What Does Serum Adiponectin Portend in Obese Nigerian Type 2 Diabetes Subjects

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Abstract

Background: Adiponectin is a protein hormone whose levels have been found to correlate with glycaemic control and lipid profile in patients with Type 2 DM. This study evaluates the relationship of adiponectin in Obese and non - obese Nigerian T2DM patients.

Method: This cross-sectional hospital-based study included two groups of 60 Obese T2DM and 60 non-obese T2DM subjects. All study participants had clinical assessment, and blood samples collected and assessed for serum Adiponectin, fasting blood glucose, glycated hemoglobin, total cholesterol, triglyceride, low density lipoprotein, high density lipoprotein.

Results: Obese T2DM subjects had lower levels of adiponectin than Non-obese T2DM subjects ($p > 0.05$). In both groups, 65% and 77% of the Obese non-Obese diabetic group had good glycemic status, which poorly correlated with serum adiponectin levels, with higher adiponectin values seen in the groups with poorly controlled glycemic status.

High density lipoprotein cholesterol (HDL-C) levels correlated positively with serum Adiponectin levels in both Obese and non-Obese diabetic groups, however this was significant only in the Obese diabetic group ($r = 0.30$, $p = 0.02$). Adiponectin correlated negatively with Triglycerides only in the non-Obese diabetic group ($r = -0.12$, $p = 0.37$), and also correlated negatively with atherogenic index ($r = -0.092$, $p = 0.316$), though not statistically significant.

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Conclusion: Adiponectin is a poor marker for glycaemic control, and does not correlate with lipids such as TG, through its anti-atherogenic properties it may be associated with reduced risk of atherosclerosis as evidenced by its weakly positive and direct correlation with HDL among Nigerian Type 2 DM subjects.

Keywords: Serum adiponectin; obese type 2 diabetes; glycaemia; lipid profile*.*

1. Introduction

Obesity is defined as an excessive proportion of body fat relative to lean body mass of sufficient magnitude to produce adverse health consequences[1]. It is an endemic health problem in both developed and developing countries [2]. Obesity is a significant risk factor for diabetes [3] as well as poor glycemic control in known type 2 diabetes patients, in whom obesity is currently driving the global diabetes epidemic [4]. Thus, in diabetes subjects, obesity is associated with poorer control of blood glucose levels as well as that of cholesterol and blood pressure [5,6] Conversely, intentional weight loss is associated with reduced mortality among overweight persons with diabetes [7]. A loss of 5-10% of body weight resulted in improved fitness, reduced HbA1c levels, decreased use of lipid lowering medications as well as improved cardiovascular disease risk [8].

Obesity therefore remains an independent risk factor for cardiovascular disease [9] and this increased risk for cardiovascular events such as coronary heart disease, is due in part to its strong association with atherogenic dyslipidemia characterized by high triglycerides and low HDL [10].

In obese type 2 DM patients, overall cardiovascular disease risk is increased due to a clustering of cardiometabolic risk factors [11,12].

Adiponectin, a novel marker with anti-atherogenic, anti-inflammatory, cardioprotective and insulin sensitizing properties, consists of 244 amino acids, which form four different domains, shares homology with collagen and compliment factor C1q family [13]. Adiponectin modulates a number of metabolic processes via the activation of 5′-adenosine monophosphate-activated protein kinase (AMPK) and peroxisome proliferator activated receptor-α (PPAR-α) [14]. A decline in plasma or serum levels of adiponectin due to genetic or environmental factors has been implicated in the development of diabetes, poor glycemic control, dyslipidemia, abdominal obesity and hypertension [15-17].

Studies have shown that increased adiponectin levels might be associated with better glycemic control, better lipid profile and reduced inflammation in diabetic subjects [18,19]. Conversely, low adiponectin levels, by regulating insulin resistance and metabolic profile, may contribute to the markedly increased risk of atherosclerosis in diabetic subjects [18]. This anti-inflammatory cytokine has been noted to have an important relationship with lipid metabolism, particularly higher levels of HDL cholesterol and lower levels of triglycerides and measures that increase adiponectin levels are therefore thought to be valuable targets for decreasing the atherosclerotic risk present in diabetes [19].

