

Intravenous iron: barriers and facilitators to use

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Title: Intravenous iron: barriers and facilitators to use at nine maternity hospitals

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ABSTRACT

Background: Anaemia in pregnancy is mostly due to iron deficiency, and the use of intravenous (IV) iron is gaining acceptance as a treatment option. Recently released obstetric transfusion guidelines recommend IV iron in maternity patients requiring iron when oral formulations are poorly tolerated, unlikely to be well absorbed, or when rapid restoration of iron stores is required.

Aim: To identify barriers and facilitators to the use of IV iron in pregnancy among 9 maternity hospitals in New South Wales.

Materials & Methods: A qualitative research study was undertaken using semi-structured interviews. Nine maternity units were chosen to cover a range of clinical settings and obstetric blood transfusion rates. Interviews were conducted with haematologists, obstetricians and midwives, and included questions about the use of IV iron in each institution. Interviews were transcribed, coded, and NVivo software was used to develop themes.

Results: 125 interviews were conducted: 61 with doctors. The use of IV iron differed between hospitals and individual doctors. There were hospital/pharmaceutical, clinician and patient factors which acted as either barriers or facilitators to the use of IV iron. Where perceived barriers outweighed facilitators in a particular hospital, doctors were less likely to use IV iron.

Conclusion: The use of IV iron, as perceived by doctors, differed across hospitals. There are some potentially modifiable barriers to the use of IV iron that may need to be addressed for

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IV iron to be available to obstetric patients not tolerating oral formulations or requiring rapid restoration of iron stores.

BACKGROUND

Iron deficiency anaemia (IDA) is the most common cause of pregnancy-related anaemia world-wide.¹ Approximately 40% of fertile, non-pregnant women have low iron stores and therefore an unfavourable iron status prior to conception.¹ A woman's iron requirements increase during pregnancy: for maternal red cell mass expansion and development of the fetoplacental unit.¹⁻³ Antepartum anaemia is associated with maternal morbidity such as poor cognitive function and reduced physical performance^{1,2,4}, and with neonatal/childhood morbidity such as preterm delivery, low birth weight^{5,6}, delayed growth and development and increased cognitive and behavioural abnormalities up to 10 years after iron repletion.⁷ Furthermore, antepartum anaemia predisposes to postpartum anaemia, which may be exacerbated by intrapartum or postpartum haemorrhage. It is therefore logical to optimise a woman's iron stores prior to birth, to maximise her ability to compensate for blood loss, and reduce anaemia-related complications.

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists advocates targeted rather than routine testing for iron-deficiency⁸, and iron supplementation in women at particular risk of or with proven IDA rather than routinely^{9,10}. Oral iron supplementation with 100-200mg/day of elemental iron^{10,11} together with dietary iron constitutes first line management of IDA. However, it is well recognised that women are often poorly compliant with oral iron due to gastrointestinal side effects. There is renewed

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interest in the use of intravenous (IV) iron to treat iron deficiency anaemia. The 2015 National Blood Authority's (NBA) Obstetrics/ Maternity Patient Blood Management (PBM) Guidelines recommend IV iron when oral iron is poorly tolerated, is unlikely to be well absorbed, or when rapid restoration of iron stores is required.¹⁰

Three formulations of IV iron are available on the Australian Pharmaceutical Benefits Scheme (PBS), and therefore at subsidised cost for Australian residents: iron sucrose, iron polymaltose and ferric carboxymaltose. They vary in their pharmacological properties and safety profiles (Appendix 1). All are effective in replacing iron, generally resulting in a more rapid rise in haemoglobin and a more rapid and sustained rise in ferritin, when compared to oral iron formulations.^{1, 2, 4, 12-14} Ferric carboxymaltose, the newest IV iron preparation, has the advantage of allowing a total dose infusion to be delivered in 15 minutes and with recent PBS-listing, is now similar in cost to other IV iron formulations.

There is evidence that IV iron has utility as an alternative to blood transfusion¹⁵, thereby reducing use of a limited resource that carries risks. Variation in hospital obstetric transfusion rates¹⁶ may be related to the use of IV iron. Our study aimed to identify the barriers and facilitators to the use of IV iron in hospitals with a range of obstetric transfusion rates.

MATERIALS AND METHODS

This study was part of a larger body of work using semi-structured interviews among 125 doctors and midwives to explore transfusion practices at 9 obstetric units from February to October 2014 in New South Wales (NSW). The interview questions were written by

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researchers (EM, JF) in collaboration with an obstetrician, haematologist and midwife (Appendix 2). The interview process was designed to be iterative, allowing themes to be progressively explored and consistency of opinion to be examined.¹⁷⁻¹⁹

Hospitals were deliberately selected to cover a range of case-mix, size, geographical location and obstetric blood transfusion rate. Hospital obstetric transfusion rates were identified using population data for the period 2008-2010.¹⁶ Selection of participants was by purposive sampling and facilitated by the site investigator or head of department at each hospital, who suggested individuals based on their seniority, expertise and experience, or knowledge of transfusion and blood management practices. Obstetricians, obstetric fellows/registrar, haematologists, haematology fellows/registrar, midwives, clinical midwifery educators and midwifery unit managers were included. Direct contact was made with each potential participant, and if willing, a face-to-face interview was arranged.

