Original Article

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Assessment of Non-HIV Comorbidities Among HIV-Infected Patients on Anti-Retroviral therapy (ART) in a Teaching Hospital Kohat, Pakistan

Fahad Naim[1], Awais Naeem[2], Fahim Shah[3], Umair-ul-Islam[4], Sohail Adnan[5], Muhammad Hamid[6]

[1,5,6] Assistant Professor, Khyber Teaching Hospital/KMU-Institute of Medical Sciences, Kohat
[2]Assistant Professor, Khyber Teaching Hospital/KMC, Peshawar
[3]Professor, KMU-Institute of Medical Sciences, Kohat, [4]Medical Consultant, KMU-Institute of Medical Sciences, Kohat

Author`s Contribution

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Address of Correspondent
Dr. Awais Naeem
Assistant Professor, Khyber Teaching Hospital/KMC, Peshawar
awaisnaeem06@gmail.com

ABSTRACT

Objective: To assess the non-HIV-related comorbidities in HIV-Infected patients surviving on anti-retroviral therapy (ART) at the HIV care center, DHQ Teaching Hospital, Kohat, Pakistan.

Methodology: This cross-sectional study was conducted for the period of 6 months at DHQ Teaching Hospital, Kohat Development Authority, Kohat from June to December 2020. Data were obtained from 446 patients on Antiretroviral therapy for at least 6 months by physicians and HIV specialist nurses., the data analysis was done using SPSS, and descriptive statistics were applied to analyze the frequencies, percentages, and comparisons.

Results: Analysis of the data from 446 patients showed that relative predominance of HIV infection in males (63.5 %), uneducated (59.42%), and middle-aged (31-60 years) (62.4%) and married (53.13%) people, with 1/3rd of the studied population being under-weight. Our study found that 54.7% of patients have non-HIV related comorbidity with (29.6%) of the patients having a single comorbidity while 25.1% had multiple co-morbidities. Among the non-communicable disease's prevalence of diabetes mellitus (26.5%). hypertension 21.3%, and ischemic heart disease 13.2% were higher compared to obesity, chronic liver disease, chronic kidney disease, stroke & non-HIV related cancers. These co-morbid conditions had no significant relation with gender but were more common in higher age groups.

Conclusion: Our study showed high rates of co morbidities in patients of HIV disease the challenge will need multidisciplinary care rather than patients just being treated with ARV therapy. Appropriate healthcare delivery models with a multidisciplinary approach will help in combating HIV and non-HIV-related comorbidities.

Keywords: Antiretroviral therapy, HIV, Non-communicable diseases, non-HIV-related comorbidities.

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Introduction

The Human Immunodeficiency Virus (HIV) is a life-threatening health condition among other chronic disease conditions and is associated with morbidities and mortalities, however, a significant reduction in morbidities has been observed with antiretroviral therapy (ART).[1] A larger number of patients living with HIV and registered with the National AIDS Control Program (NACP) were found in Pakistan, the estimated number was 165000 in 2019.[2] With the increasing availability of antiretroviral therapy for HIV-positive patients, there is a significant rise in the number of patients with non-HIV related, non-communicable co-morbidities.[2] The burden of these co-morbid diseases in HIV patients is unknown in Pakistan, hence also a lack of appropriate management protocols. This study was an initial step in estimating the new challenge of Non-Communicable Diseases in HIV-

infected patients. HIV infection once thought to be a fatal disease has become a chronic infection with the use of effective antiretroviral therapy.[3] Previously the cancers associated with HIV were the important factor of HIV associated mortalities and infections with the advent of newer antiretroviral therapy, there has been a paradigm shift in HIV-related comorbidities.[4] Life expectancy has increased substantially and referral to HIV care Centers has led to the aging of people having HIV infection. This can lead higher risk of non-HIV-related comorbidities, Non-Communicable Diseases, and other diseases common in the geriatric age group.

In countries having easy availability of antiretroviral treatment (ARV), non-communicable diseases increasingly account for complications and mortalities among patients, Aging, lifestyle factors, HIV infection, immune suppression and adverse effects of the antiretroviral medication can be attributing factors.[2] The longer life expectancy in HIV-infected patients has led to a paradigm shift in the management of these patients. The persistent immunosuppression and inflammation caused by HIV infection could cause early aging and an increase in the prevalence of degenerative diseases.[3] In countries like North America & Europe, approximately one-third of HIV-positive patients are of 50 years of age according to the reports. [4] The burden of comorbidities in HIV infection is quite high and it's important to identify and treat modifiable comorbidities like Diabetes, Cardiovascular disease, and hyperlipidemia.