While some studies, showed no significant relationship between adiponectin levels and glycemic control, a significant correlation is seen between adiponectin levels and the lipid profile [17,20-22].

This study evaluated the relationship of adiponectin in obese Nigerian type 2 diabetes subjects and its usefulness as a marker of cardiometabolic risk among them.

2. Methods

This cross-sectional study involved 120 consecutive adult Nigerians with type 2 diabetes attending the diabetes out-patient clinic of a tertiary hospital in South-West Nigeria. Ethical approval was sought and granted by the

hospital's Ethics and Research Committee. Written informed consent was obtained from participants. Patients with type 1 DM, chronic medical diseases, acute conditions or medications that affect inflammation were excluded

Similarly, patients who were known to have chronic debilitating diseases such as chronic heart failure, chronic liver disease and chronic renal failure, were also excluded. Clinical history and relevant clinical examination were performed and documented. Anthropometry and blood pressure were measured and documented using standard protocols [23,24].

2.1 Laboratory investigation

Blood samples were collected after eight hours overnight fast for determination of blood glucose, serum levels of total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), and triglycerides. Glycated hemoglobin was measured using Ichromax HbA1c kit (Dongnae-myeo, Republic of Korea). Serum adiponectin level was measured using enzyme-linked immunosorbent assay (Aviscera Bioscience, INC, USA)

2.2 Definition of terms

Type 2 diabetic subjects were defined based on the WHO classification and diagnostic criteria (25). Controlled diabetic subjects were taken as subjects with HbA1c < 7.0% while the poorly controlled diabetic subjects were subjects with HbA1c ≥ 7.0% (26). Dyslipidemia was defined as: LDL > 100mg/dl (2.6mmol/l); HDL < 40mg/dl (1.0mmol/l) in men or < 50mg/dl (1.3mmol/l) in women. Triglycerides > 150mg/dl (1.7mmol/l) [27].

2.3 Data Analysis

Data was analyzed using the Statistical Package of Social Sciences (SPSS) version 23.0. and is presented using descriptive statistics such as frequency tables, bar chart, box & whisker plots and scatter diagrams with the choice depending on whether the variables are categorical or continuous. Measures of central tendency such as mean, median and measures of dispersion such as standard deviation and interquartile range were used to describe all the variables with the choice depending on whether the variables were normally distributed or not. Independent Sample T-test was used to determine the difference between serum adiponectin, serum insulin and the glycemic control status of obese and non-obese diabetic subjects. Pearson's correlation used to assess the linear relationship between serum adiponectin and components of the FLP including: HDL, TC, LDL & TG.

Level of statistical significance was taken as $p \leq 0.05$.

3. Results

Sixty (60) obese and 60 non obese T2D subjects whose age range was 34 – 70 years. The median age was 62 (13.5) years for the obese type 2 DM group and 63 (17.8) years for the non-obese type 2 DM group. Twenty - eight (46.7%)) subjects were males while 32 subjects (53.3%) were females (in both groups). There was no statistical difference among these two groups for both sexes (p = 1.000). The male to female ratio was 1:1.14 for both groups.

Subjects diagnosed with Hypertension was seen in 50(83%) of the obese subjects and 44(73%) of the non- obese subjects (p = 0.184)

Eighty-five (71%) of the diabetic subjects had HbA1c < 7% while 35 (29%) diabetic subjects had poorly-controlled glycemic status (HbA1c ≥7%). The overall mean glycated hemoglobin value was 6.8 ± 2.1. The mean value of glycated hemoglobin obtained in the Obese diabetic group is shown on Table 1.

