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Seroprevalence of Hyperglycaemia in HIV Positive Patients Visiting the Cape Coast Teaching Hospital in Ghana

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Abstract

Background: Hyperglycaemia is a metabolic syndrome and common endocrine disease where there is increased blood glucose level. It can result in long-term damage and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels and finally cause death. This study was conducted to determine the prevalence of hyperglycaemia in HIV subjects visiting the Cape Coast Teaching Hospital (CCTH) in Cape Coast and its relationship with Highly Active Antiretroviral Therapy (HAART). **Methods**: A cross sectional study was carried out and blood samples of 120 HIV positive subjects of age groups ranging from 2 to 74 years were collected for screening and confirmation after an informed consent was obtained from them. The blood glucose level was then tested using OneTouch glucometer and test strips. The results were analysed using chi square goodness-of-fit and cross tabulation. **Results**: A total of 9 patients out of the 120 HIV subjects had an increased glucose level, giving a prevalence rate of 7.5%. They were within the ages of 20-60 years and were significantly lower compared to those without hyperglycaemia ($p<0.05$), those married ($p=0.001$) and those divorced ($p=0.001$). There was an inverse relationship between the period of living with HIV and the high glycaemia status ($r= -0.949$, $p=0.017$). There was also an inverse relationship between the use of HAART and high glycaemia status ($r=-0.071$, $p=0.0028$). There was a significant number of participants, who were experiencing increased thirst ($p=0.003$). Also a significant number of participants experienced increased hunger ($p=0.010$). **Conclusion**: The study revealed that there was hyperglycaemia among the study population. This may be reduced during therapy and changes in their lifestyle. Regular monitoring of glucose levels in HIV infected patients and counselling on lifestyle changes are recommended.

Keywords: Seroprevalence, hyperglycaemia, HIV

1. Introduction

Hyperglycaemia is a condition in which there is excess amount of sugar or glucose in the blood and may occur as result of imbalance glucose homeostasis in the body. This may eventually lead to diabetes mellitus condition, an endocrine disease affecting all age groups of which the underlining cause has not been well elucidated (Ford *et al*., 2004). However, sedentary lifestyle coupled with different forms of eating habits might have partly contributed to the imbalance blood sugar levels in the body (Fitch *et al*., 2006; Obirikorang *et al*., 2016b). With the normal blood glucose level in the fasting state between 3.9- 5.8mmol/L blood, individuals with a consistent range of 6.1- 6.9 mmol/l level of sugar are considered hyperglycaemic, while those with levels above 6.9mmol/l are generally known to have diabetes (W.H.O, 1999). Excess glucose in the blood stream is normally regulated by insulin produced by the pancreas into the cells to give them energy (Kalra *et al*., 2011). When the pancreas fails to produce enough insulin due to infection or damage resulting in insulin not being used in the right proportion by the body, hyperglycaemia occurs. There are over 200 million diabetic individuals in the world (Smyth and Heron, 2006) and this creates a need to understand the etiology of the disease and the influencing factors that may contribute to its onset especially in HIV infected patients.

HIV patients are known to present with metabolic syndrome and altered glucose metabolism as the CD4 counts declined and viral load increases (Fichtenbaum *et al*., 2005; Norris and Dreher, 2004). Non adherence to antiretroviral drug therapy may result in chronic complications of HIV with non-communicable diseases such as hyperglycaemia or diabetes (Mulligan *et al*., 1993). The presence of these conditions is influenced by many risk factors that include age, sex, higher body mass index, low socioeconomic standard of living and certain ethnic background or culture (Fichtenbaum *et al*., 2005; Norris and Dreher, 2004). Furthermore, the condition becomes more complicated with the development of impaired glucose tolerance, hyperlipidemia, insulin resistance and abnormal redistribution of body fat that has emerged as secondary problems following weight loss (Gkrania-Klotsas and Klotsas, 2007; Mondy *et al.,* 2007; Strawford and Hellerstein, 2001). Insulin resistance is much

implicated in the pathogenesis of diabetes in HIV-infected patients. This is associated with the destruction of beta cells of the pancreas during antiretroviral treatment (Abebe *et al*., 2014; Kalra *et al*., 2011). Eventually, there is an increase in nonoxidative glucose disposal and subsequently high level of glucose from the liver with no changes in their cycling (Heyligenberg *et al*., 1993). This suggests that HIV infection also affects the general metabolic homeostasis including glucose level of the body. Recently, it has been noted that autoimmune diabetes also occur in some HIV infected patients where antibodies are developed to glutamic acid decarboxylase during HAART and CD4 counts steadily recovered (Kalra *et al*., 2011). It therefore suggests that HIV infection gradually predisposed patients to metabolic syndromes which become complicated in absence of treatment with antiretroviral drugs.

