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Original Article

# The Prevalence of Metabolic and Endocrine Disorders Among HIV-infected Patients in a Population From the South of Iran

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**Abstract**

**Background**: Since the beginning of the acquired immunodeficiency syndrome (AIDS) pandemic, the number of people infected with human immunodeficiency virus (HIV) has shown a steady increase. Previous evidence exists regarding the evaluation of endocrine dysfunction in HIV-infected individuals. The present study sought to investigate the prevalence of metabolic and endocrine disorders in HIV-positive patients.

**Materials and Methods:** In this cross-sectional study, 72 HIV-positive patients supported by the Behavioral Diseases Center of Bandar Abbas, Iran were recruited from April, 2016 to September, 2017. Patients who did not consent to participate were excluded from the study. Several parameters were measured, including serum free T3, free T4, thyroid-stimulating hormone (TSH), luteinizing hormone (LH), adrenocorticotropic hormone (ACTH), free testosterone, cortisol, fasting plasma glucose (FPG), 2-hour plasma glucose, cholesterol, triglyceride, and low- and high-density lipoprotein levels. Finally, data were analyzed using chi-square and Mann-Whitney tests.

**Results**: High serum lipoprotein levels, diabetes, and prediabetes were observed in 28/72 (38.9%), 13/72 (18.1%), and 17/72 (23.6%) patients, respectively. The prevalence of overt hypothyroidism and subclinical hypothyroidism, as well as overt hyperthyroidism and subclinical hyperthyroidism was 32.8% (22/67), 9% (6/67), 1.5% (1/67), and 7.5% (5/67), respectively. Primary and secondary gonadal dysfunction were found in 1/47 (2.1%) and 9/47 (19.1%) patients, respectively. Primary and secondary adrenal insufficiency were detected in 8/53 (15.1%) and 1/53 (1.9%) patients, respectively. Diabetes was significantly more frequent among older patients and those with a history of addiction.

**Conclusions:** The results of this study indicated a relatively high frequency of metabolic and endocrine disorders, especially dyslipidemia and hypothyroidism in HIV-positive patients.

**Keywords:** HIV, Metabolic disorder, Endocrinopathy

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## Introduction

Since the introduction of the human immunodeficiency virus (HIV), 78 million people have been infected with the virus, with a prevalence of approximately 0.7% in people aged 15-49 by the end of 2019 (1). According to the World Health Organization (WHO), the number of Iranian people with recent HIV infection was 4400 in 2019 (2).

HIV is associated with several endocrine and metabolic disorders (3). The disorders of the endocrine system, including thyroid, gonadal, adrenal, and metabolic disorders have largely been reported in HIV-infected patients (4-6). The systemic effects of HIV, along with the complications of highly active antiretroviral therapy (HAART) have been suggested as underlying reasons for the endocrine disorders in HIV patients (7, 8). Some studies have implicated the adrenal gland as the most common endocrine target in HIV-positive patients (9,

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10).

Endocrine disorders substantially affect organ development, muscle mass, and sexual function, leading to a significant reduction in the quality of life in HIV-infected individuals (11). Limited data exist on the clinical symptoms of thyroid disorders in these patients (12). Considering that endocrine disorders are easily controlled by hormone replacement therapy (13), accurate estimates of the prevalence of these disorders in HIV-positive patients are of importance. Hypogonadism is another common endocrine disorder in HIV-positive patients. Low $CD4^+$ cell count, disease progression, and weight loss are associated with low testosterone levels, indicating testicular dysfunction (14). The association of HIV with diabetes has also been well described (11), and diabetes may exist before or after the onset of HIV infection. The pathogenesis of diabetes is mainly insulin resistance rather than insulin deficiency in HIV infection.

Given the significance of metabolic and endocrine disorders in HIV-positive patients, the straightforward management of these conditions, and the required clinical attention in the case of a considerable prevalence, the present study was conducted to investigate the frequency of metabolic and endocrine disorders in HIV-positive patients in Bandar Abbas in 2016-2017.

