potential predictors for the primary result. ROC curves were also used to determine the optimal exclusion threshold as well as the sensitivity and specificity of each predictor. A bilateral value of $p < 0.05$ was considered statistically significant. All statistical analysis was conducted using «JMP Pro 14 for Mac» (Tokyo, Japan).

3. Results

The research patients were women who had received blood transfusions for postpartum haemorrhage. The required sample size was calculated using the `pwr.f2.test()` function from the PWR package. At the level of reliability (Significance level (Type I error probability)) $p = 0.01$ and power (Power of test (1 minus Type II error probability)) power = 0.9, the minimum sample size is 26.72966 ($f2 = 0.9781187$) observations.

Mean postpartum blood loss was 1844.3 ± 632.8 ml (from 1200 to 2500 ml). All haemorrhages were successfully treated according to the current guidelines [6].

Studying the functional systemic circulation parameters concerning haematocrit and haemoglobin levels in case of blood loss (**Table 1**) it was determined that there were no statistically significant differences in HR values among all examined patients. In group I this parameter constituted 120.4 ± 8.2 bpm, in group II – 117.6 ± 7.1 bpm, in group III – 112.5 ± 3.5 bpm, in group IV – 107.3 ± 8.5 bpm ($p > 0.05$).

Table 1

Systemic hemodynamic parameters and haematocrit and haemoglobin levels in the examined groups of patients ($N = 113$)

Parameter	Ht and Hb values (%)			
	Group I Ht = 20.0–22.9 %, Hb = 45.1–50.4 g/L ($n = 29$)	Group II Ht = 23.0–25.9 %, Hb = 52.3–60.2 g/L ($n = 30$)	Group III Ht = 26.0–28.9 %, Hb = 63.4–68.9 g/L ($n = 26$)	Group IV Ht = 29.0–30.0 %, Hb = 70.1–79.9 g/L ($n = 28$)
HR, bpm	120.4 ± 8.2	117.6 ± 7.1	112.5 ± 3.5	107.3 ± 8.5
BPs, mm·Hg	88.5 ± 5.1	98.4 ± 6.01	$115.4 \pm 10.91.2$	$126.6 \pm 6.21.2.3$
BPD, mm·Hg	51.7 ± 3.6	53.1 ± 4.2	57.6 ± 5.4	60.9 ± 6.1
MAP, mm·Hg	63.97 ± 4.7	68.2 ± 3.9	76.87 ± 6.21	$82.8 \pm 5.31.2$
CVP, mm·Hg	7.5 ± 1.5	7.7 ± 1.2	8.0 ± 0.8	8.2 ± 1.3
CI, L/min/m ²	2.8 ± 0.21	3.0 ± 0.19	3.3 ± 0.22	$3.5 \pm 0.181.2$
ΔS , %	22.1 ± 0.5	23.3 ± 0.7	26.4 ± 0.91	$28.2 \pm 1.31.2$
SVRI, dynes·sec/cm ⁵ /m ²	1215.5 ± 100.2	1313.5 ± 108.1	$2203.7 \pm 117.81.2$	$2421.3 \pm 124.21.2.3$

Note: 1 – $p < 0.05$ compared to GrI; 2 – $p < 0.05$ compared to GrII; 3 – $p < 0.05$ compared to GrIII; HR – heart rate; BPs – systolic blood pressure; BPD – diastolic blood pressure; MAP – mean arterial pressure; CVP – central venous pressure; CI – cardiac index; ΔS – contractility index; SVRI – systemic vascular resistance index

However, during the systolic BP measurement, the following differences were found: in patients of group I BPs were 88.5 ± 5.1 mm·Hg, which was 10.1 ± 0.7 % less compared to patients

of group II, where this parameter was 98.4 ± 6.0 mm·Hg ($p = 0.0419$), 23.31 ± 3.6 % less compared to group III (BPs = 115.4 ± 10.9 mm·Hg) ($p = 0.0142$), and 30.1 ± 2.9 % less compared to patients of the group IV with BPs 126.6 ± 6.2 mm·Hg ($p = 0.0105$) (**Table 1**).

Despite the significant differences in systolic BP values no statistically significant difference in diastolic BP values was observed ($p > 0.05$). In patients of the GrI the abovementioned parameter was 51.7 ± 3.6 mm·Hg, in GrII it was 53.1 ± 4.2 mm·Hg, in GrIII this parameter was 57.6 ± 5.4 mm·Hg, while for haematocrit 29.0–30.0 % and Hb = 70.1–79.9 (GrIV) – 60.9 ± 6.1 mm·Hg (**Table 1**).

In the mean arterial pressure measurement, no statistically significant differences in this parameter between patients of GrI and GrII were discovered. In patients of GrI, this parameter was 63.97 ± 4.7 mm·Hg, in GrII it was 68.2 ± 3.9 mm·Hg ($p > 0.05$). In GrIII MAP was 76.87 ± 6.2 mm·Hg, which was 16.8 ± 3.2 % higher compared to the first group of patients ($p = 0.0103$). There also was a statistically significant difference in MAP values in patients of the group IV, the respective MAP being 82.8 ± 5.3 mm·Hg, which was 22.7 ± 3.6 % higher compared to GrI ($p = 0.0027$) and 17.6 ± 2.1 % higher compared to GrII ($p = 0.00281$) (**Table 1**).

There was also no statistically significant difference in CVP values ($p > 0.05$), which may be related to the fact that during the examination all patients received massive plasma expanders and blood derivatives infusions to stabilize this parameter. In patients of group I this parameter was 7.5 ± 1.5 mm·Hg, in group II – 7.7 ± 1.2 mm·Hg, in group III – 8.0 ± 0.8 mm·Hg, in group IV – 8.2 ± 1.3 mm·Hg ($p > 0.05$) (**Table 1**).

A statistically significant difference in CI values was observed. In patients of the group I the abovementioned parameter was 2.8 ± 0.21 L/min/m², in group II – 3.0 ± 0.19 L/min/m². In group III CI was 3.3 ± 0.22 L/min/m², which was 15.15 % higher compared to corresponding values in GrI ($p = 0.00132$). In group IV this parameter was 3.5 ± 0.18 L/min/m², which was 25.0 ± 1.5 % higher compared to GrI ($p = 0.0255$) and 16.67 ± 1.1 % higher compared to GrII ($p = 0.0326$) (**Table 1**).

Thus, even though in case of low haematocrit and haemoglobin levels (GrI ra GrII) MAP remained within 63.97 ± 4.7 and 68.2 ± 3.9 mm·Hg respectively, CI values indicated the systemic hemodynamic hypofunction (**Table 1**).

