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RESEARCH

Adherence to iron prophylactic therapy during pregnancy in an urban regional hospital in South Africa

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Background: Iron and folic acid supplementation plays a major role in the prevention and control of iron-deficiency anaemia in pregnancy. Therefore, this study assesses adherence to prophylactic iron supplementation during the antenatal period in South Africa.
Methods: An observational study was conducted in a regional hospital from January to December 2016. HIV-uninfected ($n = 100$) and HIV-infected ($n = 100$)] women were enrolled and subdivided into three groups: (a) ≤ 34 weeks ($n = 33$), (b) 34–36 weeks ($n = 34$) and (c) ≥ 37 weeks ($n = 33$) gestational age respectively. A structured questionnaire was used for data collection. Data were coded and statistically analysed using SPSS software. Pill count and self-reported data from women ($n = 24$) at ≤ 34 weeks and 34–36 weeks reflected $< 50\%$ adherence and 46% non-adherence, being higher in the HIV-infected women (75%). Nausea was the commonest side effect across all trimesters (79. 2%). Adherence (27.8%) and non-adherence (72.1%) to iron, folic acid and calcium supplementation were found in 88% of women.
Conclusion: This study found that adherence to micronutrient supplementation is low in pregnancy, albeit higher in HIV-infected women receiving antenatal care at a regional hospital in Durban, South Africa.

Abbreviations: Haemoglobin (Hb), Human Immune Deficiency Virus (HIV), antiretroviral therapy (ARV), zidovudine (ZDV), tuberculosis (TB), low to middle- income countries (LMICs), World Health Organization (WHO), antenatal clinic (ANC).

Keywords: adherence, anaemia, iron deficiency, pregnancy supplements, reticulocyte

Introduction

Iron deficiency is a widespread pathologic cause of anaemia in pregnancy.[1] The World Health Organization (WHO) defines anaemia as a haemoglobin (HB) concentration of ≤ 11 g/dl.[2] Globally, particularly in low- to middle-income countries (LMICs), anaemia is the commonest nutrient deficiency affecting both pregnant women and children.[3] Approximately 56% and 23% of pregnant women in LMICs and high-income countries, respectively, are anaemic.[4] In South Africa, 42.7% of maternal deaths are associated with anaemia, irrespective of micronutrient supplementation.[5]

Iron is necessary for haemoglobin synthesis and its requirement increases during pregnancy, therefore women receive prophylactic iron and folic acid supplementation throughout pregnancy and the puerperium.[1,3,6] Folic acid prevents neural tube defects and macrocytic anaemia, especially when initiated prior to conception and continued in early pregnancy during neural system development.[7] In pregnancy, the physiological demands of a growing foetus, changes in red cell volume, vomiting and increasing nutrient demand support the need for iron supplementation.[8] A decrease in iron stores during pregnancy is accompanied by a significant rise in the reticulocyte count (RC) that eventuates in an increase in erythropoiesis, therefore RC is used to monitor progress after iron supplementation.[9]

The efficacy and success of any medical intervention such as prophylactic iron/folic acid therapy throughout pregnancy is dependent on compliance and adherence to pill usage. The major reasons that national iron supplementation programmes fail include non-adherence to pill taking and other factors such as poorly functioning health systems.[6] Compliance describes the degree to which an individual accurately follows a medical instruction. Non-adherence is defined as missing two or more doses repeatedly.[6] The concurrent use of other medications affects adherence and may increase the severity of anaemia during pregnancy. It is unknown whether the use of antiretroviral drugs increases the severity of anemia.[10] However, a study by Odhiambo *et al*. demonstrated that anti-retroviral therapy including zidovudine improved haemoglobin levels.[11]

Despite the South African national Department of Health guidelines on supplementation of micronutrients to pregnant women, the prevalence of anaemia remains high, thus it is important to investigate adherence and compliance of micronutrient supplement intake amongst pregnant women.

Methods

This questionnaire-based study received institutional ethical (BE 485/15) and regulatory hospital approval prior to commencement. The study was conducted between January and December 2016 at a regional hospital (RH) that serves a largely low socioeconomic Black South African population group. Inclusion criteria included Black South African women ($n = 200$) attending their first antenatal clinic at a regional hospital, who provided written informed consent and were ≥ 18 years of age. HIV-infected ($n = 100$) and HIV-uninfected ($n = 100$) women were

All authors contributed to aspects of the research proposal and submission of article.

recruited and stratified into: (a) ≤ 34 weeks ($n = 33$), (b) 34–36 weeks ($n = 34$) and (c) ≥ 37 weeks ($n = 33$) respectively. Women with medical complications such as cardiac, diabetes, hypertension and haematological disease were excluded. Women who declined to participate were excluded.