In Ghana, most of the studies on metabolic syndromes including dyslipidemia and hyperglycaemia were carried out in diabetes mellitus patients in Accra, Kumasi as well as Tamale in the Northern part of the country (Amartey *et al*., 2015; Amoah *et al.,* 2002a; Amoah *et al*., 2002b; Danquah *et al*., 2012). There has also been a study on the development of metabolic syndrome in HIV infected patients mainly on HAART (Obirikorang *et al*., 2016a). We therefore, decided to determine the level of hyperglycaemia in individuals diagnosed with HIV infection and have been on ART for various years in the Cape Coast Metropolis.

2. Materials and Methods

2.1 Study site/area

This study was conducted at the Cape Coast Teaching Hospital in Ghana. Cape Coast is located within latitudes 5˚.07' to 5˚.20' North of the equator and between longitudes 1˚.11' to 1˚.41' West of the Greenwich meridian. It covers a total land area of approximately 122 square kilometres and a settlement population of 169,894 people according to the Population and Housing census (GSS, 2013). The city is bordered by the Gulf of Guinea to the South, Komenda-Edina-Eguafo-Abirim districts to the West, Abura-Asebu-Kwamankese districts to the East and by Twifo Hemang-Lower Denkyira district to the North. It is one of the most historical cities in Ghana and was the center of British colonial administration and the capital of Gold Coast by 1700 until 1877 when the capital was moved to Accra.

Most of the inhabitants are traders, teachers, fishermen and farmers. A number of them are unemployed and about half of the teenagers are attending school. The educational standard in the area is very high due to the presence of some of the best second cycle institutions and a University. These have made the city very busy during the weekends and on any organised events. There are also a lot of restaurants and night clubs for fast food, drinks and entertainment purposes. The economic activities of the metropolis are enhanced by many shops and vibrant market places for trading purposes.

2.2 Study Design

The study involved quantitative research methods using cross sectional research design. Blood samples were collected from 120 HIV suspected patients who visited the Central Regional Hospital's HIV/ART unit. The samples were screened and confirmed as positive for HIV. Questionnaires were administered to patients for demographic data that focused on age, sex, occupation, marital status, HIV history, family history on diabetes, lifestyle, some symptoms that indicated the presence of hyperglycemia, and other information that was relevant to the patients.

2.3 Ethical Clearance

Ethical clearance was sought from the University of Cape Coast Institutional Review Board and the Medical Director at the Cape Coast Teaching Hospital. More importantly, informed consent was obtained from each patient before their blood samples were taken and used to run the test. In situations where the patients were minors, parental consent was sought.

2.4 Collection of sample and laboratory tests

Two millilitres (2 ml) of blood was taken from patients into Ethylene Diamine Tetraaceticacid (EDTA) anticoagulant tubes and centrifuged after which the plasma were aspirated into new EDTA tubes and stored at a temperature of 4˚C. The stored plasma was later tested for the presence of HIV using Alere DetermineTM HIV-1/2 as described in (Baah, 2014). Briefly, the biological principle behind this procedure was that Alere DetermineTM HIV-1/2 was an immunochromatographic test that had a conjugate or sample pad through which the plasma migrated. The plasma reconstituted and mixed with the selenium colloid-antigen conjugate. The mixture formed continued to migrate through the solid phase to the antigen immobilized recombinant antigens and synthetic peptides at the patient window site. Antibodies to HIV-1 and/or HIV-2 present in the sample bound

to the antigen-selenium colloid and to the antigen forming a red line at the patient window site. However, the absence of antibodies to HIV-1 and/or HIV-2 allowed the antigen-selenium colloid moved past the patient window site, and no red line was formed.

