Factors Associated with Metabolic Syndrome among HIV-positive Patients at a Health Facility in Botswana

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Author’s contribution

This whole work was carried out by the author NM.

ABSTRACT

Aims: To investigate the prevalence and factors associated with development of metabolic syndrome among people with HIV on antiretroviral treatment (ART) in Botswana.

Study Design: Cross-sectional study design

Place and Duration of Study: Princess Marina Hospital in Botswana (Africa). Only patients that had been on treatment from 1st January to 31st December 2010 were included.

Methodology: A structured questionnaire and a data collection form were used to collect data on demographic, socioeconomic, lifestyle, clinical and laboratory data. Bivariate analysis was used to assess characteristics associated with the presence of metabolic syndrome by calculating odds ratios.

Results: A total of 190 subjects participated in the study, 141 (74.2%) females and 49 (25.8%) males. The mean age of participants was 42 (±9.04) years, ranging from 24 to 71 with a median age of 40.5 years (IQR: 35 – 49). The overall prevalence of metabolic syndrome in this study was 11%. In the bivariate analysis, the odds for developing MS were higher among participants who were male, obese, 41 years old and older, and those who used ART regimens containing PIs.

Conclusion: Overall, the prevalence of metabolic syndrome was 11.1% among the study participants. The factors associated with it were increasing age above 41 years.
old, male gender, obesity, longer duration of treatment and the use of PIs drugs. It is recommended that patients with such characteristics should be targeted for regular monitoring of parameters defining metabolic syndrome and that a culturally appropriate lifestyle intervention program needs to be designed and implemented for Botswana patients.

Keywords: Metabolic syndrome; antiretroviral treatment; Botswana; African.

1. INTRODUCTION

Botswana was the first country in Africa to initiate universal antiretroviral treatment to all its citizens suffering from Human Immuno-deficiency Virus (HIV) in 2001. This brought about a significant improvement in survival and quality of life of HIV-infected patients as well as a dramatic decrease in the incidence of opportunistic infections. Several reports about metabolic syndrome among people with HIV infection have been published elsewhere. The documented prevalence of metabolic syndrome (MS) was usually higher in HIV-infected patients than in those HIV-negative and ranged from less than 14% to 26% [1-3]. Although little is known about the extent of MS in HIV-positive patients in Botswana, metabolic syndrome is defined as an aggregation of central obesity and metabolic abnormalities that confer and increased risk of cardiovascular disease and type 2 diabetes mellitus. It consists of a cluster of metabolic risk factors including dyslipidemias, impaired carbohydrate metabolism, obesity and high blood pressure [4-5]. The purpose of this study was to investigate the prevalence and factors associated with metabolic syndrome among patients suffering from HIV who had been on ART at Princess Marina Hospital, Gaborone, Botswana.

2. MATERIAL AND METHODS

This was a cross-sectional study based on patient interviews and review of records. A structured questionnaire and a data collection form designed for the study were used to collect data on demographic, socioeconomic, lifestyle, clinical and laboratory data. The age of participants was categorized based on the median age.

Metabolic Syndrome was defined using the International Diabetes Federation (IDF) criteria as follows: a waist circumference of > 80 cm (woman) or > 94 (man) plus two of the following: fasting blood triglycerides > 150 mg/dL or use of triglycerides lowering drugs; blood pressure (BP) of >140/90 mm Hg or using antihypertensive drugs; fasting plasma glucose of ≥ 5.6 mmol/L or using anti-diabetic drugs; fasting high-density cholesterol of ≥ 5.2 mmol/L [5-6].

Patients who consented to participate were interviewed and their records were reviewed to collate data. Only patients aged 18 years and older that had been on treatment for at least 6 months during the study period, from 1st January to 31st December 2010, were included. Questionnaires were administered by the Researcher and two trained research assistants, who were qualified nurses during November 2010. The interviews were conducted during three weeks as data were also collated from patients’ files.

