This manuscript includes an opportunistic analysis of haemoglobin changes during pregnancy as recorded in the medical records of 600 pregnancies (to 300 women). It has not been published since it was critiqued by reviewers as not representing new information (despite a lack of Australian data) and because it included women experiencing postpartum haemorrhage. However, only half of the pregnancies were followed by a postpartum haemorrhage and a comparison of pregnancies with and without postpartum haemorrhage revealed no differences in haemoglobin profiles across pregnancy. In the absence of other Australian data on haemoglobin change during pregnancy we think it is important that these data be made available.

Haemoglobin changes during pregnancy: a retrospective cohort study of consecutive pregnancies

JANE B. FORD[1], FRANCES H. ALGERT[1], JILLIAN A. PATTERSON[1]

[1]Clinical and Population Perinatal Health Research, Kolling Institute of Medical Research, University of Sydney

Corresponding author:

Dr Jane B. FORD

Senior Research Fellow

Clinical and Population Perinatal Health Research

University of Sydney

c/- University Department of Obstetrics and Gynaecology

Building 52, Royal North Shore Hospital

St Leonards NSW 2065, Australia

Email: jane.ford@sydney.edu.au

Ph: 02 9926 6285

Fax: 02 9906 6742

Ms. Frances H. ALGERT

Student

Clinical and Population Perinatal Health Research, University of Sydney

Email: falg9356@uni.sydney.edu.au

Ms. Jillian A. PATTERSON
Biostatistician,
Clinical and Population Perinatal Health Research, University of Sydney
Email: jillian.patterson@sydney.edu.au

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ABSTRACT

Aim: Normal ranges of haemoglobin change during pregnancy and in consecutive pregnancies do not appear to have been characterised in Australia. The aim of this study was to describe haemoglobin patterns for first and second pregnancies.

Methods: Booking and antenatal haemoglobin measures were collected as part of a study investigating consecutive pregnancies for a cohort of 300 women across 11 hospitals between 2002 and 2006 in New South Wales, Australia.

Results: Booking haemoglobins were the same for first and second pregnancies. Consistent with expectations, a U-shaped distribution of haemoglobin levels by gestational age was observed with higher mean haemoglobin in early pregnancies (mean 129,~12 weeks) and in late pregnancies (mean 120, ≥37 weeks) than in mid-pregnancy (mean 118, 28-33 weeks).

Conclusions: We demonstrated a U-shaped distribution of haemoglobin levels by gestational age across pregnancies. Booking haemoglobins were consistent in first and second pregnancies. These results demonstrate similar patterns of haemoglobin levels by gestational age to those reported in other countries, however we report lower mean haemoglobin at the end of pregnancy than some studies.

Keywords: Haemoglobin; haemoglobin change; pregnancy; consecutive pregnancies; Australia.

INTRODUCTION

The World Health Organization (WHO) defines anaemia in pregnancy as haemoglobin values <110 g/L[1] and the Centers for Disease Control and Prevention (CDC) as a haemoglobin level <110 g/L during the first and third trimesters and <105 g/L during the second trimester[2]. Both low and high haemoglobin levels have been reported to be associated with adverse neonatal outcomes[3-5]. It has been acknowledged that haemoglobin status can be affected by multiple factors including altitude, fetus size, number of fetuses, athletic training and prolonged bed rest and is therefore likely to vary across populations[6].

Australian studies of haemoglobin in pregnancy report mean booking haemoglobins between 122 and 126 g/L[7, 8], although these have been single hospital studies. Based on normal pregnancy haemoglobin values reported in other settings, there is likely to be a drop in haemoglobin in the early part of the first trimester, declining to a low near the end of second trimester, followed by a gradual rise during third trimester[2]. However, normal ranges of haemoglobin change during pregnancy in Australia do not appear to have been characterised.

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists recommend all women have their haemoglobin level checked at the first antenatal visit and again at approximately 28 weeks' gestation. While it is recommended that any anaemia be investigated and treated, routine iron supplementation is not recommended for every pregnancy[9]. Given the potential importance of pre-delivery iron status for helping women cope with blood loss

associated with childbirth, it is important to understand normal ranges of haemoglobin in the Australian pregnant population.

The aim of this study was to describe haemoglobin patterns during first and second consecutive pregnancies.

METHODS

The study population included women giving birth between January 2002 and December 2006 to at least two babies (first and second) in a single Area Health Service in New South Wales (NSW) and who experienced a postpartum haemorrhage (PPH) at either birth as identified in hospital discharge data. These data were collected as part of a broader study investigating the validity of postpartum haemorrhage reporting.

