Anaemia in early childhood among Aboriginal and Torres Strait Islander children of Far North Queensland: a retrospective cohort study

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Abstract

Objective: Early childhood anaemia affects health and neurodevelopment. This study describes anaemia among Aboriginal and Torres Strait Islander children of Far North Queensland.

Methods: This retrospective cohort study used health information for children born between 2006 and 2010 and their mothers. We describe the incidence of early childhood anaemia and compare characteristics of children and mothers where the child had anaemia with characteristics of children and mothers where the child did not have anaemia using bivariate and multivariable analysis, by complete case (CC) and with multiple imputed (MI) data.

Results: Among these (n=708) Aboriginal and Torres Strait Islander children of Far North Queensland, 61.3% (95%CI 57.7%, 64.9%) became anaemic between the ages of six and 23 months. Multivariable analysis showed a lower incidence of anaemia among girls (CC/MI p<0.001) and among children of Torres Strait Islander mothers or both Aboriginal and Torres Strait Islander mothers (CC/MI p<0.001) compared to children of Aboriginal mothers. A higher incidence of anaemia was seen among children of mothers with parity three or more (CC/MI p<0.001); children born by caesarean section (CC/MI p<0.001); and children with rapid early growth (CC/MI p<0.001).

Conclusion: Early childhood anaemia is common among Aboriginal and Torres Strait Islander children of Far North Queensland. Poor nutrition, particularly iron deficiency, and frequent infections are likely causes.

Implications for public health: Prevention of early childhood anaemia in 'Close the Gap' initiatives would benefit the Aboriginal and Torres Strait Islander children of Far North Queensland – and elsewhere in northern Australia.

Key words: anaemia, Aboriginal, Torres, child, mother, Queensland

Anaemia is a global health issue that particularly affects women and young children.[1] Causes of anaemia include nutrient deficiencies – lack of folate, vitamin B12 and/or iron-infections, inflammation and genetic conditions.[1]

Anaemia in the first thousand days, from conception to age two years, can compromise the health of mothers and their pregnancy outcomes as well as the health and early childhood development of their children.[2] The most common cause of anaemia in early life is iron deficiency, as iron requirements increase due to expanding blood supply and other tissue growth.[1,3] Prevention of iron deficiency and/or anaemia is necessary for optimal child health and development.[2,4]

During the first months of life, the main source of iron is not breast milk or infant formula but the iron provided to the baby by its mother during the last ten weeks of pregnancy.[5] Iron status of an infant at birth reflects the iron status of the mother during pregnancy.[6] In low-income settings, anaemia of a mother in pregnancy is a strong predictor of anaemia in the early life of her child.[7] Birthweight matters, as smaller babies have smaller iron endowment.[6] Cord clamping practices at birth are also important, as delayed clamping can increase body iron of the newborn by about 30% compared to early clamping.[8,9]

A baby of healthy birthweight, born at full term to a well-nourished mother, typically has sufficient iron for the first six months of life.[6,8] After this, nutrient-dense solid foods rich in iron are required.[10,11] Traditionally, Aboriginal and Torres Strait Islander Australians consumed many iron-rich foods such as insects, shellfish, animal blood and organs.[12-14] Today, however, Aboriginal and Torres Strait Islander people consume diets that are less nutritious than the diets of other Australians.[15] These nutrient-poor diets, often commencing from early life, are associated with high rates of food insecurity compared to other Australians, especially among those living in remote locations.[15-17] Food insecurity increases the risk of anaemia among women and their children.[18]

Anaemia among Aboriginal and Torres Strait Islander children is a long-standing concern in remote communities in the Northern Territory and Western Australia.[19-22] A recent Northern Territory report showed 29.0% of children

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Submitted: December 2018; Revision requested: March 2019; Accepted: April 2019
The authors have stated they have no conflict of interest.

Aust NZ J Public Health. 2019; 43:319-27; doi: 10.1111/1753-6405.12911

aged six to 23 months (n=956) were anaemic in 2016/17.[23]

Comparable information on anaemia among other Australian children is limited. Localised surveys (2010) reported 1–6% of toddlers had iron deficiency anaemia increasing to 14% among those of Asian background, while one national survey from 1995 reported that 2% of 1–4-year-old children were anaemic.[24-26]

In remote Far North Queensland (Map 1), 71.5% of the population are Aboriginal and/or Torres Strait Islander people (n=14,107).[27] A recent audit from eight Cape York Aboriginal communities reported that 32.3% of children aged six to 23 months were anaemic.[28] However, published information is lacking for the wider Far North Queensland region.

The current study was undertaken to investigate anaemia among Aboriginal and Torres Strait Islander mothers and their children in Far North Queensland. Here we describe early childhood anaemia, defined as anaemia at age six to 23 months, and the characteristics associated with early childhood anaemia among Aboriginal and Torres Strait Islander children.

Methods

This retrospective cohort study used information from three existing health service data collections, extracted, linked and de-identified by the Queensland Health Statistical Services Branch. The process of securing this information has been previously described.[29] Briefly, data recorded between 2000 and 2015 were extracted from the Queensland Perinatal Data Collection (PDC)[30]; the Queensland Health Pathology Services Data Collection (Auslab)[31]; and the community health services electronic record system, Ferret,[32] used mainly in remote Far North Queensland (Map 1 and Supplementary Table 1).

Study data were provided for two cohorts of Aboriginal and Torres Strait Islander children and their mothers: the Cape York cohort and the 2009–2010 cohort. The Cape York cohort includes children of the remote Cape York communities only, born between 2006 and 2008. The 2009–2010 cohort includes children born to Aboriginal and/or Torres Strait Islander mothers with a Queensland Perinatal Data Collection (PDC) record of birth in 2009 or 2010 in Far North Queensland, which includes the Torres region, Cape York and Cairns and Hinterland. Children included in this analysis are those with a Ferret record in addition to a PDC record. The Ferret system was implemented mainly in discrete Aboriginal and Torres Strait Islander communities across Far North Queensland (Map 1). Twelve of these localities were in Cape York, 21 in the Torres region and five in the Cairns and Hinterland region.