Confirmation of the HIV status was carried out using INNO-LIA HIV I/II (Innogenetics, Gent, Belgium). Briefly, recombinant antigenic proteins and synthetic peptides from HIV-1, HIV-2, and HIV-1 group O were coated as discrete lines on a nylon strip with plastic backing. Plasma samples were incubated in a test trough together with the multiple antigen-coated test strip. HIV antibodies in the samples, bound to the individual HIV antigen lines on the strip. Afterwards, a goat anti-human IgG labelled with alkaline phosphatase was added to bind to any HIV antigen/antibody complex previously formed and incubation with the enzyme substrate (BCIP/NBT) produced a dark brown colour in proportion to the amount of HIV antibody present in the samples. Colour development was stopped with sulphuric acid. Samples containing no HIV-specific antibodies, the labelled antihuman antibody did not be bound to antigen/antibody complex so that only a low standard background colour develops.

In performing the blood glucose test, the forearm was selected at the puncture site and wiped with alcohol. A test strip was removed and inserted into the test port. The Glucometer turns on automatically and the apply sample symbol was displayed. A drop of the plasma sample was applied to the narrow channel in the top edge of the test strip and held until the confirmation window was full. The result was read on the display in mmol/L and recorded. Depending on whether the patient had eaten or was fasting, the result was recorded as random blood glucose (RBG) level or fasting blood glucose (FBG) level. These were compared to the normal ranges for either RBG (3.9mmol/L- 8.9mmol/L) or FBG (3.9mmol/L- 5.8mmol/L)

2.5 Statistical Analysis

The data from this study were subjected to statistical analysis using SPSS (version 21) software. The differences among subject groups (age, occupation, gender, year of HIV diagnosis, HAART duration, family history of diabetes, lifestyle and diabetes symptoms) were examined using Chi-Square goodness-of-fit method and cross tabulations. There were also Binomial test carried on Binomial Random Variables. Spearman correlation was also used to determine the relationship between hyperglycaemia and period of living with HIV/AIDS, and treatment.

3. Results

3.1 Demographic Data

A total of one hundred and twenty (120) HIV-1 positive patients were selected for blood glucose level test. These were made up of 50 males and 70 females. The frequency of those that belong to the age group 40-49 years was the highest, 30.90% (Figure 1). This was followed by 30-39 year groups 23.60%, then 50-59 years group, 22.80%. The number of participants in the three age groups were similar but were significantly higher than the other age groups ($p<0.05$). The frequency of other age groups was less than 10% with 70 years groups being the least. In Figure 2, 44 (37.00%) patients were single, 48 (39.50%) were married, 18 (15.10%) were divorced and 10 (8.40%) had lost their partners. There were significant lower number of those who had lost their partners ($p<0.001$) than married partners but similar to unmarried as well as divorced participants ($p>0.05$). The occupation of the studied participants also varied with 8 (7.00%) patients being students and 7 (6.10%) office workers (Figure 3). Those who were self-employed were 85 (73.90%) and 15 (13.00%) patients were unemployed. There were significant number of self employed participants than any other occupational groups ($p<0.05$).

3.2 Blood Glucose Level Test

For the 120 HIV positive patients, 44 (36.67%) were diagnosed with HIV-1 within 2 years out of which 5 (4.17%) had the condition of hyperglycaemia (Table 1). Thirty-eight (31.67%) were living with HIV-1 for about 5 years and 2 (1.657%) were detected to be having the condition of hyperglycaemia. Those who were living with HIV-1 for about 8 years were 25 (20.83%) and also 2 (1.67%) were hyperglycaemic. About 13 (10.83%) patients were living with HIV for more than 9 years but were not having the condition of hyperglycaemia. There was an inverse relationship between the period of living with HIV and the high glycaemia status ($r= -0.949$, $p=0.017$).

In Table 2, 113 (94.17%) patients were on the Highly Active Anti-Retroviral Therapy (HAART) out of which 105 (87.5%) had a normal blood glucose level and 8 (6.67%) had an increased blood glucose level. It was noticed that hyperglycaemia decreases with the number of years one has been on HAART. Three (2.5%) patients within 0 -1 year on HAART were having high level of sugar in their blood, 2 (1.67%) patients each within the

range of 2 -3 and 4 – 5 years on HAART were hyperglycaemic, the number reduced to 1 (0.83%) in the 6 – 7 years on HAART usage and no patient was hyperglycaemic above 8 years on HAART. There was also an inverse relationship between the use of HAART and high glycaemia status (r=-0.071, p=0.0028). However, the trend of reduced glycaemia condition with longer period of being on HAART may indicate that the use of HAART aid in restoring the normal metabolic function of the body thereby controlling sugar levels as well. There were 7 (5.83%) who were not on HAART at the time of the study. The patients with normal glucose levels exhibited no relationship between their glucose level and the period of living with HIV and also on HAART.

