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DIABETES DEVELOPMENT & INSULIN RESISTANCE PROMOTION ASSOCIATION WITH HIGHER LEVELS OF SERUM FETUIN-A: A CROSS-SECTIONAL RESEARCH

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Abstract:

Objective: *We aimed to determine Fetuin-A role in the initiation of resistance of insulin that ultimately leads to T2DM (Type II Diabetes Mellitus) development.*

Methods: *Our research was case-control and cross-sectional in nature which was carried out on 150 patients at Services Hospital, Lahore (March 2016 – April 2017). Random sampling method was employed for the selection of the sample which included fifty cases in each including T2DM, impaired fasting glycaemia and normal healthy participants. A detailed history of the BMI and clinical assessment was taken before the commencement of the research. We measured fasting glucose serum, serum Fetuin-A and serum insulin levels through ELISA Kit. HOMA IR was used for the calculation of resistance of insulin. Statistical analysis of the outcomes was carried out through SPSS software.*

Results: *It was learned through research that level of Fetuin-A was high in the patients of T2DM than the other patients of healthy controls and IFG with a significant P-value of (< 0.01). There was a significant increase in the HOMA IR and serum insulin in the cases who were diagnosed with T2DM than healthy and IGF patients (< 0.01). T2DM cases were observed with increased BMI than healthy controls and IGF with a significant P-value (< 0.01).*

Conclusion: *The outcomes of our research showed increased level of Fetuin-A serum associated with the promotion of the insulin resistance and T2DM development in the patients.*

Keywords: *Type 2 Diabetes Mellitus (T2DM), Fetuin-A and Impaired Fasting Glycaemia (IFG).*

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INTRODUCTION:

All the world faces T2DM as major healthcare issue with a projected incidence observed as 285 million back in 2010; which is projected to increase to 438 million till 2030 [1]. Asia faces adult involvement more than elder age group in the disease; whereas, in the West, the situation is vice versa [2]. Increased diabetes proportion in Pakistan is counted at number seven in the countries of the world, which will further increase and bring Pakistan in the list of top four countries at the ongoing rate by 2030 [3].

Pre-diabetic stage leads to diabetes development. General population faces the IFG disorder which is also considered as a pre-diabetic state [4]. Over the recent year, greater attention has been paid to IFG as it is intermediate stage that leads to CVD and diabetes [5, 6]. IFG is also considered as an indicator which has a preventive importance for the CVD and diabetes [7].

Diabetes (T2DM) development is also caused by the resistance of insulin in the patients [8]. The actions of the insulin are mediated with the help of receptors of insulin which has two extracellular subunits which bind to the insulin and another two transmembrane subunits having an activity of internal tyrosine kinase (TK). Insulin binding to insulin receptors initiates an activity of internal TK and outcome is in the shape of tyrosine autophosphorylation receptor residues followed by the subsequent several insulin receptor phosphorylation substrates which help in the mediation of the insulin [9]. Fetuin-A is a (60 k Da) glycoprotein which is produced in the liver and it helps in the binding of the insulin receptors in the adipose, muscular tissue and also restricts the activity of the insulin receptor tyrosine kinase at the same time vivo and vitro insulin receptor autophosphorylation [10]. It is therefore responsible for insulin resistance promotion and T2DM pathogenesis.

In the same background, our aim was to determine Fetuin-A role in the initiation of resistance of insulin that ultimately leads to T2DM (Type II Diabetes Mellitus) development.

SUBJECTS AND METHODS:

Our research was case-control and cross-sectional in nature which was carried out on 150 patients at Services Hospital, Lahore (March 2016 – April 2017). Random sampling method was employed for the selection of the sample which included fifty cases in each including T2DM, impaired fasting glycaemia and normal healthy participants. A detailed history of the BMI and clinical assessment was taken before the commencement of the research. The age of the patients was in the age bracket of (35 – 60) years. All the cases having any disorder such as Cushing's syndrome, hepatic disease, hyperthyroidism, alcoholism, renal diseases or abuse of drugs were not made a part of this research. All female pregnant cases, oral contraceptive pills or lactation were also excluded from the research study.