Anthropometric measurements including weight, height, waist circumferences were obtained using respectively a calibrated scale and a meter-ribbon. The weight and height measurements were used to calculate the body mass index (BMI). A BMI of >30 kg/m² was
regarded as obesity [5]. Blood pressure was measured using a standardized digital blood pressure measuring machine. Blood samples were collected by qualified phlebotomists and transported immediately to the laboratory for analysis. Tests done on the equipment at the laboratory were calibrated as regularly as required and were also subjected to daily internal quality control monitoring. Blood glucose, total cholesterol, HDL cholesterol and triglycerides levels were measured using the Roche Cobas 400 Plus analyzer.

Data on the participant’s socioeconomic status and lifestyle were obtained from responses elicited from using a structured questionnaire. Sources of income were coded as employment, government social grant, or support from family members. Alcohol intake, tobacco use and use of recreational drugs was evaluated and classified as current use and non-current use. Data collected was captured into Microsoft Excel (Microsoft Corporation) and then exported to STATA v.11 (STATA Corporation, College Station, Texas) for analysis. Baseline characteristics were summarized using medians and inter-quartile range (IQR) for continuous variables. Bivariate analysis and logistic regression were used to assess characteristics associated with the presence of metabolic syndrome by calculating odds ratios. The level of statistical significance was set at p<0.05.

3. RESULTS AND DISCUSSION

This study sought to determine the prevalence and risk factors associated with metabolic syndrome in patients on ART in Botswana. The mean age of participants was 42 (±9.04) years, ranging from 24 to 71 with a median age of 40.5 years; the majority of them were females (74.1%). The main finding from this study is that 11% of patients at the study site suffered from metabolic syndrome based on the IDF definition. This level of prevalence is higher than the figure reported by Garrido and colleagues in a sample of hospital workers from Botswana. Although the HIV-status of these workers was not known, it seems that MS in HIV-positive patients varies significantly between subgroups of populations [7]. It is known that Europeans and white Americans have high rates of MS than ethnic groups from developing countries [6,8-10].

With regard to clinical components of MS, it is interesting to note that before the start of antiretroviral treatment, none of the patients suffered from diabetes, or hypertension in the sample. At the time of the study, 9.5% and 19.5% of patients had become respectively diabetic and hypertensive (Table 1). Among those who suffered from hypertension, those older than 41 years suffered significantly from this than the younger participants (28.4% versus 10.6%, p=0.001). This finding is consistent with reported findings that up to 25.5% of Botswana patients aged at least 40 years old are hypertensive [11].

In a bivariate analysis, male participants had significantly higher levels of triglycerides than females (26.5% versus 14.5%, p=0.03). Moreover, more patients aged 41 years and older had also higher levels cholesterol but the difference was not significant (22.1% versus 12.8%, p=0.07). These findings concur with reports from Okafor [12].

In respect of anthropometric data, based on the IDF definition of metabolic syndrome, a waist circumference of > 80 cm in women or of > 94 cm in men is one of the criteria. Based on this criterion, 8 (16.3%) out of 49 men and 13 (8.5%) of 141 women met this criterion. The mean waist circumference for males was 83.8±8.6 cm, while for females it was 75.5±6.6 cm (Table 2). Among those with high waist circumference, 19 (10%) patients were obese as their body mass indexes (BMI) were 30 kg/m² or more. The mean BMI was 26.9 (±4.1) kg/m², ranging from 20.7 to 44.4 kg/m² with a median of 27.0 kg/m². More females
than males were obese but the difference was not significant (11.3% versus 6.1%, p=0.22). This finding is consistent to observations from other African countries where obesity is known to be more prevalent in females [11-13].