In relation to the symptoms of hyperglycaemia, the result shows that out of 120 patients 65 (54.17%) experienced increase urination and 55 (45.83%) similarly did not increase urination (p=0.241) (Table 3). There was a significant number of participants, 77 (64.17%), who were experiencing increased thirst as against 43 (35.83%) participants with normal thirst experienced (p=0.003). Also a significant number of participants, 68 (55.50%), experienced increased hunger as against 52 (43.33%) who experienced normal hunger (p=0.010). However, 58 (56.67%) similarly got tired easily as against 62 (51.67%) who did not get tired easily (p=0.854). Twenty-three, (19.17%) participants also had experienced slow wound healing lately with a significant higher number 95 (79.17%) who experienced fast wound healing (p=0.0001).

Table 4 shows that participants in the age group of 0-9, 60-69 and 70 and above were not having hyperglycaemia 0(0.00%). Correspondingly, three (2.50%), 7 (6.83%) and 1 (0.83%) of them were having normal glucose levels. One (0.83%) belonging to ages 10-19 and 30-39 year range each were having high glucose level. In the same age group levels 3 (2.50%) and 27 (22.50%) respectively were having normal glucose levels. Also 2 (1.67%) belonging to 20-29 and 50-59 age ranges each were having hyperglycaemia with 9 (7.50%0 and 27 (22.50%) respectively were having normal glucose levels. The age group of 40-49 year range were highest number of participants, 3 (2.50%), with increased glucose level and 34 (28.30%) having normal glucose levels. There were higher significant number of participants in 20 -59 age groups with normal blood glucose against those with hyperglycaemia ($p<0.05$).

There was also a significant lower number of unmarried participants (singles), 4 (3.33%), who had an increased blood glucose level against, 33 (27.50%), having normal glucose levels (p=0.001). Fifty-three (44.17%) married patients were having normal blood glucose with nobody 0 (0.00%) having high glucose levels. Three (2.50%) of the divorced patients were having high glucose levels with 8 (6.67%) having normal levels. Two (1.67%) of the widowed also had hyperglycaemia as against 17 (14.17%) having normal blood glucose levels (p=0.001).

The number of patients who were students was 7 (5.83%) of which 1 (0.83%) was having hyperglycaemia. For formal occupation, significant number of them were having normal glucose levels, 8 (6.67%) against 1 (0.83%) with hyperglycaemia (p=0.039). Six (5.00%) patients who were self-employed were having hyperglycaemia which was significantly lower than those, 85 (70.83%), with normal glucose level (p=0.0001). The unemployed patients were 13 (10.83%) and also a significant number, 12 (10.00%), was having normal blood glucose levels (p=0.003).

4.0 Discussion

Hyperglycaemia is a common condition present in the general population, mostly in diabetic individuals. It can occur as a result of an infection, certain medication, stress and obesity mostly due to decreased activity and excessive fat intake. Abnormalities of glucose homeostasis, primarily insulin resistance, are common in HIV infected patients receiving protein inhibitors (PIs) (Kalra *et al*., 2011; Robinson *et al*., 2007). It is likely HIV infection initiate the imbalances in glucose homeostasis which may develop into hyperglycaemia. In this study, the prevalence of hyperglycaemia in HIV patients visiting the Cape Coast Teaching Hospital was found to be 7.5%. According to the Ministry of Health 2011 report on National Policy for the Prevention and Control of Chronic Non-Communicable Diseases in Ghana, the prevalence of adult diabetes ranged from 6% to 9% (Ghana Health Service, 2011). Therefore the prevalence rate of hyperglycaemia in this study falls within the National prevalence rate of adult diabetics in Ghana. This is quite interesting and could suggest that the hyperglycaemia or diabetes may be common among people in the Cape Coast Metropolis.

