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Evaluation of Some Prominent Biomarkers in Rural Type – 2 Diabetes mellitus Cases in Kanyakumari District, Tamil Nadu, India

Murugan. A., Jerlin Nirmala. F.

Abstract**—**Life is beautiful. But, it is decided by genes, environment and the individual and shattered by the natural and / or the invited problems. Most of the global rural helpless masses are struggling for their survival since; they are neglected in all aspects of life including health. Amidst a countless number of miserable diseases in man, diabetes is becoming a dreaded killer and ramifying the entire globe in a jet speed. Diabetes control continues as a Herculean task to the scientific community and the modern society in the 21st century also. T_2DM is not pertaining to any age and it can develop even during the childhood. This multifactorial disease abruptly changes the activities of certain vital biomarkers in the present rural T_2DM cases. A remarkable variation in the levels of biomarkers like AST, ALT, GGT, ALP, LDH, HbA_1C, C- peptide, fasting sugar, post-prandial sugar, sodium, potassium, BUN, creatinine and insulin show the rampant nature of T_2DM in this physically active rural agrarian community.

Keywords**—**Alanine aminotransferase, Aspartate aminotransferase, Blood urea nitrogen, Glycated haemoglobin, Thyroid stimulating hormone

I. Introduction

DIABETS, a mundane problem [1] is marching towards an unstoppable speed [2]. Environmental, genetic factors [3], environmental mechanism [4] and maternal transmission [5], [6] are found to be the main risk factors of this metabolic disorder. Diabetes control continues as a cumbersome task to the modern world also.

This multifactorial disease abruptly changes the activities of certain vital biomarkers in the present rural Type – 2 diabetes mellitus (T_2DM) cases. Biomarkers are circulating molecules, proteins, enzymes, whose levels provide independent diagnostic (or) prognostic value for an underlying disease state (or) complications thereof [7].

Analyses of appropriate biomarkers are more likely to provide useful information to optimize these biochemicals in the diseased subjects. The present study is to try to understand the levels of certain prominent safety molecular biomarkers such as transaminases, alkaline phosphatase (ALP), lactate dehydrogenase (LDH), glycated haemoglobin (HbA1C), C-peptide, creatinine, blood urea nitrogen (BUN), insulin, etc. , which can be advocated to monitor the disease status as well as to avoid the disease, diabetes.

Murugan. A, Associate Professor in Zoology, S.T. Hindu College, Nagercoil -629002, Tamil Nadu, India. Phone: +9104652 261879, email: dr.a.murugan@gmail.com

Jerlin Nirmala. F. is Ph.D., Student in Department of Zoology, S.T. Hindu College, Nagercoil -629002, India

II. Materials and Methods

A. Study area

The present study on the evaluation of biomarkers in rural T_2DM cases is undertaken in Kanyakumari District, the southern terminus of the Indian sub-continent [8].

B. Study subjects

"Nanjil Nattu Vellala", the study population is an agrarian, endogamous, native, non-vegetarian, forward caste, Hindu community settled across the eastern parts of Kanyakumari district. The word "vellam" (water) and "anmai" (management) means cultivation (or) tillage [9]. The study covers a sizable number of 80 subjects, which includes 40 males and 40 females of age between 19-60 yrs, who are settled near the coastal, plain and hilly areas with a spread of more than 40 km distance (on road). The control (non-diabetics) and experimental (diabetics) subjects are age and area matched.

Screening of diabetics are followed by the method described [10]. Standard methods are ***used*** for the estimation of serum insulin [11], sugar (fasting and post-prandial) [12], C-peptide [13], HbA_1C [14], AST [15], ALT [16], GGT [17], ALP [18], LDH [19], BUN [20], creatinine [21], sodium [22], [23] and potassium [22], [23]. Statistical analyses are made with SPSS statistical package (version 11) [24]. Priority has been given to human values during blood collection and Ethics Committees' guidelines have been strictly followed.