All interviews were conducted by a single researcher (EM) following informed consent, and most took place in a dedicated room either in the hospital maternity unit or in private consulting rooms. Field notes were written to provide contextual data. Each interview was audio-taped and was generally 30-45 minutes duration. Once commenced, all interviews progressed to completion, and no participant requested that their interview be removed from subsequent analysis.

Audio files were transcribed and checked as previously described.²⁰ Data analysis occurred in two stages by two researchers (EM and AA). Interviews were open coded into main themes and then coding was refined to develop sub-themes using NVivo10®. The two researchers compared codes to optimise ascertainment and fidelity, and where the themes differed, consensus was reached by discussion.

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This paper focuses on the management of low ferritin in a pregnant woman, and the use of IV iron. While one question specifically explored iron infusion, the entire interview was coded with relevance to these aspects. Once themes were refined, quotes were selected from the interviews to expand on these themes. Analysis of barriers and facilitators to the use of IV iron was limited to doctors' interviews only, since they were the prescribers of iron.

Ethics approval to conduct the study was granted by the South Western Sydney Local Health District Human Research Ethics Committee and from the governance units of each hospital.

RESULTS

Sixty-one interviews were with doctors, the majority of whom had obstetric training (69%).

There were 28 obstetricians, 11 obstetric fellows/ registrars, 3 GP- obstetricians, 16 haematologists and 3 haematology fellows/ registrars. Participating doctors varied in how long they had worked in their specialty (2 to 45 years), and how long they had worked in their current hospital (2 weeks to 30 years). Obstetricians/ GP-obstetricians were the main decision-makers with respect to IV iron, and rarely involved haematology personnel in clinical consultation.

Characteristics of the nine hospitals and doctors' perceptions of the use of IV iron are presented in Table 1. Four of the nine hospitals were located outside Sydney. All hospitals had IV iron available, however there were differences in the preparation stocked by pharmacies, the logistics of administration, and perceived frequency of use at each site. All of the five high transfusing hospitals stocked iron polymaltose, however women at two of these hospitals could access iron carboxymaltose with outside prescriptions. Perceived

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infrequent use of IV iron did not appear to correlate with high hospital obstetric transfusion rates.

INSERT TABLE 1: Characteristics of study hospitals

Themes pertaining to the use of IV iron were grouped into hospital and pharmaceutical factors, clinician factors and patient factors (Figure 1). Factors such as the prescribing doctor's specialty (obstetricians or GP-obstetricians), involvement of haematology personnel, and the specific location of IV iron administration, did not appear to be related to frequency of use.

INSERT FIGURE 1: Factors influencing the use of intravenous iron in obstetric patients

Hospital and pharmaceutical factors

Hospital and pharmaceutical factors were identified as influencing IV iron use (Table 2).

Some doctors felt that IV iron had now become easier to prescribe, while others felt that it was still expensive. All hospitals stocked IV iron in their pharmacy, however availability of ferric carboxymaltose varied between institutions. In three hospitals stocking iron polymaltose only, doctors stated that they asked their patients to purchase ferric carboxymaltose privately.

INSERT TABLE 2: Hospital and pharmaceutical factors influencing the use of IV iron in obstetric patients

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All of the hospitals in which IV iron was frequently used reported that it was easy to arrange (Table 1). Important facilitators for IV iron use were a suitable location to administer it, and having staff adequately trained and comfortable with administration and monitoring for side effects. Many doctors stated that arranging IV iron in their hospital was easy due to a streamlined system of referral. For many, newer preparations such as ferric carboxymaltose requiring shorter infusion times meant that IV iron was used more readily. However, some doctors stated that they found IV iron difficult to arrange.

The extent to which IV iron was a locally accepted practice influenced its use. Some doctors perceived that it was used often and had become firmly entrenched into obstetric practice by local “champions”. In contrast, other doctors felt that IV iron was used either infrequently or not at all in their departments. Doctors stated that the existence of hospital protocols did not influence the use of IV iron within a hospital.

Clinical factors

In this study there were four clinician factors related to likelihood of IV iron use: perceived utility, education, experience/familiarity with IV iron and concerns about its safety profile (Table 3).

INSERT TABLE 3: Clinician factors influencing the use of IV iron in obstetric patients

Most doctors preferred to use IV iron ahead of blood transfusion in the antepartum setting and in the absence of bleeding, however opinion varied about its appropriateness in a stable, postpartum woman. Some doctors thought IV iron could potentially obviate the

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need for a blood transfusion at any stage, while others saw no use for iron infusion during pregnancy, or felt that it offered no advantage over oral iron.

All doctors had heard about IV iron, and many felt that the new iron formulations were now considered safer and faster to infuse than the older formulations. Doctors received education about IV iron through in-services, their own research, or by exposure to other doctors' practices. They differed greatly in how much exposure and experience they had with IV iron, and how comfortable they were using it. Obstetricians who had practised for many years had seen practice change over time, from former reluctance, to comfort and confidence using IV iron. Obstetricians who were more recently trained were generally more familiar and inherently comfortable using IV iron.

Generally there was consensus among doctors about the potential risks of allergy and anaphylaxis. Where doctors were extremely concerned about the safety profile, either due to personal or anecdotal experience of an adverse outcome, they were reluctant to use it. Several obstetricians who had been in practice the longest, spoke about the adverse safety profile particularly associated with older formulations of IV iron and how historical obstetric practice had shaped contemporary practice. While many obstetricians described contemporary IV iron formulations as safer, some felt they still carried significant risk.