This inference was also confirmed by the contractility index evaluation (ΔS). There was no observed statistically significant difference in contractility index values (ΔS) between the patients of groups I and II, in which these parameter values were within 22.1 ± 0.5 % and 23.3 ± 0.7 %, respectively ($p > 0.05$). However, in patients of GrIII, this parameter was statistically significantly different and constituted 26.4 ± 0.9 %, which was 16.29 ± 0.4 % higher than in GrI ($p = 0.0013$). In group IV this parameter was 28.2 ± 1.3 %, which was 21.63 ± 0.3 % higher than in group I ($p = 0.0035$) and 17.38 ± 0.2 % higher than in group II ($p = 0.0011$) (**Table 1**).

Thus, the systolic-diastolic left ventricular function, depending on the haemoglobin levels, was statistically significantly decreased in comparison to normal values at haemoglobin levels from 45.1 g/L to 60.2 g/L ($p < 0.005$).

Significant differences were also observed in systemic vascular resistance index values. In patients of group I this parameter was 1215.5 ± 100.2 dynes·sec/cm⁵/m² and did not statistically differ from the SVRI values in patients of group II, where it was 1313.5 ± 108.1 dynes·sec/cm⁵/m² ($p > 0.05$). In group III this parameter fell within 2203.7 ± 117.8 dynes·sec/cm⁵/m², which was 44.84 ± 7.8 % more compared to the first group of patients ($p = 0.0011$) and 40.4 ± 8.4 % higher compared to the second group ($p = 0.0085$). In the patients of group IV with haematocrit levels being 29.0–30.0 % and Hb = 70.1–79.9 g/L, SVRI was 2421.3 ± 124.2 dynes·sec/cm⁵/m², which was 49.8 ± 6.9 % higher compared to patients from the GrI ($p = 0.00021$), 45.75 ± 5.4 % more compared to the corresponding values in patients of the GrII ($p = 0.00014$), and 8.99 ± 1.1 % more compared to the third group of patients (GrIII) ($p = 0.6208$) (**Table 1**).

Thus, an examination has shown that at low hematocrit and haemoglobin levels with maintained adequate CVP levels there was a compensatory increase in afterload in postpartum women experiencing blood loss to maintain circulation, which, coupled with CI decrease, could have been the reason for cardiac decompensation.

To identify the causal link between CI values and haemoglobin levels a correlation analysis for these two variables was conducted (**Fig. 1**).

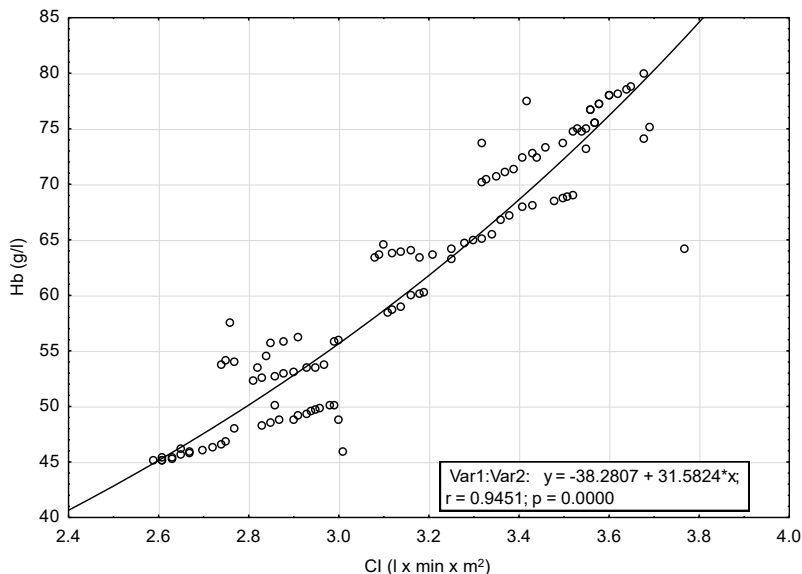


Fig. 1. The correlation between CI and haemoglobin levels in the groups studied ($r = 0.9451$; $p = 0.00000107$)

As shown in the diagram above, the correlation coefficient (r) for these two parameters was 0.9451 (**Fig. 1**), which means a high degree of correlation between CI and haemoglobin levels. And given the probability of error (p) that equalled 0.00000107 (**Fig. 1**), one can conclude that this correlation was statistically significant. In other words, myocardial contractility directly depended on the haemoglobin levels.

This inference was also confirmed by the correlation analysis for ΔS and reported haemoglobin levels in the groups studied (**Fig. 2**), which has shown a strong correlation between these two parameters ($r = 0.9615$; $p = 0.000011$).

As a result of the conducted correlation analysis for SVRI and haemoglobin levels, we identified a strong positive statistically significant correlation between these parameters ($r = 0.9364$; $p = 0.000023$) (**Fig. 3**), which demonstrated that vasoconstriction of the microcirculatory system was observed in the groups of patients with low haemoglobin levels within 45.1–60.2 g/L (GrI and GrII), while their TBV was restored.

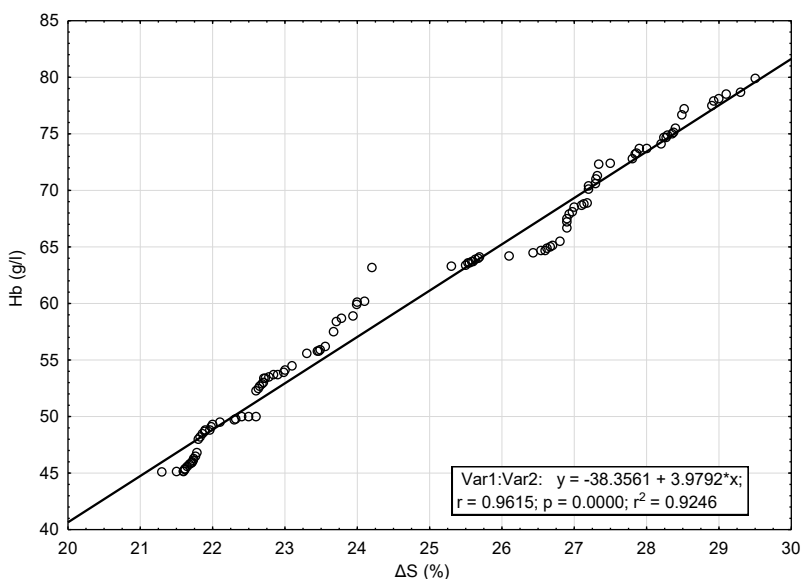


Fig. 2. The correlation between ΔS and haemoglobin levels in the groups studied ($r = 0.9615$; $p = 0.000011$)