Table 1. Metabolic syndrome components among HIV patients on antiretroviral treatment in Botswana (n=190)

| Variables                        | Frequency (%) |
|----------------------------------|---------------|
| **Waist circumference**          |               |
| >80 cm (women)                   | 13 (9.2%)     |
| >94 cm (men)                     | 8 (16.3%)     |
| **Hypertension status**          |               |
| Hypertensive                     | 37 (19.5%)    |
| **Fasting Plasma Glucose**       |               |
| Abnormal                         | 18 (9.5%)     |
| **Fasting Triglycerides**        |               |
| Abnormal                         | 33 (17.4%)    |
| **HDL-Cholesterol**              |               |
| Abnormal                         | 12 (6.3%)     |
| **Metabolic syndrome status**    |               |
| Yes                              | 21 (11.1%)    |

Table 2. Anthropometric data of HIV patients on antiretroviral treatment in Botswana

| Waist parameters | Male (n=49) | Female (n=141) | p-value |
|------------------|-------------|----------------|---------|
| Mean             | 83.8        | 75.5           | 0.8     |
| Standard Deviation | 8.6        | 6.6            |         |
| Variance         | 74.4        | 44.2           |         |
| Median           | 82.0        | 75.0           |         |
| Maximum          | 103.0       | 102.0          |         |
| Minimum          | 71.0        | 66.0           |         |

In this study, increasing age and being male were features associated with increased risk of the presence of metabolic syndrome. Not only was the mean age of individuals who had metabolic syndrome higher than in those who did not have it (48.1 years versus 41.1 years, p<0.05); patients aged 41 years and older were about two times more likely to have metabolic syndrome than their younger counterparts (OR [95% CI] = 1.85 [0.28-12.10]). This finding is consistent with the established fact that metabolic syndrome increases with age [14-15].

Though, 45.3% of participants had completed high school level of education (Table 3), more females than males had achieved this level of education (52.5% versus 24.5%, p=0.01). Among those who were married, 64.5% of them were over 41 years old. Male participants were more four times likely to be married than females (OR [95% CI] = 3.9 [1.78, 8.42]). More male participants had been employed than females (65.3% versus 58.2%, p=0.14). These findings suggest that male patients because of regular income and being married may have the ability to afford a rich diet that may unfavorably predispose them to MS [16].
Table 3. Socio-demographic characteristics of HIV patients on antiretroviral treatment in Botswana (n=190)

| Variables                  | Frequency (%) |
|----------------------------|---------------|
| Age category (years)       |               |
| 21-30                      | 15 (7.9%)     |
| 31-40                      | 80 (42.1%)    |
| 41-50                      | 57 (30.0%)    |
| 51-60                      | 34 (17.9%)    |
| >60                        | 4 (2.1%)      |
| Sex                        |               |
| Female                     | 141 (74.1%)   |
| Male                       | 49 (25.8%)    |
| Marital status             |               |
| Not Married                 | 156 (82.1%)   |
| Married                     | 34 (17.9%)    |
| Level of education         |               |
| Primary                    | 86 (45.3%)    |
| High School                 | 86 (45.3%)    |
| Tertiary                   | 18 (9.5%)     |
| Source of income           |               |
| Employment                 | 114 (60.0%)   |
| Family                      | 76 (40.0%)    |
| Smoking status             |               |
| Current smoker             | 107 (56.3%)   |
| Alcohol drinking status    |               |
| Current drinker            | 83 (43.7%)    |

With respect to medicines used by participants, only two patients had been prescribed with non-nucleosides reverse transcriptase inhibitors (NNRTIs) drugs; while 14.2% and 82.0% were prescribed respectively Nucleosides reverse transcriptase inhibitors (NRTIs) and protease inhibitors (PIs) drugs. Patients on NRTIs were one and half times more likely to suffer from MS than those not on these drugs (OR [95% CI] =1.5 [0.46, 4.83]) but the difference was not statistically significant (p=0.50). Based on age category, NRTIs have been prescribed more to patients over 41 years old (63%); while PIs were prescribed more in those younger than 41 years old (51.3%); however, in both cases the difference was not significant (p>0.05). Of the patients on PIs, 30.8% of them had MS as compared to those not taking PIs (p=0.01). This finding is consistent with the well-established fact that PIs are associated with MS. It has been reported that there is a significant elevation in the Low Density Lipoprotein (LDL) cholesterol levels and a decrease in High Density Lipoprotein (HDL) cholesterol levels in the individuals take protease inhibitors [12,17].