Patient factors

This study found three patient factors which appeared to influence the use of IV iron: clinical indication, maternal characteristics and maternal consent (Table 4). Most doctors described similar clinical indications for using IV iron: women who were intolerant of or non-

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compliant with oral iron, or who did not respond satisfactorily to oral iron, or who were at later gestation with insufficient time for oral iron to work (Table 4).

INSERT TABLE 4: Patient factors influencing the use of intravenous iron in obstetric patients

The particular characteristics of women attending each hospital varied. Some doctors mentioned that they cared for women of low socioeconomic status in whom iron deficiency was common, or who had lifestyles not amenable to being compliant with oral iron. Others mentioned treating women of cultural backgrounds where both vegetarianism and iron deficiency were prevalent.

Clinicians treating women who were unwilling to have a blood transfusion due to cultural, religious or personal beliefs might offer iron infusion. One clinician mentioned that occasionally women requested an iron infusion upfront, either because they were more educated about the risk of blood transfusion, or they had had a successful iron infusion in the past.

CONCLUSION

Our study found that the use of IV iron differed between hospitals regardless of the obstetric blood transfusion rate, and both barriers and facilitators to use were present in all hospitals. Where perceived barriers outweighed facilitators in a particular hospital, doctors appeared to use IV iron less frequently. Facilitators included availability of ferric carboxymaltose, incorporating IV iron into usual obstetric practice, and favourable logistics including well-trained staff, a suitable location and a streamlined system of referral and delivery – all potentially modifiable factors. The only identified facilitator of IV iron use that

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may not be modifiable was the patient characteristics. All identified barriers were potentially modifiable, including lack of perceived utility, lack of knowledge about the risk profile of the new formulations of IV iron, lack of experience with the newer formulations of IV iron and unfavourable logistics.

Many of the current barriers to the use of IV iron identified in this study could be modified through targeted education reinforced by local champions. Strong proponents of IV iron feel that it is currently under-utilised,^{2, 21, 22} and our study suggests that a lack of perceived utility, influence of colleagues and concerns about its safety may all contribute to this.

Concerns about the safety profile of IV iron are likely to be a carryover from earlier formulations which were associated with a greater risk of anaphylaxis. High molecular weight dextran irons are no longer available and newer formulations bind iron more tightly to their carbohydrate core, thereby minimising labile iron release.⁷ While all IV iron formulations are associated with minor infusion reactions, these disappear upon ceasing the infusion. Similarly, while all infusions carry a risk of hypersensitivity reactions and anaphylaxis, this risk is reported as <1%, especially with the newer formulations.^{7, 14, 15, 23, 24} However, there is uncertainty in the literature about the overall safety of IV iron, with meta-analyses finding either increased¹⁵ or decreased²⁵ risk of infection. A trial in obstetrics and gynaecology patients found an increased rate of severe adverse events associated with the use of IV iron.²⁵ Studies investigating the safety and efficacy of IV iron specifically in obstetrics patients are needed. Adherence to new guidelines may require further education about the safety profiles of the IV iron formulations currently available for use in Australia.

There were two factors which did not appear to influence the use of IV iron: involvement of haematology personnel in IV iron decision-making and the existence of hospital protocols.

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The autonomy of obstetricians may reflect a perceived level of comfort in managing anaemia. While all hospitals had a protocol related to administration of IV iron, the use of this and other such protocols varied amongst clinicians, and therefore did not appear to consistently influence decision-making.

To our knowledge, this is the first study using qualitative data from obstetricians and haematologists to describe the current use of IV iron in Australian maternity hospitals. It offered a unique opportunity to describe current perceptions of IV iron use prior to the release of the NBA Obstetrics/ Maternity PBM Guidelines. The strength of our study was that we were able to explore an individual's expertise and specialty-specific perspective through purposive sampling. There were several limitations however. While we wanted to ascertain hospital IV iron practices, many of the influential factors identified by clinicians related to their personal IV iron use. Furthermore, this data reflects doctors' perceptions: we did not have access to quantitative data reflecting a hospital's actual pattern of IV iron use. While studies have emphasised the utility of IV iron in both the postpartum and antepartum setting, the data presented mostly focus on the antepartum setting.

In conclusion, our study has found that the use of IV iron differs across and within hospitals. Hospital/ pharmaceutical factors, clinician factors and patient factors influence decision making and act as either perceived barriers or facilitators. Barriers to use can be addressed by optimising both the logistics of IV iron administration and also through education on appropriate use, reinforced by local champions. Addressing these barriers may result in increased availability of IV iron for obstetric patients not tolerating oral formulations or requiring rapid restoration of iron stores.

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REFERENCES

1. Milman, N. Prepartum anaemia: prevention and treatment. *Ann Hematol* 2008; **87**(12): 949-59.
2. Bhandal, N., Russell R. Intravenous versus oral iron therapy for postpartum anaemia. *Br J Obstet Gynaecol* 2006; **113**(11): 1248-52.
3. Breyman, C., Honegger, C., Holzgreve, W., Surbek, D. Diagnosis and treatment of iron-deficiency anaemia during pregnancy and postpartum. *Arch Gynecol Obstet* 2010; **282**(5): 577-80.
4. Reveiz, L., Gyte, GML., Cuervo, LG., Casasbuenas, A. Treatments for iron-deficiency anaemia in pregnancy. *Cochrane Database of Systematic Reviews* 2011, Issue 10, DOI:10.1002/14651858. CD 003094.pub3.
5. Levy, A., Fraser, D., Katz, M et al. Maternal anemia during pregnancy is an independent risk factor for low birthweight and preterm delivery. *Eur J Obstet Gynecol Reprod Biol* 2005; **122**(2): 182-6.
6. Malhotra, M., Sharma, J., Batra, S et al. Maternal and perinatal outcome in varying degrees of anemia. *Int J Gynaecol Obstet* 2002; **79**(2): 93-100.
7. Auerbach, M. Iron in hematology: Danger with IV iron: Real or perceived? *Am J Hematol* 2014; **89**(6): 664.
8. RANZCOG College Statement C-Obs 3(b): Routine Antenatal Assessment in the Absence of Pregnancy Complications. Australia: Royal Australian and New Zealand College of Obstetricians and Gynaecologists; 2013.