Three groups were made on the basis of clinical fasting outcomes in the guidelines of Diabetes Association of America [12]. These groups were Controls having normal level of glycemic with measurement of blood glucose fasting as (< 100 mg/dl); level of IFG as (100 – 125) mg/dl and T2DM cases having blood glucose fasting measurement as (126 mg/dl). Fasting time was observed in the limit of 8 – 10 hours and ELISA Kit was used for the measurement of fasting glucose level. An enzyme immunoassay kit was used for the measurement of level of Fetuin-A. HOMA IR was used for insulin resistance measurement [13]. With the help of BMI formula, we calculated BMI of the patients that is (kg / m^2) [14]. Statistical analysis of the outcomes was carried out through SPSS software (P-value < 0.05).

RESULTS:

It was learned through research that level of Fetuin-A was high in the patients of T2DM than the other patients of healthy controls and IFG with a significant P-value of (< 0.01). There was a significant increase in the HOMA IR and serum insulin in the cases who were diagnosed with T2DM than healthy and IGF patients (< 0.01). T2DM cases were observed with increased BMI than healthy controls and IGF with a significant P-value (< 0.01). Table – I & II shows the gender distribution and biophysical and demographic information of the patients respectively. Mean values of age in controls, IFG and diabetes were calculated as (51.9 ± 4.8), (52.2 ± 4.9) and (53.8 ± 4.6) years respectively. Gender distribution in percentage has been shown in Table – I. Increased BMI, weight and systolic blood pressure was observed in the patients of T2Dm with increased IFG as well than controls (P-value < 0.001). Table – III shows the biochemical variables of our research. Insulin, HOMA IR and blood fasting sugar were increased in IFG and T2DM cases with a significant P-value as (< 0.001). It was observed in the post-hoc test that T2DM and IFG cases had higher levels of serum concentrations of Fetuin-A in comparison to the healthy controls of the research as shown in Table – III with P-value as (< 0.001).

Table – I: Gender Distribution

Gender	Controls		Impaired fasting glycemic		Known type 2 diabetics	
	Number	Percentage	Number	Percentage	Number	Percentage
Male	26	52	28	56	24	48
Female	24	48	22	44	26	52
Total	50	100	50	100	50	100

