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THE UNDERSTANDING AND ADHERENCE OF HIV-INFECTED PREGNANT WOMEN TO THERAPY IN A SOUTH-EASTERN STATE OF NIGERIA: A CROSS-SECTIONAL ASSESSMENT

A. Isah *, I. E. Ogbu, K. C. Amorha, M. O. Adibe, J. M. Okonta, C. N. Aguwa

Department of Clinical Pharmacy and Pharmacy Management, University of Nigeria, Nsukka, Enugu State, Nigeria.

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Correspondence to Author:
Abdulmuminu Isah

M. Pharm,
Department of Clinical Pharmacy and Pharmacy Management, University of Nigeria, Nsukka, Enugu State, Nigeria.

E-mail: abdulmuminu.isah@unn.edu.ng

ABSTRACT: Introduction: Appropriate understanding and adherence to antiretroviral regimens are important requisites to the presentation of good outcomes in the Prevention of Mother-to-Child Transmission (PMTCT) of HIV/AIDS. **Objectives:** This study aimed to evaluate the understanding and level of adherence to antiretroviral regimens among HIV-infected pregnant women. The factors that affect the level were also determined. **Methods:** Questionnaire was used to measure the knowledge while a modified Morisky Medication Adherence Scale (MMAS-8) and formula were used prospectively to determine their adherence level and the contributing factors. Data were analyzed using statistical products and services solution version 20. Chi-square test was conducted to determine the relationship between factors that affected knowledge and its level while logistic regression was used to determine the predictors of adherence. **Results:** A total of 394 women participated in the study, out of which 353 (89.6%) women had a good understanding of their PMTCT regimen, which was not affected by their educational levels. They had a low level of adherence among 301(76.4%) respondents. The adherence was not related to their knowledge score. Forgetfulness was a statistically significant ($p<0.001$) barrier to adherence, as availability of support groups and the understanding of the effectiveness of the regimen, were strong motivators to adherence at $p = 0.011$ and $p = 0.003$ respectively. **Conclusion:** This study concludes that there is a good level of understanding of but the suboptimal level of adherence to PMTCT regimens among the HIV-infected pregnant women in Enugu State, Nigeria.

INTRODUCTION: Vertical transmission from mother to child and horizontal transmission are the two major modes of transmission of HIV/AIDS [1]. The former occurs in three stages: transplacentally in the uterus, perinatally and postnatally while breastfeeding [2, 3].

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Vaginal delivery accounts for 60-70% of mother-to-child transmission (MTCT), while breastfeeding contributes 20-30% [4, 5]. MTCT is therefore regarded as the greatest route of infection by HIV in children [5, 6, 3]. It is more an issue in sub-Saharan Africa where many women are not only in their reproductive ages but with a high rate of childbirth and a prolonged period of breastfeeding [7].

To stem the increasing rate of MTCT, prevention of mother-to-child transmission (PMTCT), a four-pronged strategy, is currently being used. The four components include: preventing HIV infection among women of reproductive age, prevention of

unwanted pregnancy in HIV-infected women, testing and provision of antiretroviral drugs (ARVs) to pregnant women and proper integration of the HIV care, treatment, and support for the HIV positive women and their families.

The success of PMTCT depends on appropriate adherence to treatment regimen [8, 9]. Adherence is the extent to which a patient takes the medication in the way intended by the health care provider. There are different approaches to measuring adherence in different disease states, and several results have been published on the impact of adherence in antiretroviral therapy (ART) success [10, 11]. A near perfect adherence level of 95% is required for full and durable viral suppression [12]. With the use of the Medication Events Monitoring System (MEMs), pill count, and self-report, only 6% of ARV patients were found to have adherence rate of greater than 95% in a study. It was also shown that while 22% of the patients with adherence ≥ 95% had virologic failure, 55%, and 61% failures were reported for those with adherence levels of 90-94% and 80-89% respectively [13]. Apart from the viral load, adherence is positively correlated with CD4 count, and decreased rate of hospitalization and hospital stay [13]. Adherence also affects resistance to ARVs, and it has been shown to transcend within classes of ARVs [14].