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9. RANZCOG College Statement C-Obs 25: Vitamin and mineral supplementation in pregnancy: review. Australia: Royal Australian and New Zealand College of Obstetricians and Gynaecologists; 2014.
10. National Blood Authority (NBA) (2015) Patient Blood Management Guidelines: Module 5- Obstetrics and Maternity. NBA, Canberra, Australia.
11. Pasricha, S., Flecknoe-Brown, SC., Allen, KJ, et al. Diagnosis and management of iron deficiency anaemia: a clinical update. *Med J Aust* 2010; **193**(9): 525-32.
12. Al, RA., Unlubilgin, E., Kandemir, O et al. Intravenous versus oral iron for treatment of anemia in pregnancy: a randomized trial. *Obstet Gynecol* 2005; **106**(6): 1335-40.
13. Khalafallah, AA., Dennis, AE., Ogden, K et al. Three-year follow-up of a randomised clinical trial of intravenous versus oral iron for anaemia in pregnancy. *BMJ* 2012; **2**(5).
14. Van Wyck, DB., Martens, MG., Seid, MH et al. Intravenous ferric carboxymaltose compared with oral iron in the treatment of postpartum anemia: a randomized controlled trial. *Obstet Gynecol* 2007; **110**(2, Part 1): 267-78.
15. Litton, E., Xiao, J., Ho KM. Safety and efficacy of intravenous iron therapy in reducing requirement for allogeneic blood transfusion: systematic review and meta-analysis of randomised clinical trials. *BMJ* 2013; **347**.
16. Patterson J, Roberts C, Isbister J, et al. What factors contribute to hospital variation in obstetric transfusion rates? *Vox sang* 2015; **108**(1): 37-45.
17. Arnold E, Lane S. Qualitative research in transfusion medicine. *Transfus Med* 2011; **21**(5): 291-300.
18. Richards LM, Janice M. Readme first for a user's guide to qualitative methods. (3 ed) Thousand Oaks, CA, USA: Sage Publications; 2013; 336

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19. School of Medicine and Public Health. Qualitative methods in health research. Newcastle: University of Newcastle, Australia; 2008.
20. Mayson, E., Shand, AW., Ford, JB. Single unit transfusions in the obstetric setting: a qualitative study. [Manuscript]. In press 2015.
21. Auerbach M. Should intravenous iron be upfront therapy for iron deficiency anemia? *Pediatr Blood Cancer* 2011; **56**(4): 511-2.
22. Auerbach M. IV iron in pregnancy: an unmet clinical need. *Am J Hematol* 2014; **89**(7): 789.
23. Froessler, B., Collingwood, J., Hodyl, NA., Dekker, G. Intravenous ferric carboxymaltose for anaemia in pregnancy. *BMC Pregnancy Childbirth* 2014; **14**(1): 115.
24. Professional National Prescribing Service, National Medicine Wise. Ferric carboxymaltose (Ferinject) for iron-deficiency anaemia: full review. NPS Radar: Rational Assessment of Drugs and Research. 2014 August 2014:14-20.
25. Mayo Clinic Proceedings. The safety of intravenous iron preparations: systematic review and meta-analysis: Dowden Health Media, Inc.; Jan 2015.
26. Clinical Information Access Portal. MIMS Online Australia 2015. Cited 8-1-2015. Available from: <http://www.ciap.health.nsw.gov.au/>.
27. Garg, M., Morrison, G., Friedman, A et al. A rapid infusion protocol is safe for total dose iron polymaltose: time for change. *IMJ* 2011;41(7):548-54.

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Table 1: Characteristics of study hospitals