Data were obtained from two sources: (1) abstracted from the medical records of 300 randomly selected women ('abstracted data'), and matched population data for these women from the (2) NSW Perinatal Data Collection ('birth data'). Five trained abstractors visited each of 11 hospitals to abstract data onto a standard data abstraction form. Training was conducted on 5% of records and involved abstraction by two people and comparison of abstracted data. Inter-observer agreement was ≥96% for the 39 data items. Booking haemoglobin (Hb) and the last antenatal Hb (and the gestational age at collection) were abstracted, where available, from pathology reports included in the medical records. Although gestational age at booking was not recorded, this is usually conducted at 12 weeks gestation. Last antenatal haemoglobin was collected since the broader study was focussed on postpartum haemorrhage. Birth data were used for

additional information on all births including maternal demographic and pregnancy factors, labour and delivery outcomes. Postpartum haemorrhage was defined according to the Australian Coding Standards[10].

T-tests and paired t-tests were used to compare differences between pregnancies and during pregnancy with statistical significance reported at the p <0.0.5 (two-tailed) level. Chi-square tests were used to measure association between categorical variables. Mean haemoglobin levels at each gestational age were compared with those reported by the World Health Organisation[2]. Mean haemoglobin levels were only reported for gestational ages where > 3 Hb measures were available.

Ethics approval for data linkage and sampling was granted by the NSW Population and Health Services Research Ethics Committee (REC). Ethics approval for the study was granted by the Northern Sydney Central Coast Area Health Service Human REC for public hospitals and individual ethics committees (private hospitals).

RESULTS

Of the 600 birth records, 588 records representing both pregnancies for 294 women were available for analysis. Complete records were not available for five women and abstracted data for another woman were for second and third births. Births occurred across 7 public hospitals and 4 private hospitals. The majority of births were singleton births (98.3%) in public hospitals (81.3%). (Table 1).

Booking haemoglobin was available for 546 pregnancies (92.9%) and antenatal Hb for 531 (90.3%) pregnancies. Both booking and antenatal Hb were available for 502 (85.4%) pregnancies.

The mean booking haemoglobin for first and second pregnancies was 129 g/L. Mean antenatal haemoglobin was 118 and 117 for first and second pregnancies respectively. The average decrease in Hb between booking and antenatal measurement was 11 g/L for first pregnancies (P<.0001) and over both pregnancies, and 12 g/L (P<.0001) for second pregnancies. Where there was a short inter-pregnancy interval (<=1 year), second pregnancy mean booking haemoglobins were lower (124 versus 129 g/L).

A plot of haemoglobin levels as measured across differing gestational ages during pregnancies shows a mid pregnancy nadir following booking – with higher readings at earlier and later gestational ages, and the lowest average seen at 25 weeks (Figure 1). Comparison with WHO reported means by gestational age illustrates slightly higher booking haemoglobin values in our study and lower readings near term, although confidence intervals are overlapping. When mean haemoglobin patterns for pregnancies with and without postpartum haemorrhage were compared, the same shape of plotted trend lines was evident (not shown).

Haemoglobin measures impacted by postpartum haemorrhage outcome?

Given that the study population over-represented pregnancies with a PPH following birth (54.8% of the births studied), haemoglobin measures for pregnancies

with and without a postpartum haemorrhage outcome were compared. Booking and antenatal haemoglobins were no different for pregnancies with or without a postpartum haemorrhage outcome. PPH pregnancies showed the same decline (as non-PPH pregnancies) between booking and antenatal Hb measurements (11 g/L).. Women with low haemoglobin at booking or antenatally (<110 g/L) were not at significantly increased risk of postpartum haemorrhage following pregnancy (P=0.56).

DISCUSSION

Our study found that haemoglobin measures changed during pregnancy – with higher readings at the lower and higher gestational ages. Mean booking haemoglobin was the same for first and second pregnancies, with similar decreases in haemoglobin during pregnancy evident for respective pregnancies (12 vs 11 g/L).

We could not identify other studies that have compared haemoglobin measures for consecutive pregnancies for the same women. One could expect lower haemoglobin levels in subsequent pregnancies given the blood loss associated with any delivery and the physical demands of looking after a young baby. Importantly, we showed no difference in booking haemoglobin in subsequent pregnancies. Among women with a short inter-pregnancy birth interval the mean booking haemoglobin in a second pregnancy was slightly lower (124 versus 129 g/L) however still within the normal range.