The duration of treatment ranged from 6 to 104 months, with a mean of 54.6 (±22.5) months. The finding from this study shows that MS has been increasing with the duration of treatment (Fig. 1).
In a bivariate analysis, age category, sex and other sociodemographic characteristics did not show any significant difference with regard to the length of treatment. However, patients who had been on treatment for more than 60 months had high levels of fasting glucose (17.4% versus 2.95%, \( p=0.01 \)), triglycerides (23.2% versus 12.5%, \( p=0.09 \)), and cholesterol (29.1% versus 18.3%, \( p=0.08 \)). Patients who had been on treatment for over 60 months were about 3 times more likely and significantly to have metabolic syndrome than those who had been on treatment for less than 60 months (OR [95%CI] = 2.69 [1.03, 7.02]). Additionally, as reported in Table 4, the mean duration on treatment of patients with metabolic syndrome had been significantly higher than for those without (66.6 months versus 53.3 months, \( p=0.01 \)). This finding is consistent with reports that HDL-cholesterol levels decrease as the duration of the therapy increases while the LDL-cholesterol levels increases with the duration of the therapy [17].

Table 4. Duration of treatment data of HIV patients on antiretroviral treatment in Botswana

| ART duration Parameters | MS (n=21) | No MS (n=169) | p-value |
|-------------------------|-----------|---------------|---------|
| Mean                    | 66.6      | 53.3          | 0.01    |
| Median                  | 68.0      | 56.0          |         |
| Standard Deviation      | 26.4      | 21.7          |         |
| Sample Variance         | 697.8     | 470.1         |         |
| Minimum                 | 8.0       | 6.0           |         |
| Maximum                 | 104.0     | 104.0         |         |

Overall, 11.1% of individuals met the criteria for metabolic syndrome. As shown in Table 5, several factors were associated with the occurrence of metabolic syndrome in this sample of Botswana patients on antiretroviral treatment. Based on the bivariate analysis performed, the mean age of participants who had metabolic syndrome was higher than that of those who did not have it (48.1 years versus 41.1 years, \( p<0.05 \)). Patients aged 41 years and older were about two times more likely to have metabolic syndrome than their younger counterparts.
(OR [95% CI] = 1.85 [0.28-12.10]). This finding has been reported also in a cohort of Nigerian patients where it was found that MS was associated with increasing age [13].

Table 5. Factors associated with the presence of metabolic syndrome among HIV patients on antiretroviral treatment in Botswana (n=190)

| Variables                                      | Odd Ratios (95% CI)       | p-values |
|------------------------------------------------|---------------------------|----------|
| Age (41 and above vs. < 41 years old)         | 1.85 (0.28-12.10)         | 0.52     |
| Alcohol Use (Yes vs. No)                      | 1.48 (0.60-3.68)          | 0.54     |
| ART Duration (60 months and over vs. < 60)    | 2.69 (1.03-7.03)          | 0.037    |
| ART Regimen (NRTI Use vs. No NRTI Use)        | 1.49 (0.46-4.83)          | 0.05     |
| ART Regimen (PI Use vs. No PI Use)            | 3.36 (1.27-8.91)          | 0.025    |
| Education (Primary vs. High school & Tertiary) | 2.14 (0.84-5.43)          | 0.16     |
| Employment (Unemployed vs. Employed)          | 1.76 (0.71-4.38)          | 0.32     |
| Marital status (Married vs. not Married)      | 6.98 (2.67-18.34)         | 0.0001   |
| Obesity status (Yes vs. No)                   | 16.16 (5.44-47.98)        | 0.0001   |
| Sex (Male vs. Female)                         | 1.92 (0.74-4.96)          | 0.27     |
| Smoking Status (Yes vs. No)                   | 1.36 (0.55-3.38)          | 0.66     |

