

## Heritability of hypoadiponectinemia in first-degree relatives of Indian population

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### Abstract

**Objective:** Diabetes is a disorder and prevention has become a global priority. Significance of hereditary factor in the advancement of Diabetes mellitus is really convincing. Sensitive factor for developing Type 2 diabetes (T2DM) is identified as adiponectin and hence the need of the study.

**Materials and Methods:** This is a cross-sectional study. Subjects with self-reported history of T2DM in both parents were selected and biochemical parameters with anthropometric were recorded. They were grouped as diabetic and non-diabetics.

**Result:** A greater level of difference of 9.45 units was seen in adiponectin levels between presence and absence of family history of diabetes (FHD). Further adiponectin continued to witness a significant difference even in diabetics and normal group with respect to family history. Hence when linear regression was made to assess relationship between adiponectin and other variables, it was found that diabetic status ( $P=0.000$ ), leptin ( $P=0.001$ ), and FH ( $P=0.000$ ) had reached statistical significance among others parameters. Moreover adiponectin was positively correlated with diabetic status ( $B=4.655$ ) and negatively correlated with leptin ( $B=-0.125$ ) and Family History ( $B=-9.034$ ).

**Conclusion:** The comprehensive relation between Family History and adiponectin is true and are inversely related. Hence the impact of familial predisposition is advocated due to genetic load and diabetic status.

**Keywords:** Adiponectin, Family history, Hypoadiponectinemia.

### Introduction

Diabetes is a chronic illness which requires long-term medical care in achieving glycemic control and decreasing the associated complications such as retinopathy, neuropathy and nephropathy with enhanced the class of life. It has become a major contributor for an increase in medical expenditure.<sup>1</sup> Additionally, diabetes has greater risk for several life-threatening diseases including cardiovascular disease.<sup>2</sup> Hence the issue of diabetes prevention has become a global priority.

Type 2 Diabetes Mellitus (T2DM) is a multi-factorial disease linked to several potential risk factors of which diabetes in the family and ethnicity are of main concern. Studies report presence of diabetes in the family to be an important independent risk factor and is known to share the same family environment with the genes.<sup>3,4</sup> The influence of developing T2DM becomes two to four fold higher in subjects depending on the number of pretentious family members along with relationship to the patient.<sup>5-7</sup> Consequently the affected degree and exact mechanism remain obscure.

Pathophysiology of type 2 diabetes mellitus are implicated mostly because of dysregulation of endocrine function and inflammation of adipose tissue (AT) triggering the changes in the levels of cytokines such as adiponectin, Leptin etc.

Heritability of 30-70% levels in plasma adiponectin is influenced by the exchange of several genes.<sup>2,8-10</sup> Gene associated studies had identified an susceptibility point in the gene, which is associated with diabetes mellitus and also metabolic disorder. This same locus is identified to have

adiponectin expression (chromosome 3q27).<sup>11</sup> Hence, Adiponectin gene may be linked with diabetes. Based on biological evidences and positional information from linkage studies, Adiponectin may be an crucial mediating factor for better perception of risk for developing T2DM. Hence to identify the heritability of hypoadiponectinemia reflecting with the plasma variation of Adiponectin in subjects with first degree relatives with T2DM was chosen.

### Materials and Methods

This study was completed in Dakshina Kannada district and is a cross sectional type of study. A total of 229 type 2 diabetic subjects, matched with controls of 205 healthy individuals were recruited for this study. Both genders with 30-70 years, confirmed diabetic mellitus subjects atleast since one year, not on insulin treatment, may be on diet control, free from any vascular disorders were identified and selected.

Family histories of diabetes were asked to be reported from the selected subjects. Subjects who failed to identify their parental status of diabetes were excluded from the study. This created a group of 157 diabetic subjects and 118 controls with a clear information of parental status of diabetes. Both the parents having diabetes mellitus were assigned as FHD +ve and both the parents free from diabetes mellitus were considered as FHD -ve.

Diabetic microvascular and macrovascular complications were ruled of with relevant examination.

Ethics committee of Yenepoya University had approved the study protocol. Selected subjects rendered their informed consent. The separated serum from fasting blood

samples were used for the assessment of adiponectin, leptin. Enzyme Linked Immunosorbent assay was the technique used. Glycated hemoglobin was done by an immune turbidometric technique in fresh fasting samples by Thyrocare Technologies Limited. Standard procedure was followed to measure the anthropometric variables like WC, HC, height and weight. BMI was calculated.

### Statistical Analyses

Baseline characteristics of the FHD +ve and FHD–ve of diabetic and Normal were compared using the independent t-test. Linear regression was used to find the association between the variables. P values <0.05 was judged as having a statistically significant difference. Statistical analysis was performed using SPSS 10.0

### Results and Discussion

Diabetes mellitus is a life style disorder which affects the Gluco regulatory mechanism. Increased physical activity provides the best protective benefit in pronounced persons with the highest risk for the disease.<sup>12</sup> Since diabetes prevention has become a global concern, to accomplish the objective of prevention, it is important for the targeted group to understand the pathogenesis of diabetes through the reports on genetic risk of diabetes among family members of type 2 diabetic patients<sup>13</sup> is recommended.

