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Journal of AIDS and HIV Research

Full Length Research Paper

Assessment of renal dysfunction and associated factors among patients on Tenofovir based antiretroviral treatment at Gondar University Hospital, North West Ethiopia: Retrospective institution based cross sectional study

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Tenofovir Disoproxil Fumarate a nucleotide reverse transcriptase inhibitor that was introduced as a preferred first line antiretroviral therapy in Ethiopia as of 2008. However, routine renal function assessment is recommended as it is known to cause renal failure and renal tubular dysfunction.
To assess the practice of renal function monitoring of patients on TDF based ART regimen. The magnitude of renal dysfunction and its associated factors are also assessed. Institutional based retrospective record review was carried out to determine the magnitude of renal dysfunction and associated factors among HIV positive individuals who have been on TDF based ART regimen in Gondar university hospital. A total of 406 records were reviewed and 96.21% were found complete. From a total of 290 patients with Creatinine determination, renal dysfunction was found in 25.2%. Patients aged between 30-41years had AOR of 2.75(95%CI 1.18, 6.37), while those aged 42-53 years had AOR of 3.10 (95%CI 1.12, 8.55) as compared to those aged less than 30 years. Low body mass index (AOR 4.39(95%CI 2.24, 8.61), low CD4 (AOR 5.87(95%CI 2.73, 12.62)) were associated with increased risk of renal dysfunction. However Advanced WHO stages (stages 3 and 4), were associated with a lower incidence of renal dysfunction. About one fourth of patients who were on TDF regimen developed renal dysfunction. Twenty nine percent of participants had no renal function monitoring. Factors which influence the renal dysfunction in patients with TDF regimen in this study are age, low body mass index, low CD4 count and advanced WHO stage.

Key words: Renal dysfunction, Tenofovir, antiretroviral therapy (ART) regimen, Gondar University Hospital

INTRODUCTION

Statement of the problem

In the world, there are an estimated 33.4 million people living with HIV/AIDS among this 22.4 million found in sub Saharan Africa and in Ethiopia 790,000 (720,000-890,000) are living with HIV virus and 45,000 die due to AIDS. There were a total of 2.1 million deaths due to HIV/AIDS in 2007 (WHO, 2007; UNAIDS, 2013)

Tenofovir Disoproxil Fumarate (TDF), a nucleotide reverse transcriptase inhibitor (Gallant et al., 2004), was introduced in Ethiopia as of 2008 as a preferred nucleotide reverse transcriptase inhibitor of first line ART (Adolescents PoAGfAa, 2011; HAPCO/MOH, 2008). It is currently eligible for use in all groups of HIV /AIDS

patients (Adolescents PoAGfAa, 2008).

WHO as at 2013 recommended Tenofovir to be used as a preferred first line antiretroviral drug used in combination with other ARV drugs (WHO, 2010). However, use of TDF can result in renal side effects that includes renal failure and renal tubular dysfunction (Peyriere et al., 2004; Perazella, 2003). It is excreted by the kidneys through glomerular filtration and active tubular secretion. When Tenofovir is administered with acyclovir, ganciclovir and protease inhibitors , its serum level may be increased (FDA Report).

It may also lead to significant proteinuria predominantly of tubular origin which is a marker of renal tubular dysfunction (Mauss, 2005). In industrialized countries, TDF has been associated with nephrotoxicity, including impaired glomerular filtration rate and proximal tubulopathyand rarely to the extent of Fanconi's syndrome (Cooper et al., 2010; Gallant et al., 2005; Mocroft et al., 2010; Scherzer et al., 2012; Laprise et al., 2013; Fux et al., 2007).

Current or past medications are other causes of renal dysfunction (Goicoechea et al., 2008; Jones et al., 2004; Zimmermann et al., 2006). Glomerular filtration (GFR) is one of the methods used to monitor and follow patients on tenofovir. This way of renal function assessment is important for monitoring and the early detection of adverse effects, as well as dose adjustment of antiretroviral therapy (ART) (Post FA, 2010). Creatinine-based estimates of GFR are widely used in clinical practice owing to its easy availability and inexpensiveness (Post FA, 2010).. Monitoring renal function decline can be assessed by CrCl using the C-G formula and eGFR using the MDRD formula. Therefore ,it is recommended to calculate either CrCl or eGFR, in addition to serum creatinine for monitoring of renal function among HIV-infected patients receiving TDF in resource-limited settings (Sasisopin et al., 2011).