Longitudinal information on child growth and haemoglobin levels was recorded on the Ferret system. To ensure independence of events for statistical analysis, only the first child born to each mother between 2006 and 2010 was included.

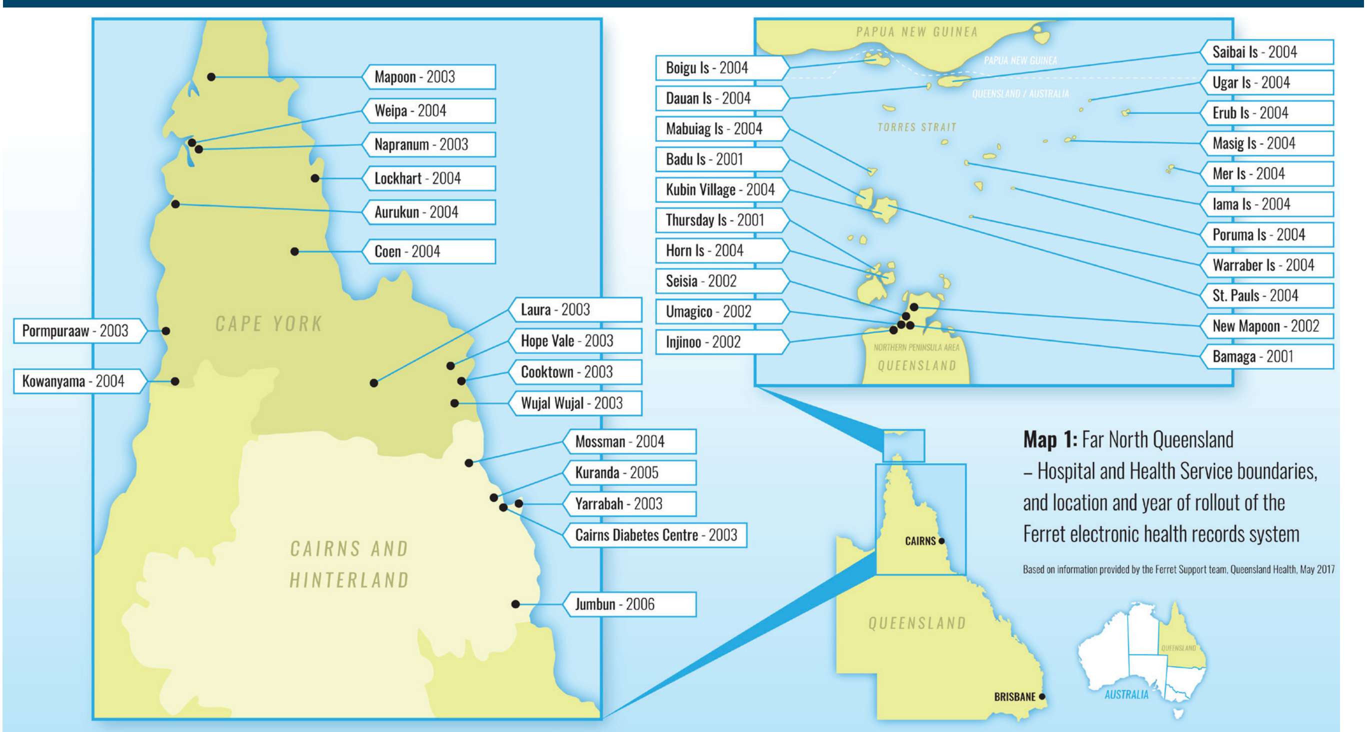
Ethics approval was granted by Queensland Health Far North Queensland Human Research Ethics Committee (HREC/15/QCH/50-980) in June 2015. Approval under the Queensland Public Health Act 2005 was granted by the Director-General of Queensland Health in February 2016. The complete linked de-identified data was provided to the research group in May 2017.

Study variables and definitions

Anaemia was defined as per Queensland Health clinical guidelines (haemoglobin <105 g/L from six to 11 months; haemoglobin <110g/L for children from 12 to 23 months).[33] Children aged six to 23 months, with at least one haemoglobin level recorded below the respective criteria for age at the date of measurement, were considered to have anaemia. The haemoglobin levels reported here for children were measured on capillary blood using a HemoCue®.

Some characteristics are as reported on the Perinatal Data Collection[30] (mother's usual residence, ethnicity, parity, smoking in pregnancy, pregnancy induced

Map 1: Caption Far North Queensland – Hospital and Health Service boundaries and localities of Ferret electronic health records system.



hypertension; baby's sex, gestational age at birth, birthweight, method of birth). Birthweight z-scores adjusted for sex and gestational age, for babies with gestational age of 33 weeks or more were calculated using the INTERGROWTH-21ST Neonatal Size Calculator.[34,35] The INTERGROWTH-21st standards for newborns are designed to complement the WHO Child Growth Standards.[34] Weight for age z-scores for the first weight measure at age four to six months recorded on the Ferret system were calculated using the STATA 'zscore06' module, which is based on the 2006 World Health Organization sex-specific child growth standards.[36,37]

Where measurements were available, z-score-change was calculated (z-score for the first weight measurement at age four to six months minus birthweight z-score for weight for gestational age). Z-score-change is a measure of change in weight for age z-scores in the first months of life. A positive value indicates an increase in weight for age, a negative value indicates a decline in weight for age, while a zero value indicates no change in weight for age (Supplementary Table 2).

