

Risk factors for anaemia in pregnancy in rural KwaZulu-Natal, South Africa: Implication for health education and health promotion

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Abstract

Background: Anaemia in pregnancy is a major public health problem in developing countries. It is associated with an increased risk of maternal and perinatal morbidity and mortality. A high rate of anaemia in pregnancy in the rural population of KwaZulu-Natal (30% according to national and 57% according to the World Health Organization [WHO] definition of anaemia in pregnancy) is observed. The risk factors for anaemia, particularly during pregnancy, are multiple and complex and their relative contributions are known to vary by geographic areas and by seasons. In order to design an intervention for treatment and prevention of anaemia in pregnancy, studies to assess the aetiological factors are necessary. The aim of this study was to evaluate the strength of association between intestinal helminthiasis, urinary schistosomiasis and HIV infection on anaemia in pregnancy.

Methods: A retrospective case-control study design was used in a rural district hospital of South Africa. A total of 300 pregnant women, 100 of them with anaemia (haemoglobin less than 10 gm/dL according to the national definition of anaemia in pregnancy) referred as cases and 200 controls were studied from Empangeni Hospital. Both cases and controls were matched for age, parity and gestational age. Data were collected from the antenatal clinic and prevention of mother-to-child transmission of HIV (PMTCT) programme registers for cases and controls at their booking visit during the months of May, June and July of 2004. Univariate and multiple logistic regression were performed to analyse the data.

Results: Of the cases, 48% and 1% among the controls had intestinal helminthiasis, resulting in the odds ratio of 42 ($p = 0.000$ and 95% CI 9.96 – 176.59). The risk of anaemia was related to urinary schistosomiasis, as 27% of the cases compared to 1% of controls was found with anaemia. The odds ratio was 12 ($p = 0.000$ and 95% CI 3.58 – 41.02). These parasitic infestations are known to cause chronic haemorrhage and iron deficiency resulting in the development of anaemia in pregnancy. Transmissions of intestinal parasitic infestation occur through the faecal-oral route. Personal hygiene and other environmental factors are therefore an important factor for the transmission of the disease. To reduce the transmission of faecal-oral diseases (e.g. intestinal helminthiasis and urinary schistosomiasis) key interventions recommended are: 1) safe disposal of human excreta, 2) hand-washing practices with soap after defecation, and 3) maintenance of drinking water free from faecal contamination.

Similarly, HIV infection increased the chance of developing anaemia in pregnancy twofold as HIV infection was more common among cases (56%) than among controls (37%), resulting in an odds ratio of 2.11 ($p = 0.003$ and 95% CI 1.123 – 3.21). The prevention of HIV infection and transmission can be achieved through the improvement of knowledge of these conditions. These can be achieved through health education and health promotion.

Conclusion: These findings confirm and conform to other studies on the association between anaemia in pregnancy and parasitic and HIV infections. Antenatal care should promote de-worming and education on personal hygiene and HIV (risk factors, mode of transmission, etc.). The provision of safe water supply and toilet facilities for the rural communities should be considered urgently to prevent and promote better health for all, including pregnant women.

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Introduction

The term anaemia implies a reduction in the oxygen-carrying capacity of the blood as a result of fewer circulating erythrocytes than normal or a decrease in the concentration of haemoglobin (Hb). The deficiency occurs through the reduced production or an increased loss of red blood cells. Pregnant women are considered to be the most vulnerable group, since the additional demands that are made on maternal stores during this period unveil the various latent deficiencies that manifest themselves as anaemia.¹ According to the World Health Organization (WHO), anaemia should be considered when the haemoglobin level is below 11 gm/dL.² In South Africa (SA), anaemia is considered during pregnancy if the

haemoglobin concentration is below 10 gm/dL. Between 9 and 12% of pregnant women were found to have iron deficiency anaemia in SA in 2000.^{3,4} Anaemia in pregnancy is found to be a common clinical problem and between 35 and 70% prevalence rates are reported. This comprises an important contribution to maternal and perinatal mortality and morbidity in most developing countries.^{2,5} Nearly 600 000 women between the ages of 15 and 44 years die each year worldwide as a result of complications of pregnancy and childbirth.⁶ The maternal mortality ratio (MMR) in the world is estimated to be 390/100 000 live births, and most of these occur in developing countries.⁷ In most countries in Africa and in some in Asia the rates are as high as 700/100 000 live births.⁸ In

SA the MMR is reported between 135 and 165/100 000 live births during 2002 to 2004.⁹