**Table 1:** Biochemical parameters of the study participants

Biochemical variables	Obese diabetic Mean (±SD)	Non-obese diabetic Mean (±SD)	P value
Glycated Haemoglobin (%)	6.9 ± 2.0	6.6 ± 2.1	0.45
Fasting Serum Adiponectin level (µg/ml)	3.0 ±1.8	3.6±1.8	0.13
Fasting Serum Insulin level (µIU/ml)	4.6 ±5.8	4.3 ±2.7	0.42

* P value significant

Obese Type 2 DM subject group, with good glycaemic control, the mean serum Adiponectin level was ~~of~~ 2.9 ± 1.4 µg/ml while those with poor glycaemic control had a mean serum Adiponectin level of 3.3 ± 2.3 µg/ml. Also, in the non-obese Type 2 DM subject group, 46 (77%) had controlled glycemic status with a mean serum Adiponectin level of 3.6µg/ml ± 1.9 while 14 subjects (23%) had poorly controlled glycemic status with a mean serum Adiponectin level of 3.8µg/ml ± 1.6. The mean serum adiponectin level in the obese type 2 DM group was 3.0 ± 1.8 (µg/ml), and was lower compared to the non-obese diabetic group which was 3.6 ± 1.8 (µg/ml). These values were however similar. (p = 0.13). Figure 1.

The mean serum adiponectin levels of the diabetic subjects with controlled and poorly controlled glycemic status were 3.3µg/ml ± 1.7 and 3.5µg/ml ± 2.0 respectively and this was also not statistically significant (t = 0.497, df = 118, p = 0.620).
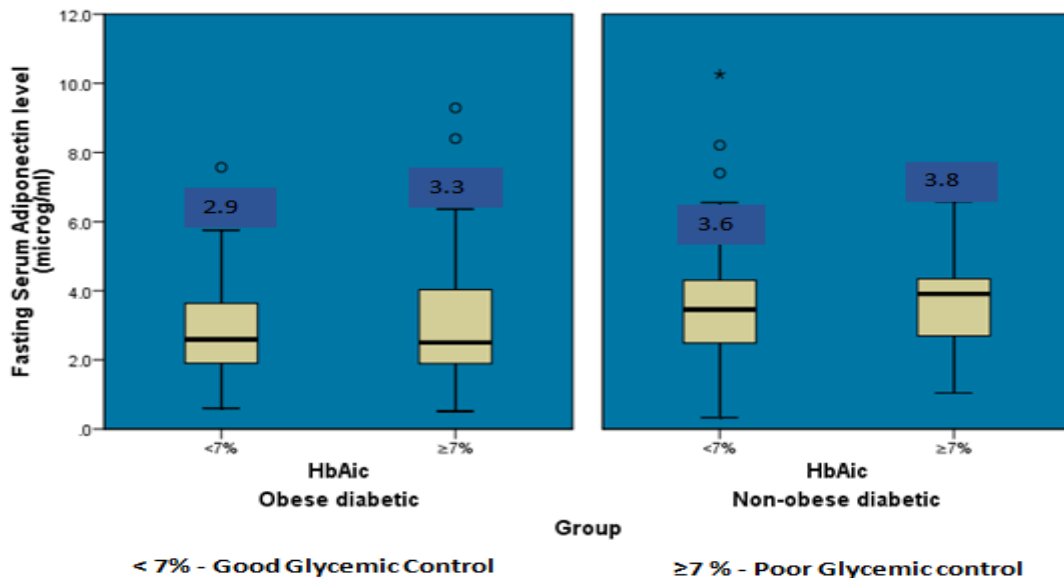
Figure 1: Adiponectin level and glycemic control among both groups of diabetic subjects

The comparison of the lipid profile in both groups is shown in table 2. There appears to be no difference in the lipid profile of both groups