Existing data suggest that persons living with HIV infection develop AIDS-related Comorbidities at significantly younger ages as compared to HIV-uninfected counterparts.[5] The achievements made in fighting against HIV are now under threat from non-HIV-related multimorbidity.[6] Pakistan is one of the countries with an increasing number of patients diagnosed with HIV.[7] Treatment for Non Communicable diseases can cause problems related to polypharmacy, Drug interactions, increase in side effects, and possible loss of ARV treatment efficacy.

The burden of non-HIV-related comorbidities is largely unknown in Pakistan. Secondly, there is no mechanism for integrating their care with other medical specialties. They have difficulty in purchasing medications for non-HIV-related comorbidities. Moreover, the National AIDS Control program may offer some support for these patients' non-AIDS-related health issues if common comorbidities are known.

There is little data on appropriate management protocols for non-HIV-related comorbidities in developing countries like Pakistan. Multi-morbidity in patients with HIV infection has an upward trend and can be challenging to manage in our local settings.9 Understanding the Noncommunicable Disease burden among those living with HIV infection is vital if the achievements already made in combating HIV infection are to be maintained especially in low-income countries. People living with HIV are taking free medications from HIV care centers and can be a vulnerable population. prevalence of comorbid conditions is high and patient care can be integrated with other specialties for proper treatment and management of these patients. By knowing common comorbidities in people living with HIV infection, they can be routinely screened and followed up for prevention and early management of non-communicable diseases. Moreover, patients with HIV are still stigmatized and they are reluctant to go to other Outpatient departments. As the prevalence of non- HIV related comorbidity is high, Patients will need a holistic approach for the management of their health issues in one place to make their access to health care facilities convenient.

This study will identify common non-HIV related comorbidities and non-communicable diseases in patients with HIV infection and can provide future directions for making appropriate guidelines for their prevention, screening, and management to provide multidisciplinary care to these patients.

Methodology

This cross-sectional study was conducted for the period of 6 months at DHQ Teaching Hospital, Kohat Development Authority, Kohat from June to December 2020. The Ethical approval was obtained from institutional review board of Khyber Medical University, Institute of Medical Sciences Ref No: ERC/KIMS/2021/05. Informed consent was taken from patients registered at the HIV care center from June 2008 till December 2020. Data were obtained from 446 patients calculated on the basis of prevalence of both genders, having age ≥15 years, and on Antiretroviral therapy for at least 6 months. Patients who did not consent to this study and were unable to come in person to the HIV care center or were not capable of responding to interviews due to cognitive defects were excluded from the study. All Personal details were kept confidential to ensure the confidentiality of study participants.

Data were collected by physicians and HIV specialist nurses at the HIV care center by using predesigned

proforma. The nurses were pre-trained on proforma before starting the study to ensure smooth and proper data collection. Data were collected related to demographics, social status, smoking, substance abuse and non-Communicable diseases that included Diabetes, hypertension, Ischemic heart disease, Chronic kidney disease, Chronic liver disease, Obesity, Stroke and Non-HIV related malignancies.[4]

Diabetes Mellitus was defined as patients who were taking oral Hypoglycemic agents or Insulin or a Single HbA1c reading of ≥ 6.5% or Two or more readings of either Fasting Blood Sugar ≥ 126 mg/dl or Random blood sugar ≥ 200mg/dl or A visit to physician or problem list diagnosis on at least two visits. Obesity was defined as Patient with BMI of 25 kg/m^2 and above.[10] Hypertension was defined as patients having visit or problem list comorbid of hypertension and prescribed any antihypertensive therapy or A visit or problem list comorbidity of hypertension and the average of 2 the systolic blood pressure readings above 140 mm Hg or diastolic blood pressure readings of 90 mm Hg. Patients with a history of documented Myocardial infarction, coronary artery vascularization, or documented coronary artery disease on coronary angiography or a Problem list of myocardial infarction or coronary artery disease on at least 2 or more visits to a Physician were considered to have ischemic heart disease. Chronic Liver disease was defined as persistent transaminitis > 2 times normal on 2 different occasions 3 months apart or a Patient having coarse shrunken liver on ultrasound abdomen or A visit to Physician or problem list of chronic liver disease on at least 2 visits. Patients having a problem list diagnosis of non-HIV related cancer (This will include only cancers that are non- HIV related like lung and breast cancers) will be considered as non-HIV related Cancer.