Severe anaemia ($Hb < 7.0 \text{ gm/dL}$) in pregnancy is associated with an increased risk of maternal and perinatal mortality.^{10,11} In sub-Saharan Africa it is estimated that 20% of maternal deaths are associated with anaemia.^{12,13} It is found to be a risk factor for infant iron deficiency, which is also associated with adverse behavioural and cognitive development of children and low birth weight, which is one of the main risk factors for infant mortality.^{14,15}

During the assessment of the nutritional status of children and their mothers it was found that 24% of preschoolers, 22% of children of 6 to 11 years of age and 22% of their mothers were anaemic in KwaZulu-Natal (KZN).¹⁶ In the context of developing countries, nutritional iron deficiency is the main cause of anaemia in pregnancy. Folate and vitamin A deficiencies, parasitic infestation (helminthiasis, urinary schistosomiasis), haemoglobinopathies (sickle cell disease, thalassaemia), infection with HIV and malaria, multiparity and seasonal variation are all important known risk factors for anaemia in pregnant women.^{17,18,19}

Most sub-Saharan African countries, including SA, currently have national policies to prevent and treat anaemia and malarial prophylaxis for all pregnant women. However, a high rate of anaemia in pregnancy in the rural population of KZN (30% according to national and 57% according to the WHO definition of anaemia in pregnancy) was observed.²⁰ Few studies have comprehensively assessed the aetiological factors responsible for anaemia in pregnancy in SA, more especially in rural settings. In sub-Saharan Africa, it is believed that deficiency of iron (nutritional deficiency) during pregnancy is the leading cause of anaemia.²¹ Vitamin A and B12 deficiencies are also described as risk factors for anaemia in pregnancy.^{22,23} Deficiency of folate has also been described in West African studies.²⁴ HIV and parasitic infections are also known to cause anaemia.²⁵⁻²⁷

The risk factors for anaemia, particularly during pregnancy, are multiple and complex and their relative contributions are known to vary by geographic areas and by seasons.^{5,10,28} Knowledge of the relative importance of the different risks or aetiological factors should therefore form the basis for public health or clinical intervention to control anaemia in pregnancy in different areas and populations.²⁹ The present study was undertaken to measure the extent of intestinal helminthiasis, urinary schistosomiasis and HIV infection on anaemia among pregnant women attending a rural hospital in KZN.

Materials and method

Settings and population

Empangeni Hospital is the only 256-bed maternity hospital in the health district of Uthungulu, which covers over 450 000 people in mainly rural areas. The hospital is a referral centre for 14 rural clinics for maternal and baby care. The affiliated clinics provide antenatal care, including prevention of mother-to-child transmission of HIV (PMTCT), delivery service (approximately 5% of total sub-district deliveries) and postnatal care, among other primary healthcare services. The hospital offers a range of services, including maternity care (antenatal, labour, postnatal), gynaecological care (termination of pregnancy, out-patient and in-patient care), theatre, neo-natal and follow-up care for premature infants and infants of women on the PMTCT programme, a crisis centre for victims of sexual abuse and voluntary counselling for and testing

of women (including non-pregnant women). The PMTCT programme was implemented in the Uthungulu health district (Empangeni Hospital and all its affiliated clinics) in May 2002 and has offered anti-retroviral treatment provision since November 2004. One consultant, two medical officers, three midwives and three professional nurses are allocated to provide comprehensive antenatal care, which includes the PMTCT programme. Medical and nursing administrators offer administrative support for optimal management of the antenatal clinic.

Study design

A retrospective case control design was used in the investigation. One hundred consecutive pregnant women who had anaemia (Hb less than 10 gm/dL) at their booking visit during the months of May to July 2004 constituted the cases. Two hundred pregnant women were selected as controls from the same antenatal population during the same study period who were non-anaemic and attended the clinic for routine antenatal check-ups. The controls were matched for age, parity and gestational age. Patients who were referred from other institutions were not included in this study as cases or controls.

Definition of cases: Pregnant women attending Empangeni Hospital antenatal clinic for their first or booking visit and who had blood Hb levels of less than 10 gm/dL (according to the SA national definition of anaemia in pregnancy).²

Data collection

Data were collected from the antenatal clinic and PMTCT registers for cases and controls. Blood Hb levels were used to select cases and controls. The results of stool and urine examination and Hb levels were obtained from the antenatal clinic register. The HIV status of the cases and controls was obtained from the PMTCT register. Permission for the study was obtained from the hospital management.

