*Original article*

# Anemia, red blood cell transfusion and administration of blood products in obstetrics: a nationwide analysis of more than 6 million cases from 2011-2020

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**Background** - The prevalence of anemia is high, especially in obstetrics. There is large evidence, that anemia during pregnancy is associated with increased maternal morbidity and mortality. Anemia and peripartum hemorrhage remain the main causes for transfusion of red blood cells (RBC). Patient Blood Management (PBM) reduces the need for RBC transfusion significantly. The present study retrospectively analyzed the impact and prevalence of anemia and RBC transfusion on pregnant women.

**Materials and methods** - Data were retrieved from the German Statistical Office on pregnant women who delivered in hospital between January 1st 2011 and December 31st 2020. The prevalence of anemia, peripartum hemorrhage, comorbidities, administration of blood products and complications were analyzed.

**Results** - A total of 6,356,046 pregnant women were analyzed of whom 78,257 (1.23%) received RBC transfusion (RBC transfusion group) and 6,277,789 (98.77%) did not receive RBC transfusion (non-RBC transfusion group). In all women analyzed anemia rate was 23.74%. The rates of anemia during pregnancy (70.39 *vs* 23.15%; p<0.0001), postpartum hemorrhage (41.42 *vs* 4.35%; p<0.0001), hospital length of stay (127.5 *vs* 87.08 hours; p<0.0001) and single complications were higher in women with RBC transfusion compared to women without RBC transfusion.

**Discussion** - The prevalence of anemia and the increased risk for RBC transfusion show that there is great potential for effective implementation of PBM in obstetrics. The treatment of anemia during pregnancy and reduction of RBC transfusions will decrease maternal morbidity and mortality.

**Keywords:** *red blood cell, transfusion, anemia, obstetrics, pregnancy.*



## INTRODUCTION

Anemia is a serious global health problem during pregnancy. According to the World Health Organization (WHO) the prevalence of anemia in obstetrics is about 42.0% worldwide and still around 18.7% in Europe[1]. The WHO defines anemia in pregnant

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women as a hemoglobin (Hb) value <11.0 g/dL irrespective of gestational age[2]. Alongside the WHO criterion, there are other definitions of anemia for the second trimester (Hb <10.5 g/dL) according to various international guidelines[3-5].

There are several potential causes of anemia during pregnancy. Physiologically, iron demand is increased, which may result in iron-deficient erythropoiesis and iron-deficiency anemia (IDA) when iron intake is inadequate. In addition, blood volume expands more than red blood cell (RBC) mass which leads to hemodilution[6]. Excessive bleeding like postpartum hemorrhage (PPH) may also lead to anemia. In Germany, PPH is defined as a blood loss of >500 mL after vaginal delivery and >1,000 mL after Cesarean section[7].

Iron deficiency (ID) and IDA during pregnancy are associated with increased maternal and fetal morbidity and mortality. Maternal complications include preterm labor, increased rates of Cesarean section, PPH and death. Fetal complications include low birth weight and small-for-gestational-age neonates[6]. In addition, anemia is an independent risk factor for single complications (e.g., renal failure and pneumonia), postoperative anemia, increased hospital length of stay (LOS) and RBC transfusion[8]. The administration of RBCs themselves is associated with adverse effects for the patients, such as acute hemolytic transfusion reactions, anaphylactic reactions or acute lung injury[9].

In 2020, Zdanowicz *et al.* analyzed data from the Swiss obstetric hospital registry (1998-2016) on 627,921 deliveries and found an increase of one to two RBC units transfused during PPH[10]. To combat complications caused by IDA and reduce the risk of RBC transfusions, international experts recommend the implementation of Patient Blood Management (PBM) in obstetrics[11,12]. There is a large body of evidence indicating that the successful implementation of PBM reduces patients' morbidity and mortality[13-15].

With this background, this study was conducted to examine the rate of anemia and administration of blood products in obstetrics over a period of 10 years in Germany, using a large database.

## MATERIAL AND METHODS

### Inclusion criteria

All pregnant women who delivered in hospital between January 1st 2011 and December 31st 2020 in Germany (No.=6,356,046) were included in the study.