III. Results

To understand the age and sex related variations of biomarkers in the study subjects, two age-groups (i.e.) 19 - 39 yrs (lower age) and 40 – 60 yrs (higher age) of both sexes are selected. Various biomarkers such as blood glucose (fasting and post-prandial), insulin, C – peptide and HbA_1C levels in the serum (fasting) are analyzed as an essential measure of the health of the study subjects and are shown in Table I.

TABLE I
EXPLAINS SOME OF THE VITAL PARAMETERS OF GLYCAEMIC CONTROL IN THE STUDY SUBJECTS (N= 80 SUBJECTS; 10 MALES + 10 FEMALES IN EACH CATEGORY) (VALUES ARE ± SD)

Parameters	Age-group (yrs)	Sex	Non-diabetics (control)	Diabetics (experimental)
Sugar *1(fasting)	19 – 39	Male	92 ± 9.8	181.4 ± 51.23
		Female	86.5 ± 8.67	160.2 ± 44.99
	40 - 60	Male	96.8 ± 3.92	178.1 ± 69.13
		Female	95.8 ± 9.53	180.5 ± 68.84

Sugar * [1](post-prandial)	19 – 39	Male	97.8 ± 12.54	145.6 ± 10.95
		Female	100.4 ± 13.26	232.9 ± 59.28
	40 - 60	Male	96.6 ± 7.86	146.2 ± 9.93
		Female	102.4 ± 13.29	234.9 ± 58.48
[2]Insulin*	19 – 39	Male	35.28 ± 0.57	19.55 ± 1.79
		Female	35.3 ± 0.49	19.75 ± 1.26
	40 - 60	Male	35.27 ± 0.72	17.06 ± 2.11
		Female	35.47 ± 0.73	16.12 ± 1.91
[3]C – peptide*	19 – 39	Male	0.43 ± 0.19	1.0 ± 0.34
		Female	0.44 ± 0.12	0.79 ± 0.25
	40 - 60	Male	0.48 ± 0.18	2.17 ± 1.17
		Female	0.44 ± 0.17	2.48 ± 1.28
[4]HbA1c*	19 – 39	Male	5.52 ± 0.51	7.46 ± 0.5
		Female	5.49 ± 0.59	7.92 ± 0.72
	40 - 60	Male	5.66 ± 0.59	9.36 ± 1.21
		Female	5.64 ± 0.64	9.42 ± 1.23

Units: mg /dL[1]; µIU / ml[2]; ng / ml[3]; %[4] t values: non-diabetics Vs diabetics P: < 0.01 highly significant*

Analyses revealed that, there is an appreciable level of increase of fasting sugar (i.e.) 97% in males and 85% in females of 19-30 yrs diabetics than the controls, while the increase is 85% in male and 88% in female diabetics of 40 – 60 yrs.

A notable level of increase of serum post-prandial sugar is also found in the diabetics than the controls. It is 49% in male and 132% in female diabetics of 19-39 yrs and 51% in male and 129% in female diabetics of 40 – 60 yrs.

A remarkable level of increase of C-peptide (i.e.) 133% in male and 79% in female diabetics of 19 – 39 yrs is seen, where as it is 352% in male and 464% in diabetic females of 40-60yrs than their respective controls.

A sizable level of increase of HbA_1C is there in diabetics than the controls. In 19 – 39 yrs males it is 33% and in females it is 44%, but in 40 – 60 yrs it is 65% in males and 67% in females.

Table II shows that there is an enhanced level of AST,ALT, GGT, ALP and LDH in both male and female patients of lower and higher age-groups than their respective controls. In male patients, we can see an increase of about 32% in 19 – 39 yrs age-groups and 49% in 40 – 60 yrs age subjects, where as it is 55% in diabetic females of 19 – 39 yrs age and it is 49% in 40 – 60 yrs old females. Moreover about 25% hike of ALT is seen in males of lower and higher age-groups, but it is 24% and 23% in females of lower and higher age-groups respectively.

