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The occurrence of Hyperglycemia among HIV positive: A Case of People Living with HIV Attending Nyeri Referral Hospital

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ABSTRACT

Background: The hallmark of HIV infection is the progressive loss of immune cells called the CD4 cells weakening the immune system and leaving individuals vulnerable to various opportunistic infections (OIs) and other illnesses, ranging from pneumonia to cancers. Diabetes/hyperglycemia complication on set among the HIV infected has been suggested by several authors although very a minimal interest has been paid on this subject. This study looked at the correlation between hyperglycemia (a risk factor of DM) and HIV infection among HIV-infected individuals in Nyeri County Hospital-Kenya. Methods: This was a case-control study involving 193 individuals who were grouped into two groups of 97 HIV-positive HIV-Negative individuals (also referred to as study control group) based on negative HIV results and fasting blood glucose level 4.4 ± 2.2mmol/L. and 96 participants who were HIV positive. Results: A total of 193 individuals were enrolled, grouped into 97 subjects of HIV-negative individuals (control group) and 96 participants who were HIV-positive. In the study 13.54% of HIV-positive were hyperglycemic compared to 6.18% HIV- ve individuals (mean glucose level 7.6 ± 5.1 and 4.4 ± 1.1mmol/L, respectively (P>0.05) r=0.023). Conclusion: The study identified Hyperglycemic as a likely complication in HIV-infected individuals with a need to study the effect of individual diabetes mellitus risk factors in HIV-infected individuals.

Key Words: Blood glucose, Diabetes Mellitus, HIV, Hyper glycemia.

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1. INTRODUCTION

This paper presents an evaluation of the existence of any relationship between HIV infection and hyperglycemia. It also presents the background and purpose of the study, study methodology as well as findings, conclusions, and recommendations.

1.1 Background and Aim of the Study

Human immunodeficiency virus infection occurs alongside other infections including diabetes. Diabetes and HIV have the same prognosis and the two diseases have similar symptoms which include weakening of immunity, reduction of body weight (body fat waste) and hyperinsulinemia with insulin resistance, glucose metabolism abnormalities, abnormal liver function with elevated activities of alanine aminotransferases, neurovasculopathies with non-healing wounds, dementia, candidiasis, chest infections among others [1]

AIDS and diabetes are both independent diseases in that the occurrence mechanisms are different. AIDS is caused by the human immunodeficiency virus (retrovirus) that causes the destruction of immune cells in the body leading to serious immune suppression and hence an onset of many other illnesses referred to as opportunistic infections (OIs). Diabetes on the other hand is a medical complication as a result of glucose metabolism abnormality with a diverse causative agent and it can also be one of the complications of advanced HIV infection [2]

Uncontrolled HIV replication have been suggested to cause diabetes mellitus in some patients [3]; Similarly, the incidence of diabetes mellitus among HIV infected individuals was observed to be high compared to the incidence in individuals not HIV infected [4]. In this case clients with advanced HIV infection had high blood sugar which resolved after viral replication was suppressed with antiretroviral therapy (ART) [4].

DM has been classified into three categories, this depend on the circumstances present at the time of diagnosis i.e. the pathogenesis. Type 1 diabetes (β-cell destruction, usually leading to absolute insulin deficiency), is further sub-divided into two subtypes as immune mediated diabetes and idiopathic diabetes.

Immune-mediated diabetes results from a cellular-mediated autoimmune destruction of the β-cells of the pancreas. Markers of the immune destruction of the β-cell include islet cell autoantibodies, autoantibodies to insulin, autoantibodies to GAD (GAD65) and autoantibodies to the tyrosine phosphatases IA-2 and IA-2β. One and usually more of these autoantibodies are present in 85–90% of individuals when fasting hyperglycemia is initially detected. In this form of diabetes, the rate of β-cell destruction is quite variable, being rapid in some individuals (mainly infants and children) and slow in others (mainly adults). Some patients, particularly children and adolescents, may present with ketoacidosis as the first manifestation of the disease. Others have modest fasting hyperglycemia that can rapidly change to severe hyperglycemia and/or ketoacidosis in the presence of infection or other stress. Still others, particularly adults, may retain residual β-cell function sufficient to prevent ketoacidosis for many years; such individuals eventually become dependent on insulin for survival and are at risk for ketoacidosis [5].

