A PROSPECTIVE OBSERVATIONAL STUDY ON QUALITY OF LIFE, ADVERSE DRUG REACTIONS AND PRESCRIPTION PATTERN OF PATIENTS UNDERGOING ANTIRETROVIRAL THERAPY

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ABSTRACT

Background: HIV/AIDS affect communities in every sector of the world making the disease openly an issue of global significance. Number of people living with HIV is 1.99 Lacs in Karnataka, and it holds the third place in India among the states. Objectives: The main objective of the study was to assess the quality of life, adverse drug reactions and prescription pattern among HIV/AIDS patients undergoing Antiretroviral Therapy. Materials and Methods: Study was carried out at ART department, Mysore Medical College & Research Institute and Associated Hospitals; K R Hospital, Mysuru, India, from October 2017 to March 2018. A total of 255 patients were enrolled in the study as per inclusion and exclusion criteria. Patients demographic data were collected by using patient data collection form and Adverse Drug Reactions were assessed by using Naranjo causality assessment scale, Hartwig scale. The Quality of Life was assessed by using WHO QOL-HIV BREF questionnaire. The domains associated with the quality of life were identified and correlated with multiple factors. Results: Majority of the patients were in the age group of 55-64 years. The frequently assessed opportunistic infection was tuberculosis. Lactic acidosis was most commonly seen as ADR. From QOL assessment the „environmental score” shows higher QOL. 48.91% ADR were “probable and most of the ADRs are mild (50%). Conclusion: The study was conducted to enhance the overall quality of life among infected individuals. A decline in infection can be obtained by giving education and awareness about the disease in the population.

KEYWORDS: HIV/AIDS, Adverse drug reaction (ADR), Quality of life (QOL), Antiretroviral Therapy (ART).

INTRODUCTION

HIV/AIDS is a leading global burden. Beginning stages of the disease heavily affect the body’s defence mechanism. Human Immunodeficiency virus seems to be a causative organism for the chronic sickness. These virus attacks host immune system through their high affinity to CD4 cells, and its counts plays a major role in the AIDS detection. Individuals with HIV are more prone to get opportunistic infections due to fungus, bacteria, virus etc. Due to the weakened immune system, patients are at a risk of developing Cryptococcal Meningitis, Toxoplasmosis, Oesophageal candidiasis and certain cancer like Kaposi’s sarcoma.¹

According to the estimation of WHO, 36.7 million people were living with HIV at the end of 2016.² In India as per the National Aids Control Organization (NACO); ministry of health and family welfare, the estimated number of People Living with Human Immunodeficiency Virus (PLHIV) is 1.99 Lacs in Karnataka (2015), 3⁴th place in India among the states.³

On the other hand, the severity of this ailment decreases by the effective involvement of health-care professionals, that makes a dramatic change through the introduction of potent ART drugs. Standard treatments consist of combinations of antiretroviral drugs. This approach is known as Highly Active Antiretroviral Therapy (HAART).⁴ It includes combinations of „two Nucleoside reverse transcriptase inhibitors and a Non- Nucleoside reverse transcriptase inhibitors”, and „two NRTI’S and a protease inhibitor.⁵

QOL is a measure of treatment in HIV. QOL is said as, those having their own views about the life regarding to the culture and value system as well as counting the goal’s standards, expectations and concerns. HRQOL is useful for documenting the persistent disease, monitoring the changes in health over time, assessing the effect of therapy and measuring the return on health care savings.
Quality of Life is mainly measured by using WHOQOL-HIV BREF scale. [6]

Use and uptake of ART has resulted in adverse drug reactions. ADR arises due to the impact of virus in the immune system and also by complex ART drug. These adverse reactions may be mild to severe. Long term ADR shows reduced efficacy of ART and act on health related quality of life. Generally, treatment needs constant remedial treatment like antiretroviral therapy. Prescribing of those costly antiretroviral drugs is an extra burden to the patients. Prescribing the quality generic drugs helps the patients. [7]