Other characteristics (maternal body mass index [BMI] and age; baby's prematurity and/or low birthweight) were derived from Perinatal Data Collection information using criteria specified by the Australian Institute of Health and Welfare and the National Health and Medical Research Council, unless otherwise referenced.[38,39] Information on maternal glucose tolerance, haemoglobin, ferritin, red cell folate (RCF) and vitamin B12 levels are as recorded on the Queensland Pathology Auslab system. Maternal anaemia in the third trimester of pregnancy was defined as an Auslab record of mother's haemoglobin level <110 g/L as per Queensland Health clinical guidelines, measured on a date between estimated day 186 of pregnancy and the date of birth of the child.[24,40] Supplementary Table 2 provides further details on definitions including implausibility criteria. Implausible values were considered missing.

The Socio-Economic Index for Areas (SEIFA 2011) ranks Australian Bureau of Statistics Statistical Local Areas (SLA) by deciles of relative socio-economic advantage and disadvantage.[41] A ranking of '1' indicates greatest relative disadvantage while a ranking of '10' indicates greatest relative advantage. The appropriate SEIFA decile ranking was allocated to each mother based on her usual place of residence.

Statistical analysis

Categorical variables were described using absolute and relative frequencies. The distributions of numerical variables were assessed; symmetrically distributed numerical characteristics were described using mean values, 95% confidence intervals (95%CI), and ranges; numerical values with a skewed distribution were described using median, inter-quartile ranges (IQR) and ranges. The cumulative incidence of anaemia between age six to 23 months was presented with 95% confidence interval (95%CI). Mean haemoglobin levels using the first haemoglobin reading for each child, and incidence of anaemia were presented by six-month age groups (six–11 months, 12–17 months, 18–23 months). Children were included in one or more of the six-month age intervals if the appropriate measurements were available at that age but once only in analysis for the six to 23-month age group. Characteristics of the children and their mothers were compared between those children who had early childhood anaemia and those who did not, using bivariate logistic regression analyses adjusted for cohort.

The following characteristics were considered during multivariable analyses (Cohort 1 "2009-2010 cohort" n=407; Cohort 2 "Cape York cohort" n=301): sex of the baby; birthing method (non-instrumental vaginal, instrumental vaginal, caesarean section); gestational age of baby; whether baby was premature or not; birthweight of baby; z-score-change (z-score for weight for age at first weight at age four to six months less z-score for birthweight); feeding method to age four months (only breast milk, only infant formula, both breast milk and formula); ethnicity of mother (Aboriginal, Torres Strait Islander, both); region of residence of mother; SEIFA category for residence of mother; age of mother when baby was born; BMI category of mother (underweight, normal weight, overweight, obese); categories of parity (0-2, >=3); smoking during pregnancy; five or more antenatal care visits; pregnancy induced hypertension; mother had pre-existing diabetes; mother had gestational diabetes); low RCF level before or during pregnancy; low B12 level before or during pregnancy; mother anaemic in the third trimester of pregnancy.

Multivariable logistic regression analyses were conducted to identify independent risk factors for early childhood anaemia for the complete case analysis. Backward and forward stepwise modelling procedures were initially conducted to establish basic multivariable models for the combined cohorts. Characteristics that were not part of the basic models were assessed for potential confounding effects. A confounder was assumed to be a variable that changed estimates of characteristics in the basic model by 10% or more.[42]

Multivariable multiple imputation was conducted using Stata's MI commands for sequential imputation using chained equations. Missing values were imputed for BMI of mother; parity; smoking during pregnancy; mother anaemic in the third trimester of pregnancy; mother with pre-existing diabetes; mother with gestational diabetes; number of antenatal visits five or more; feeding method to age four months; and z-score-change from birth to age four to six months. Low RCF and B12 levels before or during pregnancy were not imputed because these characteristics were missing in close to 80% of cases. Examination of patterns of missing data was conducted using Pearson's chi-square and Fisher's exact tests to compare the occurrence of missing values in characteristics (Supplementary Table 3). Patterns of missing values were assessed and judged to be "missing at random".[43] Linear regression was used to impute missing values of continuous characteristics; logistic regression was used to impute missing values of dichotomous characteristics; ordinal logistic regression was used to impute missing values of the categories of BMI. Imputation models were based on the following variables with nil missing data: early childhood anaemia; sex of baby; gestational age of baby; baby premature; birthing method; birthweight of baby; pregnancy induced hypertension, ethnicity of mother, age of mother, SEIFA index; antenatal care received; and cohort. Forty imputed data sets were created. Multivariable logistic regression analyses were conducted to identify independent risk factors for early childhood anaemia for imputed data.

Results of multivariable models for complete case and imputed data analyses are presented as odds ratios (OR) and 95% confidence intervals. P values of less than 0.05 were considered statistically significant.

Figure 1: Flow diagram – early childhood anaemia among two cohorts of Aboriginal and Torres Strait Islander children and their mothers in Far North Queensland; data available and exclusions.

