PUB: 16/2014

International Journal of Biochemistry. Photon 195 (2014) 352-360
https://sites.google.com/site/photonfoundationorganization/home/international-journal-of-biochemistry
Original Research Article. 4438-5728

International Journal of Biochemistry Photon

Evaluation of HbA_1c, Fasting insulin and Lipid profile in the assessment of Diabetic Nephropathy in Type 2 diabetes Mellitus in Males: A rural Hospital Study

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The authors receive Thomas Edison Award-2014 in Biochemistry for Inspiration and Knowledge Distribution among young research scholars.

Article history:
Received: 21 November, 2013
Accepted: 28 November, 2013
Available online: 10 February, 2014

Key Message:
The farmers here are constantly exposed to insecticides and pesticides. This chronic exposure to pesticides and effect on protein peptide insulin needs further evaluation at the molecular level, where not only insulin but other proteins could have been damaged or the coding genes might have been mutated.

Keywords:
Diabetic Nephropathy, Fasting Insulin, HbA_1c

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Abstract
Worldwide diabetic nephropathy (DN) is the leading cause of end stage renal disease, prompting for increased renal replacement therapy in these patients. Most studies conducted till now in Type 2 Diabetes Mellitus (T2DM) are in urban population. There's scarcity of the data regarding occurrence of diabetic complications in a rural setting and increasing trend of non-communicable diseases. Present study focuses on anthropometric and glycemic variability in males in a rural tertiary setting. All the anthropometric and biochemical parameters were assessed by standard methods. The analysis showed forty five subjects were found to be suffering from DN. Screening of T2DM and monitoring for incipient DN would benefit the rural population who are in their "golden years of life" and contribute towards the country's economy in a major in an agrarian nation like India. This dictates the comprehensive evaluation of anthropometric and biochemical evaluation of males aged 55 years and above in conjunction with clinical assessment for improving the renal outcome of patients with diabetes mellitus. In this study only rural setting was considered where people's occupation is agriculture and depends on monsoon rains, effect on the seasonal variation on the availability of food and its effect on nutrition should be kept in mind.

Citation:
Munilakshmi U., Shashidhar K.N., Harish R., Reddy M., Lakshmaiah V., 2014. Evaluation of HbA_1c, Fasting insulin and Lipid profile in the assessment of Diabetic Nephropathy in Type 2 diabetes Mellitus in Males: A rural Hospital Study. International Journal of Biochemistry. Photon 195, 352-360.

1. Introduction

Diabetes mellitus (DM) a group of metabolic diseases characterized by hyperglycemia results from defects in insulin secretion, insulin action or both. DM is not only known to constitute 5% of global death annually, but also associated with long term damage, dysfunction and failure of various organs mainly the eyes, kidneys, nerves, heart and blood vessels (Taloyan et al., 2009).

With increased industrialization, endi stage renal disease (ESRD) in patients with diabetic nephropathy (DN) has become a major medical challenge for experts and major financial burden for the patients (Taloyan et al., 2009).

Known risk factors for the onset of diabetic nephropathy are (1) genetic predisposition

(indicated by a history of hypertension and cardiovascular events in first-degree relatives), (2) quality of glycemic control, (3) level of blood pressure, and (4) smoking. Among these, the strong risk factor for nephropathy in type 2 diabetic males was smoking. According to several studies elevated urinary albumin excretion rates (AER) at the time of diagnosis of type 2 diabetes are significantly more frequent in smokers than in non-smokers (Olivarus et al., 1993).

Kidney, being one of the target organs for action of insulin, undergoes flow and pressure changes at glomerular level due to chronic hyperglycemia ultimately resulting in Diabetic Nephropathy.

Glycated hemoglobin (HbA_1c) is a well-known marker for long-term glycemic control. It indicates mean blood glucose levels and predicts the risk for developing complications in diabetic population (Mahato et al., 2011). Along with dyslipidemia, elevated HbA_1c is regarded as risk factor for cardiovascular disease (CVD) with or without DM. In diabetic population for every 1% increase in absolute HbA_1c risk of CVD was increased by 18% (Selvin et al., 2004).