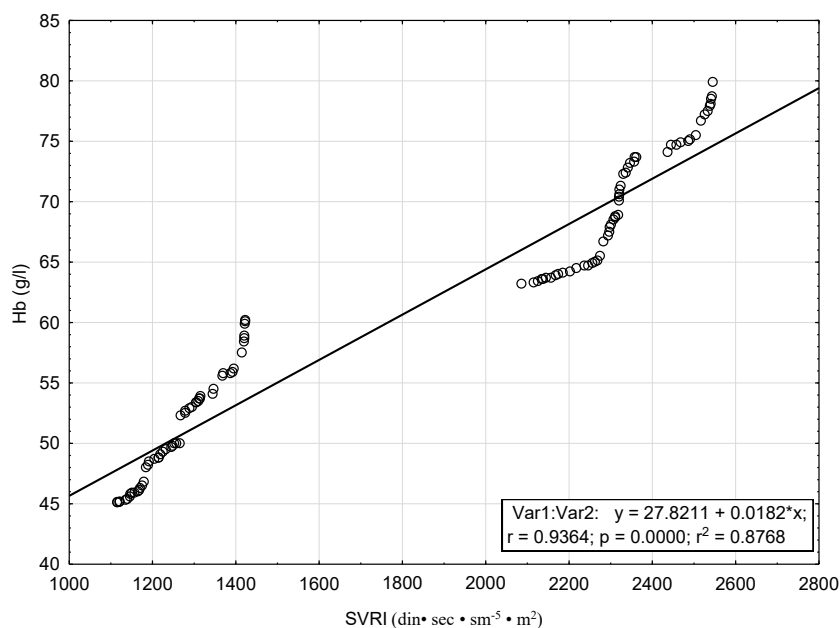


Fig. 3. The correlation between SVRI and haemoglobin levels in the groups studied ($r=0.9364$; $p=0.000023$)

Studying systemic oxygen transport concerning haematocrit and haemoglobin levels in case of blood loss we found that at Ht values within 20.0–22.9 % and Hb levels within 45.1–50.4 g/L (GrI), DO_2 was 226.6 ± 40.7 mL/min/m² (Table 2). It is noteworthy that such IDO_2 values are outside of the physiological range for the human body and correspond with hemic hypoxia, which is a risk factor for the adverse clinical outcome in these patients during the postpartum period.

Table 2

Parameters of gas transport function of the blood and haematocrit levels in the groups studied ($n = 113$)

Parameter	Ht and Hb values (%)			
	Group I Ht = 20.0–22.9 %, Hb = 45.1–50.4 g/L ($n = 29$)	Group II Ht = 23.0–25.9 %, Hb = 52.3–60.2 g/L ($n = 30$)	Group III Ht = 26.0–28.9 %, Hb = 63.4–68.9 g/L ($n = 26$)	Group IV Ht = 29.0–30.0 %, Hb = 70.1–79.9 g/L ($n = 28$)
IDO_2 , mL/min/m ²	226.6 ± 40.7	272.3 ± 51.41	$345.8 \pm 47.31.2$	$434.5 \pm 44.21.2.3$
IVO_2 , mL/min/m ²	78.3 ± 6.2	95.7 ± 9.21	$116.5 \pm 22.91.2$	$130.3 \pm 29.61.2.3$
O_2ER , %	37.4 ± 2.5	36.1 ± 1.9	$31.8 \pm 1.71.2$	$26.1 \pm 1.51.2.3$

Note: 1 – $p < 0.05$ compared to GrI; 2 – $p < 0.05$ compared to GrII; 3 – $p < 0.05$ compared to GrIII; IDO_2 – systemic oxygen delivery index; IVO_2 – systemic oxygen consumption index; O_2ER – tissue oxygen extraction ratio

With an increase in haematocrit levels up to 23.0–25.9 % and haemoglobin levels up to 52.3–60.2 g/L (GrII), a directly proportional increase in IDO_2 up to 272.3 ± 51.4 mL/min/m² was observed, which was 20.17 ± 1.7 % higher compared to IDO_2 in the patients of the first group ($p = 0.0347$) (Table 2).

With a further increase in haematocrit levels, a linear increase in IDO_2 was also observed (Table 2).

In group III the abovementioned parameter was 345.8 ± 47.3 mL/min/m², which was 52.6 ± 4.2 % higher than the corresponding parameter in group I ($p = 0.0138$) and 27.0 ± 2.2 % higher than in group II ($p = 0.0305$) (Table 2).

In group IV IDO_2 was 434.5 ± 44.2 mL/min/m² and this parameter was 25.66 ± 1.6 % higher than the corresponding parameter in group III with haematocrit levels within 26.0–28.9 % and Hb = 63.4–68.9 ($p = 0.0329$) (Table 2).

Experimentally found changes in IDO_2 in the groups studied are shown in **Fig. 4**.

The correlation between IDO_2 and haemoglobin levels appeared to be the following (**Fig. 5**).

As a result of the conducted correlation analysis for IDO_2 and haemoglobin levels, we identified a strong positive statistically significant correlation between these parameters ($r = 0.9385$; $p = 0.000011$) (**Fig. 5**).

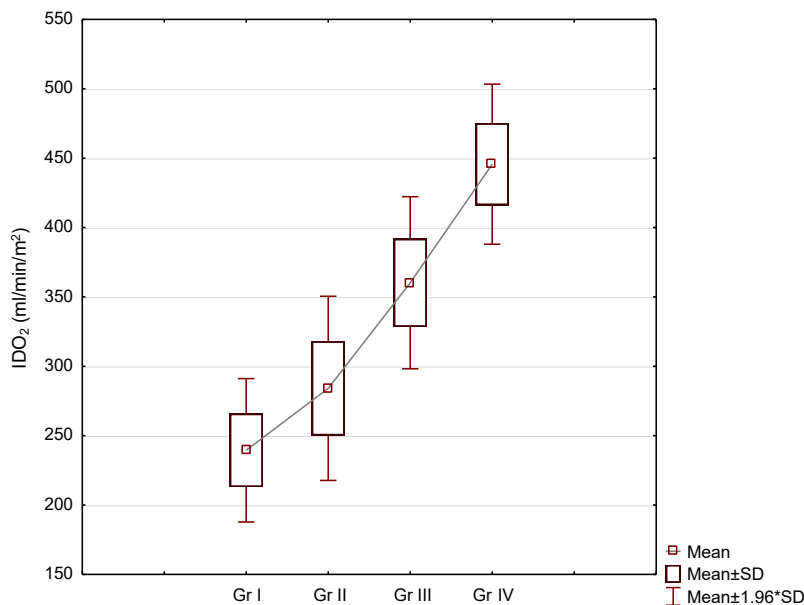


Fig. 4. Diagram of the midrange IDO_2 values in the groups studied in relation to the haemoglobin levels: GrI/GrII : $p = 0.000002$; $F = 1.649957$; $t\text{-value} = -5.4052$; GrI/GrIII : $p = 0.0000013$; $F = 1.440838$; $t\text{-value} = -15.2355$; GrI/GrIV : $p = 0.0000011$; $F = 1.247935$; $t\text{-value} = -27.1171$)