## Materials and Methods

### *Study Population*

This cross-sectional study was conducted on HIV-positive patients in Bandar Abbas, Iran. Patients were selected by the census method, and 72 HIV-positive patients supported by the Behavioral Diseases Center of Bandar Abbas were recruited from April 2016 to September 2017. Written informed consent was obtained from all the patients. Patients who did not consent to participate were excluded from the study.

### *Sampling and Data Collection*

Patients' demographic data including age, gender, history of addiction, and history of tuberculosis were collected through face-to-face interviews. The symptoms of endocrine diseases, including weight loss, muscle weakness, polydipsia, polyuria, impotence, and intolerance to cold and heat, along with amenorrhea and oligomenorrhea in afflicted women were evaluated. Subsequently, patients were examined in terms of thyroid, height, weight, and wasting. Other data such as the duration of HIV infection, the presence of AIDS, and antiviral treatments were recorded as well.

Patients' $CD4^+$ cell count, plasma glucose, and lipid profile had been measured on a monthly basis. The results of the latest tests were recorded, including $CD4^+$ cell count, fasting plasma glucose (FPG), 2-hour postprandial plasma glucose (2-h PPG), total cholesterol, triglyceride, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) levels. In addition, patients' blood samples were sent to the laboratory of Shahid Mohammadi Hospital of Bandar Abbas for further investigations. Due to a history of injectable drug use, the blood samples of some patients were not sufficient for the performance of all tests. Thus, thyroid function tests were prioritized in these patients. The serum cortisol levels were evaluated in the fasting blood samples of 47 patients using the chemiluminescence method via the Abbott ARCHITECT® Instrument System. Furthermore, serum levels of thyroid-stimulating hormone (TSH), free T4, and free T3 were measured in 72 patients, using the same system. Then, serum levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), and adrenocorticotropic hormone (ACTH) were estimated in 47 patients using the Elecsys® kit and the Roche Cobas E411 analyzer. Next, enzyme-linked immunosorbent assay (ELISA) was used to measure free testosterone in 47 patients in blood samples collected at 8:00 in the morning after 10 hours of fasting.

### *Variable Definition*

Diabetes was defined as FPG ≥126 mg/dL and/or 2-hour plasma glucose ≥200 mg/dL after the ingestion of 75g oral glucose.

Primary adrenal insufficiency was defined as serum cortisol <18-20 g/dL and ACTH above the normal limit, while secondary adrenal insufficiency was defined as ACTH lower than or within normal limits.

Primary hypogonadism in men or hypogonadotropic hypogonadism was defined as decreased serum free testosterone due to a decrease in LH and FSH, whereas secondary hypogonadism was defined as decreased serum free testosterone level with elevated LH and FSH.

Hypothyroidism was characterized as TSH above the normal limit and decreased FT4. Subclinical hypothyroidism was defined as TSH above the normal limit and FT4 within normal limits.

Likewise, dyslipidemia was determined as the presence of at least one abnormality of any lipid profile components, including total cholesterol, LDL, triglyceride values above the normal limit, and HDL lower than normal value according to the lipid guideline (15).

### *Statistical Analysis*

The Statistical Package for the Social Sciences (SPSS) software (Version 25.0, SPSS Inc., Chicago, IL, USA) was applied for analysis. Data were analyzed using descriptive statistics (i.e., percentage, mean, standard deviation, and the like) and chi-square and Mann-Whitney tests. $P$ values <0.05 were considered statistically significant.

## Results

### *Demographic Findings*

The mean age of the participants was 43±9 years, including 43 (59.7%) men and 29 (40.3%) women. The

mean weight and height of the patients were 61.1±11.5 kg and 169±8 cm, respectively. The body mass index (BMI) of 35 (48.6%) patients was within the normal range while 24 (33.3%), 12 (16.7%), and 2 (2.8%) patients were underweight, overweight, and obese, respectively.

The average duration of HIV infection was 4±7 years, and more than half of the patients had been infected with the virus for more than 8 years.

Thirty-four patients (47.2%) had a history of tuberculosis and 63 (87.5%) received HAART. The most common type of treatment was zidovudine + lamivudine + efavirenz or Vonavir (Table 1). Table 2 presents the laboratory findings of HIV-positive patients.