Hyperlipidemia is common in patients with renal failure. In addition, atherogenic changes in lipoprotein composition occur in most of these patients (Massy et al., 1996). It has long been hypothesized that lipoproteins play a role in renal injury similar to their established involvement in atherosclerosis. A number of experimental investigations have provided relevant evidence that lipids may contribute to progressive renal damage (Keane et al., 1994). However, there are only a few prospective studies that have addressed a possible relationship between dyslipidemia observed in patients with renal failure and the rate of progression in kidney disease (Hunsicker et al., 1997). Hence the present study was undertaken to investigate glycated hemoglobin (HbA_1c), fasting insulin and total lipid profile in the assessment of diabetic nephropathy in type 2 diabetes mellitus of male patients.

2. Subjects and Methods

Eighty six Type 2 Diabetes Mellitus males and non-diabetic male subjects with a median age of 56 years visiting R L Jalappa hospital attending Medicine Out Patient Department attached to Sri Devaraj Urs Medical College, Kolar, India from October 2011 to January 2012 were included in the study. Exclusion criteria comprised of Type 1 diabetes mellitus, peripheral vascular disease, acute or chronic infection, cancer, hepatic disease, myocardial infarction. The study was approved by institutional ethical committee who provided ethical clearance and a written informed consent was obtained from all the participants.

Anthropometric measurements such as: age, gender, body weight, height, body mass index (BMI), waist circumference (WC), hip circumference (HC), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were noted. Anthropometric measurements were measured with standard scale and measuring tape and all units of measurements were expressed in SI units. Patient weight and height were measured to the nearest 0.1 kg and 0.1 cm respectively. BMI was calculated by Quelet index formula (Ashwell et al., 1982), WC was recorded as the smallest girth between the rib cage and the top to the lateral border of the iliac crest during the minimal respiration. SBP and DBP were measured in all subjects in the supine position, inflating the cuff tied at the level of heart to the left arm after confirming that the patient was in the relaxed state.

Biochemical parameters were measured after an overnight fast, and the parameters were estimated using Johnson & Johnson vitros 250 dry chemistry auto analyzer which works on the principle of reflectance Photometry. However the biochemical values we have estimated in our study were analyzed only after confirming with Internal Quality Assurance Scheme (IQAS) by using Bio-Rad lyophilized serum sample and all the parameters were within ± 2 Standard Deviation. The blood glucose estimation was done by Glucose Oxidase Peroxidase method (GOD-POD) (Edmund Lamb et al., 1999), glycated hemoglobin was estimated by HPLC, serum creatinine was estimated by jaffes test (Lamb et al., 1999), uric acid estimation by uricase method (Lamb et al., 1999), total cholesterol was estimated by cholesterol oxidase-peroxidase method (Lamb et al., 1999), triglycerides estimation was done by Enzymatic colorimetric test- GPO PAP (Lamb et al., 1999), HDL cholesterol estimation was done by poly anion precipitation method (Lamb et al., 1999). LDL-c, Non-HDL-Cholesterol, eGFR and VLDL was calculated (Lamb et al., 1999, Holewijn et al., 2010, Levy et al., 1990). Spot urine albumin was estimated by sulfo-salicylic acid method, urine creatinine by jaffes method and albumin:

creatinine ratio was calculated (Waugh et al., 2003).

Value of HbA_1c was given as percentage of total haemoglobin and values of all other parameters were given in mg/dl. Dyslipidemia was defined by presence of one or more than one abnormal serum lipid concentration. Diabetes was defined as per American Diabetes Association (ADA) criteria (ADA suppl., 2011). The data was evaluated by SPSS statistical package version 16.0. Independent 't'test (2-tailed) was used to compare means of different parameters.

All values are expressed as mean ± standard error of mean. The results were considered significant with p-value < 0.05.

3. Results

With respect to the Anthropometric measurements (Table: 1) the mean age (56 years), height (166.19 cm), weight (67.64 kg), WC (96.05 cm), HC (94.97 cm), WHR (1.01) in diabetic males and in non-diabetic male subjects are age (57 years), height (164.84 cm), weight (69.74 cm), WC (94.60 cm), HC (97.22 cm), WHR (0.97) was observed respectively. Among these variables only WC and WHR were statically significant. The mean SBP in diabetic males was 128 ± 4.64 mm Hg and in non-diabetic males was 124 ± 15.76 mm Hg and the mean DBP in diabetic and non-diabetic males was 80 mm Hg and 82 mm Hg respectively which was statistically significant (p=0.02).