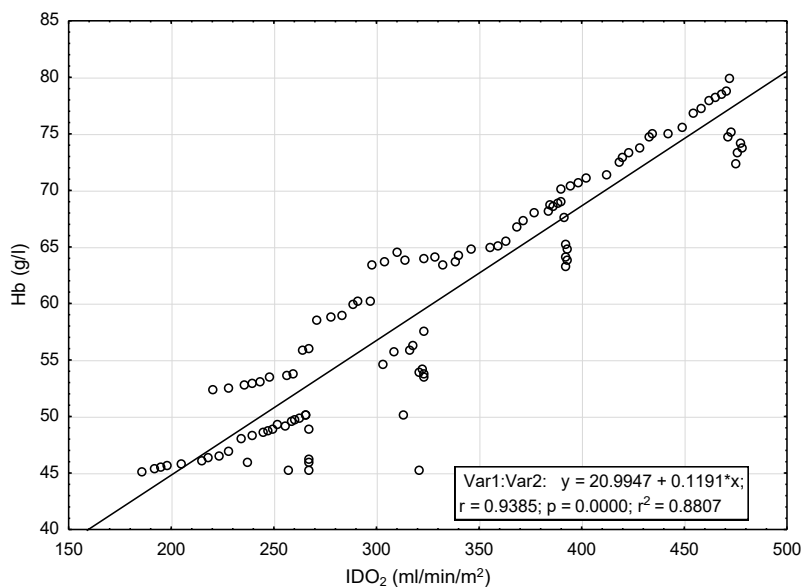


Fig. 5. The correlation between IDO_2 and haemoglobin levels in the groups under study ($r = 0.9385$; $p = 0.000011$)

As shown by the diagram in **Fig. 5**, there is a directly proportional linear relationship between systemic oxygen delivery and haemoglobin levels. It is noteworthy that at Ht levels within 20.0–28.9 % and equal $\text{FiO}_2 = 100\%$ there was a 2-3 times worse deviation of IDO_2 values

compared to the normal gas transport status in patients from groups I, II and III; and only in the patients from group IV IVO_2 values were close to normal physiological range. Such an oxygen metabolism state in postpartum patients was interpreted as hemic hypoxia.

A linear increase concerning haemoglobin and haematocrit levels was also observed in systemic oxygen consumption index values. Studying the relation between VO_2 values and Hb and Ht levels we found that at Ht=20.0–22.9 % and Hb = 45.1–50.4 g/L (GrI) IVO_2 was 78.3 ± 6.2 mL/min/m² (Table 2).

In patients from the group with Ht=23.0–25.9 and Hb = 52.3–60.2 (GrII), IVO_2 was 95.7 ± 9.2 mL/min/m², which was 22.2 ± 2.0 % higher in comparison to group I ($p = 0.0314$). However, this IVO_2 value in group II was 17.84 ± 1.5 % less compared to GrIII, in which the above-mentioned parameter was 116.5 ± 22.9 mL/min/m² ($p = 0.0415$) (Table 2).

As shown by the data in Table 2, with an increase in hematocrit levels a linear increase in IVO_2 values was observed (Table 2).

In group IV IVO_2 was 130.3 ± 29.6 mL/min/m², which was 11.85 ± 1.1 % higher than the corresponding parameter in group III ($p = 0.0439$) (Table 2).

Changes in IVO_2 concerning the groups studied are shown in Fig. 6.

The correlation between IVO_2 and haemoglobin levels appeared to be the following (Fig. 7).

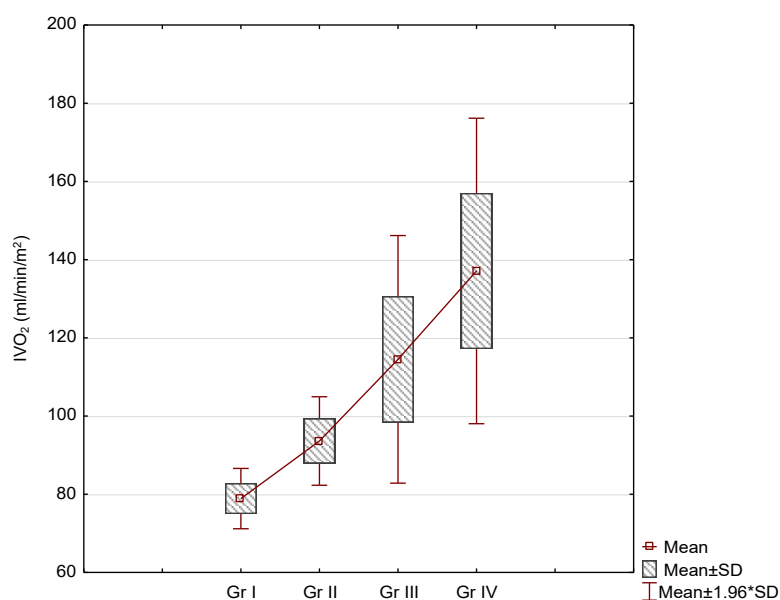


Fig. 6. Diagram of the midrange IVO_2 values in the groups studied in relation to the haemoglobin levels: GrI/GrII : $p = 0.000001$; $F = 2.15390494$; t -value = -10.9514 ;
GrI/GrIII : $p = 0.0000012$; $F = 16.83880$; t -value = -11.12876 ;
GrI/GrIV : $p = 0.0000014$; $F = 25.636263$; t -value = -14.88914)

As a result of the conducted correlation analysis for IVO_2 and haemoglobin levels, we identified a strong positive statistically significant correlation between these parameters ($r = 0.8881$; $p = 0.000001$) (Fig. 7).