Cohort analysis and case studies reported tubular damage suggestive of Fanconi's syndrome. Diagnosis of this syndrome is based on the presence of hypophosphatemia, hypokalemia, glucosuria, hyperchloremic metabolic acidosis and mild proteinuria. The incidence of this syndrome is 22.4/100,000 after 7 months of treatment and disappear 4-8 months after stopping the drug (Hassane et al., 2004).

In cohort studies, serum Creatinine increased to (2.7 mg/dl) and reduced to slightly higher than the starting level once Tenofovir was discontinued. Risk factors of TDF associated renal impairment were advanced HIV level once Tenofovir was discontinued. Risk factors of TDF associated renal impairment were advanced HIV infection with low CD4 counts, raised Creatinine at

initiation of HAART, low BMI, history of kidney disease , diabetes mellitus, hypertension, sepsis and dehydration (Moreno, 2006).

In the first year of treatment with Tenofovir, HIV patients with baseline normal renal function must be monitored at monthly interval, and then after every three months. However patients with abnormal renal function are monitored more frequently. In cases of unavoidable administration of nephrotoxic drugs like aminoglycosides, amphoterecin B and so on, then weekly assessment of the renal function is important (HIV Medicine, 2007).

A follow-up of serum Creatinine, urinalysis and electrolytes should be performed in patients taking Tenofovir. Early diagnosis is important for timely discontinuation so that life-threatening electrolyte imbalances can be avoided. Patients should be screened after initiation of TDF for renal dysfunction (Ansari and Ansari, 2008).

LITERATURE REVIEW

Magnitude of the problem and associated factors for renal toxicity

Different retrospective and prospective studies conducted in USA from 2001 to 2007 on HIV infected patients on TDF containing regimen showed that the prevalence of renal failure due to TDF administration varied from 4 to 14% (Joel et al., 2005: Michael et al., 2010; paul et al ., 2011).

Table 1 summarizes the literatures concerning renal side effects of tenofovir and its associated factors.

Justification

A study done in Zambia from 2007 to 2011 recommended renal function test monitoring is needed before and during ART use in Africa (Wandeler et al., 2014).

A favourable safety profile for TDF in the treatment of adults with HIV infection is essential. Risk factors for development of nephrotoxicity can be identified and may be useful in managing those patients at greatest risk (Nelson et al., 2007).

Intensive renal monitoring with creatinine clearance, GFR, proteinuria, and glucosuria, is essential at baseline and during treatment with tenofovir. Risk factors of nephrotoxicity and pertinence of therapeutic drug monitoring of tenofovir should be evaluated.

According to WHO ART (2010) guideline, there are limited data on the use of TDF without renal screening

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Table 1. Socio-demographic characteristics of patients who have taken TDF antiretroviral regimen in Gondar University Hospital, Gondar, Northwest Ethiopia.

Variable	No.	%
Sex		
Male	173	42.6
Female	233	57.4
Age		
18-29	108	26.6
30-41	204	50.2
42-53	82	20.2
54-65	12	3.0
Address		
Urban	360	88.7
Rural	46	11.3
Educational Status		
Unable to read and write	127	31.3
Able to read and write	6	1.5
Primary education	130	32.0
Secondary education	94	23.1
College and above	49	12.1

or monitoring in resource-limited settings.

This study is conducted to assess the practice of renal function monitoring based on the recommendations and to find out the magnitude of renal dysfunction and its associated factors in Gondar University Hospital, and these were not studied before in this set up.

Objectives

The general objective of this paper is to assess the magnitude of renal dysfunction among patients who have been taking TDF based ART regimen in Gondar University Hospital, Gondar, Northwest Ethiopia. Its specific objectives are to i) determine the proportion of patients with renal dysfunction who have taken TDF based ART regimen, and ii) identify associated factors of renal dysfunction.