With respect to the biochemical parameters (Table: 2) significant difference were observed between diabetic and non-diabetic males with FBS 143 mg/dl in diabetic males and 99.80 mg/dl in non-diabetic males, percentage of HbA_1c in diabetic males was 10% and 6% in non-diabetic male subjects, Fasting Insulin in diabetic males 20.51 mcU/ml and in non-diabetic males was 12.21 mcU/ml. The insulin resistance or receptor defect

or may be due to nephropathy the insulin levels might have increased in diabetic males compared to non-diabetic male subjects. The SCr was 1.17 mg/dl and 0.1 mg/dl in diabetics and non-diabetic males respectively. We also estimated uric acid in both study groups and the levels were slightly higher in diabetic males (5.36 mg/dl) compared to non-diabetic male subjects (5.22 mg/dl). However it was not statistically significant. With respect to lipid profile the mean values of HDL-c (37.20 mg/dl) in diabetic males and (36.34 mg/dl) in non-diabetic male subjects which was statistically significant (p=0.005). The TG levels, TC and LDL-c levels were lower in diabetes compared to non-diabetes with no significant difference. However to what extent their dietary habits, life style modifications etc. would have led to reduced LDL-Cholesterol and Total Cholesterol has to be considered. But, whatever the LDL value we have observed in our study is true to the fact that there is no selection bias or calculation bias, and moreover we have considered the limitations of Friedewald equation.

We have also estimated Spot urine creatinine, in diabetic males it was 63.09 mg/dl and non-diabetic males was 89.96 mg/dl. This observation has shown that there is increased excretion of creatinine in urine in diabetics compared to non-diabetic males. We also compared the spot urine creatinine and spot urine albumin and the ratio between these were statistically significant (p=0.000). The values obtained for the parameters (Table: 3): LDL-c, Non-HDL-c, VLDL and eGFR was calculated using the formulas; we observed slightly decreased levels of Non-HDL-c in diabetic males (128.97 mg/dl) compared to non-diabetic male subjects (150.66 mg/dl) with a non-significant p-value.

Table 1: Showing the comparison of parameters between diabetic and non-diabetic males

Parameters	Diabetes	Non diabetes	p value
Age (years)	56.01±0.76	57.74±13.55	0.18
Height (cm)	166.19±7.96	164.84±14.47	0.13
Weight (kg)	67.64±10.83	69.74±15.63	0.10
Waist circumference (cm)	96.05±11.05	94.60±8.01	0.00**
Hip Circumference (cm)	94.97±9.55	97.22±9.19	0.71
Waist Hip Ratio	1.01±0.13	0.9784±0.09	0.01*
Systolic BP (mmHg)	128.67±4.64	124.60±15.76	0.67
Diastolic BP(mmHg)	80.74±11.24	81.01±9.13	0.02*
Obesity Index	66.18±7.96	64.83±14.47	0.13
Body Mass Index	24.47±3.51	28.63±33.73	0.12

* considered as significant p-value (< 0.05), ** <0.001considered as strongly significant

Table 2: Showing the comparison of biochemical parameters between diabetic and non-diabetic male subjects

Parameters	Diabetes	Non-diabetes	p value
FBS (mg/dl)	143.74±72.98	143.74±72.98	0.002*
Fasting Insulin	20.51±36.80	12.21±10.60	0.001**
HbA_1c (%)	10.01±7.84	6.64±1.83	0.02*
SCr (mg/dl)	1.17±0.94	0.92±0.22	0.01*
Uric Acid (mg/dl)	5.36±5.97	5.22±1.30	0.25
Total Cholesterol (mg/dl)	166.17±40.36	187.00±40.47	0.69
Triglycerides (mg/dl)	208.64±152.01	217.01±113.94	0.41
HDL (mg/dl)	37.20±5.45	36.34±8.25	0.00**
Spot Urine Albumin (mg/dl)	716.5±056.88	174.57±238.17	0.00*
Urine Creatinine	63.09±54.42	89.96±115.19	0.17
Spot urine Alb/ creat ratio	29.34±72.54	2.91±4.50	0.00**

* considered as significant p-value (< 0.05), ** <0.001considered as strongly significant

Table 3: Showing the comparison of calculated biochemical parameters between diabetic and non-diabetic males