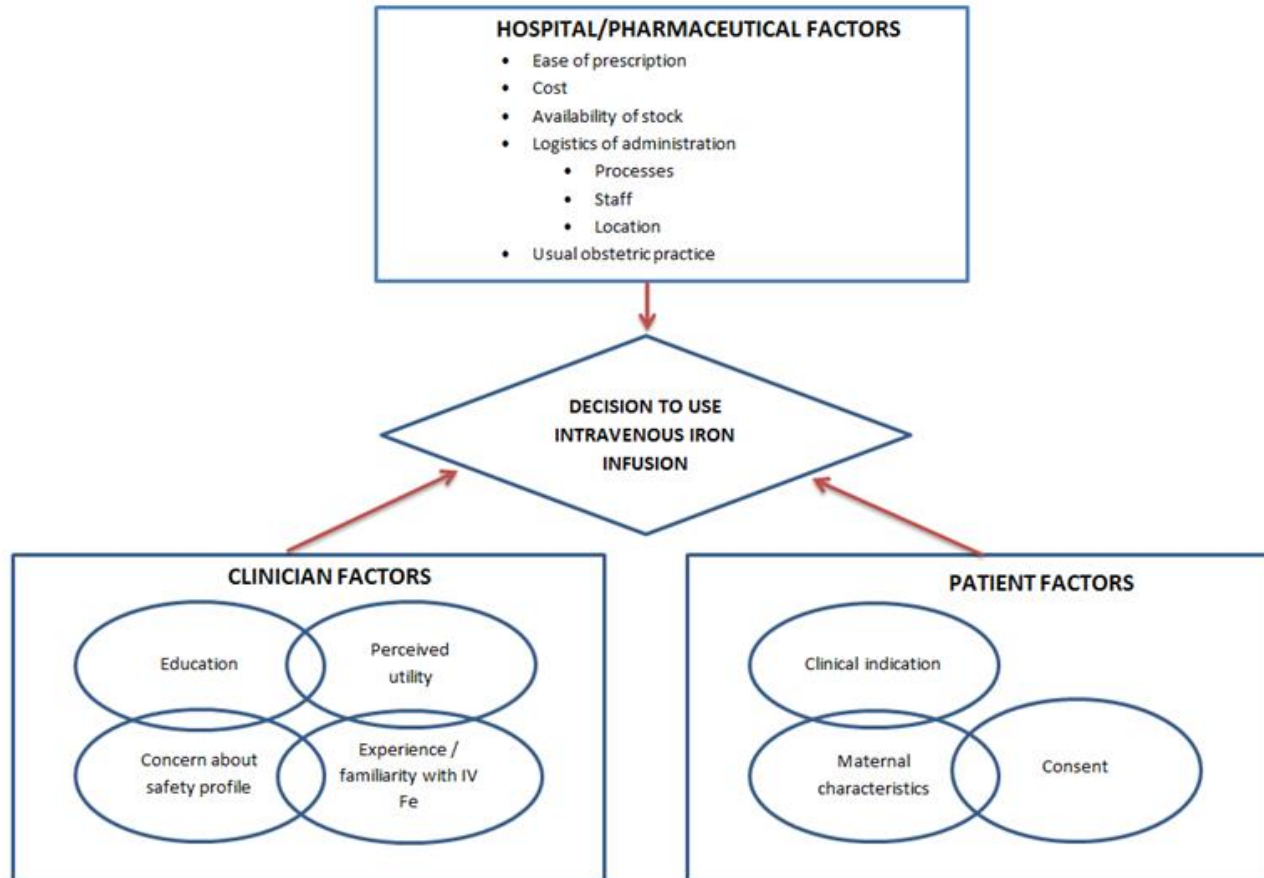
Hospital	Rurality	Obstetric service levels [†]	Average births/year (2008-2010)	Frequency of IV iron use among obstetricians [‡]	Easy to arrange	Preparation of IV iron stocked by hospital	Main prescribers in obstetric patients	Involvement of haematology department	Common setting of IV iron administration	Common location of IV iron administration	Obstetric transfusion rate
A	Metro	4	2000-3000	Infrequent	Yes	Polymaltose	Obstetricians	No	Outpatient	Ambulatory care unit	High
B	Rural	3	<500	Infrequent	Yes	Polymaltose	GP- obstetricians	No	Inpatient	General medical ward	High
C	Rural	4	<500	Infrequent	Yes	Polymaltose	Obstetricians or GP- obstetricians	No	Inpatient	Maternity ward	High
D	Metro	4	500-2000	Infrequent	No	Polymaltose	Obstetricians	No	Outpatient	Ambulatory care unit	Low
E	Metro	6	≥3000	Infrequent	No	Polymaltose [§]	Obstetricians	Rarely	Inpatient	Maternity ward	Low
F	Metro	5	2000-3000	Frequent	Yes	Polymaltose [§]	Obstetricians	Rarely	Outpatient	Ambulatory care unit	High
G	Metro	6	≥3000	Frequent	Yes	Polymaltose [§]	Obstetricians	Rarely	Outpatient	Maternity day assessment unit	High
H	Metro	Private	2000-3000	Frequent	Yes	Carboxymaltose	Obstetricians	No	Inpatient	Maternity ward	Low
I	Metro	6	2000-3000	Frequent	Yes	Carboxymaltose	Obstetricians	No	Outpatient	Maternity day assessment unit	Low

[†]Obstetric service level denotes a public hospital unless otherwise specified

[‡] This refers to the perception by obstetricians about how frequently intravenous (IV) Fe is used in their hospital

[§] Patients from these hospitals were permitted to purchase iron carboxymaltose privately from a community pharmacy, and bring it into the hospital for infusion

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Table 2: Hospital and pharmaceutical factors influencing the use of IV iron in obstetric patients