METHODS

Study design

The study design was institutional based cross-sectional retrospective record review.

Study setting and period

The study was conducted in the University of Gondar Hospital ART

follow-up clinic which is located in Gondar town in the northwest part of Ethiopia. Free HAART was started in the Hospital as part of a national program in 2003. The total number of people living in the town is 206,987, among which 98,085 are male and 108,902 are females. The hospital is a referral academic center serving a catchment area of nearly 7 million peoples. In the University of Gondar Hospital ART follow-up clinic, the number of patients on ART was 4379, and those who have ever started were 8036 at this ART clinic. The 2008 Ethiopian ART-guideline recommended TDF to be used as a preferred first-line drug. The University of Gondar Hospital began to implement this guideline since then. The clinic gives routine clinical assessment, laboratory evaluation like CD4 counts, complete blood counts, liver and renal function tests, urinalysis; drug refill from one to two months, and adherence support. Patients would be assessed clinically by medical practitioners, health officers for eligibility of initiation of ART. The medication would be offered by trained nurses. Patients would be seen by physicians if they have only new complaints during follow-up. Drugs are refilled every one or two months. CD4 count and complete blood counts would be done every 6 months. This study was conducted from April to June 2015.

Source population

The source populations constituted all HIV positive patients and had been on ART drugs at the University of Gondar ART follow-up clinic.

Study population

The study populations were all PLWHA who had taken TDF

containing regimen at the University of Gondar Hospital ART treatment clinic.

Inclusion and exclusion criteria

Inclusion criteria: Those PLWHA aged 18 years and above taking TDF containing regimens. Those PLWHA having at least three months follow-up visits to the hospital ART clinic.
Exclusion criteria: Records with poor documentation and patients who have renal failure before Tenofovir initiation were excluded from the study.

Sample size determination

The proportion of renal dysfunction and renal function monitoring of PLWHA on TDF containing ARV regimen was unknown from previous Ethiopian studies. Therefore, to get the largest sample size, 50% proportion was taken for sample size determination. Moreover, the degree of precision was assumed for generalization as 0.05 and degree of confidence with which to conclude equals 95%. With the above assumptions, the sample size was calculated by using a single population proportion sample size calculation formula with a source population as follows:

$$n = (Z\alpha/2)^2 \times P(1-P)/d^2$$

$$(1.96)^2 \, 0.5(1-0.5)/(0.05)^2$$

Where
$Z\alpha/2$ = Critical value for normal distribution at 95% confidence interval which equals to 1.96 (Value at alpha= 0.05).
P = 0.5% there is no previous research
D =0.05 is the margin of error.
The calculated sample is= 384.

The required minimum sample will be obtained from the above estimate adding the non-response rate.

= 384 + 38
Add 10% non-response rate = 38
Required sample size = 384+ 38 = 422

Sampling procedure

A total of 2743 subjects who had been taking TDF containing regimen were stratified from the GUH ART database. Patients were classified based on the year they started the ART treatment. All HIV/AIDS patients who were taking TDF based regimens had an equal chance of being selected. A simple random sampling method was used for selecting the sampling units by a computer-generated method.

Study variables

These include *dependent variable (*renal dysfunction) and independent variables like i) demographic factors: age, sex, educational status, occupation, address, and ii) Other factors: Co-morbidities (DM, HTN), CD4 count, BMI, WHO Stage, HBV co infection, presence of malignancy, HIV/HCV co infection, duration on TDF/ART and other drugs (NNRTI/PI).

Data collection procedure

Data was collected using pretested and structured questionnaire

from selected patient records. The data was collected by trained data collectors who were not working in the ART clinic.

Data quality management

The questionnaires were pre-tested on patients who were attending in Gondar Military Hospital ART clinic. Training was given for two data collectors before the start of data collection.
Data processing and analysis

The collected data was cleaned for its consistency, checked for its completeness, coded, and entered to SPSS version 20 for analysis and data was re-cleaned for completeness. Descriptive statistics was computed to determine the prevalence of renal dysfunction and the pattern of renal function monitoring for patients taking tenofovir containing regimens. Logistic regression was done for determining association between dependent and independent variables. The result was presented with odd ratio and 95% confidence interval.