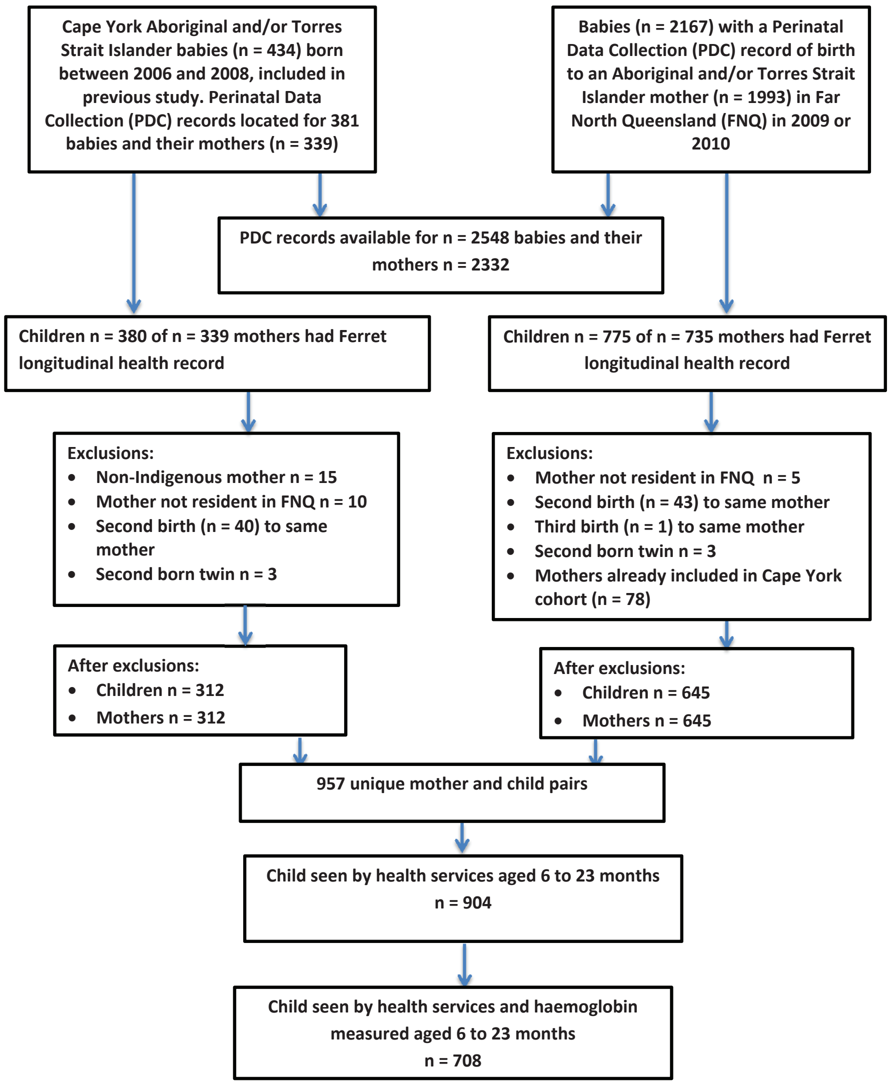
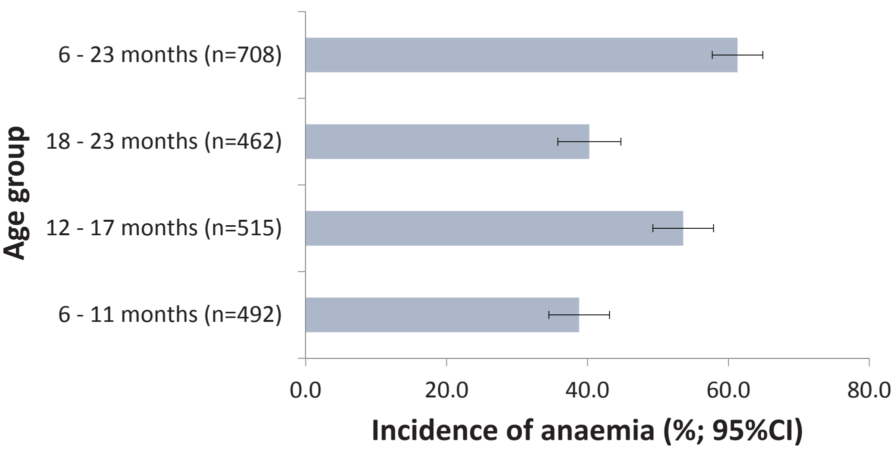


Figure 2: Incidence of anaemia among Aboriginal and Torres Strait Islander children (n = 708) of Far North Queensland from age six to 23 months, and by six-month age groups (%, 95% confidence interval).



Analysis was conducted using Stata version 13 (StataCorp, Lakeway Drive, College Station, Texas).

Results

Linked de-identified data was provided in May 2017 for 2,548 Aboriginal and Torres Strait Islander children born to 2,332 mothers in Far North Queensland between 2006 and 2010. Ferret records were available for 1,155 children of 1,074 mothers. The number of children for whom this information was available is close to the estimated 1,147 child residents based on census population figures for those localities (Figure 1, Map 1, Supplementary Table 4). Information was excluded where the mother was non-Indigenous (n=15), not resident in Far North Queensland (n=15) and where the child was not the first child born to his/her mother in the cohort years (n=90). Seventy-eight mothers were excluded from the 2009–2010 cohort because they were already included in the Cape York cohort. After exclusions, the number of unique mother and child pairs was 957 (Figure 1).

Ferret records showed at least one visit to health services between age six and 23 months for 904 (94.5%) of these 957 children, of whom 708 (74.0%) had a haemoglobin level recorded at least once between the ages of six and 23 months (Supplementary Tables 5 and 6). No significant differences were seen between children for whom haemoglobin measurements were available and those without haemoglobin measurements, except that children from Cape York were more likely to have been seen by health services and have had a measurement of haemoglobin made, compared to children from elsewhere (p<0.001), see Supplementary Tables 5 and 6.

Of these 708 children, 61.3% (95%CI 57.7%, 64.9%) had at least one haemoglobin measure showing anaemia; the incidence of anaemia by six-month age groups was highest at 12–17 months (Figure 2). Mean haemoglobin was above the level indicating anaemia (105 g/L) at six to 11 months; 109.8 g/L (95%CI 108.7,110.9) but below the level indicating anaemia (110 g/L) at 12–17 months; 109.3 g/L 95%CI 108.3, 110.3) and close to that level (110 g/L) at 18–23 months; 111.8 (95%CI 110.8, 112.8), see Supplementary Figure 1. Among children anaemic at six to 11 months who had subsequent haemoglobin measurements, 102 out of 150 (68%) were also anaemic at

12–17 months and 69 out of 138 (50%) at 18–23 months.

