Patterns of red-cell transfusion use in obstetric practice in Sweden 2003–2017: A nationwide study

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Abstract

Background There is a paucity of data on patterns of red-cell transfusions in obstetrical care, but some studies have suggested an increase in transfusion rates during the last decade. The purpose of this study was to investigate maternal characteristics, temporal trends and hospital variations in red-cell use in a large contemporary obstetric cohort in Sweden.

Study design and methods Nationwide observational cohort study of maternal red-cell transfusions for all deliveries in Sweden between 2003 and 2017.

Results The proportion of deliveries that received red-cell transfusions was stable during the study period, although the number of red-cell units administered per delivery declined. Among transfused women, most received a low-volume transfusion of 1 or 2 units. Red-cell transfusion was more common among the nulliparous, for instrumental and caesarean deliveries, and with increased maternal age. We saw large variations in transfusion rates between hospitals in Sweden, despite adjusting for age and parity.

Conclusions In comparison to other high-resource countries we see a high proportion of deliveries with maternal red-cell transfusions. However, we do not see an increase in red-cell use over time.

Background

While the overall incidence of red-cell transfusions has decreased in Sweden and other high-resource settings such as the US and England [1–3], there are studies that suggest increasing transfusion rates in obstetric patients [4–6]. The reasons for this are not fully understood.

It has previously been observed that a significant fraction of maternal red-cell transfusions in obstetrics may be considered inappropriate [7]. In a 2017 study, it was observed that obstetricians were more likely to prescribe transfusion with two red-cell units, although estimated blood loss and haemoglobin level suggested that one unit would suffice [8]. A single centre study from the same year showed that almost half of red-cell transfusions were administered despite no ongoing blood loss and a haemoglobin level (Hb) of >7 g/dl [9].

A recent Swedish study showed that the majority of red-cell units administered to women between the ages 25–35 were used in an obstetric context [1]. Besides this, little is...
known about the transfusion patterns in these patients. There is limited data on any long-term effects of allogeneic blood transfusion in the obstetric population, and given that blood products are a scarce and a costly resource, any upward trend in utilization warrant further investigation.

Therefore, we conducted a nationwide, long-standing study to describe maternal red-cell transfusion in Sweden. Specifically, we characterized trends over time and in relation to maternal age, as well as variation across hospitals.

**Methods and materials**

**Data sources and setting**

The study was based on the Swedish Medical Birth register and the Swedish portion of the third iteration of the Scandinavian donations and transfusion database (SCANDAT3-S). The registers were linked using the unique national registration number assigned to all Swedish residents.

The Swedish Medical Birth Register is a nationwide population-based health register established in 1973 and managed by the National Board of Health and Welfare, containing 96-99% of all births. The register contains demographic and gestational data, as well as information on diagnoses and medical procedures classified according to the Swedish version of the International Classification of Diseases (ICD) system and standardized procedural codes. Details on the register have previously been described [10]. Antenatal and in-hospital obstetric care is part of the government-funded public health-care system in Sweden, and virtually all women attend.

The SCANDAT databases are a series of bi-national databases that contains computerized information on blood donors, donations, blood products, transfusions and transfused patients since 1968 in Sweden and 1981 in Denmark. SCANDAT3-S is the third iteration of the Swedish portion of the database, containing data on blood transfusions and donations until 2017, extracted from Blood Bank laboratory information systems, with nationwide coverage in Sweden since 1996 [11].

**Study design**

All deliveries in women aged 15–50 years between January 1, 2003 and December 31, 2017 were identified in the Swedish Medical Birth Register. Information on all maternal red-cell transfusions was extracted from the SCANDAT3-S database.

**Statistical analysis**

A maternal peripartum red-cell transfusion was defined as a recorded administration of one or more red-cell units in the time period from 14 days prior to and until 14 days after delivery. If maternal transfusion occurred, the delivery was categorized as ‘transfused’. The total number of transfused units administered during this period was also counted and categorized as ‘1 or 2 units’, ‘3 to 9 units’ or ‘10 units or more’.

Maternal demographic and gestational characteristics were described for transfused and non-transfused deliveries, and according to the number of administered units per delivery (in mentioned categories). Multi-foetal births were counted as one delivery.

Considered variables include maternal age at delivery, parity (nulliparous, one previous delivery and more than one previous delivery), body-mass index (BMI, kg/m²), gestational length (preterm < 37 weeks, at term and post-term > 42 weeks), plurality (singleton or multi-foetal pregnancy), foetal presentation at delivery (cephalic, breach, flexed, other), delivery mode (spontaneous vaginal, instrumental vaginal or caesarean) and hospital category (county, regional or university hospital).