Pharmacist supports the patients and other health care providers to achieve goals such as decreasing toxic effects, staying away from drug interactions, concise the treatment regimen, minimizing drug cost, managing co-morbid conditions and promote long term adherence. [8]

MATERIALS AND METHODOLOGY
This is a hospital based prospective observational study. It was conducted at Mysore Medical College and Research Institute and Associated Hospitals,(K R Hospital); Mysuru. The study was carried out at ART department of HIV patients who are undergoing Anti Retroviral Therapy as health care and the study duration was the period of 6 months from October 2017 to March 2018. The data were collected from the patient medication history and their bystanders respectively after getting informed consent. The department of ART comprise of doctors specialized in infectious disease, two counselors, pharmacist, ICTC. CD 4 test can be done at the same department. Nursing students are also available for the services. During the study period we attended 255 patients who are above 15 years old. Female patients with pregnancy and lactation, incomplete information, unconscious patients and age below 15 are excluded from the study.

Ethical approval was obtained from the Institutional Ethical Committee of Mysore Medical College and Research Institute, K R Hospital; Mysuru.

Importance of the study was explained to the participants and informed consent was taken from the patients or their bystander. WHO QOL-HIV BREF questionnaire was used to investigate the quality of life of people living with HIV receiving ART. And it is filled by patient itself and recorded the same. The data collected from the patients from questionnaire and data collection form. The statistical analysis was done by using SPSS and analysed using the statistical test like ANOVA and two-tailed t-test and the results were compared.

RESULTS
Demographic details
Table 1: Gender Distribution of the Study.

<table>
<thead>
<tr>
<th>Sl. No</th>
<th>Gender</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>154</td>
<td>60.4%</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>101</td>
<td>39.6%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>255</td>
<td>100%</td>
</tr>
</tbody>
</table>

Quality of Life
Table 2: Mean Of Domains.

<table>
<thead>
<tr>
<th>Sl. No</th>
<th>Scores</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Physical domain score</td>
<td>9.60</td>
<td>3.090</td>
</tr>
<tr>
<td>2</td>
<td>Physiological domain score</td>
<td>9.49</td>
<td>2.965</td>
</tr>
<tr>
<td>3</td>
<td>Level of Independence domain score</td>
<td>8.85</td>
<td>2.509</td>
</tr>
<tr>
<td>4</td>
<td>Social relationship domain score</td>
<td>10.41</td>
<td>4.14</td>
</tr>
<tr>
<td>5</td>
<td>Environmental domain score</td>
<td>10.99</td>
<td>3.036</td>
</tr>
<tr>
<td>6</td>
<td>Spirituality/Religion/Personal belief domain score</td>
<td>10.17</td>
<td>2.649</td>
</tr>
</tbody>
</table>

Figure 1: Mean of Domains.
Adverse Drug Reactions

Table 3: Suspected Medication.

<table>
<thead>
<tr>
<th>Sl. No</th>
<th>Medication</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Zidovudine</td>
<td>48</td>
<td>52.17%</td>
</tr>
<tr>
<td>2</td>
<td>Efavirenz</td>
<td>10</td>
<td>10.86%</td>
</tr>
<tr>
<td>3</td>
<td>Tenofovir</td>
<td>26</td>
<td>28.26%</td>
</tr>
<tr>
<td>4</td>
<td>Atazanavir</td>
<td>8</td>
<td>8.61%</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>92</td>
<td>100%</td>
</tr>
</tbody>
</table>

Prescription pattern

Table 4: Type of ART Regimen.