Haemoglobin measurements were not available for 249 children between the age of six and 23 months. If it is assumed that all these children did not have anaemia, the number of children without anaemia (n=249 + 274) would be n=523. Under this hypothetical assumption, the incidence of early childhood anaemia would be 45.4% (95%CI 42.2%, 48.5%).

Bivariate analysis (n=708) showed the incidence of early childhood anaemia was higher among boys (65.8%) compared to girls (56.5%, *p*<0.001) and among children born by caesarean section (69.5%) compared to those born by vaginal birth (57.7%, *p*<0.001). Children who had early childhood anaemia had lower mean birthweight (3,159g vs. 3,217g, *p*=0.01) and lower mean birthweight z-score (+0.082 vs. +0.274, *p*=0.001), and higher mean gains in z-score (+0.254 v-0.013, *p*<0.001) for weight for age in early life, see Tables 1a and 1b).

Children of Aboriginal mothers (71.4%) had higher incidence of early childhood anaemia than children of mothers who were Torres Strait Islander (46.9%) or both Aboriginal and Torres Strait Islander (43.9%, *p*<0.001), see Table 2).

Multi-variable analysis (Table 3) showed higher incidence of early childhood anaemia among children born by caesarean section compared to children born by vaginal birth (*p*<0.001), children with higher gains in weight for age (*p*<0.001) and children of mothers with a parity of three children or more (*p*<0.001), and lower incidence of early childhood anaemia among girls compared to boys (*p*<0.001). Children whose mothers were Torres Strait Islander (*p*<0.001) or both Aboriginal and Torres Strait Islander (*p*<0.001) had lower incidence of early childhood anaemia compared to children whose mothers were Aboriginal (Table 3). The analysis was repeated using mother's region of residence instead of mother's ethnicity. Children of mothers who were resident in the Torres Strait and Northern Peninsula Area (MI *p*=0.003) and children of mothers resident in Cairns and Hinterland (MI *p*=0.005) had lower incidence of early childhood anaemia compared to children of mothers resident in Cape York (Supplementary Table 7).

Multi-variable analysis showed disparate results in respect of smoking in pregnancy. Multiple imputation analysis, but not complete case analysis, showed significantly higher incidence of early childhood anaemia among children of mothers who smoked in pregnancy compared to children of mothers who did not smoke in pregnancy (MI *p*=0.023), see Table 3. Birthweight, age of mothers and anaemia of mothers in the third trimester of pregnancy were found to be confounding factors in multivariable analyses.

Discussion

This study shows that early childhood anaemia was common among these (n=708) Aboriginal and Torres Strait Islander children of Far North Queensland with the incidence of anaemia being 61.3% between the age of six and 23 months. Many children with anaemia before the age of 12 months were still anaemic in the second year of life. Mean haemoglobin levels were low; below the diagnostic level for anaemia from 12 to 17 months. Our findings are consistent with reports of high rates of early childhood anaemia among Aboriginal and Torres Strait Islander infants and young children elsewhere in northern Australia.[24,44,45]

Table 1a: Incidence of Early Childhood Anaemia (anaemia between age six and 23 months) among Aboriginal and Torres Strait Islander children (n=708) of Far North Queensland by characteristics of the children.

Characteristics of children	n	Child ever anaemic age 6–23 months n (%) [95%CI]	P value (logistic regression adjusted for cohort – unless stated otherwise)
Cohorts:			
Both combined	708	434 (61.3%) [57.7%, 64.9%]	n/a
2009–2010 births cohort	407	199 (48.9%) [44.1%, 53.8%]	chi2 <0.001
Cape York cohort	301	235 (78.1%) [73.4%, 82.8%]	
Gender:			
Male	363	239 (65.8%) [60.9%, 70.7%]	<0.001
Female	345	195 (56.5%) [51.3%, 61.8%]	
Birth method:			
Vaginal	473	273 (57.7%) [53.2%, 62.2%]	base
Vaginal/Instrumental	35	22 (62.9%) [46.0%, 79.7%]	<0.001
Caesarean	200	139 (69.5%) [63.1%, 75.9%]	<0.001
Birth Weight category:			
Low birth weight (<2,500g)	81	52 (64.2%) [53.5%, 74.9%]	0.008
Normal (2,500–4,000g)	580	355 (61.2%) [57.2%, 65.2%]	base
Marcosomic (>=4,000g)	47	27 (57.4%) [42.8%, 72.1%]	0.782
Gestational age category:			
Preterm (<37 weeks)	82	50 (61.0%) [50.2%. 71.8%]	0.893
Full-term (>=37 weeks)	626	384 (61.3%) [57.5%, 65.2%]	
Feeding method birth to 4-6 months; n=544 (164 missing)			
Only breast milk	228	157 (68.9%) [62.8%, 74.9%]	base
Only infant formula	56	30 (53.6%) [40.1%, 67.0%]	0.249
Breast milk and formula	260	159 (61.2%) [55.2%, 67.1%]	0.018

Table 1b: Incidence of Early Childhood Anaemia (anaemia between age six and 23 months) among Aboriginal and Torres Strait Islander children (n = 708) of Far North Queensland by characteristics of the children.