**Table 1.** Frequency of Addiction, AIDS, History of Tuberculosis, and Type of HAART Treatment in HIV-positive Population

| Variable | | Number (%) |
|---|---|---|
| Addiction | Positive | 38 (52.8) |
| | Negative | 34 (47.3) |
| | Injection | 5 (6.9) |
| | Common syringe | 20 (27.8) |
| AIDS | Positive | 45 (62.5) |
| | Negative | 27 (37.5) |
| Tuberculosis | Positive | 34 (47.2) |
| | Negative | 38 (52.8) |
| HAART | Zidovudine + Lamivudine + Efavirenz | 22 (30.6) |
| | Vonavir | 22 (30.6) |
| | Zidovudine + Lamivudine | 8 (11.1) |
| | Combivir + Efavirenz | 8 (11.1) |
| | Zidovudine + Lamivudine + Nelfinavir | 2 (2.8) |
| | Abacavir + Lamivudine | 1 (1.4) |
| | No medication | 9 (12.5) |

*Note*. HAART: Highly active antiretroviral therapy; AIDS: Acquired immunodeficiency syndrome; HIV: Human immunodeficiency virus.

### *Diabetes*

Metabolic and endocrine disorders were statistically analyzed by age, gender, BMI, history of tuberculosis, duration of virus infection, CD4⁺ cell count, and HAART treatment (Tables 3-6). Among 72 HIV-positive patients, 41 cases had normal FPG and 2-hour PPG. However, 17/72 (23.6%) and 13/72 (18.1%) patients had prediabetes and diabetes based on FPG, respectively. The correlation analysis of glycemic complications including FPG, 2-h PPG, prediabetes, and diabetes by age, gender, BMI, history of tuberculosis, duration of virus infection, CD4⁺ cell count, and HAART treatment showed that patients with a history of addiction were more frequently diabetic or prediabetic. A significant correlation was observed between glycemic disorders and age ($P=0.025$), and the rate of glycemic disorders was higher at older ages.

### *Dyslipidemia*

Metabolic and endocrine disorders were statistically analyzed by age, gender, BMI, history of tuberculosis, duration of viral infection, CD4⁺ cell count, and HAART treatment. Among 72 HIV-positive patients, 44 tested normal for cholesterol, triglycerides, HDL, and LDL. Cholesterol, triglyceride, HDL, and LDL levels were at the borderline of dyslipidemia in 14/72 (19.4%) patients. In addition, 14/72 (19.4%) patients had high levels of cholesterol, triglycerides, HDL, and LDL. There was no significant difference regarding dyslipidemia and normal serum levels of cholesterol, triglyceride, HDL, and LDL by age, gender, BMI, history of addiction, history of tuberculosis, duration of virus infection, CD4⁺ count, and HAART treatment.

### *Thyroid Dysfunction*

The results of TSH, T3, and T4 tests were normal in 33 patients. One patient had overt hyperthyroidism, and 5/67 (7.5%), 6/67 (9%), and 22/67 (32.8%) patients had subclinical hyperthyroidism, subclinical hypothyroidism, and overt hypothyroidism, respectively. Statistical analysis

**Table 2.** Laboratory Findings in HIV-positive Population

| Variable | Mean ± SD | Min. | Max. | Variable | Mean ± SD | Min. | Max. |
|---|---|---|---|---|---|---|---|
| Duration of HIV infection (y) | 7 ± 4 | 1 | 15 | ACTH (pg/mL) | 23.41 ± 17.15 | 2.53 | 87.8 |
| Free T4 (ng/dL) | 6.98 ± 2.83 | 0.81 | 13.14 | FPG (mg/dL) | 109 ± 42 | 69 | 327 |
| Free T3 (pg/dL) | 2.33 ± 0.80 | 0.81 | 4.23 | 2-hour PG (mg/dL) | 143 ± 55 | 97 | 363 |
| TSH (mIU/L) | 4.93 ± 3.09 | 0.24 | 14.37 | Total cholesterol (mg/dL) | 165.1 ± 40 | 79 | 281 |
| FSH (mIU/L) | 17.21 ± 19.31 | 1.3 | 82.12 | HDL (mg/dL) | 44 ± 17 | 12 | 86 |
| LH (mIU/L) | 16.44 ± 14.31 | 1.9 | 74.65 | LDL (mg/dL) | 91.5 ± 32.8 | 43.1 | 193.8 |
| Free testosterone (pg/mL) | 8.27 ± 9.29 | 0.1 | 40.47 | TG (mg/dL) | 129 ± 89 | 43 | 642 |
| Cortisol 8 p.m. (μg/dL) | 11 ± 6.1 | 1.1 | 28.6 | CD4⁺ cell count (/μL) | 633 ± 413 | 76 | 1791 |