Low IVO_2 values with corresponding low Ht and Hb levels observed in this study might have been caused by patients experiencing peripheral spasms, as demonstrated by the increase in SVRI (Table 1).

It is noteworthy that at Ht = 20.0–22.9 % and Hb = 45.1–50.4 g/L (GrI), IVO_2 values were 2 times lower than the lowest normal physiological limit, while in the patients of group IV this parameter's values were within the normal range (Table 2).

No less important criterion of systemic oxygen metabolism is a tissue oxygen extraction ratio (O_2ER). The importance of this parameter lies in the relationship between the actual oxygen delivery and its consumption by tissues.

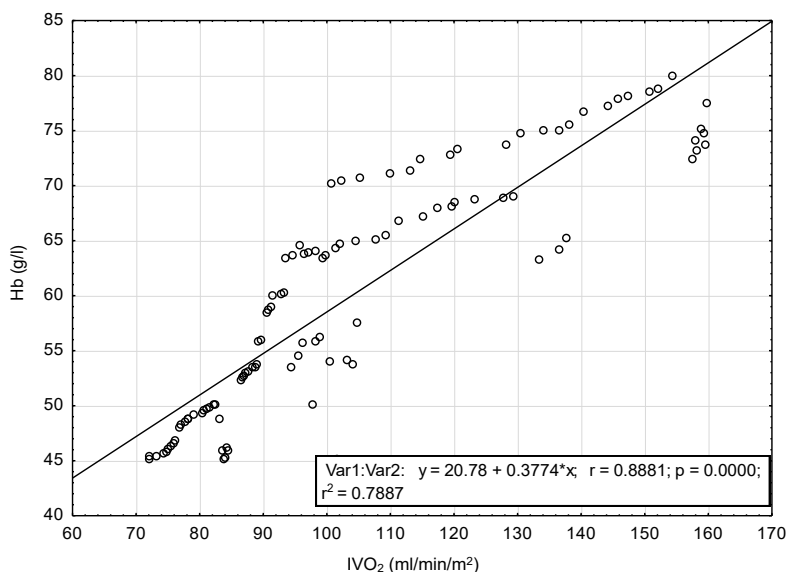


Fig. 7. The correlation between IVO_2 and haemoglobin levels in the groups studied ($r = 0.8881$; $p = 0.000001$)

In study of the O_2ER values no statistically significant difference between patients of groups I and II was observed: at $Ht = 20.0\text{--}22.9\%$, $Hb = 45.1\text{--}50.4$ g/L this parameter was $37.4 \pm 2.5\%$, while at $Ht = 23.0\text{--}25.9\%$, $Hb = 52.3\text{--}60.2$ g/L O_2ER was within $36.1 \pm 1.9\%$ ($p > 0.05$) (**Table 2**).

With a further increase in hematocrit and haemoglobin levels, a linear decrease in O_2ER was observed.

At $Ht = 26.0\text{--}28.9\%$, $Hb = 63.4\text{--}68.9$ g/L (GrIII), this parameter was within $31.8 \pm 1.7\%$, which was $14.97 \pm 0.9\%$ lower compared to patients of group I ($p = 0.0425$) and $11.91 \pm 0.7\%$ lower compared to patients of group II ($p = 0.0372$) (**Table 2**).

In patients of group IV, O_2ER levels were within $26.1 \pm 1.5\%$. It was $17.92 \pm 1.1\%$ lower compared to the corresponding parameter in group III, which was also statistically significant ($p = 0.0354$) (**Table 2**).

To identify the causal link between O_2ER values and haemoglobin levels a correlation analysis for these two variables was conducted (**Fig. 8**).

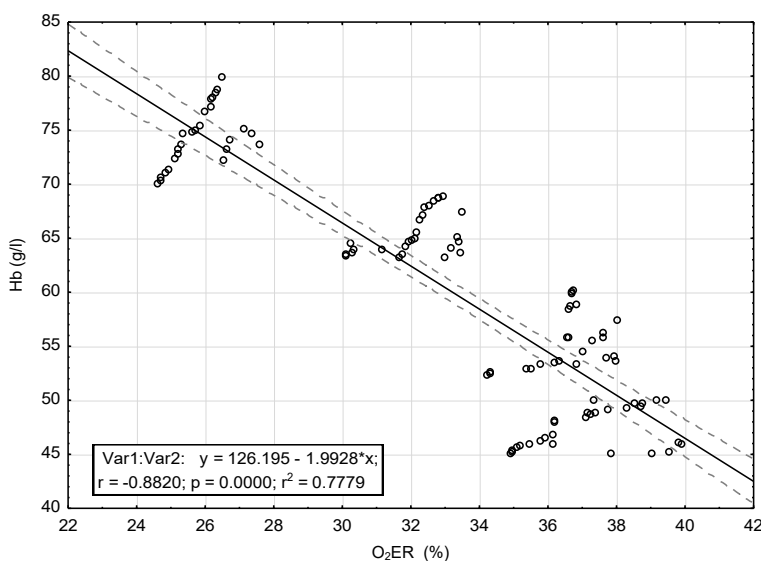


Fig. 8. The correlation between O_2ER and haemoglobin levels in the groups studied ($r = 0.8820$; $p = 0.0000014$)

As shown in the diagram above, the correlation coefficient (r) for these two parameters was 0.8820 (**Fig. 8**), which means a high degree of correlation between O_2ER and haemoglobin levels. Given the probability of error (p) that equalled 0.0000014 (**Fig. 8**), one can conclude that this correlation was statistically significant.

It is noteworthy that at $Ht = 20.0\text{--}25.9\%$, $Hb = 45.1\text{--}60.0\text{ g/L}$ (GrI and GrII), O_2ER values were 1.5–2 times higher in comparison to normal physiological values for this parameter. However, in patients of group IV this parameter's values were within the normal range (**Table 2**).

Calculation of minimum allowable haemoglobin level in postpartum women in case of blood loss was conducted via the R programming language, using an integrated development environment RStudio [https://www.r-project.org/; https://www.rstudio.com/].

To calculate the minimum allowable haemoglobin value, we used linear regression with coefficients calculated through the method of least squares (**Fig. 9**).