Detailed history was obtained from all participants to gather detailed information on their past medical history, personal history, social history, and medications they are using. Detailed clinical examination was done including blood pressure checkup, weight measurement, height measurement, body mass index, and detailed systemic examination. The routine laboratory tests including blood sugar, creatinine, and Urine routine analysis, and used records already mentioned In the HIV Patients personal file. All patients were screened for chronic liver disease if clinically indicated and this included ultrasound imaging and liver function tests. All patients were assessed to check for non-HIV-related comorbidities as per operational definitions given above. Any clinical condition that was present in patient apart from HIV related complications as per WHO clinical staging was considered as a Non HIV related comorbidity.[11] We also assessed patients having multi morbidity which was defined as patient having 2 or more different Non-HIV related comorbidities. [12, 13] The data analysis was done using SPSS version 23. Descriptive statistics applied to calculate frequency of each comorbidity. Distribution of comorbidities were compared in different genders and age group patients to check any significant difference in various groups using Chi- Square test and p value of lesser than 0.05 was considered significant.

Results

We recruited 506 patients registered at HIV care center, DHQ Teaching hospital, KDA, Kohat out of which 60 patients were excluded as per our exclusion criteria and final analysis was done on 446 patients. There were 283(63.5%) males and 163(36.5%) female patients in our study. Most patients were aged between 31 to 60 years (62.4%) and were unemployed (59.42) % of our study population The patient's details are presented in table I.

Table I: Socio-Demographic Characteristics of Patients in HIV care center, DHQ Teaching Hospital, Kohat. (N=446)

Variable	N	%
Gender		
Male	283	63.5%
Female	163	36.5%
Age		
Less than 30 years	91	20.4%
31-45 years	151	33.9%
46-60 years	127	28.5%
Greater than 60 years	77	17.3%
Body Mass Index		
Under weight	177	39.7%
Normal Weight	208	46.6%
Over weight	56	12.6%
Obese	5	1.1%
Employment		
Employed	181	40.58%
Un-Employed	265	59.42%
Educational status		
Primary Education	147	33%
Secondary Education	109	24.4%
Intermediate Level	63	14.1%
Higher Education Level	32	7.2%
Uneducated	95	21.30%
Marital status		
Married	237	53.13%
Un-Married	196	43.94
Widow	13	2.91%

Distribution of Non-HIV related comorbidities were checked in patients living with HIV & Diabetes mellitus

was the most common comorbidity (26.5%) of patients followed by Hypertension (21.3%) and ischemic heart disease (13.2%) in our study population. The distribution of different non-HIV related comorbidities is shown in Table II.

Table II: Prevalence of Non-HIV related Comorbidities among patients in HIV care center, DHQ Teaching Hospital, Kohat

Non- HIV related Comorbidity	(%)	(95% Confidence Interval)
Diabetes Mellitus	26.5	22.4-.30.8
Hypertension	21.3	17.6-25.4
Ischemic heart Disease	13.2	10.2-16.7
Obesity	1.1	0.4-2.6
Chronic Liver Disease	7.6	5.3-10.5
Chronic Kidney Disease	6.5	4.4-9.2
Stroke (CVA)	5.4	3.5-7.9
Non- HIV related Cancer	3.4	1.9-5.5

We also analyzed our data for number of comorbidities present in our patients and it showed that 102 (29.6%) of patient had only one comorbidity while 112 (25.1%) patients had multimorbidity (2 or more comorbidities). The distribution of comorbidities among different genders was stratified to check for any difference between males and females. (Table III)

Table III: Prevalence of Single comorbidity and Multimorbidity among patients in HIV care Center, DHQ Teaching hospital, Kohat. (N= 446)

Comorbid distribution	Total Patients	Distribution in Percentage
No comorbidity	202	45.3
Single Comorbidity	132	29.6
Multi morbidity (2 or more comorbidities)	112	25.1

There was no significant difference in distribution of Non – HIV related comorbidities in our study population and P values were more than 0.05 for each comorbid condition. (Table IV)

Table IV: Distribution of Non- HIV related comorbidities among different Genders.