Operational definitions

Renal dysfunction: defined as a decrease in glomerular filtration rate [GFR] to less than 60 ml/min with at least one follow-up elevated serum creatinine and lower GFR (KDIGO, 2012).

Patients with renal function test: Patients who have got renal function monitoring according to WHO guideline (2010) before initiation and every six months once on treatment (WHO, 2010).

Ethical approval and consent to participate

Retrospective data analysis was approved by the Review Board of the University of Gondar. Patient informed consent was waived because of the retrospective characteristics of the study

RESULTS

Socio-demographic characteristics of patients

A total of 422 charts of HIV/AIDS patients taking TDF regimen were collected and 16 of which were found to be grossly incomplete and inconsistent in response. Only 406 charts were thoroughly reviewed and data were collected with a response rate of 96.21%. Two hundred thirty-three participants (57.4%) were females and 173 (42.6%) were males. The mean age (±SD) was 35.5(±8.76) years and the majority (50.2%) of the participants was in the age group of 30-42. About 26.6% were from 18 to 29 years. About 360(88.7%) participants were living in urban areas and 46(11.3%) in rural areas. Thirty-one percent of the participants were unable to read and write and 12% had college-level education or above (Table 2).

Clinical characteristics of participant

Thirty three percent (33.3%) of patients on TDF containing regimen were WHO stage 3 HIV, 13.1%

Table 2. Clinical characteristics of participants who are taking TDF regimen at Gondar University Hospital, Gondar, Northwest, Ethiopia (N=406).

Variable	No.	%
CD4		
<=199	234	57.6
>=200	172	42.4
WHO Stages on initiation of TDF		
1	161	39.7
2	57	14
3	135	33.3
4	53	13.1
Duration of TDF		
<=6 month	46	11.3
7-12 month	39	9.6
13-18 month	41	10.1
19-24 month	50	12.3
>=24 month	230	56.7
Duration of total ART		
<=6 month	41	10.1
7-12 month	29	7.1
13-18 month	23	5.7
19-24 month	28	6.9
>=24.1 month	285	70.2
HBV (HBsAg)		
HBV reactive	9	2.2
Non-reactive	25	6.2
Not done	372	91.6

patients were WHO stage 4 and stage 1 accounted for 39.7%. Baseline blood pressure and serum creatinine before or upon initiation of TDF regimen were recorded in 44.6% and 83.3% of study participants respectively. The mean systolic BP ($\pm$SD) and diastolic BP ($\pm$SD) were 102.72($\pm$11.21) and 67.54($\pm$7.47), respectively. The mean ($\pm$SD) CD4 count was 243.23($\pm$212.93) cells/mm^3. Two hundred and thirty-four (57.6%) patients had baseline CD4 <199 cells/mm^3 and the remaining 42.4% were having CD4 count above 200 cells /mm^3 (Table 3).

Patterns of renal function monitoring

Pattern of renal function monitoring and renal dysfunction at baseline, 3rd, 6th, 9th, 12th, 18 and above 24 months for patients who are taking TDF regimen is depicted in Figure 1.

Renal dysfunction

The mean ($\pm$SD) baseline GFR (calculated using the C-G

equation) and serum creatinine on initiation of TDF were 89.70 ml/min$\pm$30.35 and 0.79$\pm$0.2, respectively. About 68(16.7%) of the patients did not have baseline serum creatinine measurement at the time of TDF initiation. The proportion of patients with renal dysfunction as measured by C-G equation was 25.2% among individuals monitored with serum creatinine in the study period. The prevalence of renal dysfunction in this study is depicted in the Figure 2.

Renal function monitoring

As a WHO guideline for HIV positive patients who are taking ART, TDF regimen should be monitored at least every six month for renal dysfunction. A total of 290(71%) patients were having renal function test monitoring and 116(29%) patients were not monitored for renal dysfunction. The detail of renal monitoring pattern in this study is shown in Figure 3.