Male patients were reported, in this study, to be about two-folds more likely to have metabolic syndrome than their female counterparts but the difference was not statistically significant (p=0.27). This finding is in contrast with what was reported by Garrido and co-workers [7]. They reported that the prevalence of metabolic syndrome and the risk for developing it was significantly higher in females than males. However, their findings concurred with the results from this study in that male participants had significantly higher levels of triglycerides than females.

The interaction between sex and marital status of patients seemed to suggest an increased likelihood of metabolic syndrome. Married patients were about 7 times more likely to have metabolic syndrome than their unmarried counterparts (OR [95% CI] = 6.98 [2.68, 18.34]) noting that male patients were about 4 times more likely to be married than females (OR [95% CI] = 3.88 [1.78, 8.42]). The finding from this study that being married is associated with metabolic syndrome concurs with reports by other investigators that marital status influences eating patterns [18].

A dietary pattern that includes cereals, fish, legumes, vegetables, and fruits was independently associated with reduced levels of clinical and biological markers linked to the metabolic syndrome, whereas meat and alcohol intake showed the opposite results [19]. It is possible that the married participants in this study may have been taking a diet comprising meat and alcohol intake but this was not assessed. Further studies should investigate this.

Other significant factors were being obese and having been prescribed PIs drugs; patients who were obese were 16 times more likely to have metabolic syndrome than those who were not (OR [95% CI]=16.16 [5.44-47.98]); while those who had been prescribed PIs were about 3 times more likely (OR [95% CI] =3.36 [1.27-8.91]). In fact, 61.9% versus 38.1% of those not taking of those prescribed PIs had metabolic syndrome (p=0.01). This is because PIs are known disrupt lipid metabolism by activating endoplasmic reticulum stress and inhibiting autophagy activity in adipocytes, thereby contributing to the onset of MS [20].

The above findings of this study are to be interpreted taking into account the limitations inherent to the design of this study; as a cross-sectional study no temporal link could be
established between variables. Nevertheless, two recommendations could be made in relation to the findings. Firstly, because this study showed that metabolic syndrome increases with age, the length of treatment, the use of PIs; patients with such characteristics should be targeted for regular monitoring of parameters defining metabolic syndrome. This would improve safety particularly for male patients aged over 41 years who show increased risk due to other co-factors such employment and their marital status. Secondly, the findings from this study suggest that lifestyle interventions are advisable for HIV-infected patients suffering of or at risk of acquiring metabolic syndrome. Fitch and co-workers had already demonstrated that a lifestyle modification program encompassing dietary counseling and physical activity is a useful strategy for HIV-infected patients [21]. This has been confirmed by a recent meta-analysis by De Lorgeril [22]. Because a lifestyle change should be contextualized, a culturally appropriate lifestyle intervention program needs to be developed for Botswana patients.

4. CONCLUSION

Overall, the prevalence of metabolic syndrome was 11% among the study participants. The factors associated with it were increasing age above 41 years old, male gender, obesity, longer duration of treatment and the use of PIs drugs. It is recommended that patients with such characteristics should be targeted for regular monitoring of parameters defining metabolic syndrome and that a culturally appropriate lifestyle intervention program needs to be designed and implemented for Botswana patients.

CONSENT

Not applicable.

ETHICAL APPROVAL

The author hereby declares that this study was examined and approved by the Medunsa Research Ethics Committee Ethics of the University of Limpopo and it has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

ACKNOWLEDGEMENTS

Mr. Desire B. Mhlabi is acknowledged for his role in the collection of data.

COMPETING INTERESTS

The author has declared that there are no competing interests.

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