*Note*. HIV: Human immunodeficiency virus; TSH: Thyroid-stimulating hormone; FSH: Follicle-stimulating hormone; LH: Luteinizing hormone; ACTH: Adrenocorticotropic hormone; FPG: Fasting plasma glucose; 2-h PG: Two-hour plasma glucose; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; TG: Triglyceride; SD: Standard deviation; Min.: Minimum; Max.: Maximum.

**Table 3.** Metabolic and Endocrine Disorders by Age in HIV-Positive Patients

| Metabolic and Endocrine Conditions | | | Age | *P* value |
|---|---|---|---|---|
| | | | Mean ± SD | |
| Glycemic status | Normal | | 41.05 ± 8.24 | 0.025 |
| | Abnormal | Prediabetes | 44.53 ± 8.43 | |
| | | Diabetes | 45.85 ± 9.44 | |
| Lipid status | Normal | | 43.34 ± 9.37 | 0.513 |
| | Abnormal | Borderline | 41.29 ± 8.32 | |
| | | High | 42.29 ± 6.62 | |
| Adrenal axis | Normal | | 44.07 ± 6.50 | 0.522 |
| | Insufficiency | Primary | 37.63 ± 11.65 | |
| | | Secondary | 51.00 ± 0.00 | |
| Gonad axis | Normal | | 42.78 ± 8.20 | 0.081 |
| | Hypogonadism | Primary | 48.00 ± 0.00 | |
| | | Secondary | 47.00 ± 5.36 | |
| Thyroid axis | Normal | | 45.00 ± 7.71 | 0.088 |
| | Subclinical hypothyroidism | | 40.5 ± 9.07 | |
| | Overt hypothyroidism | | 40.32 ± 10.25 | |
| | Subclinical hyperthyroidism | | 42.2 ± 9.04 | |
| | Overt hyperthyroidism | | 42.0 ± 0.00 | |

*Note*. SD: Standard deviation; HIV: Human immunodeficiency virus.

**Table 4.** Metabolic and Endocrine Disorders by Gender in HIV-positive Patients

| Metabolic and Endocrine Conditions | | | Gender | | *P*-value |
|---|---|---|---|---|---|
| | | | Male | Female | |
| | | | No. (%) | No. (%) | |
| Glycemic status | Normal | | 23 (53.5) | 19 (65.6) | 0.310 |
| | Abnormal | Prediabetes | 12 (27.9) | 5 (17.2) | |
| | | Diabetes | 8 (18.6) | 5 (17.2) | |
| Lipid status | Normal | | 27 (62.8) | 17 (58.8) | 0.722 |
| | Abnormal | Borderline | 8 (18.6) | 6 (20.6) | |
| | | High | 8 (18.6) | 6 (20.6) | |
| Adrenal axis | Normal | | 23 (85.2) | 21 (80.8) | 0.728 |
| | Insufficiency | Primary | 3 (11.1) | 5 (19.2) | |
| | | Secondary | 1 (3.7) | 0 (0.0) | |
| Gonad axis | Normal | | 19 (70.4) | 18 (90.0) | 0.104 |
| | Hypogonadism | Primary | 0 (0.0) | 1 (5.0) | |
| | | Secondary | 8 (29.6) | 1 (5.0) | |
| Thyroid axis | Normal | | 20 (50.0) | 13 (48.1) | 0.882 |
| | Subclinical hypothyroidism | | 5 (12.5) | 1 (3.8) | |
| | Overt hypothyroidism | | 11 (27.5) | 11 (40.7) | |
| | Subclinical hyperthyroidism | | 3 (7.5) | 2 (7.4) | |
| | Overt hyperthyroidism | | 1 (2.5) | 0 (0.0) | |

*Note*. HIV: Human immunodeficiency virus.

demonstrated no significant correlation between thyroid disorders and age, gender, BMI, history of addiction, history of tuberculosis, duration of virus infection, $CD4^+$ count, and HAART treatment.