It is standard clinical practice in South African public sector hospitals to prescribe prophylactic iron and folate supplementation throughout pregnancy. In the present study, all participants received a month's supply of iron 'Pregamal' tablets (a combination of ferrous fumarate [200 mg/day] and folic acid [100 mg/day]) at every antenatal visit. For anaemic women, ferrous sulphate (FSO_4; 200 mg/day) and folic acid (5 mg/day) was prescribed. In addition, women received calcium carbonate supplementation (1250 mg/day) as a preventative measure against the development of pre-eclampsia.

Women recruited were followed up for adherence at their next scheduled antenatal visit. All adherence and non-adherence information, including side effects, was obtained at each follow-up visit. Women were requested to return the balance of their supplements at each visit. Adherence was assessed via self-reporting and by manual pill count. Self-reporting referred to women who had left pill containers and reported verbally, whereas pill count refers to the number of pills remaining in their container. Full blood count, reticulocyte and serum ferritin (SF) tests were analysed. Patient data including demographic (age, area of residence, social status), clinical (parity, gestational

Table 1: Clinical and demographic data of all study groups

Parameters	1st attendees ≤ 34 weeks HIV uninfected ($n = 33$)	1st attendees ≤ 34 weeks HIV infected ($n = 33$)	34–36 weeks HIV uninfected ($n = 34$)	34–36 weeks HIV infected ($n = 34$)	≥ 37 weeks HIV uninfected ($n = 33$)	≥ 37 weeks HIV infected ($n = 33$)	*p*-value
Residence:							
Urban (%)	100	100	88	91	79	82	0.01
Rural (%)	0	0	12	9	21	18	
Maternal age (years)	24 ± 5	28 ± 7	25 ± 5	31 ± 6	27 ± 7	30 ± 6	0.0001
Maternal height (cm)	158 ± 6	159 ± 7	159 ± 7	157 ± 5	160 ± 7	158 ± 7	0.54
Maternal weight (kg)	69 ± 16	66 ± 12	76 ± 13	76 ± 17	80 ± 16	84 ± 18	0.0001
BMI (kg/m^2)	28 ± 6	27 ± 5	30 ± 5	30 ± 6	32 ± 6	34 ± 6	0.0001
Systolic pressure (mmHg)	12 0 ± 13	115 ± 14	112 ± 10	111 ± 12	112 ± 9	111 ± 11	0.01
Diastolic pressure (mmHg)	70 ± 10	70 ± 12	70 ± 9	70 ± 11	71 ± 8	70 ± 7	0.1
Parity	0 ± 1	1 ± 1	1 ± 1	1 ± 1	1 ± 1	1 ± 1	0.0001
Gravidity	2 ± .755	2 ± 2	3 ± 2	3 ± 0.9	3 ± 2	3 ± 1	0.0001
GA (weeks) current visit	19 ± 7	20 ± 7	35 ± 0.72	35 ± 2	39 ± 2	38 ± 1	0.0001
GA at birth	38 ± 2	39 ± 2	39 ± 2	39 ± 2	40 ± 2	39 ± 2	0.019
Baby weight (kg)	3.06 ± 0.56	3.21 ± 0.45	2.98 ± 0.52	2.86 ± 0.62	3.41 ± 0.43	3.15 ± 0.40	0.004
NVD (%)	54.5	33.3	50	32.3	27.2	27.2	
Scheduled C/S (%)	18.1	18.1	14.7	14.7	15.1	9	
Emergency C/S (%)	0	3.0	9	23.6	42.4	48.4	0.67
Male/Female ratio (%)	45:27	24:30	28:44	29:44	52:33	48:39	0.23
Stillbirth: FSB-MSB-NND (%)	0-3-3	0-0-0	3-0- 0	0-3- 0	0-0-0	0-0-0	0.14
Complications:							
Severe PE (%)	4	0	4	0	0	0	
CPD (%)	8	0	4	0	4	0	0.97
FD (%)	0	20	8	13	4	4	
Preterm labour (%)	13	0	0	0	0	0	
Contraceptives:							
	66	79	68	76	79	64	
Injectable (%)	16	0	18	3	9	3	0.53
Oral (%)	9	12	9	15	12	30	
Tubal ligation (%)							
Feeding:							
Breast (%)	79	79	76	59	91	52	0.003
Formula (%)	21	21	24	41	9	48	