Regardless of the significance of hereditary factor in the advancement of Diabetes mellitus, patients with diabetes and their relatives don't completely comprehend the danger. Studies report that less than 40% of human beings with a family history of the T2DM really see themselves to be at an expanded danger of conceiving diabetes.<sup>14,15</sup> To evaluate the perception of risk of diabetes through family history and a marker, the study was taken up.

The baseline characteristics of the study group are shown in Table 1. It is obvious that Anthropometric variables were higher in subjects with a parental history of diabetes than those without. Biochemical parameters like FBS, HbA1c, Leptin levels also followed the same trend. The serum levels of Adiponectin showed a difference of 9.45 units between the presence and absence of parental history of diabetes. (Fig. 1) represents the biochemical parameters of the groups according to family history of diabetes mellitus. The use of BMI as an indicator of adiposity is well known, however recent evidence represents WC as a strong predictor of obesity related health risk<sup>16</sup> because it is a indicator of abdominal fat.<sup>17</sup> This was very much clear in our study that overall a positive family history of diabetes had a higher WC though both the groups had similar BMI, a weak significant remained among the waist circumference in the normal group between the family history but in any case it was not reflected in the obesity marker the leptin level.

Table 2 depicts the group statistics of diabetic and normal subjects according to family history. When compared between the family history, a significant difference between all the biochemical parameters-FBG, HbA1c, Leptin and Adiponectin was observed among the

diabetic subjects. Where as this significant difference was lost in the normal group (except for adiponectin). Both the groups showed no significant difference among anthropometric variable except for weak significance for WC among the Normal group. It is observed that the predisposition to increase fat mass is due to greater genetic susceptibility in such offspring's with FHD.<sup>13</sup> Compelling evidence in of our study was in FHD group, with increased WC, HC though the BMI was the same. This substantiates that FHD mediates the pathogenesis of the disease. Also observed that the group with FHD had a higher level of FBS, and HbA1c. Also Leptin levels were much higher with a low adiponectin in subjects with FHD. This association of hypoadiponectinemia in FHD is also supported by other studies.<sup>18,19</sup> It is observed that diabetic subjects with positive Family history were younger and less bulkier as tabulated by BMI, WC and HC. Whereas in the Normal group, persons with both parents of diabetes has shown an opposite effect. They were more massive as seen by anthropometric variables like BMI, WC and HC when compared to no family history of diabetes. In both the group, positive family history has low Adiponectin and high Leptin, HbA1c when compared to negative family history.

To substantiate the increase in the levels of the parameters, group statistics of diabetic and normal subject was considered. In our study FBG, HbA1c, Leptin and Adiponectin showed a significant difference among the diabetic group between the family history whereas this difference was lost among the normal group, except for Adiponectin to be statistically significant. This shows that Adiponectin is grossly reduced in diabetic subjects and in susceptible persons with FHD which is also supported by sull et al and others.<sup>18,19</sup> Observational studies have also seen decreased plasma adiponectin levels in several metabolic disorders and its associated risk factors.<sup>20-22</sup> Studies demonstrate that adiponectin assumes to play a vital part on insulin resistance and  $\beta$ -cell dysfunction. It has been proposed that genetic polymorphisms in the *AdipoQ* gene are clinically associated with diseases.<sup>9,23,24</sup>

Since Adiponectin alone showed significant difference in the normal and diabetic group, linear regression was analyzed for Adiponectin as the dependent variable. Table 3 shows the variables which independently determines the Adiponectin levels. It was found that diabetic status (B=0.38, p=0.000), Leptin (B=-0.140, p=0.001) and Family history (B=-0.732, p=0.000) were significant. The observed independent association between adiponectin and other variables like diabetic status, leptin and parental history are worth highlighting. In Multiple linear regression analysis, Adiponectin was negatively correlated with other parameters though leptin and family history were significant. This implies that Adiponectin is positively associated with diabetic status of the individual and is inversely related with leptin and family history, the impact on familial predisposition may be due to a strong genetic load that exists in diabetic state with a FH than the presence of a weak effect on individual without FH.<sup>25</sup> The latter

effect may be covered by other unidentified hereditary components.