Majority of the participants were between the ages of 20 to 60 years and these age groups showed the high hyperglycaemia. This is an indication that high sugar levels in the blood may be associated with age and has to do with the eating habit or lifestyles of the people (Feigenbaum and Longstaff, 2010; Perreault *et al*., 2008). More so, it was noted that majority of the married participants did not show any condition of hyperglycaemia suggesting living a healthy life by taking in a balance diet. The frequent exercise in addition to taking well balance diet ensures the healthy condition of individuals against metabolic syndrome (Robinson *et al*., 2007).

The next groups were those who were not married, divorced or widowed but showed hyperglycaemia condition which is also an indication of not having time to take in a well-balanced diet (Fitch *et al*., 2006) or living a sedentary lifestyle and probably might not have been doing much exercise. Increased diabetes prevalence is associated with patterns of development, changes in employment, residence, use of time, diet and nutrition, and increased sedentary lifestyle (Naemiratch and Manderson, 2007). All these factors are very important in controlling diabetes and adhering to the normal standards of living by observing the kind of food intake with much exercise could control blood sugar level of the body. Also most of those with high hyperglycaemia were self-employed and might have had this condition as a result of their sedentary lifestyles. However, the fact that there was at least one person, under various occupations, with hyperglycaemia shows that the condition may not be solely associated with the type of occupation one is involved in but rather affluent living standard may play a major role in increasing blood sugar level of the body. Obesity and sedentary lifestyles are risk factors for type II diabetes (Haupt and Newcomer, 2001; Hu, 2003) and high blood sugar level prevention activities include balanced diet intake, exercise and counselling (Fitch *et al*., 2006). The type of exercise, the duration and the frequency at which it is done result in effective control of blood sugar level. Other factors like stress management, diet and weight reduction are also important in controlling hyperglycaemia.

The factors involved in raising blood sugar levels include infections, certain medicines, increased stress, decreased activity, hormone imbalances or severe illnesses (A.D.A and Association, 2013). Therefore all these factors should be considered in the management of HIV because infected people are immune-compromised and are prone to many infections. Also the drugs intake can predispose them to getting hyperglycaemia. There are also confirmations that the antiretroviral therapy has effect on metabolic activities (Dagogo-Jack, 2008; Hoerger *et al*., 2008) as hyperglycaemia significantly declined with the number of years a patient has been on the therapy. This may suggest that the development of glucose imbalances depends on the treatment received or patient adherence to treatment regime. It is likely HIV infection initiate disorderliness in metabolic activities of the body resulting in hyperglycaemia but assume normal activities with introduction of antiretroviral therapy. It was also observed in this study that hyperglycaemia declined with the number of years the patient has been living with the disease. Some of the patients had been on antiretroviral therapy which might have accounted for restoring their normal blood glucose level with the HIV infection. This confirmed the earlier observation that infection affects metabolic activity of the body (Dagogo-Jack, 2008) but treatment with antiretroviral therapy affect abnormal metabolic activities of the body by reducing the blood sugar level (Brown *et al.,* 2005). Also some of the patients experienced increased thirst and hunger with normal wound healing suggesting early sign of diabetes or recovering due to HIV treatment (Casqueiro and Alves, 2012; De Wit *et al*., 2008). It is likely HIV treatment has effect on the development of hyperglycaemia into chronic diabetic condition by restoring the normal metabolic homeostasis.

5. Conclusion

In conclusion, the study has revealed that hyperglycaemia could develop along with HIV infection in most patients due to defect in homeostasis from infection. The condition might also be related to sedentary standard of living and HIV therapy may restore the normal blood sugar homeostasis. Therefore glucose level of HIV patients must be regularly measured in order to reduce the complications and mortality associated with diabetes. .

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Table 1: The presence of hyperglycaemia in HIV infected patients

Glycaemia Status	**Living with HIV (years)**					
	0-2	3-5	6-8	9-11	≥12	Total
High (%)	5(4.17)	2(1.67)	2(1.67)	0 (0.00)	0 (0 .00)	9(7.5)
Normal (%)	39(32.5	36(30.0)	23(19.17)	5(4.17)	8(6.67)	111(92.5)
Total (%)	44(36.67)	38(31.67)	25(20.83)	5(4.17)	8(6.67)	120(100)

r=-0.948, p=0.0167

Table 2: The presence of hyperglycaemia and the use of HAART in HIV infected subjects.