In idiopathic diabetes, type 1 diabetes have no known etiologies. Some of these patients have permanent insulinogenic and are prone to ketoacidosis, but have no evidence of autoimmunity. Although only a minority of patients with type 1 diabetes fall into this category, Individuals with this form of diabetes suffer from episodic ketoacidosis and exhibit varying degrees of insulin deficiency between episodes. This form of diabetes is strongly inherited, lacks immunological evidence for β-cell autoimmunity [5].

Type 2 diabetes, range from predominantly insulin resistance with relative insulin deficiency to predominantly an insulin secretory defect with insulin resistance. This form of diabetes which account for 90–95% of those diabetics encompasses individuals who have insulin resistance and usually have relative (rather than absolute) insulin deficiency at least initially and often throughout their lifetime, these individuals do not need insulin treatment to survive. There are probably many different causes of this form of diabetes. Although the specific etiologies are not known, autoimmune destruction of β-cells does not occur [6].

Other specific types of diabetes include; Genetic defects of the β-cell diabetes that is associated with monogenetic defects in β-cell function, genetic defects in insulin action diabetes that result from genetically determined abnormalities of insulin action, diseases of the exocrine pancreas diabetes which involves any process that diffusely injures the pancreas can cause diabetes. Acquired processes include pancreatitis, trauma, infection, pancreatectomy and pancreatic carcinoma, Endocrinopathies diabetes-Several hormones e.g., growth hormone, cortisol, glucagon and epinephrine, antagonize insulin action, drug or chemical-induced diabetes. Many drugs and toxins can impair insulin secretion they include Vacor (a rat poison) and intravenous pentamidine which can permanently destroy pancreatic β-cells, Infections diabetes is diabetes resulting from infection by certain viruses have been associated with β-cell destruction e.g. Congenital rubella, coxsackievirus B, cytomegalovirus, adenovirus and mumps have been implicated in inducing certain cases of the diabetes [7].

The long-term consequences of uncontrolled diabetes include neuropathy, retinopathy and heart disease. It is also associated with vascular disease and is one of the major reasons for amputations [10]. Insulin is a hormone that enables the body cells to absorb glucose from the blood for use as fuel, for conversion to other needed molecules, or for storage. Insulin is also the principal control signal for conversion of glucose to glycogen for internal storage in liver and muscle cells. The principal biochemical

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function of glucose is to provide energy for life processes. Glucose oxidation by the glycolytic and tricarboxylic acid pathways is the primary source of energy for the biosynthesis of ATP [9].

Independent risk factors in diabetes are old age, larger BMI category, liver damage and diseases and viral infections. In type 1 diabetes the pancreatic cells that make the insulin are destroyed causing severe lack of insulin (hypoinsulinemia). It is not clear what causes type 1 diabetes which account for about 5-10 % of diagnosed diabetes and develops most often in children and young adults, but the disorder can appear at any age, symptoms usually develop over a short period although beta cells destruction begin months, even years earlier. Symptoms appear when at least 80% of the cells are affected [10].

The destruction of beta cells is thought to be the result of the body attacking and destroying its own cells in the pancreas, also known as autoimmune reaction. It is not clear why this happens, but a number of explanations and possibilities could trigger this reaction. These may include infection with a specific virus or bacteria (e.g. Cytomegalovirus whose induction of DM in mice has proven to be an excellent experimental model for the pathogenesis of viral diseases). Other include exposure to food-borne chemical toxins, disorder in the immune systems caused by virus infection whereby immune system cannot kill infectious agents or autoimmune systems response, as seen in type 1 diabetes mellitus, where by lymphocyte infiltration of the islet cells of the pancreas occur with concomitant beta cells destruction and the appearance of antibodies to islet cells components before the manifestation of diabetes [11].