<table>
<thead>
<tr>
<th>Sl. No</th>
<th>Types of regimen</th>
<th>Number</th>
<th>Regimen</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>First line</td>
<td>194</td>
<td>TDF+3TC+EFV AZT+3TC+EFV AZT+3TC+NVP TDF+3TC+NVP d4T+3TC+EVF</td>
<td>23</td>
<td>11.8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>22</td>
<td>11.34%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>30</td>
<td>15.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>97</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>22</td>
<td>11.34%</td>
</tr>
<tr>
<td>2</td>
<td>Second line</td>
<td>61</td>
<td>AZT+3TC+ATV+RTV TDF+3TC+ATV+RTV</td>
<td>43</td>
<td>70.49%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>18</td>
<td>29.50%</td>
</tr>
</tbody>
</table>

Table 1 shows that, out of 255 patients, 154 patients were males (60.4%) and 101 patients were females (39.6%). The table 2 & figure 1 explains mean of various domains considered in this study and the study summarises that Environmental domain (10.99%) have the highest mean comparing with other domains. The social relationship was found to be 10.41%. Finally, the level of independence (8.885%) shows the least mean among the domains. Figure 2 shows, various types of ADRs associated with ART drugs. Major ADRs 21.73% were seen as lactic acidosis. Least percentage of ADR was found to be psychosis (1.08%). From the table 3, It is understood that, out of 92 ADRs 48 were related with Zidovudine (52.17%), followed by Tenofovir (28.26%) and Efavirenz (10.86%). Atazanavir were found with least adverse reaction (8.61%) ie, 8 out of 92 patients. The table 4 shows a clear picture regarding the two different regimens used in the treatment. The first line regimens were used in 194 cases. Among these first line regimens, the most commonly used regimen was Tenofovir + Lamivudine + Nevirapine (50%). Least used first line regimens were Zidovudine + Lamivudine + Efavirenz (11.34%) and Stavudine + Lamivudine + Efavirenz (11.34%) respectively.

On the other side, Second line regimens used were 61. From this the most prescribed regimen was Zidovudine + Lamivudine + Atazanavir + Ritonavir (70.49%) followed by Tenofovir + Lamivudine + Atazanavir + Ritonavir regimen (29.50) used. In this study all patients were prescribed with generic drugs.

In causality assessment by Naranjo scale, 48.9% were probable 25% were possible, 23.91% were definite and 2.1% doubtful respectively. The severity assessment done by Hartwig scale, most of the ADRs are mild (50%) followed be moderate (43.47%) and severe (6.52%).

Quality of Life

The “overall quality of life” was done by the direct interaction with the help of WHOQOL – HIV BREF
questionnaire with patients during the study. 39.6% of individuals rated their lives as neither poor nor good. The health perception was 43.9% of individual having neither satisfied or nor dissatisfied life. The study also observed the significance of domain in which the physical domain score viewed with a p value < 0.05 with respect to gender. And the female showed as a better quality of life than the males with a p value = 0.002.

The physiological, level of independence, social relationship and environmental score showed that “p value” of 0.001, 0.013, 0.001 and 0.00 respectively with respect to the age group of 54-64 years. From this we can clear that quality of life is less in the age group of 54-65. The marital status varied significantly (p < 0.05) with respect to physical score, P value = 0.001. Two-tailed t-test is used for identifying the significance of income and domains. Income varied significantly with physical score (p = 0.00), physiological score (p=0.001) and level of independence(p = 0.002). From this result, the rate who have more annual income had good quality of life. Social relationship score significantly varies with HIV stages, p=0.003.

DISCUSSION
Demographic
The study was carried out in the Department of ART, Mysore Medical college and Research Institute and Associated Hospitals,(K R hospital) over a period of 6 months from October 2017 to March 2018. This is a prospective observational study assessing the Quality of Life, Adverse Drug Reactions and prescription pattern of patients undergoing antiretroviral therapy in HIV or AIDS. The study observed significant morbidity associated with the use of Highly Active Antiretroviral Therapy (HAART). In this study, out of 255 patients, 60.4% were males and 39.6% were females. The male patients were affected with the diseases more than the female patients. The result is similar to the study conducted by Biradar SM et al. In this study, the selected 103 patients were divided gender wise, in which males were 73 (70.8%) and females were 30 (29.1%). The study results also correlated with the study of Anand D et al.