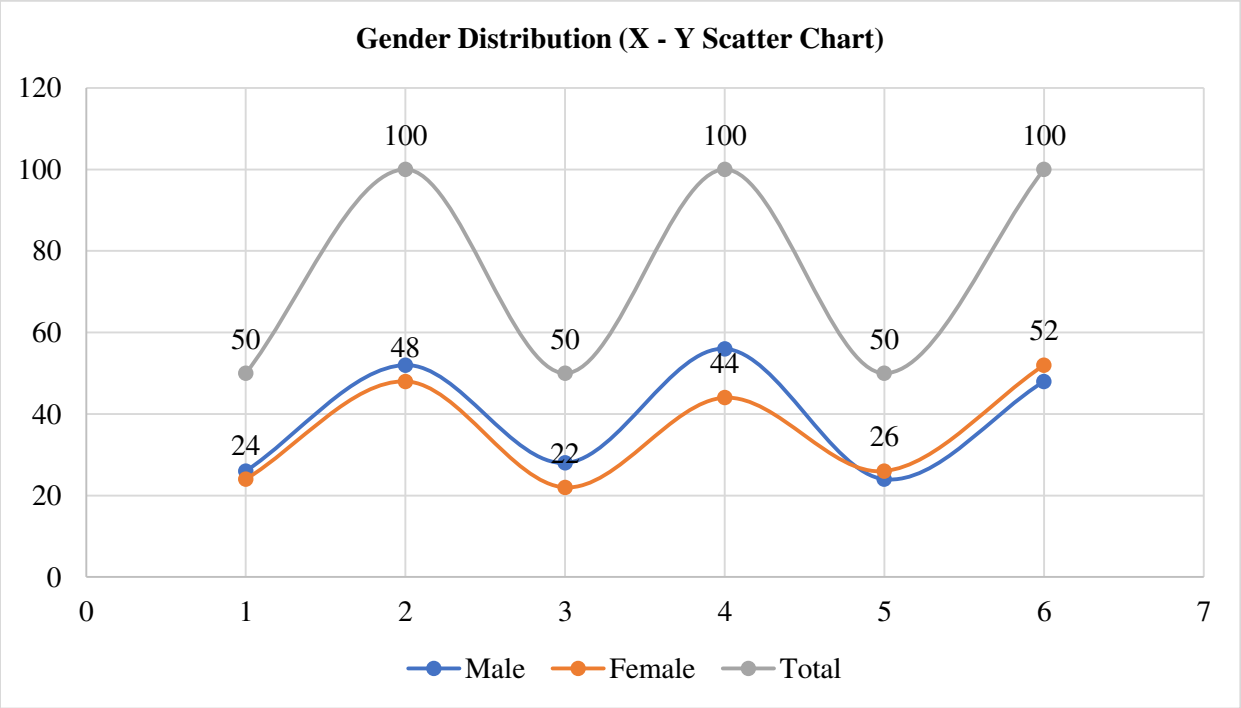


Table – II: Study Group Characteristics

Variables	Controls (50)		Impaired fasting glycemic (50)		Known type 2 diabetics (50)	
	Mean	± SD	Mean	± SD	Mean	± SD
Age (years)	51.9	4.8	52.2	4.9	53.3	4.6
Systolic BP (mm Hg)	115	11.7	122	14.4	123.1	15.6
Diastolic BP (mm Hg)	76.9	7.8	78.8	11.4	80.1	9.5
Weight (kg)	63.9	9.3	69	8.9	72.4	11.1
Height (cm)	163.9	9.7	165.9	9.1	164.7	9.6
BMI (kg/m^2)	23.6	2.9	25.5	3	26.5	3.6