Mean ± SD

NVD = normal vaginal delivery, C/S = Caesarean section, FSB = fresh stillbirth, MSB = macerated stillbirth, NND = neonatal death, CPD = cephalopelvic disproportion, FD = foetal distress, PE = pre-eclampsia, GA = gestational age, Kg = kilograms, CM – centimetres.

age, blood pressure, maternal height and weight) biochemical (urine dipsticks and routine blood results) infection data (HIV and TB infection), dietary habits (including types of food, smoking, alcohol consumption, recreational drugs and herbal medication) as well as birth details, feeding choice and family planning were recorded.

The Statistical Package for the Social Sciences (SPSS Statistics version 24, IBM Corp, Armonk, NY, USA) was used for analysis. Independent sample t-test and ANOVA were used for parametric data. Categorical data are presented using Fisher's exact chi-square test. Parametric data are expressed as mean ± standard deviation. A p-value ≤ 0.05 was considered statistically significant.

Results

Clinical and demographic data are outlined in Table 1. Birthweight was significantly different between the HIV-infected vs. HIV-uninfected groups (p = 0.004). Birthweight at ≤ 34 weeks and ≥ 37 weeks gestation for the HIV-infected vs. HIV-uninfected group was 3.06 ± 0.5 kg vs. 3.21 ± 0.45 kg and 3.41 ± 0.43 kg vs. 3.15 ± 0.40 kg respectively.

The haematological, reticulocyte profiling and SF levels taken at antenatal visits across the study population are shown in Table 2. Haemoglobin levels were below the normal reference range for pregnancy in the HIV-uninfected ≤ 33 weeks (52%), HIV-infected ≤ 34 weeks (58%), HIV-uninfected 34–36 weeks (50%) and HIV-infected 34–36 weeks (56%). The ≥ 37 weeks groups (both HIV uninfected and infected) displayed lower haemoglobin levels (18%, 33%) respectively. Based on HIV status, SF levels were similar across all groups. In the HIV-uninfected ≤ 34 weeks, the reticulocyte percentage (RC) was 6% above the normal range compared with other groups ($p = 0.44$). The reticulocyte production index (RPI) was significantly higher and within the reference range for the HIV-uninfected ≥ 37 weeks(1 ± 0.34) compared with the other groups ($p = 0.0001$; Table 2). Maternal haemoglobin levels at delivery were significantly different between groups ($p = 0.006$; Table 2).

After the initial enrolment visit, a loss to follow-up was noted at subsequent antenatal visits, particularly in the 34–36 weeks group (Table 3). Haematological profiles such as haemoglobin and SF as well as reticulocyte data did not differ across groups and were within the normal reference range (Table 3). However, the mean reticulocyte production index (RPI) for the HIV-infected < 34 weeks (0.77 ± 0.30%) was below the normal reference range (1–2%). The percentage of pill count, self-reported adherence and reasons for non-adherence across the study groups are outlined in Table 4.

In the groups that were followed up, a higher percentage of patients returned empty pill containers (50%) compared with those returning two or more pills (20.8%) and in those that did not know the number of pills remaining in the container (29.1%). These women reported an unknown pill number remaining in the container and gave no reason for their non-adherence. Notably in the HIV-infected groups there was a higher percentage that were unaware of the number of pills remaining (41.7%) compared with the HIV-uninfected groups (16%). The number of patients returning empty containers was lower in the HIV-infected (25%) compared with the HIV-uninfected (75%) groups. Moreover, at ≥ 37 weeks' gestation, the percentage of women unaware of the number of pills remaining was higher (67.6%) compared with those