Factor	Illustrative Quote
Availability of ferric carboxymaltose	<p><i>"Now that that's on the pharmaceutical benefits scheme, that also becomes a much more user friendly option"</i> [G_H_Cons_03][†]</p>
	<p><i>"It is more expensive...I mean not for the patient, they'll just pay the co-payment...but for the pharmacy"</i> [G_H_Cons_02]</p>
	<p><i>"well our pharmacy tells me that when they run out of polymaltose they'll stock the carboxymaltose"</i> [G_H_Cons_03]</p>
	<p><i>"I was aware that our pharmacy was getting it, but I'm not necessarily sure if it's rolled out yet or not"</i> [G_O[‡]_Reg[§]_01].</p>
Logistics of administration	<p><i>"You're saving a whole day....So if you look at it, you're actually saving your resources"</i> [E_H_Cons_01]</p>
	<p><i>"they would have to go down to the cancer centre, which is going to freak them out"</i> [I_H_Cons_01]</p>
	<p><i>"be hooked up, shoot it up, walk out"</i> [H_O_Cons_02]</p>
	<p><i>"But the hassle involved in organising it is just not worth the effort"</i> [D_O_Reg_03].</p>
	<p><i>"...it's a performance. You've got to admit the patient and do the regular observations to give intravenous iron"</i> [E_O_Cons_03]</p>
Usual obstetric practice	<p><i>"..Obstetricians around here are very proactive in giving iron"</i> [G_H_Cons_01]</p>
	<p><i>"There's a real push for IV iron....that probably started by an obstetrician who's now retired from here...who was one of the pushers in getting that going"</i> [F_H_Cons_01]</p>
	<p><i>"..iron infusion is generally handled well within the unit"</i> [I_O_Cons_06]</p>
	<p><i>"I think it's slowly building but I think no maybe not....I don't think the take up's been that fast"</i> [H_O_Cons_04]</p>
	<p><i>"I don't have recourse to an iron infusion over here"</i> [D_O_Reg_03]</p>

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† Identifier for each interview transcript (G_H_Cons_03 refers to: G= hospital identifier_H= Haematology_Cons= Consultant_03= 3rd haematology consultant interviewed from hospital G)

‡ O= Obstetrics

§ Reg= Registrar

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Table 3: Clinician factors influencing the use of IV iron in obstetric patients

Factor	Illustrative Quote
Perceived utility	<p><i>"iron infusion may be all they need and might sort of save them from being transfused" [A_H_Cons_02][†] "</i></p> <p><i>"I've got to really be convinced to transfuse a young woman, pregnant or otherwise. I don't like to transfuse them. Most of them are iron deficient or have lost blood and in that case I tend to - I favour fluid resuscitation and iron" [A_H_Cons_03].</i></p> <p><i>"I don't support iron infusion during pregnancy..." [D_O[‡]_Cons_02]</i></p> <p><i>"I can't see why people can't take iron tablets...it seems to me iron tablets have worked very well for the last thousands of years" [I_O_Cons_03].</i></p>
Experience/ familiarity with IV iron	<p><i>"..intravenous iron preparations in the older obstetricians was something that was a last resort" [I_O_Cons_03]</i></p> <p><i>"we grew up in an era where we didn't use them" [I_O_Cons_06]</i></p> <p><i>"The tide is turning. Um, I think – I think we're doing more doctor initiated iron infusions antenatally" [I_O_Cons_06]</i></p> <p><i>"Certainly from some of the newer consultants who've come out, who've been exposed to it here" [H_O_Cons_07]</i></p> <p><i>"So I think now that we have better iron products available" [H_O_Cons_02]</i></p> <p><i>"I'm not very much scared of giving infusions....I'm comfortable" G_O_Cons_04]</i></p> <p><i>Gosh, I haven't given intravenous iron since - 45 years....No, I don't think I've seen it here in decades" [D_O_Cons_01].</i></p>
Concern about safety profile	<p><i>"when I was brought up iron transfusions were dangerous and unpleasant" [I_O_Cons_03]</i></p> <p><i>"but there is a real hangover, this stigma from the past of adverse side effects, um, and particularly anaphylaxis" [I_O_Cons_06]</i></p> <p><i>"..iron infusion I'm a little bit, ah, not, um, confident to give for pregnant lady...because I have seen few anaphylactic shock with iron infusion....this is in my, my back home.....that's probably make me to think 100,000 time before I decide "Yes, she's okay for iron transfusion". D_O_Cons_02]</i></p> <p><i>"...as products which have - or at least are perceived to have less anaphylactic risk" [H_O_Cons_03]</i></p> <p><i>"It seems to me that any injectable medication is eventually going to start getting side effects and- and occasionally anaphylaxis and we'll probably knock someone off with that because we're now getting so blasé about squirting this stuff in...I think we're going to get burnt with that sometime in the future" [I_O_Cons_03].</i></p>

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† Identifier for each interview transcript (A_H_Cons_02 refers to: A= hospital identifier_H= Haematology_Cons= Consultant_02= 2nd haematology consultant interviewed from hospital A)

‡ O= Obstetrics

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Table 4: Patient factors influencing the use of intravenous iron in obstetric patients

Factor	Illustrative Quote
Clinical indication	<i>"To get that built up before they go into labour and potentially have a PPH" [A_O_Cons_01] †.</i>
	<i>"Oh ones that are grossly anaemic" [I_O-Cons_02]</i>
	<i>"...in some cases asymptomatic anaemia they can get away with an iron infusion over time" [D_O_Reg‡_03]</i>
Maternal characteristics	<i>"We've got people who live off coke and chips" [G_O_Cons_02]</i>
	<i>"Or they are just so chaotic in their lifestyle that you just know they're not going to take it" [I_O_Cons_02].</i>
Maternal consent	<i>"If she says that no, she would prefer not to have the blood transfusion, we could go ahead and give her an iron transfusion" [C_O_Cons_01]</i>
	<i>"Because we've had quite a few Jehovah's Witnesses come through...who've had significant bleeds who had iron infusions who've recovered quite quickly" [I_O_Reg_01]</i>
	<i>"Certainly most mothers are quite savvy these days. They'd prefer to have – to regenerate their own haemoglobin, so iron infusions are becoming popular, not only from doctors but also mothers who demand – that's probably the way they'll take" [H_O_Cons_03].</i>