Non-HIV related comorbidity	No. of patients having disease	Male	Female	P-Value
Diabetes Mellitus	118	77	41	0.6
Hypertension	95	60	35	0.9
Ischemic heart Disease	59	41	18	0.3
Chronic Liver Disease	34	22	12	0.8
Chronic Kidney Disease	29	16	13	0.3
Stroke (CVA)	24	16	8	0.7
Non- HIV related Cancer	15	10	5	0.7

We also assessed for distribution of comorbidities among different age groups and a significant difference was observed in groups in patients with Diabetes Mellitus, Ischemic heart disease and Hypertension having P value of less than 0.05. These comorbidities were more common in patients with higher age. (Table V)

Table V: Distribution of Comorbidities in Different Age groups

Non-HIV related comorbidity	No. of patients having disease in different age group	No. of patients having disease	P-Value
Diabetes Mellitus	<30 years	11	0.000
	31-45 years	28	
	46-60 years	44	
	> 60 years	35	
Hypertension	<30 years	3	0.000
	31-45 years	28	
	46-60 years	34	
	> 60 years	30	
Ischemic heart Disease	<30 years	5	0.007
	31-45 years	18	
	46-60 years	18	
	> 60 years	18	
Over Weight & Obesity	<30 years	8	0.1
	31-45 years	24	
	46-60 years	21	
	> 60 years	8	
Chronic Liver Disease	<30 years	5	0.24
	31-45 years	8	
	46-60 years	12	
	> 60 years	19	
Chronic Kidney Disease	<30 years	6	0.3
	31-45 years	8	
	46-60 years	12	
	> 60 years	3	
Stroke (CVA)	<30 years	1	0.2
	31-45 years	4	
	46-60 years	10	
	> 60 years	9	
Non- HIV related Cancer	<30 years	1	0.3
	31-45 years	5	
	46-60 years	7	
	> 60 years	2	

Discussion

Our study aimed to find non-HIV related comorbidities in patients living with HIV infection and under treatment at HIV care center, DHQ teaching hospital, Kohat, Southern part of Khyber Pakhtunkhwa, Pakistan. This was an initial step in estimating the new challenge of Non-Communicable Disease in HIV infected patient. Our study found that 54.7% patients have non-HIV related comorbidity showing the similarities with the other study conducted on the HIV patients.[17] Among patients with non-HIV related comorbidity 29.6% patients had single

comorbidity and 25.1% had multimorbidity which is quite high.

Different Studies done worldwide also showed high number of patients living with HIV suffer from non-HIV related comorbidities. A study done in USA showed that there were more comorbidities in HIV-infected patients as compared to HIV infected matched controls for comorbidities like hypertension, Obesity, Diabetes Mellitus and hyperlipidemia from 2003 to 2013.[3] Another study conducted at Lubowa, Uganda showed Overall, 20.7% (80/387) of the participants had a non-communicable disease.[14] Similar results have also been reported in other parts of Africa, Europe and studies conducted in India where significant number of patients were suffering from non-HIV related diseases and Non communicable diseases.[11,15,16] In another study conducted in Europe from Danish based population, 21.9 % patients had at least one non communicable disease at HIV diagnosis which increased to 42.2 percent at 10 years.[17]

Multimorbidity has also been reported in different studies where patients infected with HIV had 2 or more comorbidities. A study conducted in Brazil showed that Non communicable disease multimorbidity increased in 2014 as compared to 2003.[1] In another study Multi morbidity was observed in 4.7% of the cases by patients had more than one non-communicable comorbidity along with HIV- infection.[15] Another study conducted in Odisha, Eastern India, the prevalence of multimorbidity was 47.7% which was higher as compared to other studies done in India as well as other parts of world.[9] Increasing multimorbidity among HIV positive patients worth noting as with the proper use of ART, their life expectancy has increased and they have more probability of dying because of non-HIV related conditions rather than HIV complication. This increasing burden of multi-morbidity & polypharmacy in elderly age group was also shown in study conducted in USA by Guaraldi G, et al.[12]

