Maternal Anaemia in Pregnancy: A Significantly Greater Risk Factor for Anaemia in Australian Aboriginal Children than Low Birth Weight or Prematurity

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Abstract

Objectives To identify maternal and perinatal risk factors associated with childhood anaemia.

Methods A retrospective cohort study was conducted in three remote Katherine East Aboriginal communities in Northern Territory, Australia. Children born 2004–2014 in Community A and 2010–2014 in Community B and C, and their respective mothers were recruited into the study. Maternal and child data were linked to provide a longitudinal view of each child for the first 1000 days from conception to 2-years of age. Descriptive analyses were used to calculate mean maternal age, and proportions were used to describe other antenatal and perinatal characteristics of the mother/child dyads. The main outcome was the prevalence of maternal anaemia in pregnancy and risk factors associated with childhood anaemia at age 6 months.

Results Prevalence of maternal anaemia in pregnancy was higher in the third trimester (62%) compared to the first (46%) and second trimesters (48%). There was a strong positive linear association ($R^2 = 0.46$, $p < 0.001$) between maternal haemoglobin (Hb) in third trimester pregnancy and child Hb at age 6 months. Maternal anaemia in pregnancy (OR 4.42 95% CI 2.08–9.36) and low birth weight (LBW, OR 2.62, 95% CI 1.21–5.70) were associated with an increased risk of childhood anaemia at 6 months of age.

Conclusions for Practice This is the first study to identify the association of maternal anaemia with childhood anaemia in the Australian Aboriginal population. A review of current policies and practices for anaemia screening, prevention and treatment during pregnancy and early childhood would be beneficial to both mother and child. Our findings indicate that administering prophylactic iron supplementation only to children who are born LBW or premature would be of greater benefit if expanded to include children born to anaemic mothers.

Keywords Anaemia · Maternal and child health · Australian aboriginal

Significance

What is already known? Maternal anaemia in pregnancy has considerable adverse outcomes for both mother and infant. Iron supplementation is effective in preventing anaemia but is not recommended as a routine supplement for Australian Aboriginal women and their children where the incidence and prevalence of anaemia is considerably higher than other Australians.

What this study adds? Maternal anaemia in pregnancy is a greater risk factor for infant anaemia than being born premature or low birth weight. The inclusion of maternal anaemia in pregnancy as a risk factor for infant anaemia in addition to premature and low birth weight infants would be benefit more children if included in the best practice guideline

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recommendations for iron supplementation at 1-month of age.

Introduction

The prevalence of anaemia in pregnant women (Bar-Zeev et al. 2014) and in children (Northern Territory Government Department of Health 2015) remains unacceptably high in remote Northern Territory (NT) Aboriginal communities despite prevention strategies that have been in place for nearly a decade (Central Australian Remote Practitioners Association 2014; Central Australian Rural Practitioners Association 2003; Central Australian Rural Practitioners Association Editorial Committee 2009). Children in these communities are unique within the broader Australian population, with a greater exposure to infection (Currie and Brewster 2001) and higher rates of undernutrition underpinned by economic and social disadvantage (Brimblecombe et al. 2013).

Surveillance data from 2015 reported 17% prevalence of anaemia in children aged under 5 years, with the highest prevalence of 34% in children aged 12–17 months (Northern Territory Government Department of Health 2015). Recently published data from six remote communities across Northern Australia identified that 42% of children had an anaemic episode in the first 2 years of life (Aquino et al. 2018). Identification of the cause of anaemia is not routinely conducted in children as it was previously assumed that all anaemia was iron deficiency (Remote Primary Health Care Manuals 2017a).

No studies have identified risk factors for the development of childhood anaemia in remote Aboriginal communities (Khambalia et al. 2011). Local best practice guidelines, Central Australian Rural Practitioners Association standard treatment manual (CARPA STM), used by all NT practitioners, acknowledge the role of prematurity and low birth weight (LBW) as risk factors for the development of anaemia and recommend routine iron supplementation from 1 month of age (Remote Primary Health Care Manuals 2017a, b).

A growing body of evidence from international literature that suggests maternal anaemia in pregnancy is an independent risk factor for infant anaemia and iron deficiency (Colomer et al. 1990; de Pee et al. 2002; Kilbride et al. 1999; Meinzen-Derr et al. 2006; Nair et al. 2016). The increased risk of developing anaemia is detectable as early as 3–5 months of age (de Pee et al. 2002) and may persist up to 56 months (Nair et al. 2016). Exclusive breastfeeding without iron supplementation or early introduction of iron rich weaning foods appears to exacerbate the risk of iron deficiency anaemia (IDA; Meinzen-Derr et al. 2006).