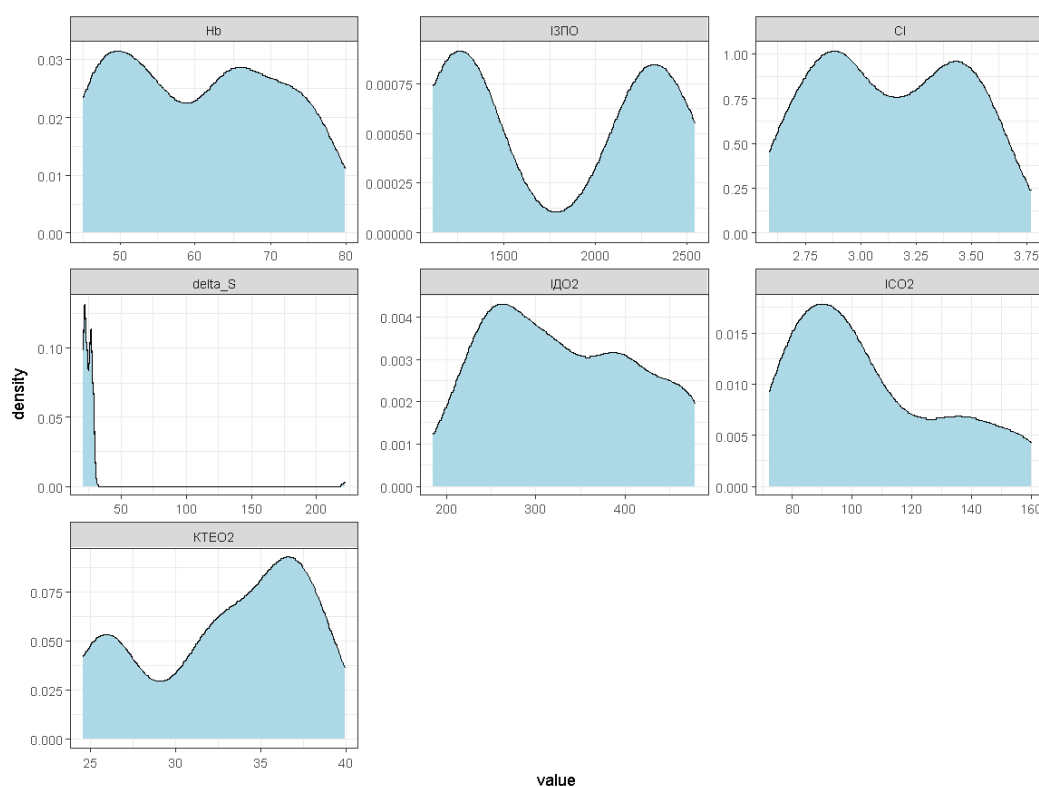


Fig. 9. Probability likelihood of the dependent and independent variables

The normality test for the dependent and independent variables was conducted using the Shapiro-Wilk method.

The normality of the residual distribution was checked using the Shapiro-Wilk method (**Fig. 10**).

In our study through a comparison of hemodynamic parameters depending on haematocrit and haemoglobin levels in patients with postpartum blood loss it was discovered that in case of blood loss and consequent intensive therapy aimed at TBV restoration statistically significant changes of BPs., MAP, CI and SVRI were observed: at Ht levels within 20.0–25.9 %, and $Hb = 45.1\text{--}60.2\text{ g/L}$ (GrI, GrII), MAP was maintained within 63.97 ± 4.7 and $68.2 \pm 3.9\text{ mmHg}$, respectively, however, CI and ΔS values indicated hypofunction of the systemic haemodynamics. At Ht levels within 20.0–25.9 % and $Hb = 45.1\text{--}60.2\text{ g/L}$ (GrI, GrII), with maintained adequate CVP levels, there was a compensatory increase in afterload in postpartum women experiencing blood loss to maintain circulation, which, coupled with CI and ΔS decrease, could have been the reason for cardiac decompensation. Also, during this study, a linear high-degree correlation between CI, ΔS and Hb levels was discovered.

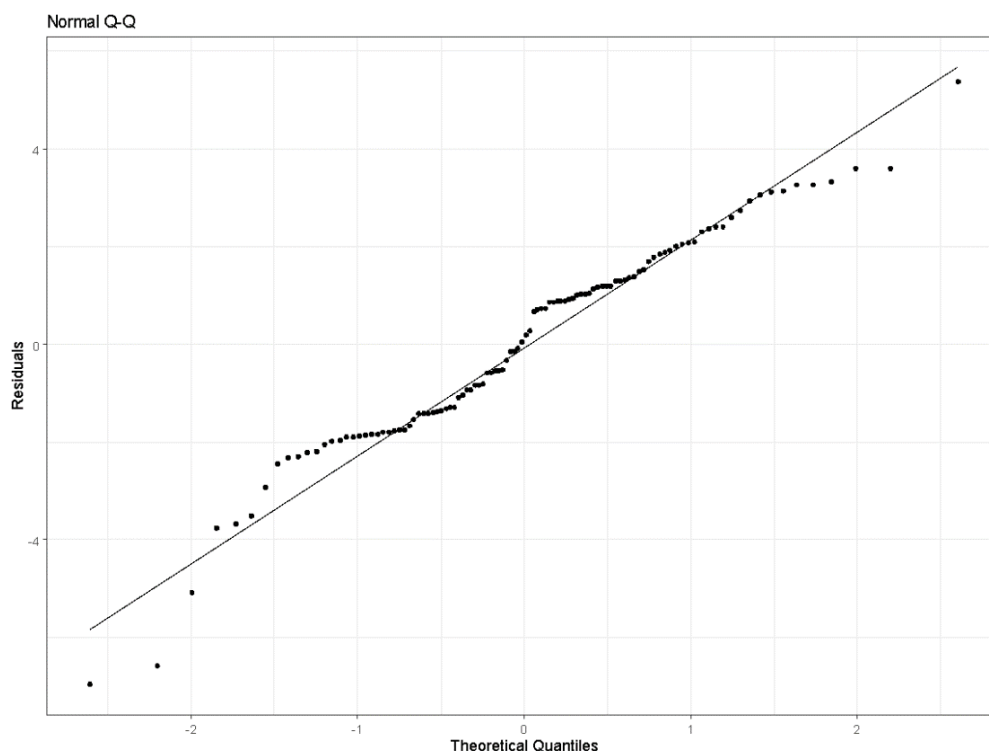


Fig. 10. Q-Q plot for the model residuals

Through a comparison of hemodynamic parameters depending on haematocrit and haemoglobin levels in patients with postpartum blood loss it was discovered that in case of blood loss and consequent intensive therapy aimed at TBV restoration statistically significant changes of BPs, MAP, CI and SVRI were observed: at Ht levels within 20.0–25.9 %, and Hb = 45.1–60.2 g/L (GrI, GrII), MAP was maintained within 63.97 ± 4.7 and 68.2 ± 3.9 torr, respectively, however, CI and ΔS values indicated hypofunction of the systemic haemodynamic. At Ht levels within 20.0–25.9 % and Hb = 45.1–60.2 g/L (GrI, GrII), with maintained adequate CVP levels, there was a compensatory increase in afterload in postpartum women experiencing blood loss to maintain circulation, which, coupled with CI and ΔS decrease, could have been the reason for cardiac decompensation. Also, during this study, a linear high-degree correlation between CI, ΔS and Hb levels was found.