Table 2: Comparison of lipid profile among both groups of diabetics

Biochemical measurements	Obese diabetic Mean (±SD)	Non-obese diabetic Mean (±SD)	T	P value
HDL (mmol/L)	1.2 ± 0.4	1.2± 0.4	0.025	0.941
TG (mmol/L)	1.0 ±0.5	1.1 ± 0.5	1.07	0.30
LDL (mmol/L)	3 .0±1.4	2.7 ±1.4	1.41	0.24
TC (mmol/L)	4.6 ±1.4	4.4 ±1.3	1.09	0.30

HDL-High density lipoprotein, TG-Triglycerides, LDL-Low density lipoprotein, TC-Total Cholesterol, *P Value Significant

The association between serum adiponectin and lipid profile of the obese and non-obese diabetic subjects is shown in Table 3**.** In figure 2, though there is a positive correlation between serum adiponectin values and High-density lipoprotein (HDL) in both obese diabetic and non-obese diabetic groups but this however, was of only of statistically significant in the obese diabetic group (p = 0.02). A negative correlation was seen with TG in the non - obese diabetic group, while a positive correlation was seen with TG in the obese diabetic group and with LDL and TC in both groups. However, these relationships were not statistically significant.

Pearson's correlation done between fasting serum adiponectin level and atherogenic index (AI) in all diabetic subjects, showed a negative association (r = -0.092) which was not statistically significant (p = 0.316).

Table 3: Correlation between Adiponectin and Lipid profile in subjects

Lipid profile	Obese diabetic		Non-obese diabetic	
	R	p-value	R	p-value
HDL	0.30	0.02*	0.20	0.13
TG	0.09	0.49	-0.12	0.37
LDL	0.13	0.31	0.08	0.56
Total Cholesterol	0.23	0.07	0.12	0.36

HDL-High density lipoprotein, TG-Triglycerides, LDL-Low density lipoprotein,

*P value significant, R- Correlation co-efficient

r = 0.30, p = 0.02*   *r = 0.20, p = 0.13*

*p value significant
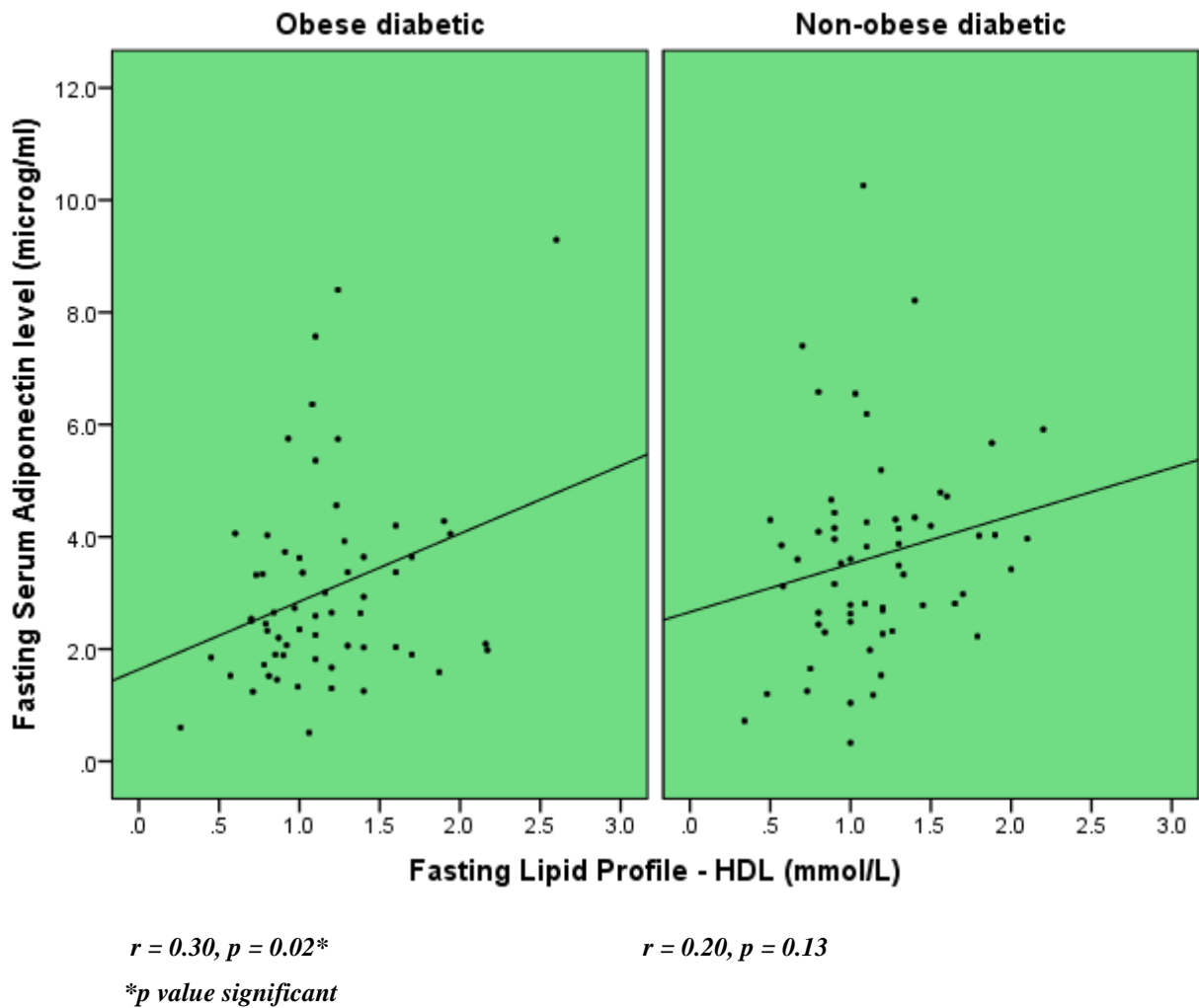
Figure 2: Relationship between Adiponectin and HDL-C among both groups of diabetic subjects