Although limited by a lack of reliable data, there is a high prevalence of maternal anaemia in pregnancy in remote communities in the NT with estimates between 14 and 50% (Bar-Zeev et al. 2014; Rumbold et al. 2011). Maternal anaemia may represent an important and under recognised risk factor for the development of childhood anaemia. If maternal anaemia in pregnancy is proven to be a risk factor, early identification and treatment may provide an upstream point of intervention in the prevention of childhood anaemia.

This study aims to identify maternal and perinatal risk factors associated with childhood anaemia to identify children who are at increased risk. Identification of children at risk will enable more effective targeted strategies of prevention and early intervention. Linking maternal and child data provided a longitudinal view of each child for the first 1000 days from conception to 2 years of age.

Methods

Study Setting

This study was part of the Sunrise Anaemia Project, a broader investigation of a childhood anaemia program in remote communities in Katherine East region, NT. The project was instigated by Sunrise Health Service, an Aboriginal community-controlled health organisation, who consented to be identified. Three communities were included: A, B and C, with populations ranging from ~300 to 1000 and with ~260 births during the study period (data from communications with Sunrise Health Data Integrity Officer).

Katherine region is located in the tropical region of Australia (23.5° South) that has a wet (October–March) and dry (April–September) season. All three communities are accessible by road in the dry season but during the wet season two of the communities are often only accessible by air (Sunrise Health Service Aboriginal Corporation 2019). Health care is provided by Remote Area Nurses and/or Midwives (RAN/Ms), Aboriginal Health Practitioners (AHPs), visiting Medical Officers and Allied Health Professionals.

Study Design and Participants

A retrospective cohort study design was used to identify risk factors associated with childhood anaemia at different ages, with the primary outcome being at age 6 months. Children enrolled were born between 1 January 2004 and 31 December 2014 in Community A and 1 January 2010 to 31 December 2014 in Community B and C, along with their respective mothers. Recruitment of participants was conducted by Aboriginal Community Based Researchers going house to house in each community. Each child's primary healthcare (PHC) presentations for the first 2 years of life and maternal antenatal records that were associated with that child were extracted from the electronic health record system

(Communicare). The Communicare data was exported as a CSV file and imported to StataCorp14.1 (StataCorp, College Station, Texas) for cleaning, linkage and analysis. Clinical notes and pathology results were manually reviewed to identify and include missing data that was not included in the initial electronic data extraction.

Ethics

Ethics approval was attained through Human Research Ethics Committee of Northern Territory Department of Health and Menzies School of Health Research (EC00153), Reference Number 2015-2525. Written informed consent was obtained from all participants or their responsible adult guardian.

Data Collection

Maternal antenatal data extracted from the electronic health records included: date of visit, age, parity, haemoglobin (Hb), iron treatment (oral or parenteral), laboratory (full blood count and iron studies) and ultrasound results. Data was not available for maternal diet during pregnancy or smoking history. Hb was measured in communities by point of care testing using capillary blood in a HemoCue machine, or from a venous blood sample sent to a diagnostic laboratory for full blood count and/or iron studies. HemoCue testing has been validated as a suitable instrument for anaemia screening with a mean Hb difference of 0.8 g/L compared to the commonly used laboratory methods (Hiscock et al. 2015).

Child data collected included: sex, birth weight and gestational age at birth, date of child health check visit, Hb measured by HemoCue, full blood count or iron studies. Scheduled health checks at 6, 12, 18 and 24 months for measurement of Hb included results conducted either 2 months prior or post the age scheduled check.

Outcome and risk factor parameters were identified from local best practice guidelines: CARPA STM (Remote Primary Health Care Manuals 2017a, b) and Women's Business Manual (WBM) (Remote Primary Health Care Manuals 2017a, b) (Table 1).

Case Definitions

IDA was determined from a full blood count that was microcytic (mean corpuscular volume < 75 fL) and hypochromic (mean corpuscular Hb concentration < 310 g/L). If iron studies were performed, IDA was diagnosed if ferritin was < 12 μg/L in children and < 30 μg/L in pregnant women.

Iron treatment was defined as: evidence of oral or parenteral iron in the prescriptions variable or documentation

Table 1 Variables definitions

Risk factors	
Maternal anaemia	Hb < 110 g/L
Premature	Born before 37 completed weeks gestation
Low birth weight	Birth weight < 2.5 kg
Outcomes	
Childhood anaemia	Hb < 105 g/L if aged 6–11 months
Severe anaemia	Hb < 110 g/L if aged 1–2 years
	Hb < 90 g/L

of iron administered in the progress notes of the extracted Communicare data.

