 DOI: 10.18231/2394-6377.2016.0004

A comparative analysis of insulin resistance among tribal and non-tribal population with Type 2 Diabetes using estimated glucose disposal rate

Bibekananda Modak[1], Bulbul Purkait[2,*], RN Maity[3]

[1]PG Student, [3]Professor, Dept. of Pharmacology, [2]Associate Professor, Dept. of Biochemistry, Midnapur Medical College

***Corresponding Author:**
Email: bulbulpurkait@gmail.com

Abstract

Objectives: To compare the Insulin resistance among Type 2 Diabetics of the local tribal and nontribal population who are reporting to OPD of Midnapur Medical College and Hospital.

Method: This was a Unicentric, cross sectional, observational study.

Estimated Glucose disposal rate which is used to analyse Insulin resistance among Type 1 Diabetics, has been utilized for the same in type 2 Diabetics.

Result: A significantly larger proportion of male non-tribals had uncontrolled FPG (> 130 mg/dl), HbA_{1c} (both ≥ 8.5% and ≥ 7%), estimated glucose disposal rate less than lower limit (i.e. < 9 mg/kg/min) of the normal range, compared to the male tribals. Compared to the male tribals, a larger proportion of the male non-tribals had PPPG ≥ 180 mg/dl. A significantly larger proportion of female nontribals had uncontrolled PPPG, HbA_{1c} and estimated glucose disposal rate less than lower limit of the normal range, compared to the female tribals. Compared to the female tribals, a larger proportion of the female non-tribals had uncontrolled FPG.

Conclusion: Tribal Population with Type 2 Diabetes showed better achievement of Treatment goal.

Keywords: Type 2 Diabetes Mellitus, Insulin Resistance, Estimated Glucose disposal rate

Introduction

The human, social and economic consequences of Non Communicable disease(NCDs)are devastating in poor and vulnerable populations. Almost three quarters of all NCD deaths (28 million), and the majority of premature deaths (82%), occur in low- and middle-income countries. NCD deaths are projected to increase from 38 million in 2012 to 52 million by 2030. [*WHO 2014.]*

The prevalence of type 2 DM is highest in certain Pacific islands and the Middle East and intermediate in countries such as India and United States. The variability is likely due to genetic, behavioral and environmental factors.DM prevalence varies among different ethnic populations in our country, with indigenous population usually having a greater incidence of diabetes than the general population of the country. The national family health survey (NHFS-3) of 2005-06 had reported that the number of diabetic women per 1,00,000 population is 1641 in West Bengal (compared to the Indian national average of 881 women), and the number of diabetic men per 1,00,000 population is 2323 in West Bengal (compared to the Indian national average of 1051 men). It can be surmised that the reported morbidity and mortality of both type 1 and type 2 DM is increasing in the state of West Bengal; and the reported morbidity and mortality from type 2 DM is increasing much more rapidly compared to that from type 1 DM.

Insulin deficiency and insulin resistance are salient elements in the pathogenesis of typical type 2 DM and both contribute to the hyperglycemia. Insulin resistance is now being implicated as a factor in hypertension, dyslipidemia, ischemic heart disease apart from being a determinant of obesity in type 2 diabetes, [*Reaven, 1988*]

There have been numerous studies in the West establishing variation in insulin resistance among different ethnic groups, which have provided us with interesting insights about not only the diabetes pandemic, but also hinted at hitherto unknown aspects of pathophysiology of type 2 DM Compared to Caucasian children, South Asian children have increased plasma insulin in the setting of normal plasma glucose levels, an early sign of insulin insensitivity [*Whincup et al, 2002; Ehtisham et al, 2005*]. There is a higher percentage of body fat and higher insulin resistance for a given BMI in South Asian children and adolescents compared to their European counterparts *[International Diabetes Federation 2013.]*

Though the Indians belonging to low socioeconomic strata (SES) are generally leaner and have less incidence of type 2 DM than those with high SES, rural-to-urban migrants who belong to low SES are adversely affected and show several features of metabolic syndrome and multiple cardiovascular risk factors[*Misra, et al, 2002; Misra, et al, 2001*].

Homeostatic model assessment (HOMA) is a method for assessing β-cell function and insulin resistance (IR) from basal (fasting) glucose and insulin or C-peptide concentrations in type 2 DM. It has been reported in more than 500 publications, 20 times more frequently for the estimation of IR than β-cell function.

The insulin-glucose HOMA model cannot be used to assess β-cell function in those taking exogenous insulin. Under such circumstances, the C-peptide

HOMA model, which uses plasma C-peptide concentrations to reflect endogenous insulin secretion, could be used.

The use of HOMA to make comparisons across ethnic and cultural groups is valid, but one should not necessarily conclude that any population has a defect compared with another simply on the basis of finding a HOMA-%S that is lower. One would need to first establish the prevailing normal HOMA-%S from a normoglycemic population in each comparative group.