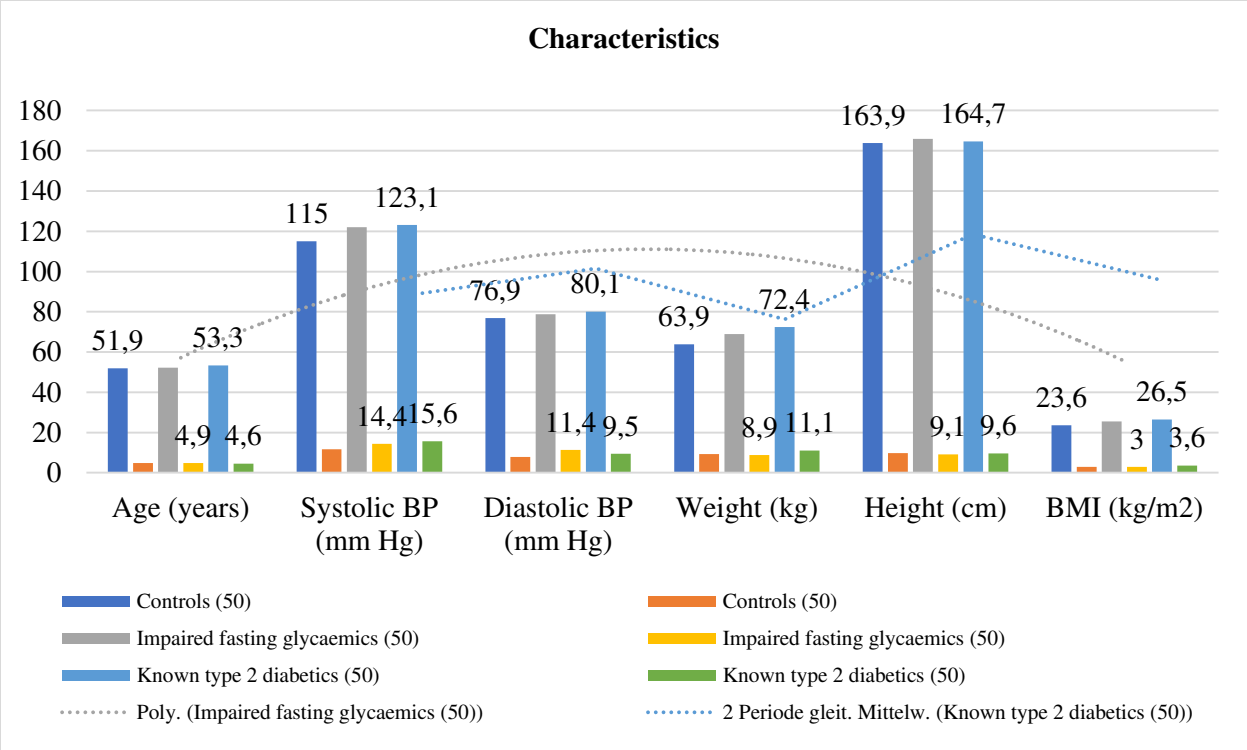
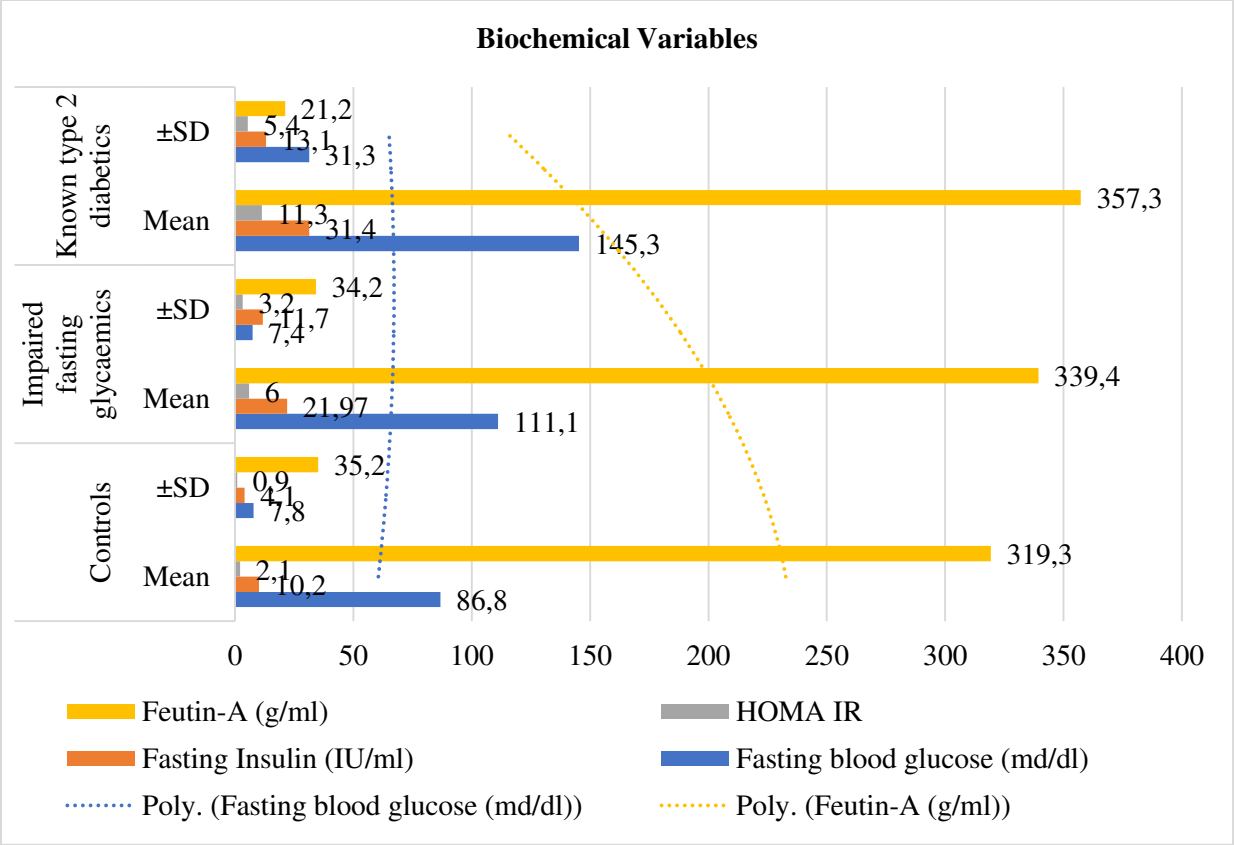


