ORIGINAL ARTICLE

IS PREGNANCY ASSOCIATED WITH BIOCHEMICAL AND HAEMATOLOGICAL CHANGES IN HIV-INFECTED NIGERIAN WOMEN?

L O Omo-Aghoja[1], *MB BS, FWACS, FMCOG, FICS*
E Abe[2], *MB BS, FWACS*
V W Omo-Aghoja[3], *BDS, FMCDS*
A Onowhakpor[1], *MB BS, FWACS*
P Feyi-Waboso[4], *MB BS, FWACS*
[1]*Department of Obstetrics and Gynaecology, College of Health Sciences, Delta State University, Abraka, Nigeria*
[2]*Department of Obstetrics and Gynaecology, Central Hospital, Benin City, Nigeria*
[3]*Department of Oral and Maxillofacial Surgery, Central Hospital, Sapele, Nigeria*
[4]*Department of Obstetrics and Gynaecology, Abia State University Teaching Hospital, Aba, Nigeria*

Background. While there is evidence that HIV affects the course and outcome of pregnancy, reports on the effects of pregnancy on HIV infection remain conflicting, especially in low-resource settings.

Methodology. A prospective study of two demographically similar cohorts of HIV-seropositive women, 154 pregnant and 151 non-pregnant, was conducted in a hospital setting in Nigeria.

Results. Cases and controls were matched for age, but parity in controls was significantly higher than in cases (p<0.0001). The time between diagnosis and treatment commencement was greater in controls compared with cases (p<0.0001). Electrolyte, urea and creatinine levels were within normal limits, with mean serum urea and potassium higher in controls compared with cases (p=0.002 and p=0.023). Aspartate aminotransferase (AAT)/serum glutamic oxaloacetic acid transaminase (SGOT), alanine aminotransferase (ALT)/serum glutamic-pyruvic transaminase (SGPT) and amylase levels were higher in controls compared with cases (p=0.001, p=0.0001 and p=0.05), but the mean CD4 count was higher in cases compared with controls (p=0.001). The haematological parameters were within normal limits and comparable in cases and controls. A comparison of CD4 count, total white blood cell count and packed cell volume across the three trimesters in the cases did not reveal any statistically significant differences in these parameters.

Conclusion. Pregnancy did not affect biochemical and haematological parameters in HIV-infected Nigerian women.

The rate of HIV infection in pregnancy is high.[1-7] There is evidence that HIV infection in pregnant women is associated with adverse maternal and fetal outcomes.[2,5,6] The effects of HIV infection include severe anaemia, infectious morbidities and vertical transmission.[2,5,8-14] In a Malawian study, AIDS and anaemia were the leading causes of maternal mortality,[15] and in Zaire maternal mortality rates in HIV-infected women were 10 times those of HIV-negative women.[16] A personal communication revealed that in a recent unpublished report from a Nigerian Teaching Hospital, HIV/AIDS accounted for 20.2% of maternal deaths.

However, the effect of pregnancy on HIV disease progression remains contentious. Evidence from developed countries suggests that pregnancy does not accelerate the progression of HIV disease,[17-21] while reports from low-resource settings imply otherwise, indicating that pregnancy may influence the rate of disease progression.[2] It has been suggested that other factors, including genetics, nutritional status and intercurrent infections, may be responsible for the rate of HIV disease progression in low-resource settings.[2,22,23] John and colleagues report an association between CCR5 promotor polymorphism and increased maternal mortality in a Kenyan cohort.[23]

The objectives of the present study were to determine the association between pregnancy and biochemical and haematological changes in HIV-infected Nigerian women as a possible indicator of disease severity.

METHODOLOGY

This study was conducted in Central Hospital, Benin City, Nigeria, which provides tertiary care to patients in Benin City and its environs. It was a prospective study of two demographically similar cohorts of HIV-seropositive women, 154 pregnant and 151 non-pregnant. The cases were pregnant women attending the antenatal clinics of the hospital from October 2005 to October 2007. Once a pregnant case was identified, the next non-pregnant HIV-seropositive patient presenting to the HIV treatment, control and prevention programme unit of the hospital and matched for social class (patient's educational status and husband's occupation,[24] location of residence, size of apartment, average weekly income, number and types of cars if any, types of electronic and electrical gadgets at home) was selected as a control. Any patient who experienced repeated attacks of malaria or other intercurrent infections was excluded from the study.