### *Hypogonadism*

Thirty-seven HIV-positive patients had a normal gonadal function. One patient had primary gonadal dysfunction while 9/47 (19.1%) had secondary gonadal dysfunction. Based on statistical analysis, no significant relationship was found between hypogonadism and age, gender, BMI, history of addiction, history of tuberculosis, duration of virus infection, $CD4^+$ count, and HAART treatment.

**Table 5.** Metabolic and Endocrine Disorders by CD4 Count in HIV-positive Patients

| Metabolic and Endocrine Conditions | | | CD4 Count | | *P* Value |
|---|---|---|---|---|---|
| | | | Low | Normal | |
| | | | N (%) | N (%) | |
| Glycemic status | Normal | | 19 (61.3) | 22 (55.0) | 0.595 |
| | Abnormal | Prediabetes | 7 (22.6) | 10 (25.0) | |
| | | Diabetes | 5 (16.1) | 8 (20.0) | |
| Lipid status | Normal | | 22 (71.0) | 21 (52.5) | 0.114 |
| | Abnormal | Borderline | 4 (12.9) | 10 (25.0) | |
| | | High | 5 (16.1) | 9 (22.5) | |
| Adrenal axis | Normal | | 21 (84.0) | 23 (82.1) | 1.000 |
| | Insufficiency | Primary | 4 (16.0) | 4 (14.3) | |
| | | Secondary | 0 (0.0) | 1 (3.6) | |
| Gonad axis | Normal | | 20 (87.0) | 17 (70.8) | 0.286 |
| | Hypogonadism | Primary | 1 (4.4) | 0 (0.0) | |
| | | Secondary | 2 (8.6) | 7 (29.1) | |
| Thyroid axis | Normal | | 13 (44.8) | 20 (54.0) | 0.457 |
| | Subclinical hypothyroidism | | 5 (17.3) | 1 (2.7) | |
| | Overt hypothyroidism | | 9 (31.0) | 12 (32.5) | |
| | Subclinical hyperthyroidism | | 2 (6.9) | 3 (8.1) | |
| | Overt hyperthyroidism | | 0 (0.0) | 1 (2.7) | |

*Note*. CD4: Cluster of differentiation 4; HIV: Human immunodeficiency virus.

**Table 6.** Metabolic and Endocrine Disorders by HAART in 72 HIV-positive Patients

| Metabolic and Endocrine Conditions | | | HAART | | *P* Value |
|---|---|---|---|---|---|
| | | | Negative | Positive | |
| | | | No. (%) | No. (%) | |
| Glycemic status | Normal | | 6 (66.7) | 36 (57.1) | 0.726 |
| | Abnormal | Prediabetes | 2 (22.2) | 15 (23.8) | |
| | | Diabetes | 1 (11.1) | 12 (19.1) | |
| Lipid status | Normal | | 7 (77.8) | 37 (58.7) | 0.467 |
| | Abnormal | Borderline | 2 (22.2) | 12 (19.1) | |
| | | High | 0 (0.0) | 14 (22.2) | |
| Adrenal axis | Normal | | 4 (80.0) | 40 (83.3) | 1.000 |
| | insufficiency | Primary | 1 (20.0) | 7 (14.6) | |
| | | Secondary | 0 (0.0) | 1 (2.1) | |
| Gonad axis | Normal | | 2 (66.7) | 35 (79.5) | 0.521 |
| | Hypogonadism | Primary | 0 (0.0) | 1 (2.3) | |
| | | Secondary | 1 (33.3) | 8 (18.2) | |
| Thyroid axis | Normal | | 3 (33.3) | 30 (51.7) | 0.536 |
| | Subclinical hypothyroidism | | 2 (22.2) | 4 (6.8) | |
| | Overt hypothyroidism | | 4 (45.5) | 18 (31.1) | |
| | Subclinical hyperthyroidism | | 0 (0.0) | 5 (8.7) | |
| | Overt hyperthyroidism | | 0 (0.0) | 1 (1.7) | |

*Note*. HAART: Highly active antiretroviral therapy; HIV: Human immunodeficiency virus.