Data Analysis

Data from the three communities were pooled as baseline characteristics were homogenous throughout. Descriptive analyses were used to calculate mean maternal age, and proportions were used to describe other antenatal and perinatal characteristics of the mother/child dyads. Pregnancy trimesters were categorised into first (≤ 12 weeks gestation), second (13–27 weeks) and third (≥ 28 weeks). A scatterplot was used to test the linear relationship between maternal Hb g/L in the third trimester of pregnancy and infant Hb g/L at age 6 months. $R^2 > 0.4$ was considered a strong association (Hamilton et al. 2015). Anaemic mothers were stratified into two groups based on whether they had received iron treatment during the third trimester of pregnancy. Univariate logistic regression analysis was used to determine any association between childhood anaemia at each age and maternal anaemia in pregnancy, LBW and prematurity. Outcomes were defined as anaemia at 6, 12, 18 and 24 months. A p-value < 0.05 was used as a threshold for statistical significance for all tests.

Results

One hundred and ninety-six mother/child dyads were recruited across the three communities. One-hundred and seventy were included for analysis after excluding 22 children born outside of the study period and 4 not usually residing in 1 of the 3 communities. There were 75 (44%) male and 95 (56%) female children records linked to maternal antenatal records that represented 65% of births during the study period.

The mean maternal age during pregnancy was 23.6 years with almost two thirds (n = 107, 63%) of women having two or more children (Table 2). All women had singleton pregnancies of which 42 (25%) were LBW and 35 (21%) were premature.

Table 2 Antenatal and perinatal characteristics of the mother/child dyads by community

Community	A n=66 (%)	B n=66 (%)	C n=38 (%)	Total n=170
Mean maternal age	23.9±4.7	23.4±3.9	24.1±5.5	23.6±4.1
Parity				
1	23 (34)	25 (38)	15 (39)	63 (37)
2	18 (27)	20 (30)	17 (45)	55 (32)
3	19 (29)	12 (18)	5 (13)	36 (21)
≥4	6 (9)	9 (14)	1 (3)	16 (9)
Antenatal visits				
0–3	11 (17)	12 (18)	7 (18)	30 (18)
≥4	55 (83)	54 (82)	31 (82)	140 (82)
Birth details				
Term and ≥2.5 kg	49 (74)	44 (67)	25 (66)	118 (69)
Low birth weight (<2.5 kg)	14 (21)	19 (29)	9 (24)	42 (25)
Premature (<37 weeks)	10 (15)	13 (20)	12 (32)	35 (21)

Table 3 Maternal anaemia screening, prevalence and iron treatment by trimester

	Total n=170 (%)
1st trimester	
Hb measured	70 (41)
Anaemic	32 (46)
2nd trimester	
Hb measured	50 (29)
Anaemic	24 (48)
3rd trimester	
Hb measured	170 (100)
naemic	105 (62)
Iron treatment 3rd trimester	46 (44)

Table 4 Childhood anaemia screening and prevalence by age

	Total n=170 (%)
6 months	
Hb measured	146 (86)
Anaemia	69 (47)
Severe anaemia	26 (18)
12 months	
Hb measured	150 (88)
Anaemia	75 (50)
Severe anaemia	17 (11)
18 months	
Hb measured	158 (93)
Anaemia	61 (40)
Severe anaemia	8 (5)
24 months	
Hb measured	153 (90)
Anaemia	61 (40)
Severe anaemia	6 (4)

Anaemia screening was documented in all 170 pregnancies in the third trimester but occurred less frequently in the first (n=70, 41%) and second trimesters (n=50, 29%) (Table 3). Taking into consideration the delayed presentation to antenatal care, 119 (70%) women were screened for anaemia at their first visit.

Almost half of the women tested in the first (n=32, 46%) and second (n=24, 48%) trimester of pregnancy were anaemic, this increased in the third trimester (n=105, 62%) when all women were tested. Of the 105 women with anaemia in third trimester, 95 (90%) had IDA however, iron treatment was recorded in the electronic health records in less than half of the anaemic mothers in the third trimester (n=46, 44%). There was no iron supplementation recorded for women who were not anaemic.

Childhood anaemia screening was high, with more than 146 (86%) children tested at each age scheduled health check (Table 4). The prevalence of anaemia was considerable across all age groups with 69 (47%) children diagnosed at 6 months of age, 75 (50%) at 12 months, 73 (46%) at

18 months and 61 (40%) at 24 months. The prevalence of severe anaemia was higher in those aged 6 months when compared with other ages.