Different levels of adherence have been reported among the general population of HIV-infected patients. A mean adherence score of 94.5% was reported in Vietnam, while 83% was reported in Tanzania. In Nigeria, the adherence rates reported include 70.5% in Ilorin [15], 62.6% in Ibadan [16], 58% in Benin [17,] and 62.5% in the North Central region [18]. These studies used a variety of instruments to measure adherence to ARVs, considering the difficulty in accurately and precisely determining adherence in outpatient settings [19]. Self-report, clinical assessment, pill count, prescription refill, *etc*. are some of the means of determination in use. One of the factors that greatly affect adherence to ART is the knowledge the patients have about their health status and the impact of the intervention. Poor knowledge about the disease is a problem in many developing nations. In India, only 36% of 609 persons surveyed ever heard of ART, 19% of whom reported that ART could cure HIV. It summarized that low levels of knowledge and access to ART were observed among HIV infected individuals [20]. In Togo, 44.4% of 99 enrollees knew the name of the specific drugs of the ART regimen, which they were placed on [21]. Studies in Nigeria showed that a good proportion of the infected individuals had good knowledge about HIV and ARTs.

A study was done by Olowookere *et al.,* revealed that 77.7% of respondents had good knowledge of HIV/AIDS while 75.2% had good knowledge of ART and tended to be more adherent to their ART regimen [22]. Another study revealed that 80% of the infected individuals had good knowledge of ARV drugs, while 77% of them had a positive attitude towards ARTs [23]. As regards PMTCT, 85% of respondents on the program in Lagos, South-western Nigeria, had very good knowledge of HIV and ART [24]. Thus, a good level of knowledge about HIV/AIDS and the benefits of ARTs is related to an improvement of adherence to prescribed regimens among HIV-positive women [25].

It is, therefore, necessary to assess the level of knowledge and adherence to ARTs in a south-eastern Nigeria, a population different from those reported in other studies.

This study aimed to assess the knowledge of and adherence to ARTs among HIV-positive pregnant women, and the associating factors.

METHODS:

Study Design: The study was a cross-sectional prospective study conducted between December 2012 and April 2014 using questionnaires.

Study Setting: The study was conducted in the five comprehensive HIV treatment and care centres in Enugu State, Nigeria, *viz*.: University of Nigeria Teaching Hospital (UNTH); Ituku-Ozalla; Enugu State University Teaching Hospital (ESUTH), Park-Lane; Cottage Hospital (CH), Agbani; Cottage Hospital (CH), Enugu Ezike and Bishop Shanahan Hospital (BSH), Nsukka. The first two are tertiary/referral centers owned and maintained by the Federal and State governments, respectively, while the other three are secondary health institutions. All centers provide outpatient PMTCT services along with adult and pediatric services.

Eligibility Criteria: The HIV-infected pregnant women who accessed HIV treatment from any of the five hospitals for at least three months (a third of the pregnancy duration) before being enrolled into the study and who gave informed consent to participate were considered eligible for the study. Expectant women below the age of 18 years were excluded from the study since they were not up to the age to give informed consent.

Sample Size Determination: Using the statistical formula of Fisher (to get an exact value because of the small size) as used in a similar study in Nigeria [22], the minimum sample size was calculated to be 358, given a 95% confidence interval and a 0.05 margin of error. A 10% adjustment gave 394, although 400 participants were finally contacted. The number was distributed among the study centers based on their patient population in the order: UNTH, ESUTH, CH Agbani, CH Enugu Ezike, and then BSH. In each clinic, systematic random sampling was used to select the eligible respondents based on the patient's list.

Ethical Consideration: Ethical approval was obtained from the Health Research Ethics Committee of the University of Nigeria Teaching Hospital Enugu State, which serves the entire region (Ref. no.: NHREC/05/01/2008B-FWA00002458-1RB00002323). Informed consent was obtained from the respondents, and confidentiality was assured and maintained throughout the study.

Instrument and Method of Data Collection: A four-part semi-structured an interviewer-administered questionnaire was used to document responses from the selected participants. The first part recorded the demographic characteristics, the second assessed understanding of HIV and antiretroviral regimen, while the third measured the level of adherence. Adherence level was measured using two tools: a modified Morisky Medication Adherence Scale (MMAS-8) and a self-report of the number of doses taken within a 7-day recall period, which was graded with a score of 95% and above for good adherence while less than 95% was considered to be poor adherence. The last part explored the factors that affect adherence to ART. To ensure consistency of the instrument, a pilot study was conducted in a hospital with similar characteristics to those of the study sites. Internal consistency test for the instrument gave values between 0.5-1.0 while the reliability test using Pearson correlation gave a coefficient of 0.9128.

Data Analysis: The data were processed using descriptive and inferential statistics with Statistical Product and Services Solution (SPSS), Version 20. Means and standard deviations were used to report knowledge and adherence levels.

Chi-square test was used to describe the levels of knowledge and adherence while logistic regression was conducted to determine the factors that predicted adherence to ART. Inferences about all responses were considered statistically significant at $p<0.05$.