† Identifier for each interview transcript (A_O_Cons_01 refers to: A= hospital identifier_O= Obstetrics_Cons= Consultant_01= 1st obstetric consultant interviewed from hospital A)

‡ Reg= Registrar

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Appendices

Appendix 1: Summary of PBS-listed parenteral iron preparations available in Australia in 2015^{24, 26}

Iron Preparation	Name of product	Elemental iron content	Pregnancy category	Cost (\$)		Common side effects	Risk of hypersensitivity reaction (including anaphylaxis)	Test dose required	Total dose infusion	Maximum dose	Infusion time
				Dispensed price for maximum quantity (DPMQ)	Maximum price to consumer						
Iron sucrose	Venofer	100mg/5mL ampoule	B3	139.82	37.70	Taste perversion, hypotension, fever, rigors, injection site reactions, nausea (0.5-1.5%) Flushing, sweating, chills, fever, nausea, vomiting, headache, rash	Rare [†]	Yes	No	100mg/5mL per dialysis session; 3 doses/week	≥ 15min
Iron polymaltose	Ferrosig Ferrum H	100mg/2mL ampoule	A	31.88	37.30	Nausea, hypophosphataemia, injection-site reactions, headache, hypertension, dizziness	Infrequent	Yes	Yes	2500mg/500mL	5 hours [§]
Ferric carboxymaltose	Ferinject	500mg/10mL ampoule	B3	317.22	37.70		Uncommon [‡]	No	Yes	1000mg/2mL per week	15 min

Intravenous iron: barriers and facilitators to use

†Rare defined by risk $\geq 1/10,000$ but $< 1/1000$ ²⁵

‡Uncommon defined by risk $\geq 1/1000$ but $< 1/100$ ²⁵

§ Infusion protocol for iron polymaltose (according to the Australian Injectable Drugs Handbook, 3rd Ed 2005) is 5hrs, but this study has shown that a reduction in the infusion time to 73min resulted in 20 infusion-related reactions during the rapid phase, 1 of which was considered severe (myalgia), all of whom completed the infusion successfully with 5 individuals requiring the infusion to be completed at the original slower infusion rate. There were 31 delayed adverse events which occurred in the 5 days following infusion, with only 2 described as severe (headache) ²⁷

Intravenous iron: barriers and facilitators to use

Appendix 2: Semi-structured interview schedule which was asked of all 125 interview participants

Preamble

*I am interested in obtaining as much information as I can about your hospital's blood transfusion practice in maternity patients, and some of your own thoughts about blood transfusion. When talking about blood transfusion, I mean specifically **red blood cells** and not other blood products. The questions being asked are not designed to scrutinize yours or your hospital's practice, and the things we discuss today will remain confidential. If a particular question falls outside your realm of responsibility or area of expertise, please tell me and I will move on.*

Information to collect prior to interview

Obtain from the participant prior to interview if possible.

- **(all)What type of obstetric/ haematology or anaesthetic service is offered by your hospital?**
- **(all)Do you have any hospital policies relating to haemorrhage, anaemia or patient blood management?**

- PROMPT (all): Specifically MTP (massive transfusion protocol), PPH (post-partum haemorrhage) prevention or management guidelines, PBM (patient blood management) guidelines, anaemia in pregnancy guidelines

- **(all)Does your hospital have a Transfusion Officer/ Transfusion Clinical Nurse Consultant (CNC)?**

- PROMPT (haem): If yes, how are they involved in blood transfusion?

Intravenous iron: barriers and facilitators to use

- PROMPT (haem): Does your hospital conduct audits on blood product usage? If so, where is the data obtained from eg: medical records, Obstetrix Database, Bloodbank Information System?
- PROMPT (haem): Does your hospital have a Transfusion Committee?

Participant Demographics

- **(all)What is your job title and specialty/ area of expertise?**
- **(all)In what way are you involved with the care of maternity patients?**

Thinking about antenatal care

- **(all): Does your hospital routinely test Hb antenatally?**
 - PROMPT (obgyn/mw): Who tests it? At what gestational age?
- **(all) What is your hospital's approach to a low Hb in a pregnant woman?**
- **(all)Does your hospital routinely test ferritin antenatally?**
 - PROMPT (obgyn/mw): If not, who decides to test it? On which women? At what gestational age?
- **(all) What is your hospital's approach to a low ferritin in a pregnant woman?**
 - PROMPTS (obgyn/haem/anaes): How can iron replacement be given to patients at your hospital (setting, personnel authorising, inpatient vs outpatient; women with low SES who can't afford Fe)?
 - PROMPTS (obgyn/haem/anaes): What preparation of iron is on your formulary (oral or IV)?
 - PROMPT (all): How is iron deficiency followed up? (by whom, mechanism for follow-up)

Intravenous iron: barriers and facilitators to use

- **(all): Does your hospital routinely perform a blood group and antibody screen?**
 - PROMPT (obgyn/mw): Which women? In which situation? At what gestation?
 - **PROMPT (obgyn/haem/anaes):** Do you know how your hospital manages a woman found to have antibodies on screening?
 - PROMPT(obgyn/haem/anaes): In **planning** the delivery, is anything special done for women found to have antibodies on screening? What about any special provisions **at the delivery** itself?