Table – III: Biochemical variables

Variables	Controls		Impaired fasting glycemic		Known type 2 diabetics	
	Mean	±SD	Mean	±SD	Mean	±SD
Fasting blood glucose (md/dl)	86.8	7.8	111.1	7.4	145.3	31.3
Fasting Insulin (IU/ml)	10.2	4.1	21.97	11.7	31.4	13.1
HOMA IR	2.1	0.9	6	3.2	11.3	5.4
Feutin-A (g/ml)	319.3	35.2	339.4	34.2	357.3	21.2



DISCUSSION:

CVD and diabetes are very much depending on the development of insulin resistance [15]. Numerous factors such as cytokines and fatty acids are influential in the signalling of molecules of insulin through so many other ways having interference with the signalling pathway of the insulin [16]. It is also considered that Fetuin-A is involved in the insulin resistance pathogenesis [17]. No research has been conducted in the comparison of T2DM, IFG and controls for the comparison of the level of Fetuin-A serum in our country. We aimed to determine Fetuin-A role in the initiation of resistance of insulin that ultimately leads to T2DM (Type II Diabetes Mellitus) development. It was observed in the outcomes that concentrations of the Fetuin-A serum were more in the T2DM cases than IFG and healthy patients. Insulin action is inhibited through level of serum Fetuin-A on target tissues as it interacts with the receptors of insulin [18].

Various research studies have prospectively investigated the relationship between diabetes risk and level of Fetuin-A. In the six years' follow-up these research studies have reflected the association between diabetes and Fetuin-A [11]. An author also discovered in his seven-year prospective follow up research that increased diabetes risks are associated with the incidence of increased level of Fetuin-A serum, these patients were observed with increased level of glucose which was not in the range of diabetes [19]. Future diabetes can be caused because of higher level of Fetuin-A and in the IFG cases as established. Whereas, Mori has observed no variation in the difference between non-diabetic and diabetic cases in terms of Fetuin-A level. Protein modification and glucose toxicity may be one of the reasons behind this hypothesis which may overcome the Fetuin-A effect on resistance of insulin. Diabetes development is also associated with the incidence of obesity. We also observed that in this particular research BMI of the T2DM and IFG cases was higher than the healthy patients considered as control. Our outcomes are comparable with the outcomes of Ishibashi and Stefan [19, 20]. It can also be deduced from the research outcomes that an increased rate of BMI in the T2DM cases and IFG patients may also contribute in the elevation of the level of Fetuin-A that as a result initiates the insulin resistance.

Outcomes about increased HOMA-IR levels are comparable with the outcomes of Jung et al. about T2DM and IFG cases and also in the control group [21]. These outcomes also second the involvement of

Fetuin-A in insulin resistance pathogenesis.

CONCLUSION:

The concentration of Fetuin-A is increased in T2DM and IFG than controls. Fetuin-A may have an association with the resistance of insulin and it may also have a part to play in the T2DM pathogenesis. These outcomes with the previous animal and human studies also increase the chances of the Fetuin-A being a potent therapeutic target in the management of T2DM. Moreover, large sample size prospective research studies may also help in the establishment of the relation between T2DM development and levels of Fetuin-A.

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