Table 2: Haematological results of all study groups

Parameters	1st attendees ≤ 34 weeks HIV uninfected ($n = 33$)	1st attendees ≤ 34 weeks HIV infected ($n = 33$)	34–36 weeks HIV uninfected ($n = 34$)	34–36 weeks HIV infected ($n = 34$)	≥ 37 weeks HIV uninfected ($n = 33$)	≥ 37 weeks infected ($n = 33$)	Reference range	p- value
Haemoglobin at recruitment (g/dl) %	11 ± 2 (51.5)	11 ± 2 (57.5)	11 ± 2 (52.9)	11 ± 2 (55.8)	12 ± 2 (18.1)	12 ± 2 (33.3)	11–12	0.0001
Serum ferritin (µg/L)	34 ± 35	28 ± 29	30 ± 42	23 ± 15	33 ± 20	30 ± 22	10–291	0.68
Reticulocyte C (%)	6 ± 23	2 ± 0.46	2 ± 0.48	2 ± 0.50	2 ± 0.43	2 ± 0.59	0.5–2	0.44
Reticulocyte CA (X 10^{12}/L)	0.06 ± 0.03	0.06 ± 0.04	0.07 ± 0.02	0.08 ± 0.06	0.09 ± 0.1	0. 07 ± 0.03	0.05–0.1	0.09
Corrected RC (%)	2 ± 0.45	0.10 ± 0.34	2 ± 0.33	2 ± 0.44	2 ± 0.34	2 ± 0.50		0.0001
Reticulocyte PI	0.78 ± 0.41	0.62 ± 0.24	0.88 ± 0.26	0.82 ± 0.33	1 ± 0.34	0.81 ± 0.37	1–2	0.0001
Haemoglobin at birth (g/dl)	11 ± 0.59	11 ± 2	11 ± 2	11 ± 2	13 ± 0.91	12 ± 0.89	11–12	0.006

Mean ± SD.
Reticulocyte C = reticulocyte count, reticulocyte CA = reticulocyte count absolute, corrected RC = corrected reticulocyte count, reticulocyte PI = reticulocyte production index.

Table 3: Clinical data collected during pregnancy follow-up

Parameters	1st attendees ≤ 34 weeks HIV uninfected (*n* = 10)	1st attendees ≤ 34 weeks HIV infected (*n* = 9)	34–36 weeks HIV uninfected (*n* = 2)	34–36 weeks HIV infected (*n* = 3)	Reference range	*p*-value
Maternal Age (years)	24 ± 5	27 ± 6	21 ± 0.71	31 ± 3	–	0.06
GA (weeks)	26 ± 8	30 ± 11	38 ± 3	37 ± 2	–	0.08
Maternal weight (kg)	65 ± 13	77 ± 13	81 ± 37	79 ± 9	–	0.16
Maternal height (cm)	158 ± 7	160 ± 6	159 ± 10	153 ± 2	–	0.31
BMI (kg/m^2)	26 ± 4	30 ± 5	33 ± 13	33 ± 3	–	0.04
Haemoglobin (g/dl)	11 ± 0.72	11 ± 2	11 ± 0.15	11 ± 0.94	11–12	0.96
Reticulocyte C (%)	2 ± 0.59	2 ± 0.45	2 ±	2 ± 0.35	0.5–2	0.31
Reticulocyte CA (x 10^{12}/IL)	0.08 ± 0.03	0.14 ± 0.3	0.19 ±	0.06 ± 0.02	0.05–0.1	0.66
Corrected R C (%)	2 ± 0.47	2 ± 0.4	2 ±	2 ± 0.31	–	0.34
Reticulocyte PI	2 ± 0.32	0.77 ± 0.30	1 ±	2 ± 0.31	1–2	0.20
Serum ferritin (µg/L)	50 ± 52	23 ± 14	18 ±	27 ± 29	10–291	0.53

Mean ± SD. BMI = Body mass index. For other abbreviations, see note to Table 2.

Table 4: Pill count and self-reported adherence

Parameters	HIV uninfected (*n* = 12)	HIV infected (*n* = 12)	Total %	Total no. of women: 24
Follow-up at scheduled dates: first attendees ≤ 34 weeks/34–36 weeks' gestation:				
Number of women who returned two or more pills	1 (8.3%)	4 (33.3%)	5 (20.8%)	Adherence (50%)
Number of women who returned zero pills	9 (75%)	3 (25%)	12 (50%)	Non-adherence (46%)
Number of women with unknown number of pills remaining	2 (16.7%)	5 (41.7%)	7 (29.1%)	

Adherence at term birth and at recruitment: first attendees ≤ 34 weeks, 34—36 weeks, ≥ 37 weeks/birth gestation:				
Parameters	**HIV uninfected (*n* = 91)**	**HIV infected (*n* = 85)**	**Total % of all groups**	**Total no. of women: 176 (88%)**
Number of women who returned two or more pills	5 (5.4%)	3 (3.5%)	8 (10.5%)	Adherence (27.8%)
Number of women who returned zero pills	22 (24.1%)	27 (31.7%)	49 (27.8%)	Non-adherence (72.1)
Number of women with unknown number of pills remaining	64 (70.2%)	55 (64.7%)	119 (67.6%)	