A full blood count was recorded for 11 children, of which 7 results (63%) identified anaemia. All were hypochromic and microcytic anaemia, suggestive of iron deficiency which was confirmed in four cases with iron studies.

There was a strong positive linear association ($R^2 = 0.46$, $p < 0.001$) between maternal Hb in third trimester pregnancy and child Hb at age 6 months (Fig. 1). For each 1 g/L change in maternal Hb there was a 0.6 g/L (95% CI 0.52–0.76) change in infant Hb. The odds of a child developing anaemia (OR 4.42, 95% CI 2.08–9.36) at age 6 months was four folds greater if their mother had anaemia in the third trimester of pregnancy compared
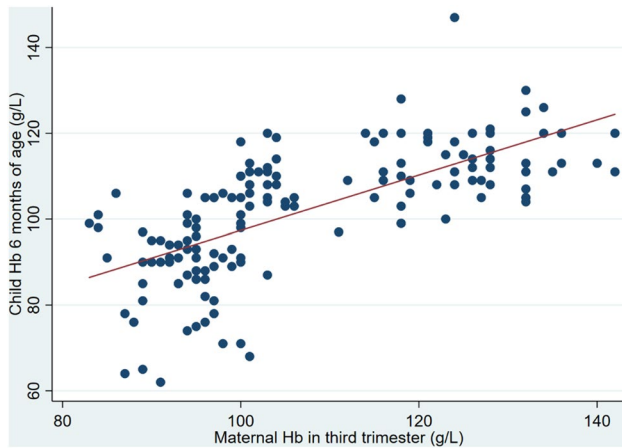
Fig. 1 The association of maternal haemoglobin in third trimester of pregnancy on child haemoglobin at age 6 months

with those born to non-anaemic mothers (Table 5). The odds substantially increased if maternal anaemia in third trimester was not treated (OR 6.17, 95% CI 2.62–14.51) however, even with treatment the likelihood of developing anaemia was still significant (OR 3.00 95% CI 1.25–7.17).

Maternal anaemia in pregnancy was also associated with an increased odds of childhood anaemia at age 12 months (OR 2.04, 95% CI 1.03–4.06) and 24 months (OR 2.08, 95% CI 1.04–4.16) but did not reach significance at 18 months (OR 1.5, 95% CI 0.78–2.88). LBW (OR 2.62, 95% CI 1.21–5.70) was associated with childhood anaemia at age 6 months. The association between prematurity (OR 1.87, 95% CI 0.84–4.15) and anaemia at 6 months did not reach statistical significance.

Discussion

The prevalence of maternal anaemia in pregnancy (62%) in these communities was alarmingly high and not dissimilar to that reported previously (50%) in two large Top End NT communities (Bar-Zeev et al. 2014). Maternal anaemia in pregnancy is not routinely reported in the NT Mothers and Babies Report (Hall et al. 2015) or as a key performance indicator to monitor how well health services are performing for their clients. Further studies or improved data collections would be beneficial to establish how widespread maternal anaemia in pregnancy is in rural and remote Australian Aboriginal communities and to ascertain the immediate and long term impact of adverse outcomes on maternal and infant health.

No previous studies have identified the trimester specific prevalence of anaemia among pregnant Australian Aboriginal women. The higher third trimester prevalence in this study may be partially explained by the physiological changes in pregnancy where increased plasma volume leads to lower Hb concentration (Churchill et al. 2019) however, a drop in MCV below normal reference ranges was noted in 84% (n = 34) of women who were not anaemic in first trimester, but became anaemic in third trimester, suggestive of depletion of iron stores. The WBM 6th edition (Remote Primary Health Care Manuals 2017a, b) identifies that a fall in MCV is the earliest sign of ID however, it does not recommend using this as an indicator for commencing iron supplementation as has been shown in other recent studies (Rabindrakumar et al. 2018).

Maternal anaemia was predominantly IDA (90%) which is recognised as the most common aetiology in pregnancy (Kassebaum 2016). The determination of IDA in this study however, was limited by a very small number of iron studies

Table 5 Association between risk factors and childhood anaemia at age 6 months					
Childhood anaemia	Yes n = 69 (%)	No n = 77 (%)	Odds ratio	95% CI	p-value
Risk factors					
Maternal anaemia 3rd trimester					
No	13 (25)	39 (75)	1.00		
Yes	56 (60)	38 (40)	4.42	2.08–9.36	< 0.001
Untreated	35 (67)	17 (33)	6.17	2.62–14.51	< 0.001
Treated	21 (50)	21 (50)	3.00	1.25–7.17	0.01
Low birth weight					
No	45 (41)	64 (59)	1.00		
Yes	24 (65)	13 (35)	2.62	1.21–5.70	0.02
Premature birth					
No	50 (44)	64 (56)	1.00		
Yes	19 (59)	13 (41)	1.87	0.84–4.15	0.07