RESULTS: Of the 400 eligible respondents contacted, 397 agreed to participate. Those that declined to participate gave reasons of not having time and being uninterested in the research. From the 397 questionnaires distributed, 394 (99.2%) were considered properly filled and used for analysis.

TABLE 1: DEMOGRAPHIC DISTRIBUTION OF THE RESPONDENTS

Demographic Characteristics	No. of Patients	Percentage
Age of Group (years)		
Below 20	3	0.8
20-29	181	45.9
30-39	208	52.8
40 and above	2	0.5
Ethnicity		
Ibo	378	95.9
Idoma	6	1.5
Yoruba	2	0.5
Hausa	8	2.0
Marital Status		
Married	358	90.9
Single	11	2.8
Widowed	23	5.8
Divorced	2	0.5
Educational status		
Primary	51	12.9
Secondary	308	78.2
Above secondary	35	8.9
Occupation		
Housewife	108	27.4
Self-employed	218	55.3%
Civil servant	68	17.3%
Number of living children		
0-1	201	51.0
2-4	182	46.2
5 and above	11	2.8

Socio-Demographic Characteristics: The mean age of the respondents was 30.4 ± 4.6 years with the majority (52.8%) being within the age group 30-39 years **Table 1**. Most of them were Ibos (95.9%) and were married (90.9%). A reasonable proportion (78.2%) had secondary education, thus being only self-employed (55.3%) with just about half (51.0%) having at most a living child. A good number 335 (88.1%) had disclosed their HIV status to their spouses, most of whom (74.4%) were reported to be HIV positive themselves.

Understanding of HIV Regimen: A great majority (97.2%) were aware that HIV could be transmitted from an infected mother to her unborn baby. All the respondents were on ART with the majority (81.2%) being on ART for more than 6 months before the study. Just 2.8% and 4.6% did not know the name of their medications nor the correct number of tablets per dose, respectively. Very few (0.8%) had incorrect knowledge of the frequency of dosing and incorrect timing of the daily intake. Slightly above half (58.1%) of the respondents had PMTCT experience, while almost all (98.7%) believed that ART was effective. The majority (85.0%) hoped to have a child free of the infection after PMTCT. In all, a good proportion (89.6%) of the women on PMTCT had a good knowledge of HIV **Table 2**.

TABLE 2: UNDERSTANDING OF HIV POSITIVE WOMEN ON THEIR HIV TREATMENT REGIMEN

Knowledge of HIV	No of Patients	Percentage
Can HIV spread from infected mother to baby in the womb?		
No	11	2.8
Yes	383	97.2
Are you on HIV medication?		
Yes	394	100.0
For how long have you been on HIV medication?		
8week-6months	74	18.8
Above 6months	320	81.2
Name of HIV medication you are taking?		
AZT/3TC/NVP	315	79.9
AZT/3TC/EFC	62	15.7
AZT/3TC/LPV/r	6	1.5
I don't know	11	2.8
Number of tablet per dose		
Incorrect dosing	18	4.6
Correct dosing	376	95.4
Number of times taken per day of dosing		
Incorrect frequency of dosing	3	0.8
Correct frequency of dosing	391	99.2
Time of daily intake of medication		
Incorrect	3	0.8
Correct	391	99.2
Have you been on PMTCT?		
No	229	58.1
Yes	165	41.9
Believe that ART is effective		
No	5	1.3
Yes	389	98.7
What patients hope to achieve from the medication?		
Childfree	335	85.0
Prolong life	14	3.6
Achieve cure	45	11.4
Who knows your HIV status?		
Nobody	8	2.0
Spouse	347	88.1
Friend	12	3.0
Sister	25	6.3
Mother	2	0.5
The HIV status of spouse		
Negative	53	13.5

Positive	293	74.4
I don't know	46	11.7
No husband	2	0.5
Knowledge score		
Poor knowledge	41	10.4
Good knowledge	353	89.6

Adherence to Antiretroviral Therapy among Pregnant Women: The MMAS-8 showed that many patients (77.9%) did sometimes forget to take their medications. Almost all (99.2%) of them never stopped taking their medications without informing their doctors, just as they (91.6%) never forgot to carry their medications along on a journey. Their overall adherence score on the MMAS-8 showed 72.3%, 12.9% and 14.7% for high, medium, and low adherence levels respectively. Concerning determining adherence based on a seven-day recall period, many of the respondents (76.4%) reported a good adherence level. The adherence parameters are shown in **Table 3**.