Data sources and screening procedure

At the booking visit the nursing staff took down relevant histories, conducted examinations and recorded findings both on antenatal record cards and in the clinic register. Screening for anaemia, syphilis and rhesus factors were done using venous blood samples as a routine procedure in the antenatal clinic. Every pregnant woman also received at least a routine obstetric ultrasound. Screenings for intestinal helminth infection was performed using light microscopy after wet preparation of slides to detect the presence of any ova, cysts or trophozoites of helminth in stools. In cases of the presence of cysts and/or trophozoites reference was made to atlas for identification and confirmation. The urinary schistosomiasis was diagnosed by using a diagnostic urine filtration technique. The urine specimen was spun for 10 minutes in the laboratory to obtain the sediment that was investigated under the microscope for the evaluation of Schistosoma eggs. The presence of a single ovum confirmed the diagnosis of schistosomiasis. Both stool and urine tests were performed at the Empangeni Hospital laboratory. These tests were undertaken as part of the routine antenatal check-up. The mother's name, age, parity and gestational age were recorded in the clinic register on the same day. The ages and parity were obtained from the mothers and gestational age was estimated by examination of the fundal height or from the women's last recorded menstrual period. A full blood count (FBC) was used to estimate the Hb level (together with packed cell volume (PCV), white blood cell (WBC) differential counts, general film reading, etc) at the hospital laboratory (using the standard cyanmethaemoglobin method with a COULTER HmX Hematology

Analyzer). A day later, the FBC, stool and urine examination reports of all routine tests were sent to the antenatal clinic. Dedicated professional nurses at the clinic, who were responsible for antenatal care during the first visit, recorded the Hb, stool and urine results in the clinic register. The original copies of the laboratory results were then kept aside in the clinic to be attached to the patients' antenatal carrying cards during the second visit. Appropriate interventions were taken according to the results. Voluntary counselling and testing for HIV were offered to all pregnant mothers for possible inclusion in the PMTCT programme. Each mother that attended for antenatal care received stocks of ferrous sulphate (200 mg daily) and folic acid (5 mg daily) doses for supplementation until the next appointment.

Data analysis

After decoding and before entering the data into the computer, individual data were scrutinised thoroughly for accuracy and consistency. The data were subsequently fed into the personal computer using the SPSS 12.0.1 software package. Association between various parameters and the risk factors was determined by comparing each group separately with the control in the univariate analysis. For each of the study factors, risk was estimated by calculating the odds ratio (OR) as approximation of the relative risk (RR), together with 95% confidence intervals (95% CI). On the basis of the results in the univariate analysis, all three variables of the study (intestinal helminthiasis, urinary schistosomiasis and HIV infection) were found to be statistically significant, and were therefore included in the final model.

Results

The distribution and comparison of age, parity, gestation and Hb of cases and controls are shown in Table I. The mean age, parity and gestational ages of the cases and controls were matched and were therefore equally distributed in cases and controls.

Table I: Frequencies and comparison of cases and controls by age, parity, gestation and mean haemoglobin at booking visit

Factors		Cases (numbers)	Controls (numbers)	Comparison
Age (years)	15–24 years	56	112	NS
	25–34 years	38	76	
	35 and above	6	12	
	Mean age (Sd)	24 years (5.91)	24 years (5.86)	
Parity	0–3	95	191	NS
	4 and above	5	9	
	Mean (Sd)	1.16 (1.46)	0.99 (1.12)	
	Median (Range)	1 (7)	1 (5)	
Gestational age	1st trimester	1	2	NS
	2nd trimester	68	136	
	3rd trimester	31	62	
Haemoglobin	Mean (Sd)	8.12 (1.12)	10.94 (1.32)	$p < 0.05$ Significant
	(Hb < 7gm)	15	0	

Table II shows the results of the univariate logistic regression analysis and the estimation of the OR of anaemia in relation to the study variables. Intestinal helminthiasis was associated with a significantly increased

risk of anaemia in pregnancy. Of the cases and controls, 48% and 1% respectively had the infection, which gave the OR of 42 ($p = 0.000$).

Table II: Results of univariate logistic regression analysis for risk factors for anaemia in pregnancy (OR and 95% CI for OR)

Risk factors	OR	95% CI	P value
Intestinal helminthiasis	41.93	9.96–176.59	0.000
Urinary schistosomiasis	12.12	3.58–41.02	0.000
HIV infection	2.11	1.27–3.21	0.003

The risk of anaemia was related to urinary schistosomiasis, as 27% of the cases compared to 1% of controls was found with anaemia and the OR was 12 ($p = 0.000$). Similarly, HIV infection was common among cases (56%) than among controls (37%), which resulted in an OR of 2.11 ($p = 0.003$).

Table III shows the final results of multivariate logistic regression analysis and the final model of risk constructing when entered into the model. Since a backward method was carried out and all the variables were included in the analysis, the final model had the variables that remained significant even after adjusting for all other variables that also showed its independent risk of association with anaemia in pregnancy. It is noted that HIV infection has lost its absolute significance. Intestinal helminthiasis was the only variable that was significantly associated with severe anaemia (OR = 9.06).