Characteristics of children	All n=708	Ever anaemic age 6–23 months n=434	Not anaemic age 6–23 months n=274	P value (logistic regression adjusted for cohort)
Gestational age at birth weeks – median (IQR) [range]	39 (38–40) [26–42]	39 (38–40) [27–42]	39 (38–40) [26–42]	0.036
Birth weight - grams mean (95% CI) [range]	3,181 (3,136, 3,225) [800–5,320]	3,159 (3,102, 3,215) [800–5,320]	3,217 (3,145, 3,288) [960–4,780]	0.010
Z-score for birth-weight for gestational age mean (95%CI) [range] n=692 (missing n=16)	+0.16 (+0.07, +0.24) [-2.9–+4.3] n=692	+0.082 (-0.021, +0.18) [-2.9–+4.3] n=426	+0.274 (+0.142, +0.405) [-2.4–+3.2] n=266	0.001
Z-score-change birth to first weight at age 4 -6 months mean (95% CI) [range] n=527(missing n=181)	0.16 (+0.057, +0.255) [-3.7–+3.7] n=527	+0.254 (+0.125, +0.382) [-3.7–+3.7] n=334	-0.013 (-0.167, +0.140) [-3.5–+3.0] n=193	<0.001

The finding of more early childhood anaemia among children born by caesarean or vaginal/instrumental births may reflect the urgency of such births, with early cord clamping reducing transfer of placental blood to the newborn.[8,9] Caesarean births are increasing among Indigenous mothers; this finding may be particularly relevant for the Torres Strait where diabetes in pregnancy and births by caesarean section are common.[46,47]

Table 2: Incidence of Early Childhood Anaemia (anaemia between age six and 23 months) among Aboriginal and Torres Strait Islander children (n = 708) of remote Far North Queensland by characteristics of their mothers

Characteristics of mothers	n	Child ever anaemic age 6–23 months n (%) [95%CI]	P value (logistic regression adjusted for cohort)
Ethnicity			
Aboriginal	423	302 (71.4%) [67.1%, 75.7%]	base
Torres Strait Islander	228	107 (46.9%) [40.4%, 53.5%]	<0.001
Both Aboriginal and Torres Strait Islander	57	25 (43.9%) [30.6%, 57.1%]	<0.001
Region of residence			
Cairns and Hinterland	56	29 (51.8%) [38.3%, 65.3%]	0.025
Cape York	442	318 (72.0%) [67.7%, 76.2%]	base
Torres Strait and Northern Peninsula Area	210	87 (41.4%) [34.7%, 48.1%]	0.023
SEIFA – usual residence			
Mother resident in SEIFA 1	620	377 (60.8%) [57.0%, 64.7%]	0.509
Mother resident in SEIFA 2 - 10	88	57 (64.8%) [54.6%, 75.0%]	
Body Mass Index of mothers (n=481, missing n=227)			
Underweight (9.8%)	47	34 (72.3%)[59.1%, 85.6%]	0.037
Healthy weight (35.8%)	172	93 (54.1%) [46.5%, 61.6%]	base
Overweight (25.2%)	121	63 (52.1%) [43.0%, 61.1%]	0.459
Obese (29.3%)	141	68 (48.2%) [39.9%, 56.6%]	0.032
Teenage mothers			
Teenage mother	163	95 (58.3%) [50.6%, 65.9%]	0.162
Mother age 20 years or older	545	339 (62.2%) [58.1%, 66.3%]	
Antenatal visits (missing n=1)			
Less than 5 visits	83	43 (51.8%) [40.8%,62.8%]	<0.001
5 visits or more	642	390 (62.5%) [58.7%, 66.3%]	
Parity (missing n=233)			
nil to 2	277	161 (58.1%) [52.3%, 64.0%]	0.103
3 or more	198	127 (64.1%) [57.4%, 70.9%]	
Smoked in pregnancy (n=703, missing n=5)			
Yes	439	275 (62.6%) [58.1%, 67.2%]	0.020
No	264	155 (58.7%) [52.7%, 64.7%]	
Gestational Diabetes (n=421, missing n=287)			
Yes	75	42 (56.0%) [44.5%, 67.5%]	0.329
No	346	198 (57.2%) [52.0%, 62.5%]	
Pre-existing Diabetes (n=587, missing n=121)			
Yes	33	23 (69.7%) [53.1%, 86.2%]	<0.001
No	554	330 (59.6%) [55.5%, 63.7%]	
Pregnancy Induced Hypertension (PIH)			
Yes	45	31 (68.9%) [54.8%, 83.0%]	0.026
No	663	403 (60.8%) [57.1%, 64.5%]	
Anaemia in third trimester (n=657, missing n=51)			
Yes	336	202 (60.1%) [54.9%, 65.4%]	0.014
No	321	199 (62.0%) [56.7%, 67.3%]	
Iron deficiency in pregnancy (n=385, missing n=323)			
Yes	185	110 (59.5%) [52.3%, 66.6%]	0.775
No	200	123 (61.5%) [54.7%, 68.3%]	
Low Red Cell Folate (RCF) before/during pregnancy (n=158, missing n=550)			
Yes	20	16 (80.0%) [60.8%, 99.2%]	<0.001
No	138	71 (51.5%) [43.0%, 59.9%]	
Low B12 before/during pregnancy (n=131, missing n=577)			
Yes	22	7 (31.8%) [10.7%, 53.0%]	0.151
No	109	62 (56.9%) [47.4%, 66.3%]	

Our findings show that children of Aboriginal mothers had higher incidence of early childhood anaemia compared to children of mothers who were Torres Strait Islander or both Aboriginal and Torres Strait Islander. Further analysis by mother's region of residence showed the same pattern. These results reflect the different history of Aboriginal people of Cape York compared to people of the Torres Strait. Government policies forcibly relocated Queensland Aboriginal people from their traditional lands to mission settlements, some of which are now the remote communities of Cape York.[48] This "large scale relocation did not occur in the Torres Strait".[48] Despite Government restrictions and impositions, Torres Strait Islander peoples largely remained on their traditional lands, a key factor in preserving cultural continuity, including traditional food systems.[48]

The high cost of nutritious food has been widely reported, while household food insecurity is exacerbated by smoking.[49,50] The implications of poor health of mothers on the future health of their children have been raised previously.[51] The intergenerational association reported here, of high parity and maternal smoking with early childhood anaemia, reflects the shared experiences of food insecurity of these mothers and their children in a context of poverty and social disadvantage that is particularly challenging in Cape York.[48]

The limitations of this study are those associated with the use of routine health service data, including missing information.[29] The multiple imputation methodology was used to adjust for missing values and results are presented for both complete case and multiple imputation analyses. However, some information was not recorded on the electronic data collections accessed for this study. For example, information about treatment of anaemia was not available for mothers or children. It may be that treatment of maternal anaemia protects the unborn child from subsequent anaemia, but this hypothesis could not be tested. Similarly, the lack of information on treatment of children meant that the effect of treatment at first diagnosis of early childhood anaemia on subsequent haemoglobin levels could not be assessed.