**Table 1: Clinical characteristics of the subjects according to family history of type 2 diabetes**

	<b>FHD -ve (n=118)</b>	<b>FHD +ve (n=157)</b>
Age (years)	47.45 ± 8.25	47.27 ± 8.39
BMI (kg/m <sup>2</sup> )	27.40 ± 3.71	27.25 ± 4.99
WC in cm	92.79 ± 5.41	94.29 ± 5.36
HC in cm	95.04 ± 6.56	96.72 ± 6.06
FBS (mg/dl)	92.44 ± 27.56	109.84 ± 37.67
HBA1c	6.26 ± 0.79	7.03 ± 1.21
Adiponectin (mg/l)	20.52 ± 5.04	11.06 ± 3.13
Leptin (ng/ml)	8.70 ± 5.00	11.86 ± 7.66

**Table 2: Group statistics of diabetic and normal subjects**

<b>Diabetic group</b>	<b>FHD -ve (n=54)</b>	<b>FHD +ve (n=96)</b>	<b>P-Value</b>
Age (years)	48.78 ± 8.05	47.99 ± 7.54	.550
BMI (kg/m <sup>2</sup> )	27.87 ± 4.13	26.68 ± 5.58	.174
WC in cm	96.07 ± 4.31	95.73 ± 4.32	.648
HC in cm	98.38 ± 4.69	98.20 ± 4.79	.828
FBS(mg/dl)	110.13 ± 29.32	131.22 ± 32.31	<.001
HBA1c	6.36 ± 0.81	7.45 ± 1.16	<.001
Adiponectin (mg/l)	23.98 ± 4.082	11.15 ± 2.63	<.001
Leptin (ng/ml)	9.44 ± 5.62	13.49 ± 8.57	.002

<b>Normal Group</b>	<b>FHD -ve (n=64)</b>	<b>FHD +ve (n=61)</b>	<b>P-Value</b>
Age (years)	46.34 ± 8.35	46.15 ± 9.55	.903
BMI (kg/m <sup>2</sup> )	27.02 ± 3.30	28.16 ± 3.76	.073
WC in cm	90.03 ± 4.68	92.04 ± 6.06	.040
HC in cm	92.23 ± 6.62	94.41 ± 7.08	.078
FBS(mg/dl)	77.53 ± 13.92	76.2 ± 12.46	.574
HBA1c	6.19 ± 0.78	6.37 ± 0.99	.249
Adiponectin (mg/l)	17.61 ± 3.8	10.93 ± 3.80	<.001
Leptin (ng/ml)	8.07 ± 4.36	9.31 ± 5.05	.144

**Table 3: Result of multiple linear regression analysis to assess relationships between adiponectin and other variable**

<b>Variables</b>	<b>B</b>	<b>P value</b>
Sex	.809	.183
Age	-.027	.309
WC in cm	.041	.592
HC in cm	-.014	.838
BMI (kg/m <sup>2</sup> )	-.006	.917
FBS (mg/dl)	-.021	.075
HBA1c	-.380	.096
Leptin (ng/ml)	-.125	.001
Family History	-9.034	.000
Diabetic status	4.655	.000

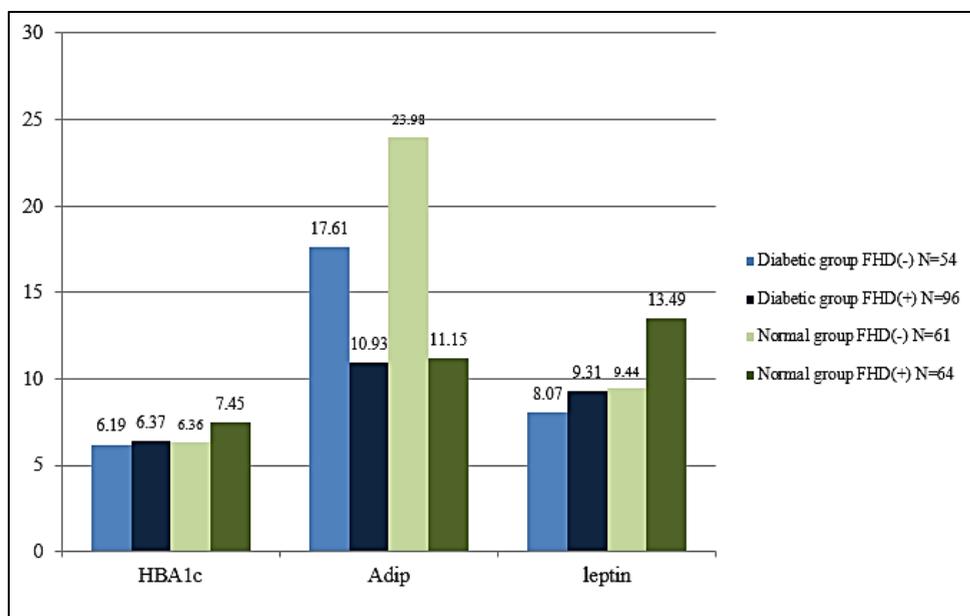


Fig. 1: Biochemical characteristics of the groups according to family history of type 2 diabetes

## Conclusion

Hence associations in individuals who are already burdened by other genetic factors needs formally adding family history as a tool for accounting the well-known risk factors for diabetes. This affiliation not just highlights the significance of shared qualities and environment in diabetes, it additionally opens the likelihood of officially adding family history to general wellbeing methodologies for distinguishing and preventing the disease.

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**Conflict of Interest:** None.

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