Analysis of systemic oxygen transport dependence on haematocrit and haemoglobin levels for patients during the early postpartum period demonstrates significant differences in IDO_2 , IVO_2 and O_2ER . At Ht levels within 20.0–28.9 %, Hb levels within 45.1–68.9 g/L and corresponding $FiO_2 = 100$ % (GrI, GrII, GrIII) there was a 2–3 times higher deviation of IDO_2 values compared to the normal gas transport status and only for patients with Ht = 29.0–30.0 %, and Hb = 70.1–79.9 g/L (GrIV), IDO_2 values were close to normal physiological range. At Ht = 20.0–22.9 % and Hb = 45.1–50.4 g/L (GrI), IVO_2 values were 2 times less than the lower normal physiological limit, while for patients with Ht = 29.0–30.0 %, and Hb = 70.1–79.9 g/L (GrIV), these parameters were within the normal range. At Ht = 20.0–25.9 %, Hb = 45.1–60 g/L (GrI and GrII), O_2ER values were 1.5–2 times higher in comparison to normal physiological values, while for patients Ht = 29.0–30.0 %, and Hb = 70.1–79.9 g/L (GrIV), these parameters were within the normal range. Correlation analysis for IDO_2 , ICO_2 , O_2ER and haemoglobin levels demonstrated a strong positive statistically significant correlation between these parameters.

$z = a_0 + a_1x_1 + a_2x_2 + a_3x_3 + a_4x_4$, analysis through the least squares method resulted in variable coefficients $a_0 = 25.4850$; $a_1 = 0.0001$; $a_2 = 13.0202$; $a_3 = -0.0222$; $a_4 = 0.0557$; $a_5 = -0.0327$; $a_6 = -0.6172$. The summary equation is:

$$Hb = 25.485 + 1e-04 \times SVRI + 13.0202 \times CI - 0.0222 \times \Delta S + 0.0557 \times IDO_2 - 0.0327 \times IVO_2 - 0.6172 \times O_2ER.$$

All the while the Adjusted R-squared coefficient was 0.9567 proving this mathematical model reliably.

After that, in order to calculate minimum allowable Hb values, the equation of linear regression was solved taking the coefficients and minimum values of the dependent variables: $CI = 3.5$; $SVRI = 2200$; $\Delta S = 26$; $IDO_2 = 560$; $IVO_2 = 120$; $O_2ER = 25$ (See Supplement A).

As a result, the $Hb = 82.5$ value was obtained, which can be considered the minimum allowable Hb level in postpartum women with postpartum haemorrhage which allows the cardiac functional status and oxygen metabolism to be maintained on the lower margin of the physiological range.

4. Discussion

In studies by Collis R. et al., the prevalence of postpartum haemorrhage in the world (with blood loss of more than 500 ml) is approximately 6 % of all pregnancies, and severe postpartum haemorrhage (with blood loss of more than 1000 ml) is recorded up to 1.96 %. According to Knight M. et al., in Great Britain, they are the cause of approximately 10 % of all deaths [8] and are the third most significant direct cause of maternal mortality [7]. According to Gallos I. et al., on average, one in 10 women giving birth in European countries is registered with PPK [9]. The reported prevalence of severe obstetric bleeding varies from 0.16 per 1000 births in Canada to 8.8 per 1000 births in Finland [10].

According to the Plenum of the Association of Obstetricians and Gynaecologists of Ukraine, the maternal mortality rate in Ukraine today is 8.2 %, exceeding a similar rate in such countries as Poland (3 %), Belarus (4 %), Spain (5 %) [11]. As noted in the order of the Ministry of Health of Ukraine No. 205 dated 03/24/2014: «obstetric bleeding remains one of the main causes of maternal morbidity and mortality worldwide. The World Health Organization (WHO) considers the prevention of obstetric bleeding and the fight against it to be a priority area of activity» [12].

Over the past 20 years, the frequency of massive obstetric bleeding in Ukraine has remained high. According to the Ministry of Health of Ukraine, «over the past 5 years, they have consistently taken second place in the structure of causes of maternal mortality» [12]. In 2013, the share of massive postpartum bleeding was 21 % and ranked second after extragenital pathology [13].

The main purpose of this study was to determine the minimum allowable haemoglobin level in postpartum women in case of postpartum haemorrhage which allows the cardiac functional status and oxygen metabolism to be maintained on the lower margin of the physiological range.

The allowable anaemia level in the postpartum period is defined as $Hb < 100$ g/L. Anaemia is an extremely important healthcare issue and can lead to short- and long-term complications if is not properly diagnosed and treated. Some of those complications include dyspnea, fatigue, dizziness, decreased functional abilities, infections, loss of consciousness, decreased quality of life, decreased cognitive abilities, emotional volatility, low weight at birth, premature delivery, increased postpartum depression risk, disturbances in mother-child interactions and increased mortality [1].

Even though postpartum haemorrhage is one of the most common childbirth complications and the leading cause of maternal death [3], the Hb and Ht level dynamic has never been the focus of studies. The majority of studies are based on later visual assessments of postpartum blood loss [7, 14]. And in rare studies of these particular parameters, only the importance of their monitoring during the first 48 hours after the delivery is mentioned [6].

In our study through a comparison of hemodynamic parameters depending on hematocrit and haemoglobin levels in patients with postpartum blood loss it was discovered that in case of blood loss and consequent intensive therapy aimed at TBV restoration statistically significant changes of BPs, MAP, CI and SVRI were observed: At Ht levels within 20.0–25.9 %, and $Hb = 45.1–60.2$ g/L (GrI, GrII), MAP was maintained within 63.97 ± 4.7 and 68.2 ± 3.9 mm·Hg, respectively, however, CI and ΔS values indicated hypofunction of the systemic haemodynamic. At Ht levels within 20.0–25.9 % and $Hb = 45.1–60.2$ g/L (GrI, GrII), with maintained adequate CVP levels, there was a compensatory increase in afterload in postpartum women experiencing blood loss to maintain circulation, which, coupled with CI and ΔS decrease, could have been the reason for cardiac decompensation. Also, during this study, a linear high-degree correlation between CI, ΔS and Hb levels was discovered.