Parameters	Diabetes	Non-diabetes	p value
Non-HDL (mg/dl)	128.97±39.80	150.66±38.76	0.49
LDL (mg/dl)	86.76±35.65	105.78±33.68	0.95
VLDL (mg/dl)	45.89±59.91	43.63±22.82	0.08*
eGFR	97.03±29.17	87.03±32.10	0.28

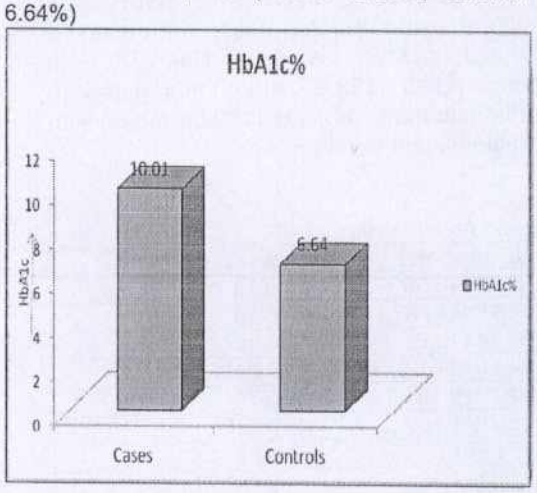
* considered as significant p-value (< 0.05)

The mean VLDL values in diabetic males was 45.89 ± 59.91 and 43.63 ± 22.82 in non-diabetic male subjects, the mean eGFR values in diabetic males 97.03 ± 29.17 and in non-diabetic males was 87.03 ± 32.10, where no significant difference was found between diabetic and non-diabetic males.

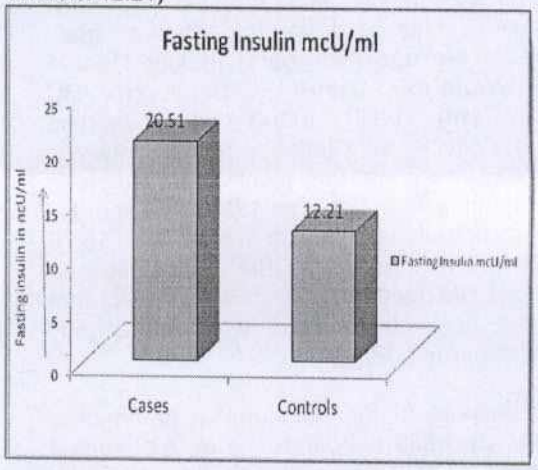
The biochemical parameters with significant p values are represented in the figures: 1, 2, 3 and 4.

Figures: Showing the significant parameters comparison between cases and controls of HbA_1c, Fasting Insulin, Serum Creatinine and HDL-cholesterol

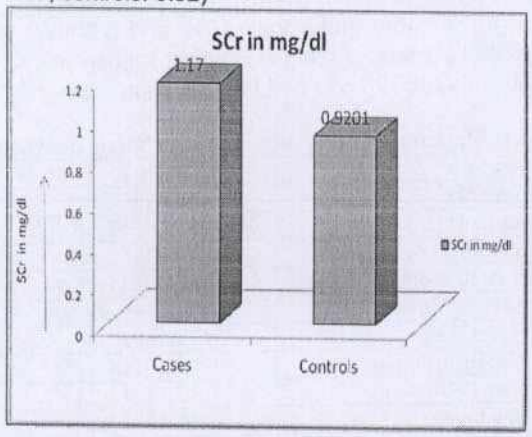
Figures 1: HbA_1c % (cases: 10.01%, controls: 6.64%)



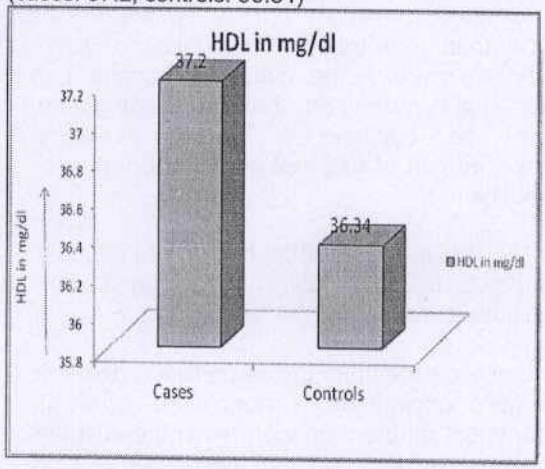
Figures 2: Fasting Insulin mcU/ml (cases: 20.51, controls: 12.21)