(n = 10) performed and relied on the FBC results of a low Hb with microcytic and hypochromic cells. The recommendation for routine iron studies at the first visit and at 28 weeks gestation in the revised WBM 6th edition is a valuable addition (Remote Primary Health Care Manuals 2017b). An assessment of iron status will not only be of clinical use for individual women in guiding anaemia prevention and treatment but will provide a more accurate insight into the true contribution of IDA in this population.

The high prevalence of IDA raises the argument for routine iron supplementation in pregnancy as advocated by WHO in areas with prevalence > 40% (World Health Organization 2016). Iron supplementation was a recommendation for all pregnant women in the WBMs (Congress Alukura and Nganampa Health Council Inc 2008) up until 2014 when conflicting information was printed in the accompanying reference document (Manuals 2014b). Despite the acknowledgement of high anaemia prevalence in Australian Aboriginal women in pregnancy at that time, iron supplementation was not recommended for women who were not anaemic (Manuals 2014a).

The positive effects of iron supplementation at delivery and post-partum do not definitively result in improved maternal and neonatal outcomes except for reducing maternal puerperal infections and preterm births (World Health Organization 2016). In this study iron supplementation during pregnancy partially mitigated the effect of maternal anaemia on increased risk of childhood anaemia however iron treatment was only included for the third trimester due to small numbers of treatment recorded in first and second trimesters. Maternal Hb measurements were not adjusted for smoking status in this study due to limited data in electronic health records and may have contributed to an underestimation of anaemia due to falsely elevated Hb in smokers (Malenica et al. 2017).

Screening for childhood anaemia was high (> 86%) at each age scheduled health check and compared favourably to the 80% coverage reported across all remote PHCs (Northern Territory Government Department of Health 2015). Prevalence of anaemia across all age groups (40–50%) was comparable to that reported in other remote communities across Northern Australia (Northern Territory Government Department of Health 2015). The assessment of anaemia aetiology in children was limited due to the very small number of FBCs and iron studies performed however, all FBCs and iron studies from anaemic children indicated IDA.

Children in this age group are further at risk of IDA when they are usually exclusively breastfed, particularly if prolonged before weaning foods are introduced (Remote Primary Health Care Manuals 2017a). The recommendation of routine iron supplementation for all exclusively breastfed babies from four months of age in the revised 7th edition CARPA STM was introduced to ameliorate this risk alongside maternal education and availability of iron-rich weaning foods (Remote Primary Health Care Manuals 2017a). However, the timing and dosage recommended by the guidelines were not evidenced based and not supported by NT health practitioners.

Maternal anaemia in the third trimester was the most significant perinatal risk factor associated with the development of childhood anaemia at age 6 months. This finding emulates evidence from international literature that is applicable in the remote Aboriginal context (Colomer et al. 1990; de Pee et al. 2002; Kilbride et al. 1999; Meinzen-Derr et al. 2006; Nair et al. 2016). The association with anaemia in the first 6 months of life is consistent with the findings of De Pee et al. in suggesting that Hb and iron stores in young infants are dependent on maternal factors (de Pee et al. 2002). The increased risk of anaemia was observed to persist beyond 6 months of age with a statistically significant association at 12 and 24 months. This supports the results of Nair et al. who reported the effect of maternal anaemia on childhood anaemia up to 56 months (Nair et al. 2016).

LBW was associated with an increased risk of childhood anaemia at 6 months of age and there was a trend towards an association with prematurity. The accuracy of gestational age at birth was limited with few first trimester dating ultrasounds performed (n = 60, 35%) and more than one fifth (n = 35, 21%) of antenatal records having no last menstrual period. The findings of this study did not take into account other potential contributors to childhood anaemia, including maternal smoking, diabetes in pregnancy, diet, other micronutrient deficiencies or infection which may have confounded results.

Conclusion

The evidence that maternal anaemia in pregnancy was the most significant risk factor for childhood anaemia has public health implications for reviewing practice and policy guidelines. A renewed focus should be placed on implementing and reporting anaemia screening, prevention and treatment in pregnancy. Current policy and best practice guidelines for children focus exclusively on LBW and infants born premature in their identification of infants at risk. Our study indicates that the current practice of administering prophylactic iron supplementation only to children who are born LBW or premature would be of greater benefit if expanded to include children born to anaemic mothers.

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