Maternal Anaemia in Pregnancy

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

Hansen, Martin; Singh, Gurmeet; Barzi, Federica; Brunette, Raelene; Howarth, Timothy; Morris, Peter; Andrews, Ross; Kearns, Therese

Published in:
Maternal and Child Health Journal

DOI:
10.1007/s10995-020-02913-7

Published: 01/08/2020

Document Version
Peer reviewed version

Maternal anaemia in pregnancy: a significantly greater risk factor for anaemia in Australian Aboriginal children than low birth weight or prematurity.

Martin Hansen,[1] Gurmeet Singh,[1,2] Federica Barzi,[2] Raelene Brunette,[3] Timothy Howarth,[2] Peter Morris,[1,2] Ross Andrews,[2] Therese Kearns.[2]

1. Royal Darwin Hospital, Darwin, Northern Territory, Australia
2. Menzies School of Health Research, Charles Darwin University, Darwin, Northern Territory, Australia
3. Sunrise Health Service Aboriginal Corporation, Katherine, Northern Territory, Australia

Corresponding author – Therese Kearns, email: therese.kearns@menzies.edu.au

Introduction

The prevalence of anaemia in pregnant women [1] and in children [2] remains unacceptably high in remote Northern Territory (NT) Aboriginal communities despite prevention strategies that have been in place for nearly a decade [3-5]. Children in these communities are unique within the broader Australian population, with a greater exposure to infection [6] and higher rates of undernutrition underpinned by economic and social disadvantage [7].

Surveillance data from 2015 reported 17% prevalence of anaemia in children aged under five years, with the highest prevalence of 34% in children aged 12-17 months [2]. Recently published data from six remote communities across Northern Australia identified that 42% of children had an anaemic episode in the first two years of life [8]. Identification of the cause of anaemia is not routinely conducted in children as it was previously assumed that all anaemia was iron deficiency (9).

No studies have identified risk factors for the development of childhood anaemia in remote Aboriginal communities (10). Local best practice guidelines, Central Australian Rural Practitioners Association standard treatment manual (CARPA STM), acknowledge the role of prematurity and low birth weight (LBW) as risk factors for the development of anaemia and recommend routine iron supplementation from one month of age [9].

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 [10-14]. The

increased risk of developing anaemia is detectable as early as 3-5 months of age [11] and may persist up to 56 months [14]. Exclusive breastfeeding without iron supplementation or early introduction of iron rich weaning foods appears to exacerbate the risk of iron deficiency anaemia (IDA) [12].

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 14-50% [1, 15]. 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 two 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 ~300-1000 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 (23.5^0 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 [16]. 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 report on the outcome of anaemia at different ages. Children enrolled were born between 1 January 2004 and 31 December2014 in Community A and 1 January 2010 to 31 December2014 in Community B and C, along with their respective mothers. Each child's primary healthcare (PHC) presentations for the first

two 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 [17].

Child data collected included: sex, birthweight 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 six, 12, 18 and 24 months for measurement of Hb included results conducted either two months prior or post the age scheduled check.

Outcome and risk factor parameters were identified from local best practice guidelines: CARPA STM [9] and Women's Business Manual (WBM) [18] (Table 1).

Table 1. Variables definitions

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

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

Iron treatment was defined as: evidence of oral or parenteral iron in the prescriptions variable or documentation 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-squared >0.4 was considered a strong association [19]. 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 six, 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 four not usually residing in one of the three 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 (<2.5kg)	14 (21)	19 (29)	9 (24)	42 (25)
Premature (<37 weeks)	10 (15)	13 (20)	12 (32)	35 (21)

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 iron deficiency anaemia 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%).

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

	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)
Anaemic	105 (62)
Iron treatment 3rd trimester	46 (44)

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 six 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 six months when compared with other ages.

Table 4. Childhood anaemia screening and prevalence by age.

	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)

A full blood count was recorded for 11 children, of which seven 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-square=0.46, $p<0.001$) between maternal Hb in third trimester pregnancy and child Hb at age 6-months (Figure 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 six months was four folds greater if their mother had anaemia in the third trimester of pregnancy compared 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 not 18 months (OR 1.5, 95% CI 0.78 – 2.88). Low birth weight (OR 2.62, 95% CI 1.21 – 5.70) was associated with childhood anaemia at age six months. The association between prematurity (OR 1.87, 95% CI 0.84 – 4.15) and anaemia at six months did not reach statistical significance.