Figures 3: Serum Creatinine (SCr) mg/dl (cases: 1.17, controls: 0.92)



Figures 4: High Density Lipoproteins (HDL) mg/dl (cases: 37.2, controls: 36.34)



4. Discussion

Diabetes mellitus is a major public-health problem worldwide. Its prevalence is rising in many parts of the developing world, and India is no exception to this. India is the diabetes capital of the world with 41 million Indians having diabetes, every fifth diabetic in the world is an Indian (ADA suppl. 2011). Individuals with type 2 diabetes mellitus (T2DM) are considered on high priority as they are potential candidates for rapid evaluation to prevent and halt the progression of complications (Shashank et al., 2007). There is a high risk of renal disease in people with type 2 diabetes, Diabetic nephropathy occurs in 20-40% of patients with diabetes and is the single leading cause of end stage renal disease (ESRD) worldwide and is associated with increased cardiovascular risk (Berry et al., 2007).

The mean age in the present study among diabetic and non-diabetic males was 56 ± 10.76 and 57 ± 13.55 years respectively. According to (Krahulec and Vazar, 2009) most of the males in 40-60 years age group developed nephropathy. The incidence of nephropathy is seen to increase consistently with age (Krahulec and Vazar, 2009). In the present study WC of diabetic males 96.05 ± 11.05 cms is found to be higher than the non-diabetic males 94.60 ± 8.01 and was statistically significant. These results indicate that the risk of developing diabetes is certainly higher in male subjects with waist circumference 90 cms and above (Imran et al., 2013). Studies conducted by Wannamethee et al., 2010 showed WC and BMI are equal predictors of diabetes in men. In our study the mean BMI of diabetic males 24.47 ± 3.51 was lower than non-diabetics 28.63 ± 33.73; however, the result was not statistically significant. Significantly higher WHR was observed in diabetic males than non-diabetic males. Similar findings were observed by Shah et al. This shows that the risk of developing diabetes is higher with WHR >1.0 (Shah et al., 2009). In this study Obesity index of diabetic males was 66.18 ± 7.96 higher compared to non-diabetic individuals 64.83 ± 14.47; however, the results are not statistically significant.

The SBP observed in our study was not significant, even though it is more in diabetic males compared to non-diabetics. These results are similar to the observations by Phan et al., 2012. This showed that SBP helps to predict several Metabolic Syndrome components in males. One Component is an increase in WC, an obesity indicator, which manifests the strongest independent contribution to elevated SBP (≥ 120 mm Hg) in males (Phan et al., 2012).

Fasting insulin levels were elevated significantly in both diabetics and non-diabetic males but the levels were found within normal reference range. However, diabetic males showed increased insulin levels compared with non-diabetics; this suggests the early risk of insulin resistance and T2DM in obese individuals. We observed the mean HbA_1c level of diabetic males 10.01 ± 7.87 was more compared to non-diabetic males 6.64±1.83. Most of the type 2 diabetic patients experience poor glycemic control irrespective of their gender. Similar findings were observed by Mcance et al, this indicates nephropathy increased significantly with increase in HbA_1c (Rosediani et al., 2006; McCance et al., 1992). This is consistent with UKPDS (United Kingdom Prospective Diabetes Study) (Adler et al., 2003) study showed that microvascular complications were benefited by better control of blood sugar levels. Also, in accordance with the fact that diabetic nephropathy and blood pressure have a strong correlation and incidence of nephropathy increased significantly with increasing dyslipidemia (Bannerji et al., 1999).

Serum creatinine levels were significantly increased in diabetic males indicating the onset of the microvascular complications. However, the mean eGFR of diabetics was increased compared to non-diabetic male subjects and this could be due to hyper-filtration and hemodynamic factors rather than the metabolic factors in pathogenesis of diabetic nephropathy (Zat et al., 1999).