### Availability of data and materials

Hospitals in Germany are legally obliged to report diagnoses and procedures according to International Classification of Diseases and Related Health Problems (ICD) codes and International Statistical Classification of Procedures (OPS) codes[16]. The German Statistical Office saves data on their local site. All calculations have been processed remotely, although individual patient and hospital identifiers were unavailable to the authors. Since the register data were anonymized to the authors, the Ethics Committee of the University Hospital Frankfurt waived the need for ethical approval (Chair: Prof. Dr. Harder, Ref: 2022-766).

### Definitions and data acquisition

All age groups and data from 2011 to 2020 were included. More recent data were not available due to accounting aspects and the internal data validation processes of the Federal Statistical Office, which processes data, evaluates their validity and releases them for further scientific analysis.

Data collected include demographics (e.g., age, LOS), comorbidities (e.g., obesity, anemia), complications (e.g., renal failure, pneumonia) and obstetric-related problems (e.g., complications due to intrapartum hemorrhage, acute hemorrhagic anemia). Diagnoses were coded according to the 10th revision of the ICD (ICD-10) and procedures according to the OPS (version 2020). **Table I** lists the ICD-10 and OPS codes for the corresponding diseases and procedures.

### Statistical analysis

Categorical variables are expressed as absolute numbers and percentages. Continuous variables were tested for normality. All the continuous variables considered (age, LOS, and mechanical ventilation) were non-normally distributed and so these are presented as medians with 25% and 75% quartiles. Group differences between categorical variables were tested for statistical significance with the chi-square test, whereas the Wilcoxon rank-sum test was used for continuous variables. Groups for predefined comorbidities, birth mode, anemia, bleeding and complications were the RBC transfusion group and the non-RBC transfusion group using their

**Table I** - *Procedural and diagnostic codes used for reimbursement purposes in Germany*

| Procedure/Diagnosis | OPS codes | ICD-10 codes |
|---|---|---|
| **Vaginal delivery** | 9-260, 9-261, 9-268 | |
| **Cesarean section** | 5-74, 5-741, 5-749 | |
| **Essential hypertension** | | I10.- |
| **Gestational hypertension** | | O13 |
| **Diabetes during pregnancy (pre-existing)** | | O24.- |
| **Gestational diabetes** | | O24.4 |
| **Nicotine abuse** | | F17.2 |
| **Obesity** | | E66.- |
| **Grade I [BMI] 30-<35** | | E66.00 |
| **Grade II [BMI] 35-<40** | | E66.01 |
| **Grade III [BMI] ≥40** | | E66.02 |
| **Iron-deficiency anemia** | | D50.- |
| **Vitamin B12-, folic acid-, any other dietary anemia** | | D51.-, D53.- |
| **Anemia of unspecified cause** | | D55.-, D64.- |
| **Anemia due to acute bleeding situations** | | D62 |
| **Anemia during pregnancy** | | O99.0 |
| **Anticoagulation therapy** | | Z92.1 |
| **Prepartum hemorrhage** | | O46.- |
| **Prepartum hemorrhage due to coagulation disorder** | | O46.0 |
| **Intrapartum hemorrhage** | | O67.- |
| **Postpartum hemorrhage** | | O72.- |
| **Pneumonia** | | J12.-, J13, J14, J15.-, J16.-, J17.-, J18.-, U69.00 |
| **Renal failure** | | N17.-, N19 |
| **Postpartum renal failure** | | O90.4, O90.9 |
| **Cardiopulmonary resuscitation** | 8-771, 8-772, 8-779 | |
| **Cardiac complications during pregnancy** | | O75.4, O75.8, O75.9 |
| **Death** | | O95 |
| **Child born dead** | | Z37.1, Z37.3, Z37.4, Z37.7 |
| **RBC transfusion** | 8-800.c | |
| **Platelet transfusion** | 8-800.6, 8-800.d, 8-800.f, 8-800.g, 8-800.h, 8-800.j, 8-800.k, 8-800.m, 8-800.n | |
| **FFP transfusion** | 8.812.6-8.812.8 | |
| **PCC transfusion** | 8-812.5 | |
| **Fibrinogen transfusion** | 8-810.j | |
| **Massive blood transfusion** | 8-800.1 | |

OPS: international statistical classification of procedures; ICD-10: 10th revision of the International Classification of Diseases and Related Health Problems; BMI: body mass index; RBC: red blood cell; FFP: fresh-frozen plasma; PCC: prothrombin complex concentrate.

respective ICD and OPS codes as defined in **Table I**. The level of statistical significance was set at 5%. Excel 2019 (Microsoft Corp., Seattle, WA, USA) was used for data handling and SAS (Version 9.4M6, SAS Institute Inc., Cary, NC, USA) for statistical analysis.