Table 3. Cross-tabulation of socio-demographic and clinical characteristics of patients who were taking TDF regimen Gondar University Hospital, Gondar, Northwest, Ethiopia.

Variable	Renal dysfunction		Total
	Yes [No. (%)]	No [No. (%)]	
Sex			
Male	40(30.5%)	91(69.5%)	131
Female	33(20.8%)	126(79.2%)	159
Age			
18-29	15(18.5%)	66(81.5%)	81
30-41	38(27.3%)	101(72.7%)	139
42-53	18(30%)	42(70%)	60
54-65	2(20%)	8(80%)	10
Address			
Urban	61(23.6%)	198(76.4%)	259
Rural	12(38.7%)	19(61.3%)	31
Educational status			
Unable to read and write	24(27%)	65(73%)	89
Able to read and write	2(50%)	2(50%)	4
Primary education	21(21.9)	75(78.1%)	96
Secondary education	15(24.6%)	46(75.6%)	61
College and above	11(27.5%)	29(72.5%)	40
BMI			
<=18.49	48(37.5%)	80(62.5%)	128
>=18.50	25(15.4%)	137((84.6%)	162
CD4 count			
<=199	57(32.8%)	117(67.2%)	174
>=200	16(13.8%)	100(86.2%)	116
WHO staging			
1	39(35.1%)	72(64.9%)	111
2	13(28.3%)	33(71.7%)	46
3	17(16.5%)	86(83.5%)	103
4	4(13.3%)	26(86.7%)	30
NNRTI			
Yes	71(24.9%)	214(75.1%)	285
No	2 (40%)	3(60%)	5
PI			
Yes	8(26.7%)	22(73.3%)	30
No	65(25%)	195(75%)	260
Duration of TDF			
<=6 month	3(15.8%)	16(84.2%)	19
7-12 month	10(40%)	15(60%)	25
13-18 month	4(15.4%)	22(84.6%)	26
19-24 month	10(28.6%)	25(71.4%)	35
>=24 month	46(24.9%)	139(75.1%)	185

Table 3. Contd.

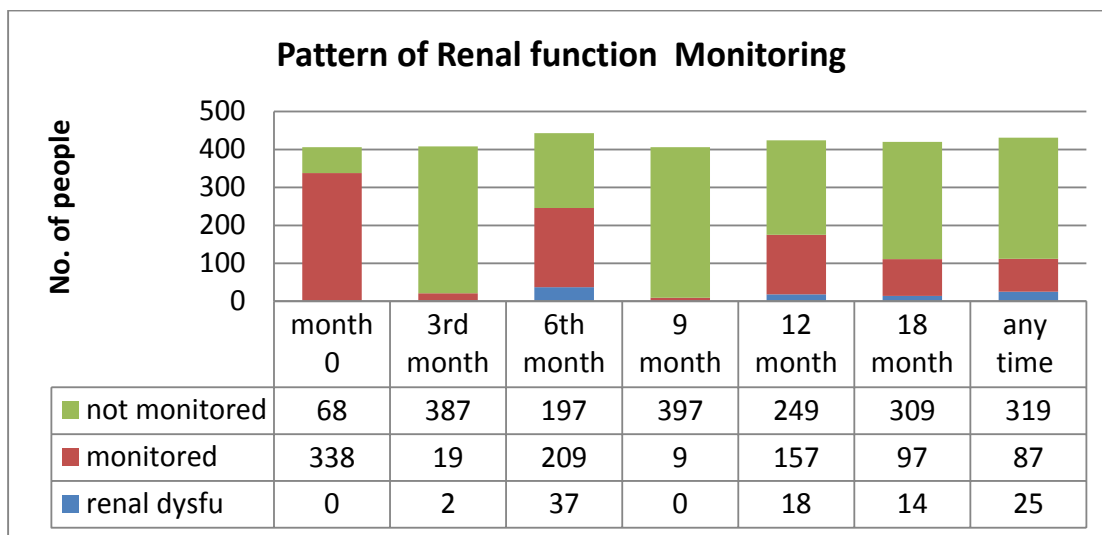|			
Duration of ART			
<=6 month	1(6.2%)	15(93.8%)	16
7-12 month	6(37.5%)	10(62.5%)	16
13-18 month	5(35.7%)	9(64.3%)	14
19-24 month	9(42.9%)	12(57.1%)	21
>=24 month	52(23.3%)	171(76.3%)	223
Hypertension			
Yes	4(23.5%)	13(76.5%)	17
No	55(24.6%)	169(75.4%)	224
Diabetes mellitus			
Yes	0(0%)	1(100%)	1
No	36(24.7%)	110(75.3%)	146
Malignancy			
Yes	4(80%)	1(20%)	5
No	69(24.5%)	213(75.5%)	282
HBV/HCV infection			
Yes	2(20%)	8(80%)	10
No	9(29%)	22(71%)	31