Other rare causes of diabetes (type 1 and 2) can include any other illness or disease that damages the pancreas affecting its ability to produce insulin, e.g. pancreatitis, alteration of the hormone or cytokine levels and interactions of the HIV's protein VPr with proteins responsible for glucose transport within cells [10]. Liver cirrhosis can cause insulin resistance and glucose intolerance [13] a sign of developing diabetes and liver cirrhosis is common HIV infected individuals [12]

Depression a common problem in HIV infected persons may trigger the body turning on itself (autoimmune response), causing pancreatitis as in case of type 1 diabetes. More often HIV is accompanied by depression and patients with HIV infection, clinical depression is the most frequently observed psychiatric disorder affecting as many as 1 in 3 HIV infected people [12]. Stress in HIV infected patients elicit a complex hormonal and immunological response that may alter various biochemical pathways, including glucose metabolism.

Clinical signs for diabetes include polyuria, polydipsia and blurred vision while thirst develops because of osmotic effects. Sufficiently high glucose in the blood is excreted by the kidneys, but this requires water to carry it and causes increased fluid loss, which must be replaced. A rarer but equally severe presentation is hyperosmolar non-ketonic state, which is more common in type 2 diabetes. Diabetes mellitus is also characterized by recurrent or persistent hyperglycemia and is diagnosed by demonstrating; Fasting plasma glucose level at or above 7.0mmol/l. Plasma glucose at or above 11.1 mmol/l two hours after glucose load in a glucose tolerance test. This is as well as random plasma glucose at or above 11.1 mmol/l [15]. In this study the hyperglycemia was diagnosis was based on random plasma glucose level estimation only.

A relationship between HIV infection and diabetes onset has been suggested by several other authors, for example, a study indicated a prevalence of diabetes of 2-7% among HIV infected individuals receiving protease inhibitors [16]. The incidence of diabetes in HIV patients has been estimated to range from 1% to 10% [16], another study showed an increased incidence of insulin resistance among HIV positive patients and hence a concern that this population in general and individual with evidence of fat redistribution common in HIV infected, in particular may be at increased risk of development of diabetes [17].

It has been observed that sometimes type 1 diabetes occurs when islet of Langerhans cells of the pancreas are destroyed probably as consequence of genetic susceptibility caused by the onset of autoimmune destruction triggered by environmental factors such as viral infection e.g. HI-virus [18], this's further compounded by metabolic complications and disorders common with diabetics

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which include hyperlipidemia, insulin resistance and fat redistribution, which are also common in HIV infected patients [16]. Minimal information exists on whether the occurrence of Diabetes Mellitus is associated with HIV. It is therefore important to assess the difference in the diabetes prognosis between HIV infected and non-HIV infected individuals. The objective of this study was therefore to evaluate the existence of any relationship between HIV infection and hyperglycemia.

2.0 METHODOLOGY

2.1 Research Site

A cross-section case control study was conducted at Nyeri Referral Hospital, Nyeri County, Kenya with a bed capacity of 320 of which 7% of these beds are occupied by HIV positive patients. Ethical approval was sought and granted by the Nyeri Provincial General Hospital. The participants were reassured of confidentiality in the handling of information and procedures involved in this study.

2.2 Methods and research design

2.2.1 Study participants

The HIV infected individuals who have lived in Nyeri district for 6 months prior to the study, not on ARVs and with no history of DM previous to infection and not obese were included. For the healthy group, (Control group) in addition to the above criteria, the subjects were excluded from the study if they had regularly consumed drugs with potential nephrotoxicity (such as analgesics/anti-inflammatory agents and aminoglycosides) and also those that could affect the blood sugar level. At the end only 193 subjects who were systematic selected (the 10th subject) were involved in this study. They were categorized into two groups i.e. healthy (control group) and HIV positive group consisting of 97, 96 subjects, respectively.

The sample size was calculated using the formulae given by Fisher *et al.* as quoted in Mugenda and Mugenda [19], method this derived a sample of 91 per group (case and control). This was adjusted the number to 100 per group in order to complement for any error due to chance variations.