## RESULTS

Data from a total of 6,356,046 pregnant women who delivered in hospital between January 1st 2011 and December 31st 2020 were analyzed in this study.

### Patients' characteristics

Vaginal delivery was conducted in 67.86% and Cesarean section in 35.36% of all coded, hospitalized deliveries. "Anemia during pregnancy" was diagnosed in 23.74%, "anemia of unspecified cause" in 11.85%, and "anemia due to acute bleeding situations" in 10.39%. Peripartum hemorrhage occurred in 5.59%; PPH accounted for the majority (4.8%) of these bleeds. In total, 98.77% of all women did not receive RBC transfusion (non-RBC transfusion group) and 1.23% received RBCs (RBC transfusion group) (**Table II**).

### Comparison of the RBC transfusion group and the non-RBC transfusion group

Cesarean section was conducted more often in the RBC transfusion group compared to the non-RBC transfusion group (50.1 *vs* 35.18%; p<0.0001). In addition, comorbidities such as gestational hypertension (2.06 *vs* 1.13%; p<0.0001) and pre-existing diabetes during pregnancy (7.23 *vs* 5.87%; p<0.0001) were more frequent in the RBC transfusion group than in the non-RBC transfusion group. All other comorbidities are displayed in **Table III**.

### Anemia, peripartum hemorrhage and complications

Overall, the rate of anemia during pregnancy was significantly higher in women who were transfused with RBCs than in women who did not receive RBC transfusion (70.39 *vs* 23.15%; p<0.0001). The most common bleeding complication was PPH, which was more frequent in women in the RBC transfusion group compared to those in the non-RBC transfusion group (41.42 *vs* 4.35%; p<0.0001). The rates of all other bleeding situations are presented in **Table III**.

The median LOS in hospital was significantly longer in transfused women compared to women who did not have RBC transfusion (128 [96-189] hours *vs* 87 [70-117] hours,

**Table II** - *Characteristics of the study population*

| Characteristic | Pregnant inpatients | |
|---|---|---|
| **Total patients, No.** | 6,356,046 | |
| **Age in years** | **Median [Q1-Q3]** | |
| | 28 [27.45-31] | |
| **Age groups** | **No.** | **%** |
| 10-14 | 1,181 | 0.02 |
| 15-19 | 134,824 | 2.12 |
| 20-24 | 711,686 | 11.20 |
| 25-29 | 1,761,944 | 27.72 |
| 30-34 | 2,245,568 | 35.33 |
| 35-39 | 1,230,025 | 19.35 |
| 40-44 | 255,547 | 4.02 |
| 45-49 | 13,163 | 0.21 |
| 50-54 | 840 | 0.01 |
| 55-59 | 96 | <0.01 |
| 60-64 | 4 | <0.01 |
| **Birth mode** | **No.** | **%** |
| Vaginal delivery | 4,313,530 | 67.86 |
| Cesarean section | 2,247,528 | 35.36 |
| **Risk factors** | **No.** | **%** |
| Essential hypertension | 10,428 | 0.16 |
| Gestational hypertension | 72,920 | 1.15 |
| Diabetes during pregnancy (pre-existing) | 374,418 | 5.90 |
| Gestational diabetes | 346,601 | 5.45 |
| Nicotine abuse | 34,050 | 0.54 |
| Obesity | 151,959 | 2.40 |
| Grade I | 25,743 | 0.41 |
| Grade II | 22,245 | 0.35 |
| Grade III | 25,405 | 0.40 |
| Vitamin B12-, folic acid-, any other dietary anemia | 1,500 | 0.02 |
| Anemia of unspecified cause | 752,965 | 11.85 |
| Anemia due to acute bleeding situations | 660,144 | 10.39 |
| Anemia during pregnancy | 1,508,664 | 23.74 |
| Anticoagulation therapy | 8,780 | 0.14 |
| **Bleeding** | **No.** | **%** |
| Prepartum hemorrhage | 24,759 | 0.39 |
| Prepartum hemorrhage due to coagulation disorder | 418 | <0.01 |
| Intrapartum hemorrhage | 26,510 | 0.40 |
| Postpartum hemorrhage | 305,610 | 4.80 |
| **Transfusion groups** | **No.** | **%** |
| No RBC transfusion | 6,277,789 | 98.77 |
| RBC transfusion | 78,257 | 1.23 |
| ICU admission | 30,540 | 0.48 |