Figure 1. Patterns of renal function monitoring for patients who are taking TDF regimen at Gondar University Hospital, Gondar, Northwest, Ethiopia (N=406).

Monitoring of other disease

Great majority of patients were not routinely screened for diabetes mellitus, HBV, and HCV. Hypertension was observed in 5.9% and about 21.4% of the subjects had no record regarding their BP measurements. It was not
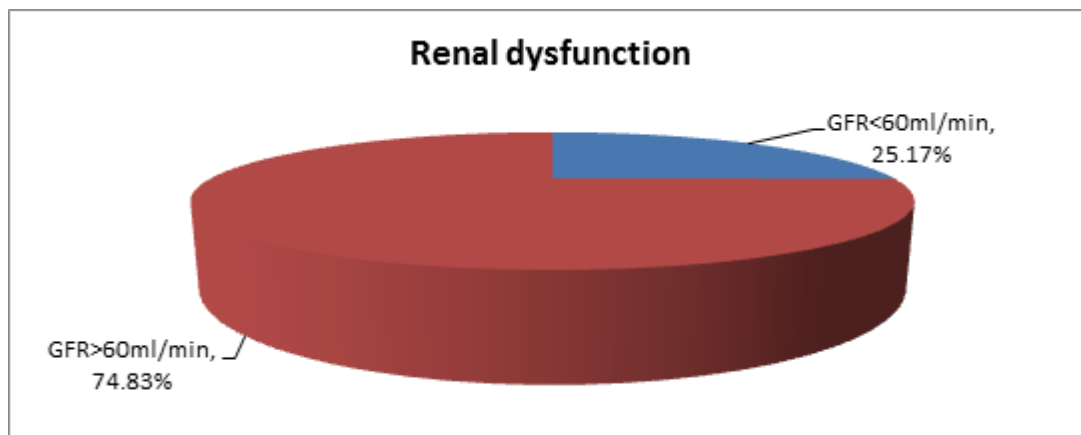
Figure 2. Renal dysfunction of patients who are taking TDF regimen Gondar University Hospital, Gondar, Northwest, Ethiopia.
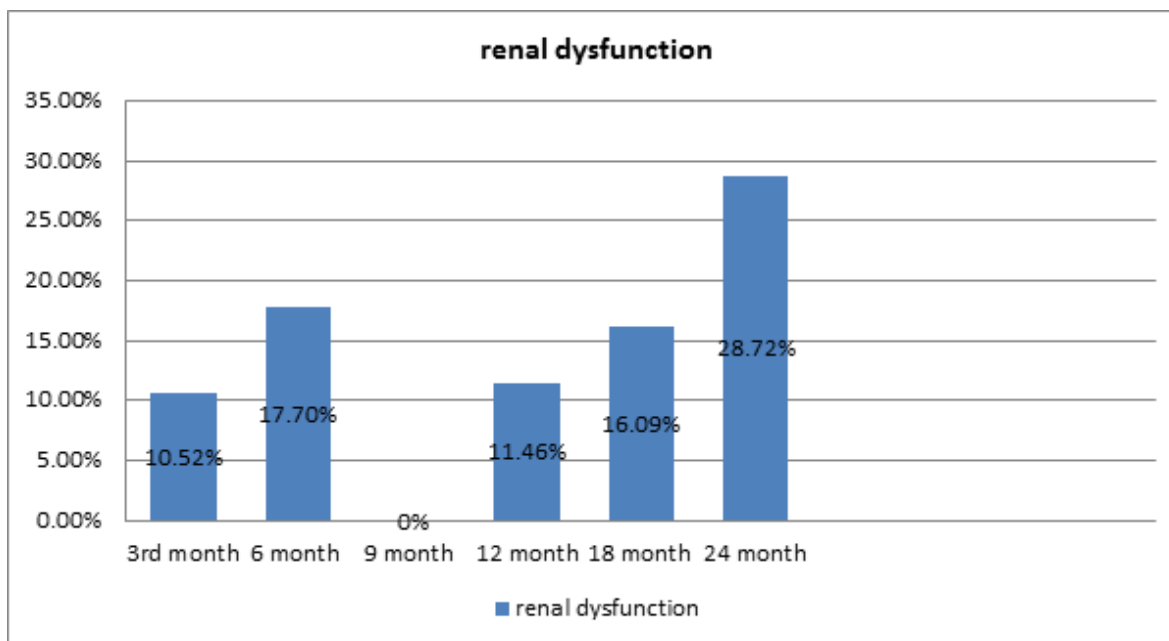