TABLE 3: LEVEL OF ADHERENCE TO ANTIRETROVIRAL THERAPY AMONG PREGNANT WOMEN

Level of Adherence	No of Patients	Percentage
Do you sometimes forget to take your HIV medication?		
No	307	77.9
Yes	87	22.1
Over the past two weeks, were there any day when you did not take your HIV medication?		
No	309	78.4
Yes	85	21.6
Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it?		
No	391	99.2
Yes	3	0.8
When you travel or leave home, do you sometimes forget to bring along your medication?		
No	361	91.6
Yes	33	8.4
Did you take your HIV medication yesterday?		
Yes	380	96.4
No	14	3.6
When you feel like your HIV infection is under control, do you sometimes stop taking your medication?		
No	394	100.0
Yes	0	0.0
Taking medication every day is a real inconvenience for some people. Do you feel like you hassled about sticking to your HIV treatment plan?		
No	384	97.5
Yes	10	2.5
Do you often have difficulty remembering to take all your HIV medication?		
No	325	82.5
Yes	69	17.5
Overall adherence (MMAS)		
High adherence	285	72.3
Medium adherence	51	12.9
Low adherence	58	14.7
Adherence level		
Non-adherence (<95%)	93	23.6
Adherence(95% & above)	301	76.4

Factors affecting Adherence: Most of the respondents of this study had similar reasons for choosing to adhere to their PMTCT medications, with all stating the desire to protect themselves and their unborn children. Other motivators of good adherence included understanding the effectiveness of the medications (95.9%) and good relationship with the HIV service providers (99.2%).

In terms of the barriers to good adherence, only the fear of being identified as being HIV positive was reported among a vast majority of respondents (92.6%). Forgetfulness and experiencing side effects were reported by 35.0% and 11.9% of the respondents, respectively. Only forgetfulness proved to be a statistically significant ($p<0.001$) barrier among them. The proportions of these factors are indicated in **Table 4** and **5**.

TABLE 4: FACTORS THAT ENCOURAGE ADHERENCE TO ANTIRETROVIRAL THERAPY IN PREGNANCY

Encouraging Factors	No of Patients	Percentage
Desire to protect the unborn child from HIV infection		
No	0	0.0
Yes	394	100.0
Desire to remain healthy and alive		
No	0	0.0
Yes	394	100.0
Availability of support group/system		
No	105	26.6
Yes	289	73.4
Understanding the need for HIV medication		
No	6	1.5
Yes	388	98.5
Understanding the effects of HIV medication		
No	16	4.1
Yes	391	95.9
A good relationship with HIV service providers		
No	3	0.8
Yes	391	99.2
Keep HIV medication in sight		
No	384	97.5
Yes	10	2.5
Making HIV medication a habit		
No	204	51.8
Yes	190	48.2
Use of daily medication reminder		
No	259	65.7
Yes	135	34.3

TABLE 5: DISCOURAGING FACTORS TO ADHERENCE TO ANTIRETROVIRAL THERAPY DURING PREGNANCY

Discourage Factors	No of Patients	Percentage
Lack of access to HIV medication		
No	394	100.0
Yes	0	0.0
Having difficulty with the dosing schedule		
No	392	99.5
Yes	2	0.5
Forgetfulness		
No	256	65.0
Yes	138	35.0
Side effects		
No	347	88.1
Yes	47	11.9
Fear of being identified as HIV positive		
No	29	7.4
Yes	365	92.6
Being too busy with other things		
No	300	76.1
Yes	94	23.9
Dissatisfaction with treatment		
No	392	99.5
Yes	2	0.5

Availability of a support group and the understanding of the effectiveness of HIV medication were among the factors that showed a statistically significant relationship with optimal adherence to ARV drugs. The regression analysis result after the bivariate analysis is presented in **Table 6**.

TABLE 6: FACTORS THAT CONTRIBUTED TO ADHERENCE TO ARVs GENERALLY

Motivating Factors	β	S.E.	P-value
Constant	19.883	23205.468	0.999
Availability of support group	0.739	0.291	0.011
Understanding the need for HIV medications	1.928	0.642	0.560
Understanding the effectiveness of HIV medications	1.928	0.642	0.003
Good relationship with HIV service providers	-20.537	23205.468	0.999
Keeping HIV medication in sight	-0.224	0.823	0.785
Making HIV medication a habit	-0.034	0.266	0.898
Use of daily medication reminder	0.304	0.285	0.286

DISCUSSION: This study assessed the understanding and adherence of patients to PMTCT regimens in Enugu State, Nigeria. Almost all the respondents were less than 40 years and of the local Ibo ethnic group. A great majority of the mothers were married while more than half have not had more than a child before. Most of them had only a secondary school certificate and thus self-employed. When their knowledge of the disease and treatment regimen was measured, most of the respondents performed excellently well. Adherence was measured using two instruments, with both showing that most of the patients had good adherence level.