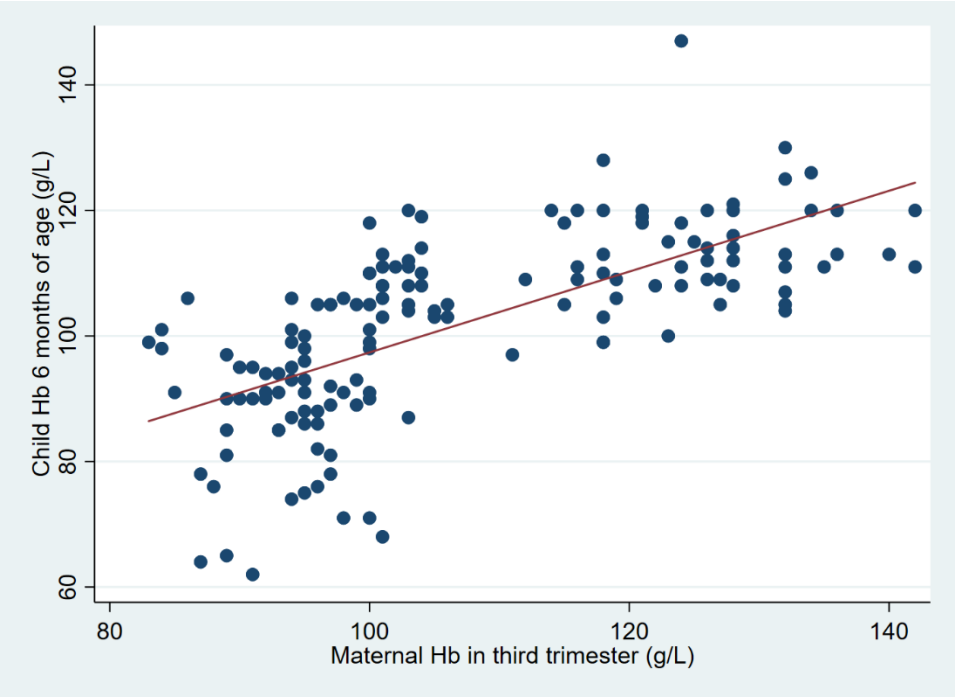

Figure 1. The association of maternal haemoglobin in third trimester of pregnancy on child haemoglobin at age 6-months.

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

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 [1]. Maternal anaemia in pregnancy is not routinely reported in the NT Mothers and Babies Report [20] or as a key performance indicator to monitor how well health services are performing for their clients. Further studies would be beneficial to establish how widespread maternal anaemia in pregnancy is in rural and remote Australian Aboriginal communities and to establish 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 haemoglobin concentration [21] 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 [18] 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 [22].

Maternal anaemia was predominantly IDA (90%) which is recognised as the most common aetiology in pregnancy [23]. The determination of IDA in this study however, was limited by a very small number of iron studies (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 [18]. 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% [24]. Iron supplementation was a recommendation for all pregnant women in the WBMs [25] up until 2014 when conflicting information was printed in the accompanying reference document [26]. 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 [27]

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 [24]. 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 [28].

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 [2]. Prevalence of anaemia across all age groups (40-50%) was comparable to that reported in other remote communities across Northern Australia [2]. 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 [9]. 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 [9]. 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 six months. This finding emulates evidence from international literature that is applicable in the remote Aboriginal context [10-14]. The association with anaemia in the first six 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 [11]. The increased risk of anaemia was observed to persist beyond six 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 [14].

LBW was associated with an increased risk of childhood anaemia at six 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 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. The current practice of administering prophylactic iron supplementation only to children who are born low birth weight or premature would be of greater benefit if expanded to include children born to anaemic mothers.

References

1. Bar-Zeev, S., et al., *Factors affecting the quality of antenatal care provided to remote dwelling Aboriginal women in northern Australia.* Midwifery, 2014. **30**(3): p. 289-96.
2. Northern Territory Government Department of Health, *Healthy Under 5 Kids Program, Growth and Nutrition Report, NT Annual Report 2015*. 2015: Darwin.
3. Central Australian Rural Practitioners Association, ed. *CARPA standard treatment manual, 4th edition*. A clinic manual for primary health care practitioners in remote and rural communities in Central and Northern Australia. 2003.
4. Central Australian Rural Practitioners Association Editorial Committee, ed. *CARPA Standard Treatment Manual: a clinic manual for primary health care practitioners in remote and rural communities in Central and Northern Australia*. 5th ed. 2009, Central Australian Rural Practitioners Association.
5. Central Australian Remote Practitioners Association, *CARPA Standard Treatment Manual (6th edition)*. 2014, Alice Springs: Centre for Remote Health.
6. Currie, B.J. and D.R. Brewster, *Childhood infections in the tropical north of Australia.* Journal of Paediatrics and Child Health, 2001. **37**(4): p. 326-330.
7. Brimblecombe, J., et al., *Characteristics of the community-level diet of aboriginal people in remote northern Australia.* Med J Aust, 2013. **198**: p. 380 - 384.
8. Aquino, D., et al., *High prevalence of early onset anaemia amongst Aboriginal and Torres Strait Islander infants in remote northern Australia.* Australian Journal of Rural Health, 2018. **26**(4): p. 245-250.
9. Remote Primary Healht Care Manuals, *CARPA Standard Treatment Manual (7th edition)*. 2017, Centre for Remote Health: Alice Springs, NT.
10. Colomer, J., et al., *Anaemia during pregnancy as a risk factor for infant iron deficiency: report from the Valencia Infant Anaemia Cohort (VIAC) study.* Paediatr Perinat Epidemiol, 1990. **4**(2): p. 196-204.