Upon recruitment, both pregnant and non-pregnant women had a data sheet completed that elicited information on socio-demographic variables, time since diagnosis of seropositive status, duration of antiretroviral therapy, and biochemical and haematological parameters. Specifically, the following biochemical measurements were done: serum electrolyte, urea and creatinine levels, serum fasting blood sugar (FBS), serum aspartate aminotransferase (AAT)/ glutamic oxaloacetic acid transaminase (SGOT), alanine aminotransferase (ALT)/ serum glutamic-pyruvic transaminase (SGPT), total bilirubin, serum amylase, serum cholesterol, very low-density lipoprotein (VLDL) and lactate dehydrogenase (LH). In addition, a full blood count (FBC - packed cell volume (PCV), white blood cell (WBC) count, platelet count and differentials) and CD4 cell count were performed.

The study was approved by the hospital's Human Ethics Committee and was carefully explained to the patients, and only those who gave informed written consent were recruited into the study.

The Statistical Package for Social Sciences (SPSS) version 13 was used for the data management and statistical analysis, with Fisher's exact test, the chi-square test or Student's *t*-test (as appropriate) being used for comparison of the mean absolute values and standard deviations (SDs). The level of significance was 0.05.

RESULTS

The socio-demographic profile and time since diagnosis and commencement of treatment are set out in Table I. The pregnant women had had their HIV diagnosis for periods ranging from 1 to 30 months (median 10 months) and had been on treatment for periods ranging from 1 to 30 months (median 8 months), while the non-pregnant women had had their HIV diagnosis for periods ranging from 14 to 29 months (median 17 months) and had been on treatment for periods ranging from 2 to 29 months (median 16 months).

The median age of the pregnant women was 29.4 years, with a range of 18 - 36 years (mean 28.6, SD 4.6) and the median age of the non-pregnant women 30.2 years, with a range of 16 - 42 years (mean 29.2, SD 3.9). The median parity in the pregnant women was 1.00, with a range of 0 - 7 (mean 1.25, SD 1.59), and that for the non-pregnant women 2.00, with a range of 0 - 13 (mean 2.10, SD 2.29). This difference was statistically significant ($p<0.0001$). The median estimated gestational age at booking was 26 weeks, with a range of 2 - 42 weeks (mean 25.8, SD 8.13). In the pregnant

TABLE I. COMPARISON OF THE SUMMARY STATISTICS OF THE SOCIO-DEMOGRAPHIC PROFILE, DURATION OF DIAGNOSIS AND TREATMENT OF CASES V. CONTROLS

Parameters	*N*	Mean (SD)	Median	*p*-value
Age (yrs)				
Cases	154	28.6 (4.2)	29.4	
Controls	151	28.9 (4.1)	30.2	0.239
Parity				
Cases	154	1.25 (1.59)	1.00	
Controls	151	2.10 (2.29)	2.00	<0.0001
EGA at booking (wks)				
Cases	154	25.8 (8.13)	26.00	
Controls	151	N/A	N/A	
Time since diagnosis (mo.)				
Cases	154	10.27 (6.12)	10.00	
Controls	151	16.86 (1.69)	17.00	<0.0001
Duration of treatment (mo.)				
Cases	154	8.86 (5.99)	8.00	
Controls	151	15.02 (3.82)	16.00	<0.0001

SD = standard deviation; EGA = estimated gestational age.

group a median of 10 months had elapsed since the diagnosis of HIV, with a range of 1 - 30 months (mean 10.27, SD 6.12), and in the non-pregnant group a median of 17 months had elapsed, with a range of 14 - 29 months (mean 16.86, SD 1.69). This difference was statistically significant ($p<0.0001$).

Serum electrolyte, urea and creatinine levels in cases versus controls are set out in Table II. The mean serum urea and potassium levels, though within normal limits, were higher in non-pregnant than pregnant women, as were the mean serum aspartate aminotransferase (AAT)/ serum glutamic oxaloacetic acid transaminase (SGOT), alanine aminotransferase (ALT)/ serum glutamic-pyruvic transaminase (SGPT) and serum amylase (Table III). However, the CD4 cell count was higher in the pregnant women than in the controls ($p=0.001$), while the haematological parameters were within normal limits and comparable between cases and controls (Table IV). Comparison of the mean CD4

TABLE II. COMPARISON OF MEANS OF SERUM ELECTROLYTE, UREA AND CREATININE LEVELS OF CASES V. COHORTS

Parameter	*N*	Mean (SD)	*p*-value
Sodium (mmol/l)			
Cases	154	139.36 (17.21)	0.260
Controls	151	142.00 (19.99)	
Potassium (mmol/l)			
Cases	154	4.15 (0.65)	0.023
Controls	151	4.48 (0.96)	
Urea (mmol/l)			
Cases	154	6.67 (9.81)	0.002
Controls	151	11.70 (14.70)	
Creatinine (mmol/l)			
Cases	154	1.16 (1.44)	0.629
Controls	151	1.24 (1.26)	