Gammaglutamyl transferase (GGT) activity is 80% in male and 84% in diabetic females of lower age-group, but it is 37 % in males and 18% in female patients of higher age-group. ALP activity is about 47% in male and 37% in female patients of 19-39 yrs age-group, likely it is about 50% in male and 39% in female diabetics of higher age-group.

It is found that LDH activity is 24% in males and 23% in female diabetics of lower age-group and 22% in male and 23% in diabetic females of higher age-group.

TABLE II
REVEALS SOME POTENTIAL BIOMARKERS RELATED TO LIVER FUNCTION.
(N = 80 SUBJECTS; 10 MALES + 10 FEMALES IN EACH CATEGORY)
(VALUES ARE ± SD)

Biomarkers	Age-group (yrs)	Sex	Non-diabetics (control)	Diabetics (experimental)
[1]AST*	19 – 39	Male	30.8 ± 4.69	40.8 ± 5.31
		Female	26 ± 5.14	40.4 ± 5.04
	40 - 60	Male	29.8 ± 3.49	40.8 ± 4.28
		Female	27.6 ± 5.1	41.1 ± 3.45
[2]ALT*	19 – 39	Male	32.3 ± 1.49	40.5 ± 4.45
		Female	32.2 ± 1.25	40.0 ± 3.79
	40 - 60	Male	34.1 ± 2.17	42.8 ± 3.63
		Female	34.4 ± 2.33	42.5 ± 3.32
[3]GGT*	19 – 39	Male	17.1 ± 4.16	30.8 ± 6.57
		Female	16.6 ± 3.61	30.5 ± 4.8
	40 - 60	Male	26.6 ± 2.2	33.6 ± 5.14
		Female	28.0 ± 1.67	33.0 ± 5.1[S]
[4]ALP*	19 – 39	Male	179.4 ± 28.97	264.1 ± 11.89
		Female	191.2 ± 13.95	261.7 ± 6.71
	40 - 60	Male	176.3 ± 30.32	263.8 ± 9.82
		Female	189.0 ± 25.32	263.4 ± 7.94
[5]LDH*	19 – 39	Male	365.4 ± 48.44	455.0 ± 20.62
		Female	369.5 ± 41.01	454.5 ± 13.86
	40 - 60	Male	371.6 ± 36.47	455.5 ± 25.83
		Female	372.0 ± 31.64	459.0 ± 19.21

Units : IU / L[1-5] t values : non-diabetics Vs diabetics P: < 0.01 highly significant*; 0.01 – 0.05 significant [S]

It is evident from the Table III that only a marginal level of increase of sodium (i.e.) 4% is noticed in lower and higher age-group diabetic males and females. A noticeable level of increase of serum potassium is found in diabetic males and females of lower and higher age-groups. The increase is around 17% in lower age-group diabetics, but it is 20% in 40 – 60 yrs old diabetics of both sexes.

A remarkable level of increase of BUN is detected in diabetic male and females of lower and higher age-groups. It is around 99% in males and 95% in females of lower age-group and 102.1 % in males and 84.9 % in females of higher age.

A narrow increase of creatinine is observed in diabetics of both sexes and age-groups. In lower age-group males it is 24% and in females it is 29%, while the percentage increase is around 14 in males and 33 in female patients of higher age-group than the control.

TABLE III
EXPLAINS SOME PROMINENT SERUM BIOMARKERS RELATED TO KIDNEY FUNCTION. (N = 80 SUBJECTS; 10 MALES + 10 FEMALES IN EACH CATEGORY) (VALUES ARE ± SD)