In our study we have observed slightly higher levels of uric acid in diabetic males than non-diabetic male subjects, which may suggest the presence of insulin resistance in T2DM. Elevated uric acid levels was a consistent feature of the insulin resistance syndrome, which are characterized by high plasma insulin levels, blood glucose concentrations and serum triglyceride concentrations and raised BMI and WHR (Bonora et al., 1999). In the present study the prevalence of microalbuminuria in diabetic subjects was statistically significant. Studies conducted by Bonora et al have reported an increased prevalence of microalbuminuria in men compared with women (Bonora et al., 1999; Johnsen et al., 2005). The causal risk factors for microalbuminuria are raised blood pressure, poor glycemic control, and older age, duration of diabetes, male sex and pre existing retinopathy. Microalbuminuria has also been reported to be associated with generalized vascular disease (Deckert et al., 1999).

Microalbuminuria in diabetics, which represents an earlier phase in the development of clinical nephropathy, is associated with many potentially modifiable risk factors. In estimating Diabetic nephropathy risk, AER (urinary Albumin Excretion Rate) is most important and should be done frequently but there are gains to be made in predictive precision by considering family history, smoking habits, glycemia, B.P., BMI and lipid levels (Faulkner et al., 2006).

Research Highlights

1. The study focuses on the glycemic variability in males in a rural tertiary setting.

2. There is an increasing trend of type 2 diabetes mellitus in rural setting which would as well be an iceberg phenomenon.

3. Screening of type 2 diabetes mellitus and monitoring for incipient diabetic nephropathy would benefit the rural population who are in their golden years of life and contribute towards the country's economy in a major in an agrarian nation like India.

4. This dictates the comprehensive evaluation of anthropometric and biochemical evaluation of males aged 55 years and above in conjunction with clinical assessment for improving the renal outcome of patients with diabetes mellitus.

Limitations

1. Comparing an adjacent urban cohort would elaborate more on the miniscule changes that might be occurring in the rural setting that might be tipping the balance towards increased risk of diabetes mellitus in the rural population.

2. Diet history and other habits which could contribute to the outcome should have been considered.

3. Since a rural setting was considered where people's occupation is agriculture which is dependent on the monsoon rains, the effect of seasonal variation on the availability of food and its effect on nutrition should be kept in mind.

4. The farmers here are constantly exposed to insecticides and pesticides. This chronic exposure to pesticides and the effect on the protein peptide insulin needs further evaluation at the molecular level where there not only insulin but other proteins could have been damaged or the coding genes might have been mutated.

5. In this study sample size is also small where the variations can be studied with larger population.

6. The gender specific glycemic variability should have been assessed by comparing with a group comprising of females.

Recommendations

1. Comparison with an urban cohort would throw light on the causal factors in a rural setting. Including females in the study would provide evidence of increased predisposition of males for diabetic nephropathy.

2. Genetic and molecular studies would provide a better understanding of the core of this issue.

Justification of Research

This study explores the iceberg of the microvascular complication of diabetic nephropathy in rural population males. Such a study is imperative for understanding the gender specific glycemic variability and it's on toward effect on progression of incipient nephropathy to overt diabetic nephropathy.

Justifying the Need of this Research and its Significance

1. Most studies conducted till now in type 2 diabetes mellitus are in the urban population. There's scarcity of the data regarding the occurrence of diabetic complications in a rural setting where recently there is an increasing trend of non-communicable diseases such as diabetes mellitus, hypertension, coronary heart disease and stroke.

2. This study looks for the gender specific glycemic variability. The males in a rural setting are heavy workers as against the sedentary lifestyles of urban dwellers. This would imply that obesity, insulin resistance and associated complications are less likely but however, there seems to be a probable effect of urbanization on the rural setting where the lifestyles are merging predisposing the rural males to type 2 diabetes mellitus and regardless of the geographical coordinates and socioeconomic status the screening of rural population should be done.

3. When the diagnosis of type 2 diabetes mellitus is established the strict follow-up should be done so that the microvascular complications can be detected early. The role of clinician and ophthalmologist should be given credit in conjunction with the biochemical markers of glycemic control.

4. This would be a milestone in management of type 2 diabetes mellitus and its associated complications especially diabetic nephropathy which would eventually progress to the fatal complication of end stage renal disease where the difference between urban and rural settings seems to be null.

Recommending how current policies need to be amended:

1. Insulin assays are limited by the expense and technical difficulties. Current policy making should incorporate mobilizing funds for these valid tests such as HbA_1c and lipid profile to be made available at level of primary care so that the complications of type 2 diabetes mellitus can be mitigated.