The reported knowledge of the study population who had a good understanding of their regimen is similar to those of some studies in Nigeria. The general HIV-patient population has good knowledge of their regimen, as reported in Ile Ife [23] and Lagos where three-quarter of the respondents had a very good knowledge of their antiretroviral regimen [24]. A study in Togo gave a contrasting result as only half of the respondents knew the names of their ARVs [21]. For the HIV-infected pregnant women, good knowledge of PMTCT has been reported in West Ethiopia, Ashanti Ghana and South Africa [26, 27, 28]. The good knowledge of this study is also not strange, considering that most respondents had at least secondary education, as was obtained for respondents of other studies in Nnewi (86.9%) and Lagos (81.1%). It must be pointed out however that educational level was not a predictor of good knowledge of ARV in this study since the women that completed lower level of education (secondary school and below) had better knowledge and adhered more than their counterparts who had higher levels of education (post-secondary). Perhaps the latter assumed that their educational level was enough for HIV/AIDS knowledge and did not give much importance to the ones provided by counselors.

This conclusion was also arrived at in another study. Moreover, patient education on their disease and medication is a standard practice in all HIV clinics. This might also account for the high knowledge score of the study. The two instruments used to measure the respondents' adherence showed good but different levels. The slight difference is attributable to the fact that whereas MMAS-8 measures adherence behavior, the determination using a seven-day recall method is more of a measure of absolute dose adherence. Nonetheless, the high adherence rates determined for the population compares favorably with the results of studies from other populations.

Two studies in Ilorin, Nigeria showed that adherence levels in the general HIV-patients population were high: 73.3% [29], 70.5% [15]. An adherence rate of 86.1% was reported among the general HIV patients population in the South Eastern Region [30]. For the HIV-infected pregnant women, adherence rate of 78.3% was reported from a commercial town (Nnewi) in South Eastern Nigeria [31]. Pregnant women in Lagos, South West Nigeria, had adherence rate of 80.6% [24] as compared to 71% reported in Rustenburg, South Africa [5]. A longitudinal study that measured adherence to regimen among HIV-infected pregnant women using three methods recorded a mean patient adherence to the medication of 71% [32].

A similar study in Zambia reported adherence rates of 82.5% pre-partum [33]. These results that are similar to that of this present study fit into the average of 75.7% adherence rate that was found to be the pre-partum rate in a meta-analysis [34]. It should be noted that adherence rates exceeding 95% are necessary to maximize the benefits of ART [24]. Therefore, the reported results of this study and those of the other mentioned studies are suboptimal. Lower rates among the general HIV-patient population have been reported in Nigeria: 62.6% [16], 58% [17], 44% [23], 49.2% [35] and 62.5% [18] in Ibadan, Benin, Ilesha, Niger Delta region and North Central region respectively. These differences are still not absolute measures of comparison since adherence is defined in different ways and is measured using different tools. It is, however clear that the motivation to protect their unborn children is such a good explanation for the high adherence rates in the pregnant women of this and related studies.

Barriers to optimal adherence in this study were similar to those of other studies in which biological and social factors showed a dynamic interaction. Only forgetfulness was found to be a statistically significant reason for missing a dose, as was also documented in other studies [18, 22, 31]. Although means of reminders like electronic daily medication reminder [36] and telephone support services have been deployed in some parts of the world, such services are yet to be engaged in the developing nations like Nigeria. Stigma and discrimination also played a role in the barriers to adherence, causing a reduction in treatment-seeking behavior [37] and effective prevention and care [38].

CONCLUSION: This study concludes that there is a good level of understanding of but the suboptimal level of adherence to PMTCT regimens among HIV-infected pregnant women in Enugu State, Nigeria. Societal education levels attained did not affect the knowledge of PMTCT. Forgetfulness was the only significant impediment to adherence, but the use of support groups and the understanding of the effectiveness of ART motivated the women to adhere to their PMTCT regimen.

Limitations: The self-report method of evaluating adherence to the regimen no doubt makes the responses subjective. The difficulty of recalling even for the seven days chosen for documentation might have affected the responses. The researchers did not also get any data from the hospitals about prescription refill/pill counts, which could have provided objective information on the adherence level.

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CONFLICT OF INTEREST: The authors declare that they have no conflict of interest to declare concerning this study.

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