Figure 3. The pattern of renal dysfunction monitoring in follow up months who are taking TDF regimen Gondar University Hospital, Gondar , Northwest, Ethiopia.

routine to follow patients with urine analysis, serum electrolyte for patient on TDF containing regimen at this study area.

Association of variables

In bivariate logistic analysis, P value ≤ 0.2 was considered for multivariate analysis. In multivariate analysis, p value < 0.05 was considered as significant.
   The multivariate logistic regression which controls the

effects of confounding variables showed patients aged 30-53 years have high risk of having renal dysfunction than 18-29 years. Patients with BMI less than 18.5 are four times (AOR 4.39(95%CI 2.24, 8.61)) at high risk of developing renal dysfunction than patients with normal BMI. Patients with CD4 count below 200 (AOR (5.87(95%CI 2.73, 12.62)) are higher risk for the outcome by five times than those with higher CD4 counts. Patients who took ART for 7-12 months and 19-24 months duration have more risk of developing renal dysfunction than others with AOR of 26.3(95%CI 2.02,343.04),

Table 4. Logistic regression on renal dysfunction and associated factors among patients on tenofovir based antiretroviral treatment at Gondar University Hospital, North West Ethiopia.

Variable	Renal dysfunction		COR (95%CI)	AOR (95%CI)
	Yes	No		
Sex				
Male	40	91	1	
Female	33	126	0.60 (0.35,1.02)	
Age				
18-29	15	66	1	
30-41	38	101	1.66(0.84,3.25)	2.75(1.18,6.37)
42-53	18	42	1.89(0.86,4.14)	3.10(1.12,8.55)
54-65	2	8	1.1(0.21,5.72)	3.78(.55,25.10)
Address				
Urban	61	198	1	
Rural	12	19	2.05(0.94,4.46)	
BMI				
<=18.49	48	80	3.29(1.89,5.74)	4.39(2.24,8.61)
>=18.5	25	137	1	
CD4				
<=199	57	117	3.05(1.65,5.63)	5.87(2.73,12.62)
>=200	16	100	1	
WHO stage				
Stage 1	39	72	1	
Stage 2	13	33	0.73(0.34,1.54)	0.79(0.31,1.98)
Stage 3	17	86	0.37(0.19,0.70)	0.19(0.08,0.44)
Stage 4	4	26	0.28(0.09,0.87)	0.10(0.03,0.36)
ART duration				
>=6 months	1	15	1	
7-12 months	6	10	9(0.94,86.52)	26.3(2.02,343.04)
13-18	5	9	8.33(0.84,83.17)	14.74(1.08,200.78)
19-24	9	12	11.25(1.25,101.640	48.75(4.21,564,105)
>24	52	171	4.56(0.59,35.4)	10.68(1.169,97.52)

48.75(95%CI 4.21,564,105), respectively. WHO stage 3 and 4 were associated with a lower incidence of renal dysfunction in TDF based regimen taking patients with AOR of 0.19 (0.08, 0.44) and 0.1(0.03, 0.36) respectively. The details of association of variables with the outcome variable are shown in the Table 4.