Upward trend in Non Communicable Diseases in people infected with HIV is supported with the results of other studies in other developing countries.[6, 18] With effective antiretroviral therapy patient infected with HIV live longer and have higher chance of developing age-related diseases and degenerative disease which can attribute towards multimorbidity. HIV infection itself may result in metabolic manifestation, Nephropathies, hepatic injury, and osteoporosis which can contribute for higher cases of non-HIV related comorbidities. Many of the conditions coexist even in non-HIV infected patients. For instance, hypertension Is a known risk factor for developing CKD or CVD. Similarly, Diabetes Mellitus is a risk factor for both chronic kidney disease & ischemic heart disease. Therefore, these comorbidities coexist in HIV infected patients specially in aging population as reported in a study.[16]

In a study conducted at South Africa, the commonest morbidity observed was hypertension showing the cases 12.4%. Diabetes mellitus was found at 4.7% & Renal impairment was found at 1.6% which has a lower prevalence as compared to our study.[11] In our study 26.5% patients were suffering from Diabetes Mellitus which was the most common non communicable disease in our patients. Hypertension was second common comorbidity with 21.3% patients suffering from it. In another study conducted in Cambodia showed the rate of diabetes among 9.4% of cases, hypertension among 15.1% however the rates of hyperlipidemia were seen among 33.7% of cases and no statistical differences was observed between diabetes mellitus and hypertension cases among male and female.[11] In another study conducted in nearly 1000 adult Malawians in HIV center, the majority of patients on ART, the prevalence of hypertension was reported as 23.7%. The combined prevalence of Diabetes and Hypertension was 26.6% in another study conducted in Malawi.[19] A small study done in Tanzania reported a very high diabetes Mellitus prevalence of 18% in their study population of whom 12% were using protease inhibitors.[13]

In our study only 59 patients 13.2% had ischemic heart disease. However Coronary artery disease was reported by a study showed the prevalence of 10.1% in patients infected by HIV.[20] Other studies have also reported of higher prevalence of IHD in patients infected with HIV.[2,21] Aging, chronic inflammation and common use of protease inhibitors can be attributing factors for ischemic heart diseases. Comorbidities like Chronic liver disease, Chronic Kidney disease, Stroke and Non-HIV related Cancer were relatively rare in our student population. Regimens including tenofovir disoproxil fumarate are commonly used in our setup have been associated with higher risk of renal dysfunction & can be the attributing factor in our setup. Similar studies have been done in other parts of world and have reported similar results.[16,22-23] People living with HIV infection are at increased risk for cancers due to associated immune-deficient state since the beginning of epidemic, although there is change in spectrum with highly active antiretroviral therapy.[14,24] The rates of other malignancies have also increased, particularly Anal, lung & liver cancers. In Our study 15 patients had non-HIV related malignancy. Thus, clinicians

will need to consider variety of oncologic manifestations as their HIV infected patients get older.

There is no large study on Non communicable diseases in patients with HIV infection in Pakistan. A study was conducted in Peshawar on neurological manifestations of HIV which mostly included HIV related diseases.[25] There have been studies on demographics, psychosocial factors and associated infections in HIV patients living in different regions of Pakistan.[23,26-27] Our study showed that increasing burden of NCD in patients with HIV will be challenging and patients living with HIV will multidisciplinary care rather than just being treated with ARV therapy. Further, as patients with HIV infection are living longer, attention should be given to management of the patients living with HIV infection especially elderly population.[28] Associated comorbidities and side effect profile of ART shall also be considered in selecting the appropriate regimen of HIV medications. Protocols should be made to manage the effect of aging, including screening and regular surveillance of the severe and common co morbidities, life style modification and optimum management of these Comorbidities which will eventually lead to the better quality of life.

Conclusion

The management of antiretroviral therapy along with Non communicable diseases will further complicate the health outcomes of patients, the guidelines on clinical management of HIV infected patients with other chronic conditions are available but further studies are required to design the optimal treatment regimens and life style changes. Appropriate health care delivery models with multidisciplinary approach will help in combating HIV & Non-HIV related comorbidities and will be of utmost importance for the care of HIV-infected patients.

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