Bio markers	Age-group (yrs)	Sex	Non-diabetics (control)	Diabetics (experimental)
[1]Sodium*	19 – 39	Male + Female	140.5 ± 0.92	146.2 ± 0.98
	40 - 60	Male+ Female	143 ± 1.34	149.3 ± 0.9
[2]Potassium*	19 – 39	Male+ Female	4.12 ± 0.1	4.94 ± 0.09
	40 - 60	Male + Female	4.3 ± 0.08	5.18 ± 0.14
[3]BUN*	19 – 39	Male	8.4 ± 1.43	16.7 ± 2.65
		Female	8.7 ± 1.62	17 ± 2.28
	40 - 60	Male	9.7 ± 1.55	19.6 ± 3.2
		Female	10.6 ± 1.91	19.6 ± 2.33
[4]Creatinine*	19 – 39	Male	0.71 ± 0.06	0.88 ± 0.12
		Female	0.69 ± 0.04	0.89 ± 0.12
	40 - 60	Male	0.79 ± 0.09	1.0 ± 0.15
		Female	0.76 ± 0.07	1.01 ± 0.12

Units : m mol /L[1,2]; mg / dL[3,4] t values : non-diabetics Vs diabetics P: < 0.01 highly significant*

IV. Discussion

Diabetes is a mundane problem and India is the leading partner to this disease. It has become an epidemic in India [25] and it reaches its peak with the highest prevalence [26]. A rapid alarming rate of prevalence of diabetes is noticed in the entire globe [1],[2] . It is recognized as one of the leading causes of death and disability worldwide [25].

Insufficient levels of insulin [27] results in hyperglycemia because of disordered metabolism. A drastic level of decrease of insulin hormone and followed by the increase of fasting and post-prandial sugar is well marked in our male and female diabetics of both lower and higher age- groups.

A statistically highly significant (P = < 0.01) low insulin and higher fasting and post-prandial sugar values are obtained in our diabetic subjects than their respective non-diabetic counterparts.

C-peptide levels are measured instead of insulin levels because; insulin concentration in the portal vein ranges from 2 – 10 times higher than in the peripheral circulation. Elevated level of C-peptide is reported by earlier researchers [28], [29].

In the present study too a remarkable level of increase of C-peptide is noticed which is statistically highly, significant (P = < 0.01).

HbA_1C levels depend on the blood glucose concentration (i.e.) the higher the glucose concentration in blood, the higher the levels of HbA_1C. Reports say diabetics with HbA_1C within the range have a significantly low incidence of complications [30], [31].

The presence of more HbA_1C level in the fasting serum in our study subjects reveals the poor glycaemic control in this survey group (P = < 0.01).

Elevated levels of ALT [32], AST [33], ALP [34], GGT [35] and LDH [36] indicate liver problems. In the present study except ALP, these marker enzymes of the liver function are noticed in an enhanced level in our subjects and the values are statistically highly significant (P = <0.01) against their respective controls.

A BUN of over 20 mg / dL is an indicator of decreased kidney function [37]. In our study, even though BUN values in the diabetics are within the range, there is a vast increase of this values in this group compared to the non-diabetic group (P = < 0.01). One study reveals the higher age and female sex specific increase of BUN values [38] and it is true in our study also.

Serum creatinine is the most commonly used indicator for renal function. One report says that, a higher serum creatinine level is associated with an increased risk for the development of T_2DM [39]. Our diabetic subjects also show a higher creatinine values which are statistically highly significant against their controls.

An elevated level of serum sodium [39] and potassium [40] in diabetics are reported by previous studies also. A slightly elevated level of serum sodium and potassium in our diabetic patients indicates that the quantitative expression of these biochemicals is noticed in accordance with the pathological conditions of the patients.

V. Conclusion

Individuals with T_2DM have a higher incidence of liver function, kidney function abnormalities, elevated levels of fasting sugar, post-prandial sugar, C-peptide, HbA_1C and decreased level of insulin reveals poor glycaemic control in diabetic subjects especially females.

Bio-chemical analyses of certain specific biomarkers reveal the extent of impact of diabetes on these agents due to the various pathological manifestations associated with diabetes. Mild chronic elevation of transaminases often reflects the underlying insulin resistance. Except ALP, elevated levels of various biomarkers in our elderly patients than the younger cases are useful additional measures in identifyin0g those at high risk of diabetes, however it should be further confirmed with large scale studies.

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