Results were presented as frequencies and percentages, and, where applicable, medians with interquartile ranges (IQR). Missing values were labelled as ‘unknown’.

We calculated the percentage of transfused deliveries where a total count of one, two, three etc. maternal red-cell units were administered, and in relation we present the cumulative percentage of total red-cell unit use. We also analysed the distribution of administered red-cell units in relation to the day of delivery (i.e. a parturient that receives two red-cell units the day of delivery and on day two after delivery contributes with two units for each of those days).

To visualize overall transfusion trends, we applied logistic regression with year of delivery modelled as a restricted cubic spline with five equally placed knots. Time-trends were further stratified in categories according to the number of administered red-cell units, parity and delivery mode and presented as the number of transfused deliveries per 1000. In the analyses on maternal age and red-cell transfusion, we used as a restricted cubic spline, with knots manually placed (at ages 22, 30, 35, 40, 45, 48) for better fit. Results were stratified and presented as above. In supplemental material, we used a logistic regression to investigate red-cell unit usage over time and in relation to maternal age.

The proportion of deliveries with maternal transfusions was also stratified by hospital category (university, regional or county). In this analysis, only hospitals with more than 500 births per year were included (comprising 42 general hospitals with 97-8% of all recorded births). We calculated the number of transfusions per 1000 deliveries, using direct standardization to the year 2003 population, with regards to age and
Results

We identified 1 599 814 recorded deliveries in the period between January 1, 2003 and December 31, 2017. We excluded births to mothers aged below 15 (n = 77) or above 50 (n = 78). The remaining 1 599 599 deliveries to 959 868 women were included in further analyses. Among these, maternal transfusion occurred in relation to 48,088 (3.0%) deliveries. Of all the included women, 45 976 (4.8%) were transfused in conjunction with at

Table 1  Characteristics of study population presented overall and stratified by transfused/non-transfused

| Number of subjects, N (%) | Overall | Non-transfused | Transfused |
|---------------------------|---------|----------------|------------|
| Age, N (%)                | 1 599 659 (100) | 1 551 571 (97.0) | 48 088 (3.0) |
| ≤24                       | 221 641 (13.9) | 215 097 (13.9) | 6544 (13.6) |
| 25–34                     | 1 032 901 (64.6) | 1 002 719 (64.6) | 30 182 (62.8) |
| 35–44                     | 342 090 (21.4) | 330 897 (21.3) | 11 193 (23.3) |
| ≥45                       | 3027 (0.2) | 2858 (0.2) | 169 (0.4) |
| Median age (IQR)          | 30 (27–34) | 30 (27–34) | 31 (27–34) |
| BMI, N (%)                | <20 | 211 434 (13.2) | 205 266 (13.2) | 6168 (12.8) |
| 20–24                     | 637 191 (39.8) | 619 172 (39.9) | 18 019 (37.5) |
| 25–29                     | 418 088 (26.1) | 405 177 (26.1) | 12 911 (26.8) |
| 30–34                     | 139 428 (8.7) | 134 895 (8.7) | 4533 (9.4) |
| ≥35                       | 62 009 (3.9) | 59 797 (3.9) | 2212 (4.6) |
| Unknown                   | 131 509 (8.2) | 127 264 (8.2) | 4245 (8.8) |
| Median BMI (IQR)          | 24 (22–27) | 24 (21–27) | 24 (22–27) |
| Gestational age, in weeks N (%) | <37 | 166 628 (10.4) | 158 056 (10.2) | 8572 (17.8) |
| 37–42                     | 1 322 787 (82.7) | 1 288 613 (83.1) | 34 174 (71.1) |
| >42                       | 109 743 (6.9) | 104 436 (6.7) | 5307 (11.0) |
| Unknown                   | 501 (0.0) | 466 (0.0) | 35 (0.1) |
| Parity, N (%)             | 0 | 705 889 (44.1) | 677 731 (43.7) | 28 158 (58.6) |
| 1–2                       | 590 940 (36.9) | 577 836 (37.2) | 13 104 (27.3) |
| ≥3                        | 302 830 (18.9) | 296 004 (19.1) | 6826 (14.2) |
| Pregnancy, N (%)          | Single | 1 576 569 (98.6) | 1 531 066 (98.7) | 45 503 (94.6) |
| Multiple                  | 23 090 (1.4) | 20 505 (1.3) | 2585 (5.4) |
| Presentation, (N%)        | Cephalic | 1 406 074 (87.9) | 1 367 596 (88.1) | 38 478 (80.0) |
| Breech                    | 52 801 (3.3) | 50 937 (3.3) | 1864 (3.9) |
| Flexed                    | 67 661 (4.2) | 64 738 (4.2) | 2923 (6.1) |
| Other                     | 33 619 (2.1) | 31 249 (2.0) | 2370 (4.9) |
| Unknown                   | 39 504 (2.5) | 37 051 (2.4) | 2453 (5.1) |
| Delivery mode, N (%)      | Vaginal | 1 237 717 (77.4) | 1 211 099 (78.1) | 26 618 (55.4) |
| Caesarean                 | 262 746 (16.4) | 248 346 (16.0) | 14 400 (29.9) |
| Instrumental              | 99 196 (6.2) | 92 126 (5.9) | 7070 (14.7) |
| Hospital, N (%)           | County hospital | 213 988 (13.4) | 207 883 (13.4) | 6105 (12.7) |
| Regional hospital         | 830 567 (51.9) | 806 260 (52.0) | 24 307 (50.5) |
| University hospital       | 555 104 (34.7) | 537 428 (34.6) | 17 676 (36.8) |
least one of their deliveries. Among transfused women, 2046 (4.5%) were transfused again in a subsequent delivery. The proportion of caesarean deliveries remained at approximately 17% (16.4–17.7%), whereas the proportion of instrumental deliveries decreased from 9.3% to 6.3% during the study period [12].