Q1-Q3: interquartile range; RBC: red blood cell; ICU: intensive care unit.

respectively; p<0.0001). Our data show an overall rate of admission to an intensive care unit (ICU) of 12.45% in women given a RBC transfusion and 0.33% in women not given a RBC transfusion. Complications such as pneumonia (0.49 *vs* <0.01%; p<0.0001), renal failure (2.09 *vs* 0.36%; p<0.0001) and cardiopulmonary resuscitation (1.25 *vs* 0.01%; p<0.0001) occurred significantly more often in the RBC transfusion group compared to the non-RBC transfusion group (**Table III**).

### Administration of blood products

The overall administration of blood products in obstetrics is presented in **Table IV**. Red blood cells were the most frequently transfused blood component, with 799 administrations per 100,000 pregnancies. Other blood components administered included fibrinogen (215/100,000 pregnancies), fresh-frozen plasma (118/100,000 pregnancies), platelets (47/100,000 pregnancies) and prothrombin complex concentrate (44/100,000 pregnancies).

## DISCUSSION

This retrospective study is based on data from 6,356,046 pregnant women hospitalized between January 1st 2011 and December 31st 2020 in Germany. One of the main findings of the study is an anemia rate during pregnancy of 23.74% in all women. Furthermore, the rate of anemia during pregnancy, PPH as well as single complications (renal failure, pneumonia, ICU admission) were higher in women in the RBC transfusion group compared to the non-RCB transfusion group.

Anemia is one of the most critical health conditions worldwide[17]. It affects 41.8% of all pregnant women worldwide and is lower in countries with high socioeconomic status (18.7%). Our findings of an anemia rate of 23.74% are in line with a meta-analysis by Karami *et al*. published in 2022. Their analysis included 52 studies involving 1,244,747 pregnant women and revealed a global prevalence of anemia during pregnancy of 36.8% (95% confidence interval [CI]: 31.5-42.4). In most cases anemia was mild (70.8% [95% CI: 58.1-81.0]) and mostly present in the third trimester (48.8% [95% CI: 38.7-58.9]). Anemia during pregnancy is mainly caused by ID due to high fetal iron demands[18]. Iron deficiency increases throughout gestation and by the end of pregnancy, around 30-50% of all women have low serum ferritin levels[6].