TABLE III. COMPARISON OF MEANS OF OTHER BIOCHEMICAL PARAMETERS OF CASES V. CONTROLS

Parameters	*N*	Mean (SD)	*p*-value
FBS (mg/dl)			
Cases	154	79.67 (8.41)	0.808
Controls	151	91.00 (13.92)	
AAT/SGOT (U/l)			
Cases	154	35.66 (35.28)	0.001
Controls	151	57.91 (68.17)	
ALT/SGPT (U/l)			
Cases	154	17.29 (16.27)	<0.0001
Controls	151	27.68 (24.89)	
Amylase (U/l)			
Cases	154	69.3 (37.86)	0.05
Controls	151	83.17 (45.36)	
VLDL (mg/dl)			
Cases	154	67.79 (162.75)	0.045
Controls	151	31.58 (53.28)	

TABLE IV. COMPARISON OF MEANS OF HAEMATOLOGICAL PARAMETERS OF CASES V. CONTROLS

Parameter	*N*	Mean (SD)	*p*-value
CD4 count (cells/µl)			
Cases	154	378.16 (272.57)	0.001
Controls	151	279.74 (230.74)	
Total WBC ($\times 10^9$/l)			
Cases	154	5.64 (1.77)	0.304
Controls	151	5.35 (2.81)	
Lymphocytes ($\times 10^9$/l)			
Cases	154	2.15 (2.04)	0.920
Controls	151	2.17 (1.96)	

count, total WBC count and PCV in the three trimesters of pregnancy did not reveal any statistically significant differences in the respective values.

DISCUSSION

A systematic review and meta-analysis of seven cohort studies from 1983 to 1996 suggested that there is an association between adverse maternal outcomes and pregnancy in HIV-infected women. The summary odds ratios for the risk of an adverse maternal outcome related to HIV infection and pregnancy were 1.8 (85% confidence interval (CI) 0.99 - 3.3) for death, 1.41 (95% CI 0.85 - 2.33) for HIV disease progression, and 1.63 (95% CI 1.00 - 2.67) for progression to an AIDS-defining illness. This association appeared to be stronger in the one study in this group conducted in a resource-poor setting.[2]

The objective of the present study was to describe any biochemical and haematological differences in the plasma of pregnant and non-pregnant HIV-infected Nigerian women. In all women, the parameters assessed were within normal limits. The CD4 count was significantly higher in the pregnant compared with the non-pregnant controls, despite the fact that the non-pregnant women had been on antiretroviral drugs for longer.

Nutritional factors and intercurrent infections have been shown to play a role in disease progression in low-resource settings. These factors were controlled for in this study, as the two groups were matched for social class and women with intercurrent infections were excluded from the study. The prognosis for HIV disease in pregnancy is worse for patients with intercurrent infections such as malaria, urinary tract infections, sexually transmitted infections and parasitic infestation.[2,24] Malnutrition, infections and infestations are generally widespread in low resource-settings.

In conclusion, this study failed to show any independent association between pregnancy and abnormal blood parameters that may suggest disease severity in HIV-infected Nigerian women. It is reasonable to suppose that any increased morbidity and mortality of pregnancy may be modulated through the combined effects of nutritional factors, intercurrent infections and genetic factors. Efforts to address these are likely to contribute to reducing the burden of HIV morbidity in infected pregnant Nigerian women.

Conflict of interest. We confirm that this study was self-funded by the authors and that the outcome is a true reflection and interpretation of the scientific findings and was in no way influenced by the authors. The work is original and it is not being considered for publication by any other journal.