Demographic and gestational information on deliveries in which maternal red-cell transfusion did and did not occur is presented in Table 1. Compared to women with a delivery between week 37 until the end of week 42, maternal red-cell transfusions were more common in both preterm and post-term deliveries. Compared to the non-transfused parturient, transfused women more often had an instrumental vaginal or caesarean delivery. Among transfused, multi-foetal pregnancy was more common than among non-transfused patients. Maternal transfusions were also more common in nulliparous women compared to women with previous deliveries.

Details of the red-cell unit distribution in transfused deliveries is presented in Fig. 1. In total, 139 424 red-cell units were administered during the study period. In deliveries with maternal red-cell transfusions, a majority received 2 units (62%), and approximately 25% received more than 3 units. More than half (52%) red-cell units were used in low-volume transfusions with three units or less.

The distribution of red-cell units in relation to day of delivery is presented in Fig. 2. Approximately 42% of all units were administered during the day of delivery and 15% were administered on and onwards from the third day after delivery. The proportion of units administered prior to delivery was very small and previous to 3 days before delivery, the percentage was <0.1% per day.

Further demographic and gestational information stratified by the number of red-cell transfusions is presented in Table 2. In deliveries with a count of 10 or more units transfused, we noted that women of advanced age were more likely to be transfused.
overrepresented, as were women with preterm deliveries, non-cephalic presentation at delivery, and caesarean delivery. Fewer deliveries were with nulliparous mothers among those that received 10 or more units, and BMI did not differ much between groups.

In Fig. 3, we present the number of transfused deliveries per 1000 over time. Overall, the number of transfused deliveries was approximately 30 per 1000 throughout the study period (A). The frequency of deliveries with maternal transfusion of 1 or 2 red-cell units increased from 17 to 22 per 1000 deliveries, whereas the proportion of deliveries with a count of 10 red-cell transfusions or more almost halved, from 0.67 to 0.32 per 1000 deliveries. Deliveries with 3–9 units also decreased from 10 to 7.6 per 1000 deliveries (B). Nulliparous women were transfused most frequently, and the trend was stable over time (C). While the proportion of transfused deliveries was stable among spontaneous vaginal and caesarean deliveries, it increased over time for instrumental deliveries from 67 to 81 per 1000 deliveries (D).

In Fig. 4, we present the overall number of transfused deliveries per 1000 in relation to maternal age. Overall, the count of deliveries with maternal transfusion was 30 per 1000 until age 35, after which we see a steady increase (A). Interestingly, the increase after age 40 was primarily seen in women receiving 1–2 units (B). Nulliparous women were more often transfused compared to parous women at all ages, with an increase in the transfused proportion with advancing maternal age (C). Spontaneous vaginal delivery was associated with the lowest risk of transfusion (D).

Figure 5 presents the overall number of transfused deliveries per 1000 across hospitals of different levels. We saw considerable variation, with a range from 20 to 54 transfused deliveries per 1000. The discrepancy was seen across all hospital categories and was not explained by adjusting for age and parity.