2.2.2 Data Collection and Analysis

Four ml of venous blood sample was collected using aseptic technique where, 2 ml was put in EDTA vacutainer for CD4 count and the remaining sample, about 2ml, was put in another EDTA vacutainer and was used for blood sugar analysis and then spun to obtain about 1ml of plasma. The plasma was for viral load analysis and it was stored at -20oC. The containers were labeled with the study number of the participant and the date of birth was also marked to tally with all the required demographic information. This was matched with the demographic information on the questionnaire form to avoid any risk of mix-ups or incorrect identification of samples [23] [24].

Blood sugar analysis was based on enzymatic method and results read spectrometric ally [23]. Determine HIV1/2 test which is a rapid diagnostic test was used to test HIV

Statistical analysis was carried out using SPSS program version 11.0. Pearson's correlation coefficients (r) were calculated to determine relationship between means of the studied markers. Results were considered statistically significant at $p < 0.05$. The reference ranges for the various markers were calculated using the normal healthy individuals (reference group).

3.0 RESULTS AND DISCUSSION

Out of the targeted 100 per group, those who responded were 96 in the case group and 97 in the control group.

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3.1 Demographics characteristics

The study noted that majority of the respondents, 41.7% for case group and 46.4% for control group were aged between 31-40 years (Table 1). However, there was a significant difference in the ages of those who were either HIV positive or HIV negative where those below 40 years were more.

3.2 The prevalence of hyperglycemia-diabetes in control and in HIV positive participants

There was no difference noted between male and female for both groups and for both glucose levels and CD4 count (P>0.005).

Table 1: Demographics characteristics among people living with HIV

		Case group		Control group		
		n (96)	%	n (97)	%	P value
Age (years)	<30	36	37.5	26	26.8	P<0.05
	31-40	40	41.7	45	46.4	
	41-50	16	16.7	16	16.5	
	> 50	4	4.2	10	10.3	
Gender	Male	18	18.8	42	43.3	P>0.05
	Female	78	81.3	55	56.7	

Table 2: The mean glucose levels of the Case group and Control Group

			Mean		P value
		Reference point	Case group	Control group	
Blood glucose levels	Male	2.13-6.5	7.8±1.4	4.3±1.3	P<0.005
	Female	2.54-6.5	7.6±5.3	4.5±1.2	

Table 3: The prevalence of hyperglycemia-diabetes in control and in HIV positive participants

		Case	Control	Total	OR	P value
Glucose status	Normal glucose	13	90	**103**	2.014	0.000
	High glucose	83	7	**90**		
	Total	**96**	**97**	**193**		

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3.3 Strength and Limitations

There are few studies and literature on the status of diabetes in HIV infected individuals or even on the relationship between HIV infection and diabetes. This relationship has been proposed, suggesting that elevated blood sugar levels could be a complication of untreated HIV infection [4]. This study will go a long way in adding up to the literature on this subject that deals with two major diseases that also affect a significant number of people in Kenya.

3.4 Discussion

The mean blood glucose concentration was higher for the case group than in the control in this study, various studies have shown active HIV infection can affect BSL [19] [3], another study found that uncontrolled HIV replication have been suggested to cause diabetes mellitus in some patients [1]. Another study noted the incidences of diabetes mellitus among HIV-infected individuals to be higher compared to the incidence in individuals not HIV infected [4].

4. CONCLUSION

The study observed that the mean blood glucose concentration in HIV positive was more than double that of the control group 7.7±2.3 and 4.4±1.1, respectively.

5. RECOMMENDATION

A study that will look at every individual diabetes risk factor and their contribution to abnormality in glucose metabolism in HIV infected persons is recommended

REFERENCES

[1] . Kalra, S., & Agrawal, N. (2013). Diabetes and HIV: current understanding and future perspectives. Current diabetes reports, 13(3), 419-427.

[2] . Reid, M. J. A., Tsima, B. M., & Kirk, B. (2012). HIV and diabetes in Africa. Afr. J. Diabetes Med, 20(2).