Majority of patient belongs to age group of 55-64 years (31.8%) and the least number of patients were in the age group of 15-25 years (7.1%). By analyzing the results, It is understood that Tuberculosis affected in 50 patients (19.6%) among 255 individuals. Our observation was similar to the study of Elizabeth ST et al says that candidiasis and tuberculosis were reported as the major infections among 245 peoples. UTI (Urinary Tract Infection) was also observed among 16.9% patients who were in the study and hence it showed the second highest infection among the people on ART treatment. Followed by, URTI (Upper Respiratory Tract Infection in 4.9% patients.

By considering Stages of disease condition, results showed that, out of 255 patients 152(59.6%) were found in stage 4, 52(58%) were in stage 3 and 45(17.6%) in stage 2.

Prescription pattern
In this all patients (255) are prescribed with the generic drugs. However these types of drugs are prescribed by categorizing them into regimens such as first line regimen and second line regimens. The first line regimens were used in 76.1% individuals concurrently whereas 23.9% treated with second line regimen. ART first line regimen TDF+3TC+NVP (Tenofovir+ Lamivudine+ Nevirapine) was the most prescribed regimen (50%). The first line regimens AZT+3TC+EFV (Zidovudine + Lamivudine + Efavirenz) as well as D4T+3TC+EFV (Stavudine+ Lamivudine+ Efavirenz) respectively prescribed in least frequency. That is 11.34%. In this study the most widely used second line regimens were AZT+3TC+ATV+RTV (Zidovudine+ Lamivudine+ Atazanavir + Ritonavir) and the least were TDF+ 3TC+ ATV (Tenofovir+ Lamivudine+ Atazanavir) was 70.49% (43) and 29.50%(18) respectively.

ADR
Out of 255 patients, 92 (36.07%) reported with Adverse drug reaction whereas 163 (64.03%) assigned with no ADR. Out of these 92 ADRs, 47 were males and 45 were females. This result is comparable with a study conducted by Lihihe RJ et al, also showed a high incidence of ADR in males with respect to female individuals. In this study the patients were initiated with both first line and second line regimens. Lactic acidosis was the most common ADRs seen in 21.73% patients. It is followed by hypersensitivity reaction (18-47%) and gastroenteritis (16.30%) and 1.08% of psychosis.

Our study results observed by Naranjo Causality assessment scale, 48.91% were “probable” and 2.17% were “doubtful”. A similar findings observed a study conducted by Mukherjee S et al. In their study Naranjo algorithm showed 88% “probable”.

In our study severity assessment done by Hartwig Scale, most of the ADRs were “mild” (50%) followed by “moderate” (43.47%) and 6.52% was “severe” type. The result is comparable with study conducted by Mukherjee S et al.

Quality of Life
A 39.6% of individuals rate their lives as “neither poor nor good” as well as 31% rate themselves as “poor” out of 255 candidates, only 10.2% are happy with their life. Later the mean of each domain were calculated and the results gave a conclusion stating that mean of environmental domain 10.99 has the highest value. The mean value of Level of independence was found to be 8.85. The result is similar to study conducted by Nirmal...
B et al so shows that highest quality of life in environment domain have a dominance over other domains.\[14\]

The quality of life among individuals is assessed by monitoring the mean of different domains. By comparing the male and female patients, the mean value of physical domain in females was 10.33. It shows a slight dominance over the male (9.12). The mean score in the physiological domain in female patients was 9.68 has a light increase than the male (9.37).

On the other hand, level of independence and social relationship undergone the estimation of their mean. Female (9.13) of level of independence are having better quality of life in compare with male (8.66). Social relationships have better effect in females (10.75) over the males (10.18). The mean of environmental domain showed superiority in females (11.18) even the male was seen in the range of 10.87.

Finally, Spirituality or Religion & Personal belief which considered as important factors in improving QOL had a great predominance in females (10.28) in comparison with males (10.10). The above information said that females had a better QOL with respect to males.