In supplemental Figure 1 (A), we present the total number of administered red-cell units per 1000 deliveries over time. Overall, red-cell unit usage decreased over the study period, from 90 to 80 units per 1000 deliveries. In (B), we present red-cell unit usage as a function of maternal age. At the maternal age of approximately 35, red-cell usage starts to increase. Across all strata,
estimates were generally imprecise above age 43 due to scarce data.

**Discussion**

In this 15-year nationwide cohort study of obstetric transfusion practice in Sweden, we saw no overall change in the proportion of deliveries with maternal red-cell transfusions, but we saw a decrease in the number of administered units per delivery. This is consistent with the finding that the number of women receiving 3–9 red-cell units decreased over time with a simultaneous rise in the proportion receiving 1–2 units. Transfused women were more likely to be nulliparous, have a multi-foetal pregnancy, a preterm delivery and instrumental or caesarean delivery. These characteristics seem to be consistent with previous findings [5,6,13,14].

### Table 2 Characteristics of study population, stratified by number of transfusions

| Number of transfused units per delivery | 1 or 2 | 3–9 | 10 or more |
|----------------------------------------|--------|-----|------------|
| Number of subjects, N (%)              | 32 049 (66.6) | 15 079 (31.4) | 960 (2.0) |
| Age at delivery, N (%)                 |        |     |            |
| ≤24                                    | 4673 (14.6) | 1800 (11.9) | 71 (7.4)   |
| 25–34                                  | 20 260 (63.2) | 9399 (62.3) | 523 (54.5) |
| 35–44                                  | 7013 (21.9) | 3823 (25.4) | 357 (37.2) |
| ≥45                                    | 103 (0.3) | 57 (0.4) | 9 (0.9)    |
| Median age (IQR)                       | 30 (27–34) | 31 (27–35) | 33 (29–37) |
| BMI, N (%)                             |        |     |            |
| <20                                    | 4259 (13.3) | 1803 (12.0) | 106 (11.0) |
| 20–24                                  | 12 087 (37.7) | 5615 (37.2) | 317 (33.0) |
| 25–29                                  | 8592 (26.8) | 4050 (26.9) | 269 (28.0) |
| 30–34                                  | 2944 (9.2) | 1481 (9.8) | 108 (11.3) |
| ≥35                                    | 1418 (4.4) | 752 (5.0) | 42 (4.4)   |
| Unknown                                | 2749 (8.6) | 1378 (9.1) | 118 (12.3) |
| Median BMI (IQR)                       | 24 (22–27) | 24 (22–27) | 24 (22–28) |
| Gestational age, in weeks N (%)        |        |     |            |
| <37                                    | 5350 (16.7) | 2888 (19.2) | 334 (34.8) |
| 37–42                                  | 23 226 (72.5) | 10 399 (69.0) | 549 (57.2) |
| >42                                    | 3453 (10.8) | 1777 (11.8) | 77 (8.0)   |
| Unknown                                | 20 (0.1) | 15 (0.1) | 0 (0)      |
| Parity, N (%)                          |        |     |            |
| 0                                      | 18 872 (58.9) | 8883 (58.9) | 403 (42.0) |
| 1–2                                    | 8774 (27.4) | 4038 (26.8) | 292 (30.4) |
| ≥3                                     | 4403 (13.7) | 2158 (14.3) | 265 (27.6) |
| Unknown                                | 20 (0.1) | 15 (0.1) | 0 (0)      |
| Pregnancy, N (%)                       |        |     |            |
| Single                                 | 30 520 (95.2) | 14 095 (93.5) | 888 (92.5) |
| Multiple                               | 1529 (4.8) | 984 (6.5) | 72 (7.5)   |
| Presentation, N (%)                    |        |     |            |
| Cephalic                               | 25 752 (80.4) | 12 074 (80.1) | 652 (67.9) |
| Breech                                 | 1205 (3.8) | 589 (3.9) | 70 (7.3)   |
| Flexed                                 | 1979 (6.2) | 889 (5.9) | 55 (5.7)   |
| Other                                  | 1547 (4.8) | 748 (5.0) | 75 (7.8)   |
| Unknown                                | 1566 (4.9) | 779 (5.2) | 108 (11.3) |
| Delivery mode, N (%)                   |        |     |            |
| Vaginal                                | 18 149 (56.6) | 8162 (54.1) | 307 (32.0) |
| Caesarean                              | 9411 (29.4) | 4443 (29.5) | 546 (56.9) |
| Instrumental                           | 4489 (14.0) | 2474 (16.4) | 107 (11.1) |
| Hospital, N (%)                        |        |     |            |
| County hospital                        | 4121 (12.9) | 1894 (12.6) | 90 (9.4)   |
| Regional hospital                      | 16 336 (51.0) | 7521 (49.9) | 450 (46.9) |
| University hospital                    | 11 592 (36.2) | 5664 (37.6) | 420 (43.8) |