Table III: Results of multiple logistic regression analysis of the risk factors for anaemia in pregnancy

Variables	Regression coefficient	P value	Odds ratio	95% CI for OR	
				Lower	Upper
Intestinal helminthiasis	4.19	0.000	65.99	8.86	492.51
Urinary schistosomiasis	2.15	0.007	8.58	1.81	40.68
HIV infection	0.53	0.050	1.70	1.00	2.90
Constant	-3.20	0.000	0.04		

Variable(s) entered in step 1: intestinal helminthiasis, urinary schistosomiasis and HIV infection.

Discussion

Anaemia in pregnant women in developing countries is generally presumed to be the result of nutritional deficiency. Iron deficiency anaemia is the most prevalent nutritional deficiency problem affecting pregnant women.³⁰ Iron deficiencies may develop during pregnancy because of the increased iron requirements on the mother's body to supply the expanding blood volume and the rapidly growing fetus and placenta. Literatures suggest that iron deficiency is responsible for about 50% of the cases of anaemia in pregnant women in developing countries.^{31,32} The net additional iron requirements during pregnancy are estimated to be 1 000 mg per day.³³ The extent of iron deficiency anaemia and the effects on maternal and neonatal health is uncertain in the Uthungulu population. Parasitic diseases (helminthiasis and malaria) are known to be contributory to iron deficiency anaemia in pregnancy. Malaria is not endemic in this population, and we have therefore not included malaria in the study. The possibility of population migration among the pregnant population may influence the result of this study and should therefore be noted. Recent research has shown that the provision of iron and folic acid is insufficient to combat nutritional anaemia.³⁴ An earlier study among black pregnant women found that age and parity are insignificant

with no association with anaemia.¹ However, this finding is more than 20 years old. The situation might have changed over time and therefore needs further investigation.

In normal pregnancy a substantial rise in plasma volume occurs compared to red cell mass, resulting in 'physiological anaemia'. Therefore, it is difficult to distinguish the causes of anaemia in pregnancy (physiological or true anaemia). It is also reported that there is a progressive increase in the prevalence of anaemia among black women as pregnancy advances.³⁵ Therefore, in order to identify specific risk factors, the adjustment of age, parity and gestational age were probably justified.

Intestinal helminthiasis (OR = 42) is strongly associated with overall anaemia and severe anaemia in pregnant women in this population. Blood loss caused by helminthiasis puts mother, fetus and child at risk of iron deficiency, which could lead to anaemia. The extent to which this deficiency occurs depends on the host's iron status, the infecting parasites and the intensity and duration of infection. It is known that the iron status of women in developing countries is frequently poor as a result of an inadequate dietary iron intake, concurrent infections and frequent or closely spaced pregnancies.³⁶ It has been found in an earlier study that micronutrient deficiency and parasitic infestations are common problems among school children in KZN.³⁷

Urinary schistosomiasis, also known as bilharziasis, is commonly caused by *schistosoma haematobium* (one of the five species of schistosome). Infected snails, which live in freshwater habitats, transmit the parasite and release infected larval forms of the parasite. Consequently, the people most at risk are those who engage in agriculture and fishing, and who use unsafe water for household chores. In a study in Kenya it was found that both male and female children spend most of their time playing in unsafe water. As they got older, playing was reduced, but girls continued to spend more time in water washing dishes and clothes than boys. Women are therefore more exposed to contract the disease in communities. This could also be the case in Uthungulu.

Studies conducted to identify risk factors for anaemia in pregnancy are mostly cross-sectional and descriptive, therefore the actual risk or association is not measured. We measured the magnitude of three risk factors for anaemia in pregnancy in this rural population. Individual pregnant women with intestinal helminthiasis are 42 times more likely to develop anaemia than non-infected ones. Similarly, pregnant women with schistosomiasis are 12 times more likely to develop anaemia than non-infected ones. These parasitic infestations are known to cause chronic haemorrhage and iron deficiency, resulting in the development of anaemia.³⁸ Deficiency of iron was the main cause of anaemia among black pregnant women in urbanised cities such as Durban. Reasons for iron deficiency could be due to physiological changes of pregnancy and infection.¹

In malaria endemic areas, the high prevalence of anaemia in general population, including pregnant women, has been observed.²⁷ Folate deficiency is also found to be responsible for nutritional anaemia. Vitamin B₁₂ was found not to be associated with anaemia in pregnancy. Transmissions of intestinal parasitic infestation occur through the faecal-oral route. Personal hygiene and other environmental factors (e.g. unsafe water) are therefore important factors in the transmission of the disease. Socioeconomic conditions, education, living condition (housing, water supply, etc.) and cultural practices play major role in transmitting the diseases in the community.