When the gender was correlated with several domains of QOL gives an exciting result as the physical domain only shows the correlation and the correlation was done by two-tailed t-test which gave a significance of 0.002 for the physical domain.

The mean of domain and the age of individuals included in the study were compared with the different domains in the QOL. In the physical domain, 15-24 years had a highest mean (10.83) where as the 8.92 was reported in age group 55-64 years. The physiological domain have a different data with respect to the physical domain. The mean of domains in the age group of 35-44 years (10.61) had a significant rate with the least mean of 8.40 in 55-64 years. In Spirituality or Religion / Personal beliefs, the highest mean analyzed among the group of 35.44 years (11.03) with respect to the lowest mean in 15-24 years (8.78). The above information concludes by giving the study report showed that, between the age group of 55-64years comparatively showed less QOL in relation with other age groups.

The domains of quality of life and age are correlated by using ANOVA technique. During the correlation methods, four domains had a significance in the age group, physiological score, level of independence, social relationship and environmental score viewed with a significance of 0.01, 0.013,0.001 and 0.000 respectively.

By Post HOC test, the data were observed in such a way that the less QOL among age group of 55-64 years. Hence, the age group is compared with other respective groups such as 25-34years, 35-44 years and 45-54 years.

In the physical domain, 55-64 years compared with 25-34years, showed a significance of 0.017. While 45-54 years observed with a significance of 0.41. Only 45-54 years monitored with a significance of 0.27 in level of independence domain. The social relationship domain in the group of 25-34 years gave a significance of 0.026. When compared with 55-64 years. Lastly, environmental domain analysed with a significance of 0.014 and 0.000 in age group of 35-44 years, 45-55 years with respect to 55-64 years. From the multiple comparison it is understood that QOL were lesser in 55-64 years.

The QOL of patient are also associated with their financial status. In our study, the financial status was mainly monitored by accessing their annual income. And the annual income was categorized as less than Rs 25000 and greater than Rs 25000.

In the physical score the mean of annual income above Rs 25000 was 9.74 where as below 25000 with 9.49 mean. If the annual income were less than Rs 25000, the level of independence showed a mean of 9.36. On the other side, a mean of 9.66 was observed above Rs 25000 annual income in the level of independence. In the case of level of independence, a mean of 8.67 and 9.08 were examined in the income of above Rs 25000 and below Rs 25000 respectively. The mean of social relationship with respect to annual income above Rs 25000 was 10.84 and below the annual income Rs 25000 was 10.07. The Environmental relationship when compared with the annual income, a mean of 11.63 seen in above Rs 25000 and 10.49 obtained in the annual income below Rs 25000. In the Spirituality/Religion/Personal belief domain, the annual income that was above Rs 25000 showed a mean of 10.20 and below Rs 25000 expressed with a mean of 10.15. When correlation done with the domains and annual income using 2-tailed t-test, a significance of 0.003 were observed only in the environmental domain. The quality of life decline as the mean increases between the domains and annual income.

As the study progresses domains were compared with marital status of individuals. In the physical domain a highest mean of 10.75 were seen in separated patients as well as the lowest was among the widowed (8.78). The separated individuals with a mean of 10.80 and single individuals with 9.34 mean was seen in level of independence with respected to the lowest mean of 8.38 in widowed. Social relationship showed a highest mean in separated (16.25) where as lowest in singles (9.64). A large mean of 12.50 in separated and the least mean 10.25 in widowed were showed in the environmental domain. The Spirituality/Religion/Personal belief domain exist with a large mean showed in separated ones (11.75) and least mean in married ones (9.80). Overall mean showed that separated having more QOL as compared with other statuses. When correlation was conducted between the domains and marital status a significance of 0.001 was seen in social relationship domain. Comparison of significant domains with the
patient marital status, the single comparison was done with married and separated individuals and gives a significance of 0.014 and 0.006 respectively. That means single showed a highest rate QOL when compared with married and separated individuals.