- ***(all) SCENARIO: A 33 year old woman G3P2 is 28/40 gestation. She is otherwise well but had a PPH of 1000mL with her last pregnancy and required a blood transfusion. Her Hb=80 today. How would this woman usually be managed at your hospital?***

Thinking about the delivery

- **(all) Who decides whether a woman needs a blood transfusion ?**
 - PROMPT (all): During the delivery?
 - PROMPT (all): In the first 24 hours postpartum?
 - PROMPT (all): Beyond 24 hours postpartum?
- **(all): What things are important to consider when making the decision to transfuse at delivery or in the early postpartum period?**
 - Probe all eg: Timing of bleeding, volume of blood loss, anticipation of further blood loss, haemodynamic stability)

- ***(all) SCENARIO: A 28 year old woman G₁P₁, experiences 1500ml of PPH at delivery due to an atonic uterus. At 12 hours post-partum she is haemodynamically stable (ie: HR= 80, BP 120/80) and is no longer bleeding.***

Intravenous iron: barriers and facilitators to use

- *How would this woman be managed at your hospital if her Hb= 71?*
- *What Hb value is used by this hospital to transfuse all women based on the Hb alone (ie: in the absence of bleeding, unstable haemodynamics etc)?*
- *Is there the tendency at this hospital to give one or more than one unit of blood when transfusing a maternity patient?*

Thinking about postnatal care

- **(all) Is a postpartum Hb checked routinely at your hospital?**
 - PROMPT (obgyn/anaes/mw) Who is responsible for checking the postpartum Hb?
 - PROMPT (obgyn/anaes/mw): When is it checked?
 - PROMPT (obgyn/anaes/mw): Which women have it checked?
- **(all) How might a blood transfusion change the care of a woman while an inpatient at your hospital?**
 - Probe all: transfer to a less acute ward; early discharge program
- **(all) How might a blood transfusion change the care of a woman after discharge (ie: as an outpatient)?**
 - Probe all: 6 week check; GP F/U of Hb/Fe studies etc

Thinking further about decision-making

- **(all) How often are you involved with maternity patients who have had large bleeds?**
 - PROMPT (all): Have you usually transfused these women or tended to manage them without transfusion?

Intravenous iron: barriers and facilitators to use

- **(all) What are some of the pros and cons of transfusing women with a low Hb?**
 - PROMPT (all): Probe risks of infection, alloimmunisation, QOL on a new breastfeeding mother, cost, adherence to guidelines
- **(all) What sort of strategies are used in your hospital to reduce blood loss and blood transfusion requirements?**
 - PROMPT (all): Are any of these special to maternity patients?
- **(all) In what situation(s) would you consider a blood transfusion to be a 50/50 call (ie: borderline)**
 - PROMPT (all) Probe whether they have a “borderline Hb” value
 - PROMPT:(obgyn/haem/anaes) What sorts of things would help you to make your decision?
 - PROMPT:(obgyn/haem/anaes) Is there a particular thing that you consider to be most important in a borderline case?
 - PROMPT:(obgyn/haem/anaes) Do you tend to give blood or tend to avoid giving blood in these borderline situations?

(all): How often is the decision to transfuse in the postnatal setting made by one person?

How often does it involve consultation with others?

- PROMPT (obgyn/haem/anaes) If so, from whom?
- PROMPT (obgyn/haem/anaes) Who do you think should ultimately be responsible for the decision to transfuse a maternity patient? Is there a hierarchy?

Intravenous iron: barriers and facilitators to use

- PROMPT (obgyn/haem/anaes) What would happen if there was a difference of opinion about whether a maternity patient should have a transfusion?
- PROMPT (obgyn/haem/anaes) What would happen if you and the patient had a difference of opinion about their need for a transfusion?
- **(all) Are you aware of any blood transfusion educational resources used in your hospital**
 - Probe all: eg: ARCBS eLearning?
 - PROMPT (all): If yes, what do you know about these?
 - PROMPT (all): If yes, what experience have you had with them and how helpful are they in your practice?

Thinking about the appropriateness of transfusion

- **(all) Previous research has found some hospitals to be low transfusing hospitals, and some to be high transfusing hospitals (with a similar obstetric case-mix). In which category do you think your hospital falls?**
- **(all) Do you feel that sometimes blood products are given inappropriately?**
 - PROMPT (all): If yes, how often (%)?
 - PROMPT (all); If yes, under what circumstances?
 - PROMPT (all): If yes, why do you think inappropriate transfusions occur?
 - PROMPT (all) Does your hospital use any strategies to reduce the number of inappropriate transfusions? How often are these things done?

Hospital Specifics

Intravenous iron: barriers and facilitators to use

- **(all)What access to blood products do you have at your hospital?**
 - PROMPT (all): How easy is it to get blood when you need it?
- **(all)Is blood transfusion regulated in your hospital?**
 - PROMPT (all): Is yes, please describe by whom, how this works etc (eg: vetting by bloodbank staff, haematology registrar approvals)
 - PROMPT (all): Does your hospital use a 1 unit transfusion policy?
 - PROMPT (obgyn/haem/anaes): Does your hospital use patient blood management (PBM) guidelines?

And finally

- **(all) How long have you worked in this hospital?**
- **(all) How long have you been a consultant/ registrar/ midwife?**

Thank you for your time and participation in this interview.