**Table III** - *Comparison of the RBC transfusion group and non-RBC transfusion group*

| | Non-RBC transfusion group | | RBC transfusion group | | |
|---|---|---|---|---|---|
| | **No.** | **%** | **No.** | **%** | |
| **Total patients** | 6,277,789 | 98.77 | 78,257 | 1.23 | |
| | **Median [Q1-Q3]** | | **Median [Q1-Q3]** | | **p-value** |
| **Age** | 28 [27.45-31] | | 31 [27-35] | | <0.0001 |
| **Birth mode** | **No.** | **%** | **No.** | **%** | **p-value** |
| Vaginal delivery | 4,270,621 | 68.03 | 42,909 | 54.83 | <0.0001 |
| Cesarean section | 2,208,323 | 35.18 | 39,205 | 50.10 | <0.0001 |
| **Risk factors** | **No.** | **%** | **No.** | **%** | **p-value** |
| Essential hypertension | 9,878 | 0.16 | 550 | 0.70 | <0.0001 |
| Gestational hypertension | 71,309 | 1.13 | 1,611 | 2.06 | <0.0001 |
| Diabetes during pregnancy (pre-existing) | 368,764 | 5.87 | 5,654 | 7.23 | <0.0001 |
| Gestational diabetes | 341,504 | 5.44 | 5,097 | 6.51 | <0.0001 |
| Nicotine abuse | 33,624 | 0.54 | 426 | 0.54 | 0.7387 |
| Obesity | 149,817 | 2.39 | 2,142 | 2.74 | <0.0001 |
| Grade I | 25,308 | 0.40 | 435 | 0.56 | <0.0001 |
| Grade II | 21,886 | 0.35 | 359 | 0.46 | <0.0001 |
| Grade III | 25,004 | 0.40 | 401 | 0.51 | <0.0001 |
| **Anemia** | **No.** | **%** | **No.** | **%** | **p-value** |
| Vitamine B12-, folic acid-, any other dietary anemia | 1,344 | 0.02 | 156 | 0.20 | <0.0001 |
| Anemia of unspecified cause | 702,304 | 11.19 | 50,661 | 64.74 | <0.0001 |
| Anemia due to acute bleeding situations | 610,792 | 9.73 | 49,352 | 63.06 | <0.0001 |
| Anemia during pregnancy | 1,453,576 | 23.15 | 55,088 | 70.39 | <0.0001 |
| Anticoagulation therapy | 8,486 | 0.14 | 294 | 0.38 | <0.0001 |
| **Bleeding** | **No.** | **%** | **No.** | **%** | **p-value** |
| Prepartum hemorrhage | 23,625 | 0.38 | 1,134 | 1.45 | <0.0001 |
| Prepartum hemorrhage due to coagulation disorder | 281 | <0.01 | 137 | 0.18 | <0.0001 |
| Intrapartum hemorrhage | 23,539 | 0.37 | 2,971 | 3.80 | <0.0001 |
| Postpartum hemorrhage | 273,193 | 4.35 | 32,417 | 41.42 | <0.0001 |
| **Complications** | **median [Q1-Q3]** | | **median [Q1-Q3]** | | **p-value** |
| Hospital LOS [h] | 87.08 [69.50-116.52] | | 127.5 [95.68-189.45] | | <0.0001 |
| Mechanical ventilation [h] | 8 [3-30] | | 20 [7-55] | | <0.0001 |
| | **No.** | **%** | **No.** | **%** | **p-value** |
| ICU admission | 20,768 | 0.33 | 9,772 | 12.45 | <0.0001 |
| Pneumonia | 266 | <0.01 | 384 | 0.49 | <0.0001 |
| Renal failure | 22,449 | 0.36 | 1,635 | 2.09 | <0.0001 |
| Postpartum renal failure | 1,542 | 0.02 | 678 | 0.87 | <0.0001 |
| Cardiopulmonary resuscitation | 675 | 0.01 | 982 | 1.25 | <0.0001 |
| Cardiac complications during pregnancy | 25,580 | 0.41 | 922 | 1.18 | <0.0001 |
| Death | 25 | <0.01 | 25 | 0.03 | <0.0001 |
| Child born dead | 1,777 | 0.03 | 946 | 1.21 | <0.0001 |

RBC: red blood cell; Q1-Q3: interquartile range; LOS: length of stay; ICU: intensive care unit.

**Table IV** - *Administration of blood products in the study population*

| Blood product (BP) | No. | BP/100,000 pregnancies |
|---|---|---|
| **Red blood cells** | 50,798 | 799 |
| **Platelets** | 3,047 | 47 |
| **Fresh-frozen plasma** | 7,508 | 118 |
| **Prothrombin complex concentrate** | 2,811 | 44 |
| **Fibrinogen** | 13,652 | 215 |
| **Massive blood transfusion** | 1,435 | 23 |

While it remains uncommon for pregnant women to be checked for ID unless anemic, a recent study indicates a prevalence of 42.0% of isolated ID in the first trimester[19]. Despite a high prevalence of ID during pregnancy, a systematic review by Daru *et al.* on the diagnosis of ID revealed a wide variation of serum ferritin thresholds used for diagnosis of ID[20]. This variation may lead to underdiagnosed, understudied, and thus undertreated ID with adverse effects on both mother and child[21]. A retrospective cohort study by Teichman *et al.* on 44,552 pregnant women revealed a screening rate for ID of 59.4%[21]. Of these, the majority of women were checked during the first trimester, when the risk of ID is lowest. Interestingly, in women with anemia, a subsequent test for ferritin was conducted in only 27.3%. The proportion of anemic patients with a ferritin test during pregnancy ranged 22-67% in the lowest and highest categories of anemia severity, respectively[21].

Our findings of an IDA rate of only 0.5% (despite an anemia rate during pregnancy of 23.74%) support the findings of Teichman *et al.* This discrepancy of our study may be explained by reimbursement coding inaccuracy. In addition, the diagnosis of IDA requires further measurement of iron parameters which are associated with increased financial expenses.