We report a U-shaped curve of haemoglobin levels across gestational age weeks of pregnancy, with higher mean haemoglobin in early pregnancies (mean 129, ~12

weeks) and in late pregnancies (mean 120 at ≥37 weeks) than in mid-pregnancy (mean 118 at 28-33 weeks). These are comparable with the overall pattern of mean haemoglobin reported in pregnancy in other studies[1].

The reported mean haemoglobins after 35 weeks gestation were lower than those reported by the World Health Organisation[1] which are based on aggregated data from four European studies of healthy iron-supplemented pregnant women[2]. We hypothesised that lower rates closer to term may be due to the over-representation of pregnancies complicated by postpartum haemorrhage in our study population. However, when we contrasted the patterns of antenatal haemoglobin among pregnancies that did and did not result in postpartum haemorrhage there were no differences in the pattern of haemoglobin readings across pregnancy. Comparisons of haemoglobin patterns across pregnancy with those of another study involving random allocation of iron supplementation and no supplementation suggest the differences in the WHO and our study patterns could potentially be due to differences in iron supplementation across the two populations[11]. A Cochrane Review investigating effect of iron supplementation on maternal haemoglobin at term found mean haemoglobin in untreated women in 17 trials ranging from 113-139, with all but one study mean being above 121; among iron-supplemented women, mean haemoglobin ranged from 97 to 132[12]. A recent study in a similar Australian birthing population near term found 52% were taking iron supplements[13]. Alternatively, other population characteristics or features of pregnancy management may explain the slightly lower haemoglobins reported in our study near term gestation.

The mean *booking* haemoglobins reported in our study (129 g/L) were consistent with those reported in other settings, both in Australia (122-126 g/L[7, 8]) and overseas (122[1] -123[14]). Overall there was no difference in mean booking haemoglobin for first and second pregnancies nor in the proportion of women with anaemia at booking at each pregnancy. This is surprising, given the high proportion of first pregnancies in our study that were complicated by postpartum haemorrhage (55% compared to population rates of around 11%)[15]. We might have expected a lower booking haemoglobin in pregnancies subsequent to those involving a postpartum haemorrhage. However, we did not have any information on subsequent treatment of women experiencing a PPH (apart from transfusion which occurred following 6% of pregnancies).

Our results show a lower mean *antenatal* haemoglobin reading for women giving birth preterm (117 g/L) compared to term (120 g/L), although confidence intervals overlap (see Figure 1). In Australia, as in many other developed world contexts, there are increases in preterm deliveries (especially iatrogenic preterm deliveries) as well as obstetric transfusions[16, 17]. It is important that gestational age of measurement is taken into account when haemoglobin levels are checked and interventions considered.

There are a number of limitations to this study. Firstly, the study collected information on the last recorded measurement of antenatal haemoglobin. Ideally haemoglobin change would be measured at pre-specified timepoints during individual women's pregnancies rather than using booking haemoglobin and last recorded antenatal haemoglobin. This also means that the distribution of haemoglobin readings

for all pregnancies is biased towards later weeks, with few measures per week before 25 weeks gestation. Secondly, we have no information available on treatment for low haemoglobin during pregnancy or post-pregnancy. Although information on transfusion post-pregnancy was available there were too few women to conduct sub-analyses. No information on iron supplementation during or between pregnancies was collected. While this study utilised an opportunistic sample of pregnancy records which included an excess of pregnancies complicated by PPH, sensitivity analyses identified no difference in the pattern of haemoglobin readings throughout pregnancy for PPH and non-PPH pregnancies.

We demonstrated a U-shaped distribution of haemoglobin levels by gestational age in pregnancies. Booking haemoglobins were consistent in first and second pregnancies. These results demonstrate similar patterns of haemoglobin levels over pregnancy to those reported in other countries, however we report lower mean haemoglobin at the end of pregnancy than some studies.

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DISCLOSURE

The authors have no competing interests to declare.

AUTHORS' CONTRIBUTIONS

JF designed the study, JF, FA and JP conducted the analyses and wrote the manuscript, JF, FA and JP contributed to interpretation of analyses and writing the manuscript. All authors approved the final manuscript.