In studies of the risk factors for cholera in KZN during 2000, it was found that the Uthungulu (Empangeni) health district had the second highest number of cholera cases and attack rate for cholera. Environmental factors such as poor sanitation facilities and a lack of provision of safe water supply to communities are the main reasons for cholera. It is also found that only half of the community members use any type of latrine.³⁹ The inhabitants of the sub-district have less toilet facilities and nearly half of them do not use toilets and have poor knowledge and practice of personal hygiene. Furthermore, nearly half of the households (43%) use unsafe water, mainly from rivers, dams or rain water.³⁹ These conditions (environmental and personal) are conducive to parasitic infestation to anyone, including pregnant women.

The HIV infection rate among pregnant women is the highest in KZN of all other provinces of South Africa.³⁵ Other studies have also found that HIV infection is a risk factor for anaemia in pregnancy.^{25,26} This could be due to the enhancement of nutritional deficiencies, opportunistic infections and the use of antiretroviral drugs in patients with AIDS. To avoid confusion in this study we matched the cases and controls for age, parity and gestational age. Other potential confounding factors such as smoking habits, alcohol consumption as well as chronic medical conditions were not considered and may have influenced the results of the study. It should also be noted that there were no antiretroviral treatment facilities for HIV-positive patients at the time of the study. A single dose of nevirapine was used only at the occurrence of labour pain, and therefore had no impact on anaemia in our study subjects.

A key component of safe motherhood is the eradication of anaemia during pregnancy. The most effective interventions against these infections are preventive and promotive in nature. The prevention should include provision of safe drinking water, clean food, control of flies, safe sex and ensuring universal precautions in human contact. In a national helminth control programme in Uganda and Tanzania, mass treatment with praziquantel and albendazole of all children by school teachers has shown a decrease in infection and morbidity and improved haemoglobin concentration.^{40,41} Concerns about the safety of antihelminthic therapy in pregnancy have been expressed from time to time. Studies have contributed to the knowledge of the consequences of using antihelminthic drugs to reduce morbidity during pregnancy. In Sri Lanka, a study examined the effect of mebendazole treatment during pregnancy on rates of major congenital defects, stillbirth, perinatal death, and low birth weight.⁴² No significant difference was observed between the rates of birth defects among infants of mothers who had taken mebendazole during pregnancy and the rates among infants of untreated mothers. Another study was conducted in western Sierra Leone to examine the role of intestinal nematode infections, including hookworm and albendazole in the second trimester. It was found that the drug minimised the decline in haemoglobin and serum ferritin concentrations during pregnancy without any extra negative effect on newborns.^{43,44} It was therefore concluded that pregnant women in this part of Africa would benefit from antihelminthic treatment after the first trimester and regular iron-folate supplements during the first trimester. After a thorough review of information about antihelminthic drugs (albendazole, levamisole, mebendazole and pyrantel) and with due regard to the seriousness of hookworm infection during pregnancy (e.g. in areas where hookworm infections are endemic and anaemia is prevalent), the WHO recommends treatment with a single, oral dose of an antihelminthic drug. These drugs can be given to pregnant and lactating women, but should be avoided in the first trimester of pregnancy.⁴⁵

The drugs used for treating schistosomiasis are not considered totally safe to use in pregnancy. The use of Praziquantel (PZQ) is found to be the safest of all. A review of the current known toxicology of PZQ over two decades of clinical experience suggests a very low potential for adverse effects on either the mother or her unborn child. The review concluded that pregnant women should be treated with PZQ that women of childbearing age should be included in all mass treatment programmes and that lactating women should not be systematically excluded from treatment.⁴⁶

We recommend chemotherapy (drug) intervention for parasitic infection during the second trimester of pregnancy (between 20–22 weeks) against both intestinal helminthiasis and schistosomiasis.

To reduce transmission of faecal-oral diseases (e.g. intestinal helminthiasis and urinary schistosomiasis), the key interventions recommended are: 1) safe disposal of human excreta, 2) hand-washing practices with soap after defecation, and 3) maintenance of drinking water free from faecal contamination. These interventions can be achieved through health education and health promotion (ensuring toilet facilities and safe water supply).

Conclusion

The findings of this study show that parasitic infections such as intestinal helminthiasis and urinary schistosomiasis and HIV infection are associated with anaemia in pregnancy in the study population. These findings confirm and conform to the findings of other studies.

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