For coding, the assumption that it might be an ID is not sufficient. Therefore, it can be assumed that undiagnosed IDA is coded as "anemia of unspecified cause" or "anemia during pregnancy". Anemia without further diagnosis should first be coded as "D64.9 Anemia, unspecified", even if iron supplements are administered "on suspicion"[22].

Since most pregnant women suffer from insufficient iron stores, iron management during pregnancy is crucial. For effective treatment of an existing ID/IDA, national (e.g., National Institute for Health Care Excellence [NICE]) and international guidelines recommend screening for hematological conditions with a full blood count at 28 weeks of gestation, as well as at any time during pregnancy if anemia is present[12,23]. The Network for the Advancement of Patient Blood Management, Haemostasis and Thrombosis (NATA) consensus statement recommends routine antenatal administration of oral iron (30-60 mg/day) and folic acid (400 µg/day) to reduce the risk of low birth weight, maternal ID and IDA[12]. This is in accordance with guidelines issued by the WHO[24]. However, the gastrointestinal side effects of oral iron salts often compromise the adherence to treatment by pregnant women. Multivitamin and mineral compounds are better tolerated but most of them do not supply sufficient amounts of iron, vitamin B12, C or D, especially for those already presenting with ID or IDA. Moreover, the EMPIRE study revealed that most pregnant Portuguese women received daily multivitamin and mineral products, as a source of iron supplementation, and 54% of them presented with ID[25]. Treatment with oral iron is recommended in mild to moderate IDA (Hb ≥8 g/dL) during the first and second trimesters. Newer, more bioavailable and better tolerated oral iron formulations may facilitate prophylaxis and treatment of ID/IDA during pregnancy[26,27]. In the third trimester, intravenous iron should be administered in severe IDA (Hb <8 g/dL) or newly diagnosed IDA[12].

Severe PPH usually leads to anemia which is associated with RBC administration[28]. This is reflected by our data, as PPH occurred more often in transfused women than in non-transfused women (41.42 *vs* 4.35%; p<0.0001). In addition, anemia was present more often in the RBC transfusion group compared to the non-RBC transfusion group (70.39 *vs* 23.15%; p<0.0001).

Prick *et al.* evaluated 521 women with anemia due to PPH (with no symptoms of severe anemia or severe comorbidities) and randomized them into a group given iron and folic acid supplementation and a group given RBC transfusions (target Hb >8.9 g/dL). Analyses revealed that significantly fewer RBC were transfused when iron was administered (88 RBC units) compared to no iron supplementation (517 RBC units; p<0.001)[29].

Postpartum anemia can be defined as a Hb <10.0 g/dL within 24-28 hours after delivery[12]. Women should have

a Hb check within 48 hours after childbirth, in cases of blood loss >500 mL or signs of anemia. In patients with postpartum anemia and symptoms of anemia, intravenous iron is efficient at increasing Hb levels[3]. In a study on women with a postpartum Hb <8.0 g/dL, Broche *et al.* found that the administration of intravenous iron increased Hb by 1.9 g/dL in 7 days and by 3.1 g/dL in 14 days[30]. In women with a Hb <10.0 g/dL within 48 hours of delivery but asymptomatic, oral elemental iron 40-80 mg daily should be offered for at least 3 months[3].

Analyses from a Swiss study on RBC transfusion in obstetrics revealed that the administration of one to two RBC transfusions during PPH increased in the last years[10]. In an analysis of 307,415 women giving birth, it was found that uterine atony, retained placenta and trauma were risk factors for severe obstetric hemorrhage (blood loss >1,500 mL or RBC transfusion) in 30.0%, 18.0% and 13.9% of women, respectively. Other diseases and complications such as pre-eclampsia, gestational hypertension, chronic hypertension and diabetes as well as anemia have also been associated with severe hemorrhage[31]. These findings are reflected by our data, as the rates of gestational hypertension (2.06 *vs* 1.13%; p<0.0001), essential hypertension (0.7 *vs* 0.16%; p<0.0001), diabetes (7.23 *vs* 5.87%; p<0.0001) and gestational diabetes (6.51 *vs* 5.44%; p<0.0001) were significantly higher in the RBC transfusion group compared to the non-RBC transfusion group.

However, as the majority of women have no known risk factors for PPH, a guideline for PBM in obstetrics should be in place to reduce the need for RBC transfusion in the peripartum period[10]. In 2019, a multidisciplinary consensus statement on the prevention and treatment of PPH was published. The aim of this statement was to generate evidence-based recommendations to assist clinical decisions in order to improve safety for mothers[32].