Reasons for non-adherence: follow-up groups: first attendees ≤ 34 weeks/34–36 weeks' gestation						
	HIV uninfected (*n* = 12)		HIV infected (*n* = 12)			
Factors	**First visits**	**34–36 weeks**	**First visits**	**34–36 weeks**	**Total %**	**Total no. of women: 24**
Side effects (%):						
Nausea	4 (33.3)	1 (8.3%)	5 (38.4%)	0	10 (40%)	
Vomiting	0	1 (50)	0	0	1 (4%)	
Dark stools	2 (16.7%)	0	1 (7.7%)	1 (7.7%)	4 (16%)	
Constipation	1 (8.3%)	0	1 (7.7%)	2 (15.3%)	4 (16%)	
Skipped doses (%)	30 (3)	50 (1)	30 (3)	33 (1)	8 (32%)	

Reasons for non-adherence at birth and at recruitment: first attendees ≤ 34 weeks/34–36 weeks, ≥ 37 weeks' gestation			
Factors	**HIV uninfected (*n* = 91)**	**HIV infected (*n* = 85)**	**Total % of all groups (*n* = 176); 88%**
Side effects (%):			
Nausea (%)	35 (38.4%)	34 (40%)	69 (39.2%)
Vomiting (%)	16 (17.9%)	8 (9.4%)	24 (13.6%)
Dark stools (%)	31 (34%)	29 (34.1%)	60 (34%)
Constipation (%)	12 (13.2%)	14 (16.5%)	26 (14.8%)
Heartburn (%)	1 (1%)	4 (4.7%)	5 (2.8%)
Other (%)		7 (8.2%)	7 (3.9%)
Skipped doses (%)	18 (19.8)	10 (11.8%)	28 (15.9%)
Forgetfulness (%)	2 (2.2%)	3 (3.5%)	5 (2.8%)
Pill overload (%)	–	3 (3.5%)	3 (1.7%

that returned two or more pills (10.5%) and with those that returned empty containers (27.8%). Women reporting unknown number of pills were higher in the HIV-uninfected compared with the HIV-infected groups (70.2% vs. 64.7%). In contrast, those that reported no pills remaining were higher in the HIV-infected (31.7%) compared with the HIV-uninfected group (24.1%). In the HIV-uninfected group only 5.4% reported two or more pills remaining compared with 3.5% in the HIV-infected groups.

Table 4 outlines the reasons for non-adherence within all study groups. In women that were followed up at scheduled visits, the main reasons for non-adherence were nausea (40%), skipped doses (32%), dark stools (16%), constipation (16%) and vomiting (4%). Nausea was highest in the < 34weeks compared with the 34–36 weeks groups irrespective of HIV status. Similarly, the women followed up at ≥ 37 weeks had a higher percentage of nausea (39.2%) followed by dark stools (34%), skipped doses (15.9%), constipation (14.8%), vomiting (13.6%), forgetfulness (2.8%) and pill overload (1.7%).

Discussion

The present study assessed compliance and adherence of pregnant women to iron and folic acid supplementation at RH. The methods of assessment of adherence used in the current study has been utilised in other studies.[12–14] In the current study, adherence to pill intake was 50% across all follow-up groups. Non-adherence to pill intake was high: 20.8% of women returned ≥ 2 pills whilst 29.1% reported not knowing the number of pills remaining at follow-up visits. The current study demonstrated that a higher percentage of women reported an unknown number of pills remaining (41.7%) in the HIV-infected compared with the HIV-uninfected cohort. Of note, most of the adherence data collected at ≥ 37 weeks' gestation were self-reported rather than by pill count. A reason for this factor is that some women consulted at their first visit were only followed up for pill taking at ≥ 37 weeks' gestation. Moreover, in the group consulted at recruitment and birth the percentage of the number of pills remaining in both the HIV-uninfected and the HIV-infected women was low (5.4%, 3.5%). However, the percentage of women reporting no pills remaining was higher among the HIV-infected women (31.7%) compared with the HIV-uninfected women (25.1%).