In addition, many (26.0%) of the 957 children with a Ferret record did not have a measure of haemoglobin recorded between the age of six and 23 months; most (n=196, 20.5%) were

Table 3: Risk factors for Early Childhood Anaemia (n=708); multi-variable analysis – complete case analysis and analysis with imputed data.

Characteristic	Complete case analysis n=329 Anaemia n=203 (61.7%)	No Anaemia n=126 (38.3%)	Odds-ratio (95% CI)[a]	*p*-value	Number of missing values (%)	Imputed data analysis n=708 Anaemia n=434 (61.3%)	No Anaemia n=274 (38.7%)	Odds-ratio (95% CI)[a]	*p*-value
Sex of child					0				
Male	115 (56.7%)	59 (46.8%)	1			239 (55.1%)	124 (45.3%)	1	
Female	88 (43.4%)	67 (53.2%)	0.63 (0.59, 0.67)	P<0.001		195 (44.9%)	150 (54.7%)	0.62 (0.55, 0.71)	P<0.001
Z-score-change from birth to 4 to 6 months	/	/	1.3 (1.2, 1.4)	p<0.001	181 (25.6%)	/	/	1.2 (1.1, 1.3)	P<0.001
Age of mother[b]	/	/	0.97 (0.92, 1.02)	P=0.224	0	/	/	0.99 (0.98, 1.00)	P=0.096
Ethnicity of mother					0				
Aboriginal	144 (70.9%)	55 (43.7%)	1			302 (69.6%)	121 (44.2%)	1	
Torres Strait Islander	46 (22.7%)	54 (42.9%)	0.34 (0.21, 0.53)	P<0.001		107 (24.7%)	121 (44.2%)	0.35 (0.22, 0.56)	P<0.001
Both	13 (6.4%)	17 (13.5%)	0.26 (0.17, 0.39)	P<0.001		25 (5.8%)	32 (11.7%)	0.28 (0.19, 0.42)	P<0.001
Parity					233 (32.9%)				
Up to 2 children	124 (61.1%)	79 (62.7%)	1			284 (65.4%)	193 (70.4%)	1	
3 or more children	79 (38.9%)	47 (37.3%)	2.1 (1.7, 2.5)	P<0.001		150 (34.6%)	81 (29.6%)	1.8 (1.4, 2.5)	P<0.001
Birth method					0				
Vaginal	125 (61.6%)	100 (79.4%)	1			273 (62.9%)	200 (73.0%)	1	
Vaginal instrumental	8 (3.9%)	3 (2.4%)	3.1 (1.9, 5.2)	P<0.001		22 (5.1%)	13 (4.7%)	1.4 (1.1, 1.9)	P=0.013
Caesarian	70 (34.5%)	23 (18.3%)	3.0 (2.9, 3.1)	P<0.001		139 (32.0%)	61 (22.3%)	1.7 (1.4, 2.1)	P<0.001
Mother anaemic in third trimester[b]					51 (7.2%)				
No	103 (50.7%)	63 (50.0%)	1			216 (49.8%)	131 (47.8%)	1	
Yes	100 (49.3%)	63 (50.0%)	1.0 (0.5, 2.2)	P=0.934		218 (50.2%)	143 (52.2%)	0.89 (0.77, 1.03)	P=0.122
Mother smoked during pregnancy					5 (0.7%)				
No	75 (37.0%)	50 (39.7%)	1			156 (35.9%)	109 (39.8%)	1	
Yes	128 (63.1%)	76 (60.3%)	1.0 (0.7, 1.5)	P=0.964		278 (64.1%)	165 (60.2%)	1.2 (1.02, 1.3)	P=0.023

Notes:
Both models were adjusted for the confounding effect of birth weight (no missing values imputed).
a: 95% CI = 95% confidence interval.
b: Mother anaemic in third trimester and mothers' age were identified as confounding variables in complete case data analysis. Imputed data are averages of 40 imputations.

seen by health services but haemoglobin levels were not recorded. Children in Cape York were more likely to be seen and to have a haemoglobin level recorded than children from elsewhere. No other differences were identified. However, the reason for this missing data is not known and there may be an unidentified bias in the availability of relevant information.

Another limitation of our study is that haemoglobin levels were measured on capillary blood using HemoCues®. The use of capillary blood and these devices may underestimate haemoglobin levels, which would result in overestimation of the incidence and prevalence of anaemia.[52] Validation studies suggest that the HemoCue® is suitable for screening purposes but, where anaemia is suspected, other methods should also be used.[53] However, health service protocols for diagnosis and treatment of anaemia in remote Far North Queensland are based on HemoCue® measurements.[33]

The information presented here is for children born between 2006 and 2010. It is possible that the situation in respect of early childhood anaemia has changed. However, in Cape York in 2014 and 2015, about one-in-three children aged six to 23 months were anaemic (n=155, 32.3% anaemic, 95%CI 24.8%, 39.7%) indicating that early childhood anaemia continues to be a problem in Cape York.[28] Comparable information is not available from elsewhere in Far North Queensland.