4. Discussion

Adiponectin is an adipokine which is known for regulating glucose, and lipid metabolism. Studies have shown that levels of adiponectin, due to its anti-atherogenic and anti-inflammatory properties correlates well with glycemic control and lipid profile in type 2 diabetics, [16-19] others however have not [17,20-22]. The glycemic control in both study groups is comparable. The mean serum adiponectin levels for both the obese and non-obese diabetic groups were also similar. Good glycemic control is known to cause a higher adiponectin level due to its insulin sensitizing properties and conversely, lower serum adiponectin levels are expected to correlate with and reflect poor glycemic control among type 2 DM patients. In this study, higher adiponectin values were seen in the groups with poor glycemic control for both the obese and non-obese subjects, showing that serum adiponectin in these subjects studied correlates poorly with glycemic control. When the subjects were classified based on their glycemic status alone the presence or absence of obesity did not influence the relationship of serum adiponectin with the glycemic control status of our type 2 DM patients. Similar findings to this study were observed by Nonogaki and his colleagues [21] a study among Japanese population in which decreases in HbA1c and plasma glucose levels were not associated with elevations in adiponectin levels. Notably, like in our study, elevations in HbA1c levels were associated with elevations in adiponectin levels. Obot and his colleagues [20] equally found

that adiponectin levels did not correlate with glycemic control status. This is however contrary to findings by Izadi and his colleagues [28] who studied an Iranian type 2 diabetic population and obtained results that showed a significant inverse relationship between adiponectin concentration and insulin resistance in these patients, as well as a significant relationship between fasting glucose and adiponectin levels.

Racial differences in the function of adiponectin may account for such differences in the usefulness of this adipocytokine in our environment [29]. A cross-sectional study by Meshkini and his colleagues evaluated ethnic differences in adiponectin levels and its association with age, gender, body composition and diet in 89 adult Australians of European, Indian and Iranian ancestries, the authors concluded that: individuals with Iranian or Indian ancestries may have lower adiponectin levels compared to Europeans. Ethnicity was found as an independent factor affecting adiponectin levels. The results of their study also highlighted age, truncal adiposity and dietary glycaemic index as other determinants of serum adiponectin, however the extent to which these factors influence adiponectin concentrations were thought to vary across ethnicities [30]. A decline in plasma or serum levels of adiponectin due to genetic or environmental factors has been implicated in the development of diabetes, poor glycemic control, dyslipidemia, abdominal obesity and hypertension.