DISCUSSION

In this study, we determined the prevalence of renal dysfunction, monitoring and factors associated with renal dysfunction of HIV patients who have been taking TDF based HAART. Renal dysfunction as defined by GFR less than 60 ml/min in this study is 25.2% and renal function was assessed at least once in 71% of the participants. The prevalence of renal dysfunction in this study is lower as compared to a study done in Germany which revealed a prevalence of 46% (FBaGS, 2005) but higher than the study done in West India which reported 6.53% (Ketan et al., 2010).

This higher level of renal dysfunction may indicate poor practice of monitoring of renal function in our study. The practice of renal function assessment and monitoring is low for early detection, management, and prevention of renal complication of tenofovir in this hospital. This could

be due to poor documentation of patient's investigation and gaps of the health care workers in applying WHO guideline to improve the patient's health and prevention of health related complications.

This study revealed that patients from age 30-53 years have a significance association with renal dysfunction. This study is similar with the study done in Multicenter EU, UK, USA, London (Nelson et al., 2007). This may be due to progressive decline in GFR as age increases.

In this study, there is a positive association between lower body mass index and renal dysfunction. Patients having lower BMI have four point four times more risk of developing renal dysfunction than patients who have normal body mass index. This is consistent with the results of studies done in Thailand (Sasisopin, 2011) and USA Maryland (Moore, 2009).

Patients who have CD4 lower than 200 per microliter have six times more risk of renal dysfunction than those with higher CD4 counts. This is in line with the studies done EU,UK, USA, London (Nelson et al., 2007) and USA Maryland (Moore, 2009).

In this study, patients having advanced WHO stage have lower risk in developing renal dysfunction than other earlier stages. Patients with advanced WHO stage are expected to have worsening of renal function. However, this group of patients may have been treated and followed more frequently that the risk decreased with advanced WHO stage. Nevertheless, this needs further research to settle this ambiguity.

The duration of ART has also a positive impact on renal dysfunction since the longer the duration of ART the higher the risk. This study is different from Thailand (Sasisopin et al., 2011) and similar with west India (Ketan et al., 2010). This may be because of prolonged exposure of different ART drug leading to transient renal function abnormality.

Limitation of the study

The study design is cross sectional which has a limitation to establish a causal association. The study is based on secondary data which has a disadvantage of incompleteness because of in appropriate handling of patient record. Also, some of the records on investigations might have been lost.

Conclusion

About one-fourth of the study patients have developed renal dysfunction and thirty percent of the cases have no renal function monitoring. These levels of renal dysfunction and unmonitored renal function have a negative effect on the ART continuum of care. It indicates that there is a gap in implementing WHO guideline. Factors like age, low body mass index, low CD4 count

and long duration of ART were associated with renal dysfunction development.

ABBREVIATION

AIDS, Acquired immunodeficiency syndrome; **ART,** anti-retroviral therapy; **ARV,** antiretroviral; **BMI,** body mass index; **BP,** blood pressure; **C-G,** Cockcroft-Gault; **CaRT,** combination anti-retroviral therapy; **CrCl,** creatinine clearance; **CKD,** chronic kidney disease; **DM,** diabetes mellitus; **eGFR,** estimated glomerular filtration rate; **HAART,** highly active anti-retroviral therapy; **HIV,** human immunodeficiency virus; **HTN,** hypertension; **GFR,** glomerular filtration rate; **GUH,** Gondar University Hospital; **MDRD,** modification of diet in renal disease; **NNRTIs,** Nucleoside reverse-transcriptase inhibitors; **NRTIs,** nucleoside reverse-transcriptase inhibitor; **PLWHA,** people's living with HIV AIDS; **SAE,** side effects; **TDF,** Tenofovir; **WHO,** World Health Organization.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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