### *Adrenal Insufficiency*

Among 53 patients evaluated for adrenal insufficiency, 8 (15.1%) cases had primary adrenal insufficiency whereas one had secondary adrenal insufficiency. The results revealed no significant relationship between adrenal insufficiency in HIV-positive patients and age, gender, BMI, history of addiction, history of tuberculosis, duration of virus infection, $CD4^+$ count, and HAART treatment.

## Discussion

In the present study, the mean age of the patients was 43± 9 years. The reported mean age in several studies (16-18) was similar to ours. Studies have shown that people living with HIV more likely have metabolic disorders regardless of age, gender, and BMI. Since these disorders constitute a significant risk factor for cardiovascular complications, regular blood glucose monitoring and lipid profile measurements are warranted in these patients (19). According to the results of the present study, representing a significant relationship between diabetes and a history of addiction in HIV-positive patients, more attention should be paid to this subgroup of patients. Bonfanti et al (20) and Alencastro et al (19) demonstrated the prevalence of metabolic syndrome as 20.8% and 24.7%, respectively. In a study by Hernandez-Romieu et al, the prevalence of diabetes in HIV-positive adults was 10.3% (21). In the current study, the frequency of diabetes was 18.1%, whereas that of dyslipidemia was 19.4%, which was lower compared to previous studies. The prevalence of thyroid dysfunction in HIV-infected individuals was also estimated in the current study. The frequency of hypothyroidism was extremely higher than other thyroid disorders in the patients. Given the similarity of hypothyroidism symptoms with those of AIDS (12, 22-24), it seems that routine thyroid function tests are necessary for the diagnosis and treatment of thyroid disorders in HIV-positive patients (12). The results of the present study regarding hypothyroidism are in line with those of Thongam et al, Bongiovanni et al, and Dev et al (22-24) regarding the function of gonads in HIV-positive patients; it was shown that the prevalence of gonadal hypothyroidism was lower than 20%, which contradicts the results of Tripathy et al with a prevalence of over 85% (13). However, our findings are in agreement with those of Rietschel et al (25). Overall, these results indicated a high prevalence of gonadal hypothyroidism in HIV-positive patients despite using HAART treatment.

Although adrenal insufficiency is considered the most common endocrine disorder in HIV-positive patients, its clinical evidence has seldom been reported in the literature (9). Conforming to the results of other studies, a high prevalence of endocrine disorder was also found in HIV-positive patients.

The limitations of this study were attempts for convincing HIV-positive patients to participate in the study and difficulty drawing blood samples in patients with injectable drug abuse. Furthermore, definitive stimulation tests were not performed for the adrenal axis. These limitations could have influenced the results of our study, and thus the results should be generalized with caution.

## Conclusion

In general, our findings showed that the frequency of metabolic and endocrine disorders was high in HIV-positive patients regardless of age, gender, or BMI. Future studies, including larger populations of HIV-positive patients, focusing on a single endocrine disorder while comparing the results to healthy individuals, would definitely help evaluate the prevalence of metabolic and endocrine disorders in HIV-positive patients.

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### Authors' Contributions

MK designed the study and MN wrote the manuscript. PD and MG analyzed and interpreted the data. GZ performed the technical revision of the manuscript. All authors read and approved the final manuscript.

### Availability of Data and Materials

The applied and/or analyzed datasets during the current study are available from the corresponding author upon reasonable request.

### Conflict of Interest Disclosures

The authors declare that they have no competing interests.

### Ethical Statement

The study was approved by the Institutional Review Board of Hormozgan University of Medical Sciences, and it complies with the statements of the Declaration of Helsinki (with the ethics code of IR.HUMS.REC.1399.404). Informed consent was obtained from all subjects.

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