[3] . Koeppe, J. and Kosmiski, L. (2006). Clinical Infectious Diseases, Apparent resolution of type 2 diabetes mellitus after initiation of potent antiretroviral therapy in man from African with HIV infection. AIDS. Map News Clinical and Infection Diseases, Publication of University of Chicago press, 42: e79-e81.

[4] . Gadd, C. (2000). Is diabetes a complication of HIV infection? Map News, page 1.

[5] . Genuth, S., Alberti, K., Bennett, P., Buse, J., Defronzo, R., Zimmet, P., (2003). Expert committee on diagnosis and classification of diabetes mellitus- follow up report. Diabetes Care 26: 3169-3173

[6] . Schranz DB, Lernmark A. Immunology in diabetes: an update. Diabetes Metab Rev. 1998; 14:3–29.

[7] . Kizmiller, J., Kwowler, W., Lernmark, A., (2009). The role of AIC assay in diagnosis of diabetes. Diabetes Care 32: 1327-1334.

[8] . Boussageon, N., Cadwell, B., Gregg, W., Benjamin, S. Engelgam, M (2006). Change in the incidence of diabetes in US adulties. American Journal of Medicine 30: 371-77.

[9] . Edelmon, D., Olsen, M., Dudley, T. and Harris, A. (2004). Ultilization of Haemoglobin A1C in predicting diabetes risks. Journal of General Internal Medicine, 19: 1175-80.

[10] .Alemzadel, R. and Wyatta, D. (2007). Diabetes Mellitus. Nelson Textbook of Pediatrics 18th edition 590: 1074-1077.

[11] .Tajima, M., Kawanabe, M.Y., Taniyama, M., Yamato, H., Maede, O. and Zentraibil, Y. (1999).Possible causes of Diabetes in cattle infected with bovine viral diarrhea virus. Zentralbl Veterinamed, 46 (3): 207-215.

[12] .Jordan, P.A. and Gibbins J.M (2006). Extracellular disulfide exchange and the regulation of cellular function. Antioxid Redox Signal, 8: 312-324.

DOI: 10.31695/IJASRE.2023.9.2.5

[13] .Selberg O, Burchert W., Hoff J., Meyer G.J., Hundeshagen H., Randoch E., Backs H.J. and Muller M. (1993). Insulin resistance in liver cirrhosis, positron-emission tomography scan analysis of skeletal muscle glucose metabolism. Journal of Clinical Investigation, 91(5) 1897-1902.

[14] .Rabkin, J. and Robert, H. R. (1999). Facts about HIV\AIDS and depressive disorders in HIV, American journal of psychiatry, 38. (3): 146-154.

[15] .UNAIDS\WHO (2006) Assessment of the epidemiological situation HIV/AIDS report: 1

[16] .Aberg, J. (2002). Insulin resistance Glucose intolerance; what does it mean? Retroviruses and opportunistic infection. 9th conference Seattle Washington, 24th Feb. to 28th Feb. 2002.

[17] .Currier, J.S., Boyd, F., Kawabata, H., Dezii, C., Burtcell, B. and Hodders, H. (2002. Diabetes in HIV Infected individuals 9th conference Seattle Washington, 24th Feb to 28th feb 2002 abstract no 677-T.

[18] .Mugenda, O.M., & Mugenda, A.G (2003). Research Methods; Quantitative and Qualitative Approach. Nairobi.

[19] .Perez, A. S., Seminario, L., Tamargo, J., Martinez, S., Campa, A., Huffman, F., & Baum, M. (2019). Lowered Fasting Blood Glucose (FBG) in a Prediabetic Individual with HIV Despite Struggle with Weight Control Management-CASE STUDY (FS17-06-19).

[20] .Standard operation guideline (2005), Phlebotomy guidelines, Nyeri provincial Hospital

[21] .WHO Guideline on Drawing Blood (2006). Best practice in phlebotomy- blood glucose test NBK138644

DOI: 10.31695/IJASRE.2023.9.2.5