Anemia and RBC transfusions are risk factors for postoperative morbidity and mortality[33,34]. Our data demonstrate that complications (e.g., renal failure and pneumonia) occurred significantly more often in the RBC transfusion group compared to the non-RBC transfusion group (p<0.0001). The rate of ICU admission (12.45 *vs* 0.33%; p<0.0001) and median LOS (128 [96-189] hours *vs* 87 [70-117] hours; p<0.0001) also differed significantly between the two groups.

The blood products administered in our study are in line with those recommended during PPH by national guidelines in Germany[35]. Red blood cells were the most frequently administered blood component (799/100,000 pregnancies). As fibrinogen levels drop early in PPH, fibrinogen should be replaced early in severe PPH[36]. This is reflected by our results, as fibrinogen was the second most commonly administered blood product (215/100,000 pregnancies).

Since this is the first investigation of such a large cohort of pregnant women receiving RBC transfusion so far, comparison with other studies is not feasable. However, further studies should be conducted to identify risk factors for RBC transfusion in obstetrics. This could help to identify women with a special risk profile at an early stage of pregnancy in order to reduce the need for RBC transfusions and complications in the peripartum period.

### Limitations

Although this study is, to our knowledge, the largest survey of pregnant women over a period of 10 years in Europe, it does have some limitations including its retrospective character and secondary reimbursement data usage. Reimbursement data are correlated with medical cases in hospital[37], although it cannot be completely avoided that conditions or events are over- or under-represented for reimbursement reasons. However, there is an increased incentive for correct documentation, since hospital reimbursements are audited by the medical service of the health insurance funds. The parameters selected were chosen according to high medical relevance to minimize coding errors. Due to the large sample size, possibly misrecorded data should be largely counterbalanced. Data were collected in a structured and representative manner according to the Declaration of Helsinki. Laboratory findings and medication are not coded for reimbursement and were therefore not available for analysis.

In addition, only information on in-hospital pregnancies and deliveries was available.

## CONCLUSIONS

The prevalence of anemia during pregnancy is high (23.74%). In women with RBC transfusion the rate of anemia, PPH and single complications (e.g., renal failure,

pneumonia, ICU admission) were higher compared to women without RBC transfusion. The implementation of PBM in obstetrics has great potential to reduce the prevalence of anemia and number of RBC transfusions during pregnancy.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Due to institutional anonymization, no conclusions can be drawn about individual patients. According to §21KHEntgG, the reimbursement data are free for scientific use. The Ethics Committee of the University Hospital Frankfurt waived the requirement for Ethics Committee approval for this study (Chairman: Prof Dr Harder, Ref: 2022-766). All data processing was performed in accordance with the tenets of the Declaration of Helsinki.

### Consent for publication

As this study involved anonymized register data, the patients' consent could not be collected.

### Availability of data and materials

The data on which the results of this study are based are available from the Federal Statistical Office with the restrictions applied. The dataset was used under license for the current study and is therefore not generally accessible. However, the data are available from the authors on reasonable request and with permission from the Federal Statistical Office.

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## AUTHORSHIP CONTRIBUTIONS

VN and JK wrote the manuscript and were in charge of planning the study in close consultation with BF and KZ. VN and JK conceived the study and were in charge of its overall direction and planning. TJ and BF conceptualized the data query. OO conducted the statistical analysis and proofread the article. All Authors contributed to the final version of the manuscript.

## DISCLOSURE OF CONFLICTS OF INTEREST

*KZ has received honoraria for participation in advisory board meetings for Haemonetics and Vifor and received speaker fees from CSL Behring, Masimo, Pharmacosmos, Boston Scientific, Salus, iSEP, Edwards and GE Healthcare. He is the Principal Investigator of the EU-Horizon 2020 project ENVISION (Intelligent plug-and-play digital tool for real-time surveillance of COVID-19 patients and smart decision-making in Intensive Care Units) and Horizon Europe 2021 project COVend (Biomarker and AI-supported FX06 therapy to prevent progression from mild and moderate to severe stages of COVID-19). KZ leads as CEO the Christoph Lohfert Foundation as well as the Health, Patient Safety & PBM Foundation. All other Authors declare no conflict of interest.*

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