2. Health education programs towards creating awareness about the complications of types 2 diabetes mellitus and diabetic nephropathy would improve the patient compliance since in a rural setting patients are lost during follow-up due to various reasons like migration from place of stay, illness, other infirmities and superstitions in findings cure in alternative therapies which are usually practiced by unqualified persons.

3. Funding for studies at molecular level is needed for better understanding of the disease process so that early markers of acute kidney injury in diabetic nephropathy can be discovered and these biomarkers can make it from bench to bedside.

Conclusion

In conclusion, these data extend our understanding by showing that higher values of fasting insulin, HbA_1c, lipid profile with anthropometric measurements and other biochemical parameters were significantly associated with commonest complications seen in T2DM i.e., Diabetic nephropathy. It further predicts CVD mortality in patients with diabetic nephropathy. However, non-diabetic male subjects showed higher weight, HC, BMI, urine creatinine, TC and triglyceride and LDL-c levels. This suggests that above the age of 55 years of males requires comprehensive evaluation of anthropometric and biochemical parameters to avoid micro and macrovascular complications and Early screening for incipient diabetic nephropathy and aggressive management of these risk factors is important in optimizing the renal outcome of patients with diabetes mellitus.

Acknowledgement

Dr. Hemalatha A., Assistant Professor, Department of Pathology, SDUMC, Kolar, India.

Authors Contributions

Munilakshmi U: Concept and Design of the study, analysis and interpretation, manuscript preparation, critical revision of the manuscript, and literature search.
Shashidhar K.N: Concept and Design of the study, clinical studies, manuscript preparation, critical revision of the manuscript, data collection, statistical analysis, and literature search.
Harish R: Concept and Design of the study, Clinical studies manuscript preparation, critical revision of the manuscript, statistical analysis, and literature search.
Madhavi R: Data collection and analysis.
Lakshamiah V: Data acquisition.

Competing Interests

Nil

Financial Competing Interest

Nil

Details of Grants

Nil

References

Adler A.I., Stevens R.I., Manley S.E., 2003. Development and progression of nephropathy in type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS 64). Kidney Int. 63:225-232.

American Diabetes Association. Standards of medical care in diabetes - 2011. Diabetes Care 2011, 34(suppl 1), S11-12.

Ashwell M., Chinn S., Stalley S., Garrow J.S., 1982. Female fat distribution - a simple classification based on two circumference measurements. Int J Obes. 6,143-52.

Bannerji M.A., Faridi N., 1999. Body composition, visceral fat, leptin and insulin resistance in Asian Indian Men. J Clin Endocrinol Metab. 84:137-144.

Berry C., Tardif J.C., Bourassa M.G., 2007. Coronary heart disease in patients with diabetes: part I: recent advances in prevention and noninvasive management. J Am Coll Cardiol. 49, 631-642.

Bonora E., Targher G., Zenere M.B., Saggiani F., Cacciatori V., Tosi F., 1996. Rrelationship of uric acid concentration to cardiovascular risk factors in young men. Role of obesity and central fat distribution. The Verona Young Men Atherosclerosis Risk Factor Study. Int J Obes Related Metab Disord. 20, 975-980.

Deckert T., Rasmussen F., Jensen B., 1999. Albuminuria reflects widespread vascular damage: the steno hypothesis. Diabetologia. 32, 219-226.

Edmund Lamb, David J. Newman, Cristopher P. 1999. Serum creatinine estimation. Carl A. Burtis, editor. Teitz textbook of Clinical Chemistry Ana Molecular Diagnostics. New Delhi, Elsevier Publications, 798.

Faulkner M.S., Chao W.H., Kamth S.K., Quinn L., Fritschi C., Maggiore J.A., Williams R.H., Reynolds R.D., 2006. Total homocysteine, diet and lipid profiles in type 1 and type 2 diabetic and non-diabetic adolescents. J Cardiovasc Nurs. 21, 47-55.

Holewijn S., Heijer M., Swinkels D.W., Stalenhof A.F., Graaf J., 2010. Apolipoprotein B, non-HDL cholesterol and LDL cholesterol for identifying individuals at increased cardiovascular risk. J Intern Med. 268(6), 567-77.

Hunsicker L.G., Adler S., Caggiula A., 1997. Modification of diet in renal disease study group. Predictors of the progression of renal disease in the modification of Diet in Renal Disease study. Kidney Int. 51, 1908-1919.