In the current study there was a high percentage of unknown number of pills remaining in both the HIV-uninfected and HIV-infected women (70.2% vs. 64.7% respectively). Self-reporting may overestimate compliance compared with pill count or biochemical methods.[13] In contrast, Ibrahim *et al.*[12] observed that self-reporting (41.1%) was a better indicator of adherence compared with pill count (36.7%). However, Bondarianzadeh *et al.* demonstrated that women may falsely report pill taking as confirmed by positive stool test.[14]

Of note, we observed that women were occasionally issued with inadequate iron tablet supplements. This may be attributed to poor antenatal attendance, incorrect follow-up dates and most often the absence of an effective logistic system to dispense the supply, or a shortage of drug suppliers at the institution. A study from another LMIC, namely Ethiopia, also reported inadequate iron supplementation at antenatal clinic visits due to poor iron tablet supply and the lack of an effective distribution system.[13]

In the current study, the reasons for non-adherence to iron prophylactic therapy included nausea, vomiting, dark-coloured stools, constipation, heartburn, skipped doses, forgetfulness and pill overload. In the HIV-infected compared with the HIV-uninfected group, nausea (40% vs. 39.2%) was the most common side effect followed by dark stools (16% vs. 34%), constipation (16% vs. 14.8%), skipped doses (32% vs. 15.9%) and vomiting (4% vs. 13.8%). Other studies have corroborated our finding of the commonest adverse event being nausea.[15–16] Notably, a high level of pregnancy-induced nausea and/or vomiting may exacerbate a women's non-adherence during the first trimester.[17] In our study, the incidence of nausea was high across all trimesters.

The finding of nausea may be attributed to the poor quality of iron supplement prescribed or due to the high level of iron intake on an empty stomach; the latter is corroborated by the low socioeconomic status of the women in the current study.[18] It is worth noting that side effects are not associated with non-compliance.[19] In contrast to our study, dark stools were not frequently reported by similar studies.[15–16]

In the current study, anaemia was higher in the HIV-infected groups compared with the HIV-uninfected groups, being higher at 34–36 weeks' gestational age compared with the term pregnancy group. Similarly, Tunkyi and Moodley[4] observed a high incidence of anaemia in HIV-infected pregnant women. The significant improvement of haemoglobin level at delivery across all groups in the current study is corroborated by a report from India[20] in which the prevalence of anaemia was reduced from 48% at first visit to 10% at fourth visit. Our findings also reveal that women enter pregnancy with an inadequate bone marrow response, as we noted a significant decrease in the production of red blood cells within the study population. The RPI levels were significantly different ($p = 0.0001$) across groups. Notably in the HIV uninfected < 34 weeks, the mean RC was higher compared with the other groups, implying an immature release of red blood cells from the bone marrow contributing to iron-deficiency anaemia and eventuating in premature labour (13%). Despite similar reticulocyte levels across the three groups ($p > 0.05$), the RPI levels in the HIV infected < 34 weeks follow-up group suggests an inadequate bone marrow response.

In the current study, age and socioeconomic income did not correlate with adherence to iron supplementation. Similarly, Roy *et al.*[20] report that age and socioeconomic status do not correlate with micronutrient adherence whilst Mithra *et al.*[6] suggest parity as a key contributor to iron supplementation compliance.

The present study also found that iron supplementation is not associated with poor birth outcome. Similar to our findings, a Tanzanian study[21] also demonstrated a non-correlation of iron supplementation with low birthweight, prematurity and small-for-gestational age babies.

It is also worthy of mention that the main limitation included self-reported data rather than pill count and a loss to follow-up. After the initial enrolment, many women did not return, particularly in the 34–36 weeks group, hence adherence data were collected only at the time of delivery. This is a common occurrence in LMIC due to cost of travel. This non-attendance led to incomplete biochemical history.

Conclusion and recommendations

In conclusion, the current study found that non-adherence to iron and folic acid supplementation in pregnant women was higher in HIV-positive than HIV-negative women in a large regional hospital in South Africa. Nausea was the commonest side effect across all trimesters and it is also the most common reason for non-adherence to iron prophylactic treatment. The reticulocyte production index should be considered a more accurate measure of iron pill adherence.

Health education sessions during the antenatal period are recommended to improve women's understanding of the importance of iron prophylactic therapy. In addition, proper information concerning the timing of taking iron and folic acid supplementation and the prescribing of high-quality iron tablets may decrease the frequency of nausea. Further research should include the use of electronic counting devices for accurate pill count including the addressing of concurrent usage of iron prophylactic therapy with other treatments.

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