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Correlation between Asymptomatic Bacteriuria and HIV-1 Viral Load Level and CD4 Count in Pregnant Women on Antiretroviral Therapy in N'djamena (Chad)

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Abstract

A cross-sectional study was conducted at the "Centre de l'Appui Psycho-Médico-Social (APMS)" which is a centre for Psychological and Medical Support in N'Djamena (Chad) from January to March 2014. The aim of this study was to evaluate the correlation between asymptomatic bacteriuria (ASB) and viral load level and CD4 count in seventy-six (76) HIV-1 infected pregnant women on antiretroviral therapy (ART). Urine culture and bacteria identification were performed by using a chromogenic culture medium (UriselectR4). T CD4+ lymphocytes count and viral load measurement were done respectively on PIMA™ test and Abbott m2000 RealTime HIV-1. In this study, 25 (32.9%) pregnant women were carrying ASB and major bacteria; *Escherichia coli* and *Streptococcus agalactiae* known to cause neonatal meningitis to newborns were identified. Bacteria were isolated mainly in women with CD4 lymphocytes < 200 cells/mm³ (60%) (15/25) and a viral load > 3log (70%) (19/25). Besides the prevention of mother to child transmission of HIV, which remains a goal, it is important to prevent also the transmission of other microorganisms causing neonatal

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infections. Our findings support the needs to do bacteriological analysis of urine in every HIV-infected pregnant woman at least in late pregnancy.

Keywords

Pregnant Women, Asymptomatic Bacteriuria, Lymphocyte CD4, Viral Load

1. Introduction

Successful antiretroviral therapy (ART) in people living with HIV (PLHIV) may leads to an undetectable viral load (VL) after 6 months treatment and be maintained undetectable or below 50 copies/ml later [1] [2]. Besides this antiretroviral drugs' effectiveness, it turned out that the immunosuppression state induced by the Human Immunodeficiency Virus (HIV) infection seems to increase asymptomatic bacteriuria (ASB) in HIV infected pregnant women in about 6% to 20% of cases [3]-[7]. ASB is a urinary tract infection without clinical signs [8] [9]. In this case, urine culture is recommended at the first prenatal visit [10].

This study is conducted to evaluate the correlation between ASB and CD4 count and HIV-1 viral load in a cohort of HIV infected pregnant women followed-up for prevention of mother to child transmission (PMTCT) in N'djamena (Chad).

2. Material and Methods

2.1. Study Site and Population

This was a cross sectional study conducted from January 1st to March 31st, 2014 among pregnant HIV-1 infected women on ART and followed-up at Centre de l'Appui Psycho-Médico-Social (APMS) of Ndjamena (Chad), a health center dedicated to people living with HIV. Pregnant women attending the site for antenatal care and not presenting any symptoms of a urinary tract infection (UTI) and not taking antibiotics for any current infection, who gave their oral consent, were included in the study.

2.2. Samples Collection

Clean-catch midstream urine samples were collected in sterile universal containers from pregnant women. They were instructed on how to collect samples and the need for prompt delivery to the laboratory the next day following their inclusion. About 10 ml venous blood were collected at the elbow on 2-Ethylene Diamine Tetra Acetate (EDTA) tubes.

2.3. Laboratory Analyses

Urine samples were seeded within 30 minutes to 1 hour after the collection onto Uriselect^{TM} 4 (Bio-Rad, France)—a chromogenic non-selective agar medium consisted of a rich nutrients base of four peptones ensuring the growth of all the germs of the urinary tract, two chromogenic substrates for the detection of bacterial enzymes (β-galactosidase and β-glucosidase), and tryptophan for the detection tryptophanase's activity (indole production) and tryptophan deaminase (TDA). Cultures were incubated at 37˚C for 24 hours. Bacterial colonies growing on the agar after the incubation period were identified as described by the Uriselect^{TM} 4 user guide.

CD4 count was performed on whole blood using Alere Pima^{TM} (Alere Technologies GmbH, Germany), a point-of-care device. Viral load samples were brought to the Virology Unit of the General Reference Hospital of N'Djamena (HGRN, Chad), using an insulated refrigerated container at 4˚C. On site, two plasma aliquots of about 1 ml were made and stored at −20˚C until the VL test was carried out. The VL was determined using Real-Time-Reverse Transcription Polymerase Chain Reaction (Real-Time RT-PCR) method using Abbott m2000 RealTime System (Abbott Laboratories, Abbott Park, Illinois, USA).

2.4. Demographic and Clinical Information

Socio-demographic information and antiretroviral treatment histories were collected using a standardized form.

2.5. Ethical Considerations

The study was approved by the ethical committee of the Centre de l'Appui Psycho-Médico-social (APMS) of Ndjamena (Chad) Coordination of the Psychological and Medical Support Unite (APMS) under the reference No. 196/PR/PM/MSPASSN/DG/PSLS-IST/PMSS/2013.

2.6. Statistical Analysis

Continuous variables were compared using the Wilcoxon rank-sum test, and comparison between two categorical variables was performed using the Chi-square test and Fisher's exact test when cell values were less than 5. For all analyses p-value of less than or equal to 0.05 was used to determine statistical significance.