There is no information to identify the cause(s) of the anaemia reported here. Nutrient deficiencies such as iron deficiency cause anaemia, as do chronic infections.[1,54] Iron deficiency is the 'usual suspect' as a nutrition-related cause of anaemia in early life because of the high requirements for iron due to rapid growth.[10] Iron requirements per kilogram of body weight are higher at six to 12 months than at other stages of the life cycle.[5] Australian estimates show that the daily iron requirements of a child aged seven to 12 months are higher than those of an adult man: Estimated Average Requirement (EAR) child seven to 12 months – 7mg; EAR male aged 19 years or more – 6mg.[55] Milk is not a rich source of iron; during the first months of exclusive breastfeeding, a baby draws on iron stores acquired before birth from the mother.[5] Subsequently the small quantity of solid food consumed by young children must provide most of these high iron requirements.[10] Consequently, iron-rich and/or iron-fortified first foods are recommended in Australia.[11]

Two studies in the Northern Territory showed the association of iron deficiency with childhood anaemia in similar settings. In one study, among young Aboriginal children (n=74) with anaemia, most (n=62, 84%) had iron deficiency anaemia, with folate deficiency and chronic infections identified as causes of anaemia in the other children.[21] Another Northern Territory study among school-age children with anaemia (n=201) found that iron therapy was effective in resolving anaemia among 83% of the 66 children for whom follow-up measurements were available.[22]

Several of the risk factors identified here are consistent with iron deficiency as a cause of the anaemia: birth by caesarean section; rapid early growth; and boys compared to girls, as boys typically have higher early weight gains than girls.[56,5]

Infections are another probable cause of anaemia in these children, with high rates of infectious diseases reported for Aboriginal and Torres Strait Islander children of remote Far North Queensland.[57] There is a bidirectional relationship between infectious disease and nutrition status; frequent illness impairs nutrition status and poor nutrition status increases susceptibility to infection.[58] The immune response to infections restricts iron availability to infectious organisms; when prolonged, this immune response can lead to anaemia.[59]

However, the diagnosis of anaemia based on haemoglobin only, as in this study, cannot identify the cause(s) of anaemia. The lack of information on the causes of early childhood anaemia is not only a limitation of this study but also a limitation of methods currently available to identify causes of anaemia in early childhood; in particular, the assessment of iron status is complex in the presence of infection.[60,54]

Prevention of early childhood anaemia is important as successful treatment of anaemia may not reverse the associated neurological deficits.[2] Where the prevalence of early childhood anaemia is high (20% or more), WHO recommends interventions that combine promotion of breastfeeding and healthy food with home fortification of solid foods using multi-micronutrient preparations for babies/children aged six to 23 months.[1,61-63] Such interventions have been demonstrated to be acceptable, safe and effective in the prevention and treatment of early childhood anaemia in low-income settings where the infectious disease burden is high.[61-63] One such intervention, the Fred Hollows Foundation Early Childhood Nutrition and Anaemia Prevention Project (ECNAPP), was successfully piloted in six remote communities across northern Australia in 2010–2012.[64] Nutrition-focused interventions will be strengthened by complementary interventions to improve food security and reduce infections in early life.[58]

Improved nutrition in the first one thousand days of life – through pregnancy up to the age of two years – provides "a golden opportunity to impact neurodevelopment and brain function through the lifespan".[2] Prevention of early childhood anaemia, included as a key strategy to 'Close the Gap' between Aboriginal and Torres Strait Islander Australians and other Australians,[65] would benefit the Aboriginal and Torres Strait Islander children of Far North Queensland – and elsewhere in northern Australia.

Acknowledgements and funding

Dympna Leonard was supported by a National Health and Medical Research Council post-graduate scholarship APP1092732.

Other agencies provided non-financial support to this research. We acknowledge and thank the Aboriginal and Torres Strait Islander leaders of the key community-controlled health service organisations in far north Queensland who considered and endorsed the proposed research, providing the support that made this research possible. In addition, we acknowledge and thank the Queensland Health Data Custodians and their research and data management staff for their assistance and support for this work.

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Supporting Information

Additional supporting information may be found in the online version of this article:

Supplementary Figure 1: Mean haemoglobin (g/L) (with 95% confidence interval) for Aboriginal and Torres Strait islander children of Far North Queensland by six month age groups.

Supplementary Table 1: Data collections used to source information to investigate Early Childhood Anaemia (anaemia at age six to 23 months) among Aboriginal and Torres Strait Islander children in Far North Queensland.

Supplementary Table 2: Definitions of variables used to describe characteristics of Aboriginal and Torres Strait Islander children (born between 2006 and 2010) and their mothers in Far North Queensland.

Supplementary Table 3: "Missingness" of characteristics in analysis of risk factors for early childhood anaemia in 708 Aboriginal children from North Queensland.

Supplementary Table 4: Early childhood anaemia among two cohorts of Aboriginal and Torres Strait Islander children and their mothers in Far North Queensland; comparisons of study participant numbers with census information.

Supplementary Table 5: Far North Queensland Aboriginal and/or Torres Strait Islander children with a Ferret record (n = 957): comparing those seen by health services at age six to 23 months (n = 904) with those not seen (n = 53).

Supplementary Table 6: Far North Queensland Aboriginal and/or Torres Strait Islander children with a Ferret record seen by health services at age six to 23 months (n = 904) - comparing those with at least one haemoglobin measure (n = 708) with those with no haemoglobin measure (n = 196) at age six to 23 months.

Supplementary Table 7: Risk factors for Early Childhood Anaemia (anaemia between six and 23 months) among Aboriginal and Torres Strait Islander children of Far North Queensland (n = 708): Results of multi variable analysis using region of residence of mother instead of ethnicity in imputed data model (all other variables as in Table 3).