11. de Pee, S., et al., *The High Prevalence of Low Hemoglobin Concentration among Indonesian Infants Aged 3–5 Months Is Related to Maternal Anemia.* The Journal of Nutrition, 2002. **132**(8): p. 2215-2221.
12. Meinzen-Derr, J.K., et al., *Risk of infant anemia is associated with exclusive breast-feeding and maternal anemia in a Mexican cohort.* J Nutr, 2006. **136**(2): p. 452-8.
13. Kilbride, J., et al., *Anaemia during pregnancy as a risk factor for iron-deficiency anaemia in infancy: a case-control study in Jordan.* Int J Epidemiol, 1999. **28**(3): p. 461-8.
14. Nair, K.M., et al., *Characterisation of anaemia and associated factors among infants and pre-schoolers from rural India.* Public Health Nutr, 2016. **19**(5): p. 861-71.
15. Rumbold, A.R., et al., *Delivery of maternal health care in Indigenous primary care services: baseline data for an ongoing quality improvement initiative.* BMC Pregnancy Childbirth, 2011. **11**: p. 16.
16. Sunrise Health Service Aboriginal Corporation. *Community Profiles*. 2019; Available from: https://www.sunrise.org.au/community-profiles.
17. Hiscock, R., D. Kumar, and S.W. Simmons, *Systematic review and meta-analysis of method comparison studies of Masimo pulse co-oximeters (Radical-7 or Pronto-7) and HemoCue(R) absorption spectrometers (B-Hemoglobin or 201+) with laboratory haemoglobin estimation.* Anaesth Intensive Care, 2015. **43**(3): p. 341-50.
18. Remote Primary Helth Care Manuals, *Minymaku Kutju Tjukurpa Women's Business Manual*. 2017, Centre for Remote Health: Alice Springs, NT.
19. Hamilton, D.F., M. Ghert, and A.H.R.W. Simpson, *Interpreting regression models in clinical outcome studies.* Bone & joint research, 2015. **4**(9): p. 152-153.
20. Hall, J., A. Case, and L. O'Neil, *Mothers and Babies 2013*, in *Nothern Territory Midwives' Collection*. 2015, Department of Health, Northern Territory
21. Churchill, D., et al., *The change in haemoglobin concentration between the first and third trimesters of pregnancy: a population study.* BMC Pregnancy and Childbirth, 2019. **19**(1): p. 359.
22. Rabindrakumar, M.S.K., et al., *The role of haematological indices in predicting early iron deficiency among pregnant women in an urban area of Sri Lanka.* BMC Hematology, 2018. **18**(1): p. 37.
23. Kassebaum, N.J., *The Global Burden of Anemia.* Hematology/Oncology Clinics if Nroth America, 2016. **30**(2): p. 247-308.
24. World Health Organization, *WHO recommendations on antenatal care for a positive pregnancy experience*. 2016, WHO: Luxembourg.
25. Congress Alukura and Nganampa Health Council Inc, ed. *Minymaku Kutju Tjukurpa Women's Business Manual, 4th edition*. 2008, Graphic Print Group.
26. Manuals, R.P.H.C., *Reference Book for the Remote Primary Health Care Manuals*. 2014, Centre for Remote Health: Alilce Springs.
27. Manuals, R.P.H.C., *Minymaku Kutju Tjukurpa Women's Business Manual, 5th edition*. 2014, Centre for Remote Health: Alice Springs.
28. Malenica, M., et al., *Effect of Cigarette Smoking on Haematological Parameters in Healthy Population.* Med Arch, 2017. **71**(2): p. 132-136.