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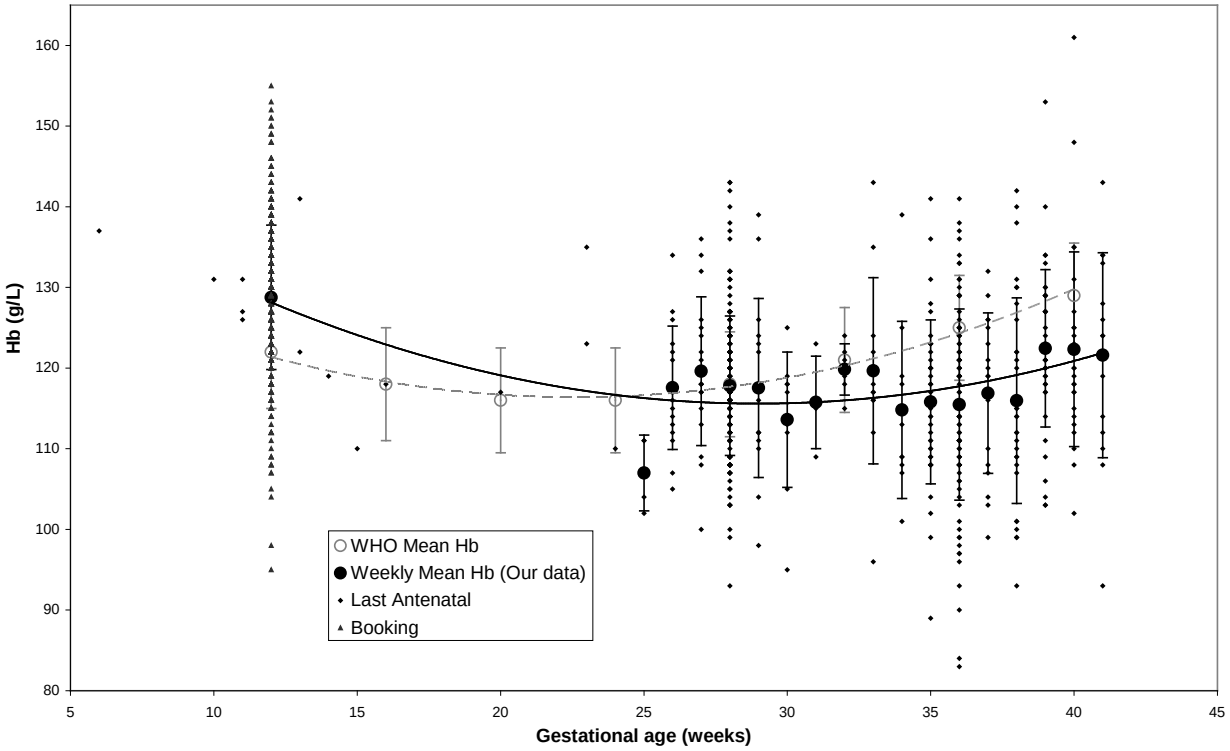
Table 1 Maternal characteristics of first and second pregnancies, 2002-2006

Maternal Characteristics	***First pregnancy*** N=294 N (%)*	***Second pregnancy*** N=294 N (%)*
Age (yrs)		
<19	10 (3.4)	2 (0.7)
20-24	46 (15.7)	31 (10.5)
25-34	202 (68.7)	186 (63.3)
35+	36 (12.2)	75 (25.5)
BMI		
Mean (SD)	23.36 (4.24)	24.03 (4.35)
Median (IQR)	23.0 (4.6)	23.4 (5.2)
Anaemia at booking (<110g/L)	29 (9.9)	25 (8.5)
Birth Hospital		
Public	240 (81.6)	238 (81.0)
Private	54 (18.4)	56 (19.1)
Gestational age at birth		
20-31 wks	3 (1.0)	6 (2.0)
32-36 wks	13 (4.4)	13 (4.0)
≥37 wks	278 (94.6)	275 (93.5)
Birthweight (g)		
<1500	2 (0.7)	4 (1.4)
1500-2499	13 (4.4)	9 (3.1)
2500-3499	126 (42.9)	115 (39.1)
>=3500	153 (52.0)	166 (56.5)
Mode of delivery		
Vaginal	153 (52.0)	181 (61.6)
Instrumental	66 (22.5)	19 (6.5)
Caesarean with labour	60 (20.4)	21 (7.1)
Caesarean, no labour	11 (3.7)	69 (23.5)
Postpartum haemorrhage	169 (57.5)	153 (52.0)
Transfusion	14 (4.8)	19 (6.5)

* Numbers in brackets are column percentages unless otherwise specified; SD = standard deviation; IQR=Interquartile range.

Figure 1 Weekly mean antenatal haemoglobin by gestational age in our study population compared to WHO reported means



Sources: Abstracted data from the current study and World Health Organisation gestation-related changes in haemoglobin; Error bars represent +/- 1 standard deviation