Glycaemia Status	**HAART Duration Range (years)**						
	0 – 1	**2 - 3**	**4 - 5**	**6 - 7**	**8 - 9**	**≥10**	**Total**
High (%)	3(2.50)	2(1.67)	2(1.67)	1(0.83)	0(0.00)	0(0.00)	8(6.67)
Normal (%)	25(20.83)	27(22.50)	27(22.50)	12(10.0)	8(6.67)	6(5.00)	105(87.50)
Total (%)	28(23.3)	29(24.16)	29(24.16)	13(10.83)	8(6.67)	6(5.00)	113(94.17)

r= -0.971, p=0.0028

Table 3: Symptoms of hyperglycaemia and the experiences of participants

Type of symptoms	**Experience**		
	Yes (%)	**No (%)**	**P-value**
Increased urination	65 (54.17)	55 (45.83)	0.568
Increased thirst	77(64.17)	43(35.83)	0.003
Increased hunger	68(55.50)	52(43.33)	0.010
Feel tired easily	58(56.67)	62(51.67)	0.624
Slow wound healing	23(19.17)	95(79.17)	0.0001

Table 4: Hyperglycaemia and demographic characteristic of the subjects

Characteristic	Glycaemia Status			
	High (%)	Normal (%)	Total (%)G	P value
Age groups				
0-9	0 (0.00)	3(2.50)	3(2.50)	-
10-19	1(0.83)	3 (2.50)	4(3.33)	0.468
20-29	2(1.67)	9(7.50)	11(9.17)	0.039
30-39	1(0.83)	27(22.50)	28(23.33)	0.0001
40-49	3(2.50)	34(28.30)	37(30.83)	0.0001
50-59	2(1.67)	27(22.50)	29(24.17)	0.001
60-69	0(0.00)	7(5.83)	7(5.83)	-
≥70	0(0.00)	1(0.83)	1(0.83)	-
Marital status				
Single	4(3.33)	33(27.20)	37(30.43)	0.001
Married	0 (0.00)	53(44.17)	53(44.17)	-
Divorced	3(2.50)	8 (6.67)	11(9.17)	0.110
Widowed	2 (1.67)	17(14.17)	19(15.83)	0.001
Occupation				
Student	1 (0.83)	6(5.00)	7(5.83)	0.110
Formal	1(0.83)	8(6.67)	9(7.50)	0.039
Self employed	6(5.00)	85(70.83)	91(75.83)	0.0001
Unemployed	1(0.83)	12(10.00)	13(10.83)	0.003

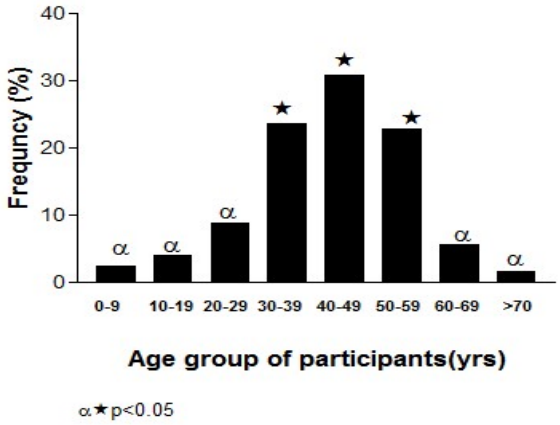

Figure 1: Age distribution of the studied participants

Figure 2: Distribution of marital status of the studied participants

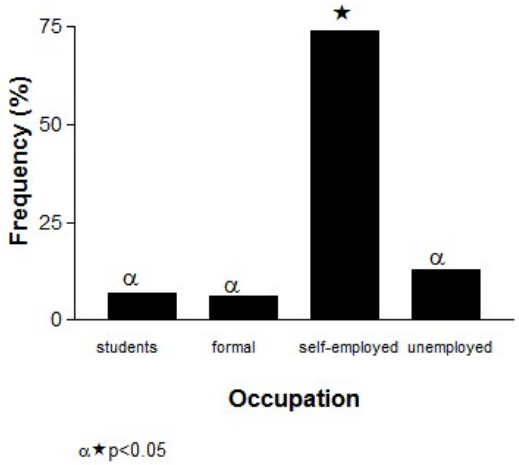

Figure 3: Distribution of the occupations of the studied participants