REFERENCES

1. McIntyre J. Maternal health and HIV. *Reprod Health Matters* 2005; 13(35): 129-135.
2. McIntyre J. Mothers infected with HIV. *Br Med Bull* 2003; 67: 127-135.
3. Offiong RA, Bunza FM, Uya AO. Prevalence of HIV infection among prenatal patients in Abuja. *Tropical Journal of Obstetrics and Gynaecology* 2001; 18: suppl. 1, 12. .
4. Urassa E, Massawe S, Mgaya H, Lindmark G, Nystrom L. Female mortality in reproductive ages in Dar es Salaam, Tanzania. *East Afr Med J* 1994; 71: 226-231.
5. Mertz KJ, Parker AL, Halpin GJ. Pregnancy-related mortality in New Jersey, 1975 to 1989. *Am J Public Health* 1992; 82: 1082-1088.
6. Huss M, Bongain A, Bertrandy M, Hofman P, Grimaud D, Gillet JY. Maternal mortality in Nice. Results of a reproductive age mortality survey using death registries in the Nice University Hospital, 1986-1993. *J Gynecol Obstet Biol Reprod* (Paris) 1996; 25: 636-644.
7. Rosenfield A, Mwaba P, Chintu C, Grange JM, Ustianowski A, Zumla A. A study of maternal mortality in resource-poor countries. *Journal of the American Medical Women's Association* 2002; 57: 167-168.
8. Public Health Service Task Force. Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV-1 transmission in the United States. June 16, 2003. http://www.aidsinfo.nih.gov/guidelines (accessed 30 March 2004).
9. Ahmed Y, Mwaba P, Chintu C, Grange JM, Ustianowski A, Zumla A. A study of maternal mortality at the University Teaching Hospital, Lusaka, Zambia: the emergence of tuberculosis as a major non-obstetric cause of maternal death. *Int J Tuberc Lung Dis* 1999; 3: 675-680.
10. Bicego G, Boerma JT, Ronsmans C. The effect of AIDS on maternal mortality in Malawi and Zimbabwe. *AIDS* 2002; 16: 1078-1081.
11. Iloki LH, G'Bala Sapoulou MV, Kpekpede F, Ekoundzola JR. Maternal mortality in Brazzaville (1993-1994). *J Gynecol Obstet Biol Reprod* (Paris) 1997; 26: 163-168.
12. MacLoed J, Rhode R. Retrospective follow-up of maternal deaths and their associated risk factors in a rural district Tanzania. *Trop Med Int Health* 1998; 3: 130-137.
13. Kumar RM, Uduman SA, Khurrana AK. Impact of pregnancy on maternal deaths AIDS. *J Reprod Med* 1997; 42: 429-434.
14. National Committee on Confidential Enquiries into Maternal Deaths. A review of maternal deaths in South Africa during 1998. *S Afr Med J* 2000; 90: 367-373.
15. McDermott JM, Slutsker L, Steketee RW, Wirima JJ, Breman JG, Heymann DL. Prospective assessment of mortality among a cohort of pregnant women in rural Malawi. *Am J Trop Med Hyg* 1996; 55: 66-70.
16. Ryder RW, Nsuami M, Nsa W, *et al.* Mortality in HIV-1-seropositive women, their spouses and their newly born children during 36 months of follow-up in Kinshasa, Zaire. *AIDS* 1994; 8: 667-672.
17. Bledsoe K, Olopoenia L, Barnes S, Delapenha R, Saxinger C, Frederick W. Effect of pregnancy on progression of HIV infection. *Int Conf AIDS* 1990; 6: 288.
18. Bessinger R, Clark R, Kissinger P, Rice J, Coughlin S. Pregnancy is not associated with the progression of HIV disease in women attending an HIV outpatient program. *Am J Epidemiol* 1998; 147: 434-440.
19. McIntyre JA. HIV in Pregnancy: A Review. Occasional Paper No. 2. Geneva: World Health Organization, 1999.
20. Weisser M, Rudin C, Battegay M, Pfluger D, Kully C, Egger M. Does pregnancy influence the course of HIV infection? Evidence from two large Swiss cohort studies. *J Acquir Immune Defic Syndr Hum Retrovirol* 1998; 17: 404-410.
21. Ahdieh L. Pregnancy and infection with human immunodeficiency virus. *Clin Obstet Gynecol* 2001; 44: 154-166.
22. Villamor E, Msamanga G, Spiegelman D, Peterson KE, Antelman G, Fawzi W. Pattern and predictors of weight gain during pregnancy among HIV-1 women from Tanzania. *J Acquir Immune Deficiency Syndr* 2003; 32 (5): 560-569.
23. John GC, Bird T, Overbaugh J, *et al.* CCR5 promoter polymorphism in Kenyan perinatal human immunodeficiency virus type 1 cohort: association with increased 2-year maternal mortality. *J Infect Dis* 2001; 184: 89-92.
24. Olusanya O, Okpere E, Ezimokhai M. The importance of social class in voluntary fertility control in developing country. *West Afr J Med* 1985; 4(4): 205- 212.
25. Ayisi JG, van Eijk AM, ter Kuile FO, *et al.* The effect of dual infection with HIV and malaria on pregnancy outcome in western Kenya. *AIDS* 2003; 17: 585-594.