3. Results and Discussions

During the 3-month study period, 76 HIV-infected pregnant women were included in the study. They aged 15 to 45 years with a median of 30 years (IQR) [22 - 28 years]. The gestational age ranged from 5 to 9 months. The women were treated by a combination ART (cART) represented by (Tenofovir (TDF) + Lamivudine (3TC) + Efavirenz (EFV)) (71.03%). The median duration on ART was 4 months. The socio-demographics characteristics of study population are summarized in **Table 1**.

We found 25 (32.9%) pregnant women of the study population carrying ASB and none of them carried more than one bacteria strain in the urinal tractus. They aged 24 to 35 years with a median of 34.5 years. All age groups were concerned by the ASB. The ASB prevalence was 32.9% CI95% [22.3% - 43.5%] and it was higher than 18.6% reported from a similar study conducted in South Africa [11].

Among, 25 women carrying ASB, 15 (60%), 5 (20%), 2 (8%) and 3 (12%) carried Enterobacteria, mainly *Escherichia coli* (11/15), *Streptococcus agalactiae* also known a Group B Streptococci (GBS), *Staphylococcus aureus* and *Candida albicans* respectively (**Table 2**). Among women with ASB, 14 (56%) had CD4 count < 200 cell/mm^3 and 18 (72%) had VL > 1000 copies/ml (3log copies/ml) (**Table 2**). Amongst pregnant women without

Table 1. Characteristics of study population.

Characteristics	n	(%)
Age Group (Years)		
15 - 24	29	38.16
25 - 34	45	59.21
35 - 45	2	2.63
Parity		
Nulliparous	11	14.47
Primiparous	27	35.53
Multiparous	38	50
Marital Status		
Married	53	69.74
Divorced	16	21.05
Single	5	6.58
Widow	2	2.63
Occupation		
Housewive	43	56.58
Trader	17	22.36
Seller	9	11.84
University Student	7	9.22

Table 2. Distribution of isolated pathogens depending on CD4 and viral load values.

Immunologic and virologic values	*E. coli* (n = 11)	*Streptococcus agalactiae*[*] (n = 5)	*Staphylococcus aureus* (n = 2)	*Klebsiella pneumoniae* (n = 2)	*Enterobacter cloacea* (n = 2)	*Candida albicans* (n = 3)
CD4 count per mm^3						
<200: n (%)	6 (54.5)	3 (60)	1 (50)	2 (100)	-[**]	2 (75)
200 - 500: n (%)	4 (36.4)	2 (40)	1 (50)	0 (0)	2 (100%)	1 (25)
>500: n (%)	1 (9.1)	-	-	-	-	
VL (log10) copies/ml						
<1.7 log: n (%)	-	-	-	-		-
<3 log: n (%)	4 (36.7)	1 (20)	-	-	11 (50)	1 (25)
>3 log: n (%)	7 (63.6)	5 (80)	2 (100)	2 (100)	11 (50)	2 (75)

[*]Streptococcus agalactiae or Group B Streptococci; [**]Bacteria not found.

ASB 19 (37.3%) had CD4 < 200 cell/mm^3 and 4 (7.8%) had VL > 1000 copies/ml. The difference between the rates of CD4 count below 200 cell/mm^3 according to bacteriuria is not statistically significant (p = 0.294), there is no correlation between ASB and CD4 rates (RR = 1.66). The difference between the rates of pregnant women with VL above 1000 copies/ml (virological failure) according to bacteriuria is statistically significant (p = 0.028), there is a correlation between virological failure (VL > 1000 copies/mm^3) and ASB in HIV-1-infected pregnant women (RR = 4.66).

Of 25 uropathogens strains isolated from urine, 14 (56%) were isolated in HIV-1 infected pregnant women with CD4 count values below 200 cells/mm^3 and 19 (76%) were isolated from women with viral load value above 3 log (1000 copies/ml) (**Table 2**).

Although results showed that most of HIV infected pregnant women with ASB had CD4 count below 200/mm^3, some studies suggested that the level of CD4 count below 200/mm^3 or higher or equal to 200/mm^3 did not have a major influence on ASB. However, viral load would have a decisive role in the development of ASB among this vulnerable group [12]. A study conducted in South Africa demonstrated a high incidence (18.6%) of ASB among pregnant HIV-positive women compared to those whom were HIV-negative (12.9%) (11). But in our previous study conducted among HIV-negative pregnant women in Lomé (31.03%) [13], we found an ASB rate similar to what we are reporting here in HIV infected pregnant women in N'djamena. These findings support conclusions from other studies, which reported that pregnancy is a major risk factor for the development of ASB [13] [14].

Although a few studies have been conducted on this subject in sub-Saharan Africa, few of them discussed the value of urinary tract infections screening during pregnancy [15] [16].

4. Conclusion

In this study, *Escherichia coli* and *Streptococcus agalactiae*—major bacteria known to cause neonatal meningitis to newborns, were isolated. Thus, evidence gathered on ASB in pregnant women infected with HIV represents a milestone for recommendation of systematic screening of urinary tract infections in Chad. The results also highlight the needs to reach viral suppression in order to reduce the risk of ASB in pregnant women.

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