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Overall, maternal red-cell transfusion occurred in 3% of deliveries, which is on the higher end compared with studies in other countries. A 2013 Finnish study on singleton births, the corresponding number was 2.3% in 2008 [6] and a 2012 Danish study found a transfusion rate of 1.9% [15]. We can only speculate on why there is a discrepancy, but there are methodological differences (e.g. we include virtually all deliveries of women between the ages of 17–50 and we include all transfusions within the 28 days encompassing delivery) that hinder direct comparison.

In case of uncontrolled massive haemorrhage, the red-cell unit obviously provides a life-saving bridge to recovery. However, there are reasons to be cautious when the patient is haemodynamically stable. In a study comparing...

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**Fig. 3** The proportion of deliveries in which red-cell transfusion occurred as a function of time for (A) the entire cohort and subdivided (B) according to the total number of administered of red-cell units, (C) per parity and (D) per mode of delivery.
Health and health service utilization among low-risk women that suffered post-partum haemorrhage, it was noted that women that received a low-volume red-cell transfusion (1 or 2 units) had poorer maternal outcomes than otherwise comparable women receiving no transfusions [16]. In a non-inferiority trial looking at quality of life, little difference was found between maternal red-cell transfusions and alternatives like iron supplementation [17] and an observational study on births complicated by post-partum haemorrhage, maternal red-cell transfusion was associated with lower rates of breastfeeding at discharge [18].

Fig. 4 The proportion of deliveries in which red-cell transfusion occurred as a function of maternal age for (A) the entire cohort and subdivided (B) according to the total number of administered of red-cell units, (C) per parity and (D) per mode of delivery.
From our data, we conclude that more than half of all units are administered after the day of delivery and that the 2-unit transfusion is most common. It is reasonable to think that a proportion of these units were administered to haemodynamically stable (albeit anaemic) patients. Current consensus guidelines, which were not in place during the study period, recommend transfusing ‘one unit at the time’ [a concept that was proposed decades ago (19)] and emphasize the use of iron supplementation in moderate to severe post-partum anaemia (20). Over time, we did see a slight reduction in red-cell units use per delivery, and time will tell if there is continued reduction in overall red-cell exposure.

Previous studies have shown that advanced maternal age is associated with adverse pregnancy outcomes (e.g. stillbirth, preterm birth, pre-eclampsia) (21,22). We found advancing maternal age to be accompanied with a larger proportion of transfused deliveries, a finding also seen in other studies [6,23]. In our study, women over 40 years were more often transfused, regardless of parity. We make no claim on a causal relationship between maternal age and red-cell transfusion on the basis of this study, but it is a topic for further study.

We saw a considerable variation in transfusion rates between hospitals, after adjusting for parity and maternal age. In an Australian study on 250,000 deliveries, difference in transfusion rates remained after careful adjustment for obstetrical case-mix, but there was no difference in patient outcomes in hospitals with lower transfusion rates compared to those with more liberal transfusion practice [24]. We cannot readily explain the differences in our study, but it is a finding that should spur further investigation.

There are important limitations to this study. In this broad overview of obstetric transfusion practice, we did not investigate the appropriateness of the individual red-cell transfusion (such as maternal Hb concentration, pre-partum anaemia etc.). Also, we did not consider other blood products than the red-cell unit.

The strength of the study is that it is, to our knowledge, the largest of its kind and has the advantage of being based on virtually complete, nationwide high-quality data over a long time period. The predictors (age, parity, delivery mode) are prospectively recorded and outcomes (red-cell transfusions) are robust and not prone to reporting or measurement error.

In our study of a Swedish obstetric cohort, we see a high proportion of deliveries with maternal red-cell transfusion in comparison to other high-resource countries. However, we do not see an increase over time, and the number of transfused units used per delivery has decreased over the study period.

Conflict of interests

The authors declare no conflict of interests.

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Fig. S1 The number of red-cell units administered per 1000 deliveries as a function of (A) time and (B) of maternal age.

Additional Supporting Information may be found in the online version of this article:

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