Persistent postpartum anaemia can lead to hypoxia of the newborn's tissues, especially in such vital organs as the brain, heart and intestines, therefore increasing the risk of adverse neural development outcomes [15]. Even liberal postoperative strategies in newborns with moderate anaemia do not improve the cerebral oxygenation index [9], which demonstrates the necessity to understand minimum allowable haemoglobin levels [16].

Haemoglobin (Hb) or hematocrit (Ht) values are widely and interchangeably used as indicators of massive bleeding [17]. However, the diagnostic value of Hb or Ht for detecting the degree of blood loss in trauma victims in the initial phase of massive bleeding remains controversial [17]. In addition, as indicated by Figueiredo S. et al., no study has yet evaluated the diagnostic value of early haemoglobin measurements and the impact of oxygen delivery on systemic homeostasis and the functional state of the heart and systemic hemodynamics at different values [17].

In a retrospective cohort of 1000 trauma patients (140 of whom were in moderate to severe shock), Knottenbelt J. D. found that a low haemoglobin level at clinic admission was associated with the severity of hypotension and mortality [18]. However, several other authors testify that the level of Hb measured at admission was not accurate in determining the degree of blood loss or the need for emergency hemostatic intervention [19]. In addition, the existing guidelines lack reasonable indications for the minimum acceptable level of haemoglobin, at which the minimum acceptable delivery of oxygen is ensured.

Several scientific publications indicate that a decrease in Ht, on the one hand, causes a proportional decrease in the content of oxygen in the blood, on the other hand, it increases the speed of blood flow through the capillaries, improves the distribution of erythrocytes in them, thereby increasing the extraction of oxygen by the cells of the body [20]. There is a point of view according to which the body satisfactorily tolerates hemodilution up to a hematocrit level of 0.2 g/l and even lower [21]. The authors explain this by the inclusion of adaptive mechanisms aimed at increasing oxygen extraction and general blood flow. However, the publications of S. M. Cain [22] provide data that at low hematocrit levels, a significant decrease in systemic oxygen consumption and a decrease in coronary blood flow is determined, which does not meet the energy needs of the heart, as a result of which myocardial hypoxia develops and a drop in the ejection fraction.

Therefore, the assessment of the state of systemic oxygen transport depending on the indicators of hematocrit and haemoglobin in the conditions of blood loss, and the determination of the minimum acceptable level of hematocrit and haemoglobin, which ensures an adequate relationship between the systemic oxygen transport and the oxygen needs of the body in the development of massive obstetric blood loss, can be an effective tool for adequate resuscitation and hemostatic therapy.

During the analysis of systemic oxygen transport depending on hematocrit and haemoglobin levels in patients during the early postpartum period significant differences in IDO_2 , IVO_2 and O_2ER were discovered. At Ht levels within 20.0–28.9 %, Hb levels within 45.1–68.9 g/L and equal $FiO_2 = 100$ % (GrI, GrII, GrIII) there was a 2–3 times worse deviation of IDO_2 values compared to the normal gas transport status and only in patients with Ht = 29.0–30.0 %, and Hb = 70.1–79.9 g/L (GrIV), IDO_2 values were close to the normal physiological range. At Ht = 20.0–22.9 % and Hb = 45.1–50.4 g/L (GrI), IVO_2 values were 2 times less than the lower normal physiological limit, while in patients with Ht = 29.0–30.0 %, and Hb = 70.1–79.9 g/L (GrIV), this parameter's values were within the normal range. At Ht = 20.0–25.9 %, Hb = 45.1–60.0 g/L (GrI and GrII), O_2ER values were 1.5–2 times higher in comparison to normal physiological values for this parameter, while in patients Ht = 29.0–30.0 %, and Hb = 70.1–79.9 g/L (GrIV), this parameter's values were within the normal range. And as a result of the conducted correlation analysis for IDO_2 , ICO_2 , O_2ER and haemoglobin levels, we identified a strong positive statistically significant correlation between these parameters.

Research limitations. The study's statistical tests could require a larger sample size to ensure that the sample is considered representative of a population and that the statistical result can be generalized to a larger population.

Prospects for further research. In the future, it is planned to expand the database of the studied parameters to increase the evidence of the obtained data and to conduct a correlation

analysis of the influence of a low haemoglobin level on the development of cognitive dysfunctions in women in labour after massive obstetric bleeding.

5. Conclusion

1. With Ht values in the range of 20.0–28.9 %, and Hb in the range of 45.1–68.9 g/l and the same indicators of $\text{FiO}_2 = 100$ % (GrI, GrII, GrIII), the deviation of IDO_2 indicators was in 2–3 times lower relative to the normal state of the blood gas transport function and only in patients with the level of Ht = 29.0–30.0 %, and Hb = 70.1–79.9 g/l (GrIV), the values of IDO_2 were close to the physiological norm.

2. At levels of Ht = 20.0–22.9 %, and Hb = 45.1–50.4 g/l (GrI), ISO_2 indicators were half as low as the generally accepted physiological norms, and in patients with a level of Ht = 29.0–30.0 %, and Hb = 70.1–79.9 g/l (GrIV), the values of this indicator were within the normal range.

3. At levels of Ht in the range of 20.0–25.9 %, and Hb = 45.1–60.2 g/l (GrI, GrII), indicators of KTEO_2 were 1.5–2 times more compared to generally accepted physiological norms of this indicator, and in patients with a level of Ht = 29.0–30.0 %, and Hb = 70.1–79.9 g/l (GrIV), the values of this indicator were within the normal range.

4. When calculating the minimum acceptable value of haemoglobin in a woman in labour under conditions of blood loss using linear regression with the calculation of coefficients by the method of least squares, the values of Hb = 82.5365 g/l were obtained, which can be considered the minimum permissible value in women in labour under conditions of postpartum blood loss, in which the functional state of the heart and oxygen exchange is at the minimum limit of the physiological norm. From the calculation of the minimum allowable haemoglobin level in postpartum women in case of blood loss using linear regression with coefficients calculated through the method of least squares the Hb = 82.5 g/L value was obtained, which can be considered the minimum allowable level in postpartum women in case of postpartum blood loss which allows the cardiac functional status and oxygen metabolism to be maintained on the lower margin of the physiological range.

Conflict of interest

The authors declare that there is no conflict of interest in relation to this paper, as well as the published research results, including the financial aspects of conducting the research, obtaining and using its results, as well as any non-financial personal relationships.

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