The drugs are given to the patient either as a first line regimen or second line regimens. The two regimens compared with the various domain of QOL. Among that mean of first line regimen used in physical domain found as a 10.13 where as the second line regimen was only 7.92. In case of physiological score have a mean of 9.83 and 8.43 for the first line as well as second line regimens. Levels of independence were observed with a mean of 9.11 in first line regimen where as 8.01 measured for second line. A mean of 10.69 and 9.51 recognized among first line and second line combinations in a social relationship score. The environmental domain concludes by giving information of mean of first line regimen (11.18) with respect to the second line (10.41). The first line and second line regimens used in the Spirituality/Religion/Personal belief domain examined with a measure of 10.10 and 10.39 respectively. As the regimen compared with the various means, except the Spirituality/Religion/Personal belief showed a highest mean for first line regimen as to second line.

When the correlation study was conducted using the two–tailed t-test between the various domains and regimens used in the treatment. The physical score, physiological score and the level of independence exhibit a significance of 0.000, 0.001 and 0.02 respectively. It concluded that second line regimens have higher QOL.

By comparing the stages of disease with various QOL domain our results states that stage 2, stage 3 and stage 4 are correlated with domains. The physical score reveals a maximum mean of 10.29 in the stage 3 whereas least mean of 9.29 in the stage 4. The stage 3 demonstrates a highest mean of 10.13 and smallest mean of 9.18 in the physiological domain. The level of independence appear with a mean of 9.24 which is the top most and least mean of 8.52, 12.02 and 9.83 are the highest and lowest mean of social relationship score. The maximal mean of environmental domain founded as 11.45 and minimal was 10.66. The Spirituality/Religion/Personal belief were established with highest mean of 10.60 and lowest with 10.17 mean. By analyzing the above data the stage 3 had the highest mean among the domains. The correlation between the various domains and the different stages of HIV/AIDS are observed with the help of ANOVA. The social relationship domain was the only score which showed a significance of 0.003.

The post Hoc tests were used for the multiple comparison of the stages of HIV infection to the domains of QOL. The social relationship domain at the stage 4 produced a significance of 0.002. That means stage 4 shows less quality of life when compared to other stages.

CONCLUSION

India is the third highest country with HIV morbidity rate. Awareness among the communities in relation to the transmission and associated problems related to HIV/AIDS should be conducted especially in rural areas which helps the society.

The current study explores the demographic characteristics, social, environmental factors affect the individuals who were suffering from HIV. The ratio of male and females were also monitored in the study. Early detection of the disease and initializing the HAART therapy prevents the progression of the infection. Co-morbid conditions as well as opportunistic infections are considered during highly Active Antiretroviral Therapy. Thus it leads to reduced severity of the disease.

In our study male patients were more in number when compared with females. And 92 ADRs were reported out of 255 patients during the study. The most common ADR was the lactic acidosis whereas the least was psychosis. The quality of life was monitored using the WHOQOL-HIV BREF Scale. The Naranjo causality assessment scale and Hartwig severity scale were used to calculate the ADRs. The "overall quality of life" and “health perceptions” were self assessed by the patient during the study, which gave most of them living with neither good nor bad in overall quality of life, and the health perception was neither satisfied nor dissatisfied.

Since, the QOL was assessed with respect to the various domains. The environmental domain showed a higher quality of life than others domains. Both the female as well as male patients were enrolled in the study. But the female exhibit an increased QOL when compared with males. The Patients between the age group 55-64 revealed a decreased QOL than the other age groups during the study. The patients having annual income of more than Rs.25000/-showed as better quality of life.

On the other hand an improved quality of life has been demonstrated by the separated one with respect to other marital statuses. Since, the disease condition was confirmed by analysing CD4 count which categorizes the condition to various stages. Stage 4 was a condition in which the CD4 count drops below 200. According to our study, the patient on stage 4 showed a declined QOL due to the gradual decrease in CD4 counts.

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