Imran S.A., Lhoret R.R., Ross M.B., 2013. Targets for Glycemic Control. Canadian Diabetes Association Clinical Practice Guidelines. Can J Diabetes. 37:S31-S34.

Johnsen B., Kreiner K., 2005. Value as predictor of cardiovascular mortality in type 1 diabetes mellitus. Br. Med. J. 294, 1651- 1654.

Keane W.F., 1994. Lipids and the kidney. Kidney Int. 46:910-920.

Krahulec B., Vazar J., 2009. Incidence of risk factors and vascular complications in patients with newly diagnosed diabetes. Unit lek. 48:1031-8.

Levy A.S., Bosch J.P., Lewis J.B., 1990. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of diet in renal disease study group. Ann Intern Med. 130, 461-70.

Mahato R.V., Gyawali P., Raut P.P., Regmi P., Singh K.P., Pandeya D.R., Gyawali P., 2011. Association between glycemic control and serum lipid profile in type 2 diabetic patients: Glycated hemoglobin as a dual biomarker. Biomedical Research. 22(3), 375-380.

Massy Z.A., Kassiske B.L., 1996. Hyperlipidaemia and its management in renal disease. Curr opin Nephrol Hypertens. 5(2), 141-146

McCance D.R., Hadden D.R., Atkinson A.B., 1992. The relationship between long-term glycemic control and diabetic nephropathy. QJ Med. 82:53-61.

Moorhead J.F., Chan M.K., Nahas E.I., Varghese Z., 1982. Lipid nephrotoxicity in chronic progressive glomerular and tubule interstitial disease. Lancet. 1309(ii)-1311.

Olivarus N.F., Andreasen A.H., Keiding N., Mogensen C.E., 1993. Epidemiology of renal involvement in newly diagnosed middle-aged and elderly diabetic patients. Cross-sectional data from the population-based study 'Diabetes Care in General Practice'. Denmark Diabetologia. 36:1007–16.

Phan W.L., Wang J.U., Liu C.C., Pei D., Yen P., Hsu C.H., Chen Y.L., 2012. Systolic Blood Pressure as an Independent Predictor of Metabolic Syndrome in Male Adolescents. Acta Cardiol Sin. 28:111117.

Rosediani M., Azidah A.K., Mafauzy M., 2006. Correlation between fasting plasma glucose, post prandial glucose and glycated hemoglobin and fructosamine. Med J Malaysia. 61:67–71.

Shah A., Bhandary S., Malik S.L., Risal P., Koju R., 2009. Waist circumference and waist-hip ratio as predictors of type 2 diabetes mellitus in the Nepalese population of Kavre District. Nepal Med Coll J. 11(4), 261-267.

Selvin E., Marinopoulos S., Berkenblit G., Rami T., Brancati F.L., Powe N.R., 2004. Meta-analysis: glycosy-lated hemoglobin and cardiovascular disease in diabetes mellitus. Ann Intern Med. 14, 421-431.

Shashank R., Rakesh M., 2007. India - Diabetes Capital of the World: Now Heading Towards Hypertension. JAPI. 55, 323-324.

Taloyan M., Wajngot A., Johansson S.E., Tovi J., Sundquist K., 2009. Cardiovascular risk factors in Assyrians/Syrians and native Swedes with type 2 diabetes: a population-based epidemiological study. Cardiovascular Diabetology. 8:59.

Wannamethee S.G., Papacosta O., Whincup P.H., Carson C., Thomas M.C., Lawlor D.A., 2010. Assessing prediction of diabetes in older adults using different adiposity measures: a 7 year prospective study in 6,923 older men and women. Diabetologia. 53, 890-98.

Waugh J., Stephen C., Kilby M.D., Lambert P.C., Blackwell C.N., Shennan A., Halligan A., 2003. Urinary microalbumin/creatinine ratios. The Biochemical Society and the Medical Research Society. 104-107.

World Health Organization 2000. The Asia-Paci c perspective: rede ning obesity. World Health Organization: Geneva.

Zat Z.R., Mayer T.N., Rennke H.G., Brenner B.M., 1999. Predominance of hemodynamic rather than metabolic factors in the pathogenesis of diabetic glomerulopathy. Proc Nah Acad sci USA. 82, 5963-7.