The components of the lipid profile done were: Total cholesterol, Triglycerides, High density lipoprotein and Low-density lipoprotein. Total cholesterol was similar across both diabetic groups and correlated positively with serum adiponectin. Triglyceride levels as well as Low density lipoprotein levels were also similar among both groups. Triglycerides (obese diabetic group) and LDL also positively correlated with serum adiponectin. A negative correlation with triglycerides was seen in the non-obese diabetic group. These associations were all not statistically significant. The High-density lipoprotein (HDL) levels in this study were similar among both groups and correlated positively with levels of serum adiponectin in both obese diabetic and non-obese diabetic groups but was statistically significant only in the obese diabetic group (r = 0.30, p =0.02). Serum levels of adiponectin are thought to correlate positively with HDL and negatively with Total cholesterol, LDL and Triglycerides due to its anti-atherogenic properties [19]. The positive correlation it has with HDL is expected due to the fact that HDL is well recognized as an independent predictor of cardiovascular risk.

Hsu and his colleagues [31] reported similar findings in a study done among Chinese population who were noted to have been on sulphonylurea and metformin therapy for more than 6 months. There was a positive asssociation between adiponectin concentration and HDL-cholesterol level in type 2 diabetes. It was also observed in their study that adiponectin concentration was the only and main predictor of HDL-cholesterol after adjusting other factors for homogenous Type 2 diabetic subjects. Obot and his colleagues [20] also reported a positive correlation between HDL levels and adiponectin in their subjects with statistical significance only in the non-diabetic group. Triglycerides and HDL-cholesterol in atherogenic index (TC/HDL ratio) reflect the balance between the atherogenic and protective lipoproteins. Atherogenic index correlates with the size of pro- and antiatherogenic lipoprotein particles. It correlated negatively with serum adiponectin in the non-diabetic population of their study. In our study, there was also a negative correlation of HDL- cholesterol with the atherogenic index, however this relationship was not statistically significant.

The correlation observed between the serum adiponectin levels and HDL in our study was however a weakly positive correlation and may not be suitable to imply the usefulness of serum adiponectin levels as a suitable marker of increased cardiovascular risk in obese type 2 DM patients. The effect of oral hypoglycemic agents the subjects had been on, may be responsible for the elevated levels of this cytokine in them. In this study, other

components of the lipid profile assayed for, namely: Total Cholesterol, Low Density Lipoprotein - cholesterol and Triglycerides as noted earlier, did not have any significant correlation among the subjects studied.

Hsu and his colleagues [31] and Obot and his colleagues [20] also observed similar findings in their studies except for the triglycerides which were significantly higher in the diabetic group in the study by Obot and his colleagues [20].

In a study done in Northern Nigeria by Ciroma and his colleagues among healthy, overweight and obese subjects, adiponectin was found to have no relationship with components of the lipid profile assayed for, namely: Low density lipoprotein - cholesterol, High density lipoprotein – cholesterol, Total cholesterol and Triglycerides, among these categories of subjects. Lipid profile was also not different among BMI classes [32].

5. Conclusion

In conclusion, this study, found no significant difference in the serum levels of adiponectin of diabetic subjects with controlled glycemic status and those with poorly controlled glycemic status. Routine measurement of serum adiponectin may not be useful as a marker of cardiometabolic risk among type 2 DM patients in our environment. Limitations: The sample size of this study may be a limitation as it may result in non-significant associations where larger studies would have shown significance as seen in the relationship between serum adiponectin levels and both glycemic control & components of the lipid profile.

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