The euglycemic-hyperinsulinemic clamp is the accepted standard for measurement of insulin sensitivity in type 1DM however, it is not practical for use in the clinical setting. The estimated glucose disposal rate (eGDR) can be calculated using routine clinical measures: glycosylated hemoglobin (HbA1c), presence of hypertension, and waist circumference *[Bannerjee et al 1995]*. The eGDR shows good correlation with IR measured by the euglycemic-hyperinsulinemic clamp and has been validated for the estimation of insulin sensitivity in individuals with type 1 diabetes*[Bonora et al 2000]*. Estimated Glucose disposal rate hitherto utilized to analyse Insulin resistance in type 1 Diabetes, has been used as a tool to assess the same in Type 2 Diabetics. This was a pilot study in an attempt to simplify the assessment of Insulin resistance in a rural outreach so that the specific treatment goals for Type 2 Diabetes could be achieved among patients of remote locations of the country.

The formula for measurement of Insulin resistance is: Estimated Glucose disposal rate:

eGDR (in mg · kg^{-1} · min^{-1}) = 21.158 – [3.407 × hypertension status (yes = 1; no = 0)] – [0.090 × waist circumference (cm)] – [0.551 × HbA_{1c} (%)].

Hypertension is defined by (1) use of antihypertensive medications and /or (2) systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg for participants aged ≥ 18 years old or systolic and/or diastolic blood pressure exceeding the age-, sex-, and height-specific 95th percentile [*NHBEP, 2004*] for those aged < 18 years. This formula was used to calculate insulin resistance in the present study.

The objective of this study was to compare the Insulin resistance among Type 2 Diabetics of the local tribal and nontribal population who are reporting to OPD of Midnapur Medical College and Hospital.

Methods

Type of Study: This was Unicentric, epidemiological, population based study.

Study area: The study was carried out at the General Medicine O.P.D. & the Department of Biochemistry of Midnapore Medical College and Hospital, a tertiary care hospital of West Medinipur district. The catchment area included the West and the East Medinipur districts, Bankura and the eastern fringes of Jharkhand – a neighbouring state.

Study population: All the type 2 diabetic patients regularly complying with treatment prescribed at the General Medicine O. P. D. who could be assessed, provided they met the inclusion & exclusion criteria.

Study period: It was conducted for one year.

Inclusion & exclusion criteria: The following inclusion and exclusion criteria were applied for selecting the cases.

Inclusion criteria

1. Age ≥ 18 years
2. Already diagnosed and confirmed, beyond reasonable clinical doubt, as type 2 DM.
3. History of taking regular anti-diabetic medication for at least the last 6 months.
4. History of taking the present anti-diabetic medication regimen, without change or alteration, for at least the last 3 months.
5. Consented to be a part of the study after the subjects were fully apprised of it.

Exclusion criteria

1. History of non compliance to prescribed anti-diabetic medications in last 6 months.
2. History of alteration or suspension of present anti diabetic treatment regimen in last 3 months.
3. History of adverse reaction to the drugs currently prescribed, at any time.
4. Non ambulatory.
5. Dyselectrolytemia.
6. Serious illness and / or complication in last 3 months.
7. Steroid use, chronic pancreatitis etc co-morbid condition or treatment that can influence the study outcome.
8. Pregnancy.

Sampling method: It was conducted by the method of systematic stratified random sampling. Four strata, namely nontribal male, nontribal female, tribal male and tribal female were defined. The website https://www.random.org/ was accessed for generating random sampling protocol. [*Das et al, 2011*].

Sample size In this study the primary outcome measures were taken to be proportion of subjects (not achieving treatment goals) having HbA_{1c} ≥ 8.5%, ≥ 7% {as per the treatment goals recommended by the *American Diabetes Association*}, and estimated glucose disposal rate (eGDR) < 9 mg/kg/min (less than the lower limit of the range of ~ 9 to 11 in those with normal insulin resistance) [*Williams et al, 2000*].

The statistical software StatCalc™ developed by Centres of Disease Control and Prevention, Atlanta, USA, was chosen for sample size calculation, as it was developed primarily for epidemiological work like the present study. The relative risks of the outcomes in each group were calculated by the software program and the results fed into StatCalc™ sample size and power

calculator for 'Unmatched Cohort and Cross-sectional Studies', with the requirement of 95% confidence level, 80% power, and 1:1 ratio between the groups to be compared. The results are tabulated below:

Table 1: Sample size for the males

Comparison amongst the males									
Different methods	**Kelsey**			**Fleiss**			**Fleiss w/ CC**		
Expected sample size	**HbA_{1c} ≥ 8.5%**	**HbA_{1c} ≥ 7%**	**eGDR < 9**	**HbA_{1c} ≥ 8.5%**	**HbA_{1c} ≥ 7 %**	**eGDR < 9**	**HbA_{1c} ≥ 8.5%**	**HbA_{1c} ≥ 7%**	**eGDR < 9**
Non-tribal	61	50	66	59	48	65	69	56	73
Tribal	61	50	66	59	48	65	69	56	73
Total	122	100	132	118	96	130	138	112	146

Table 2: **Sample size for the females**

Comparison amongst the females									
Different methods	**Kelsey**			**Fleiss**			**Fleiss w/ CC**		
Expected sample size	**HbA_{1c} ≥ 8.5 %**	**HbA_{1c} ≥ 7 %**	**eGDR < 9**	**HbA_{1c} ≥ 8.5 %**	**HbA_{1c} ≥ 7 %**	**eGDR < 9**	**HbA_{1c} ≥ 8.5 %**	**HbA_{1c} ≥ 7 %**	**eGDR < 9**
Non-tribal	39	45	50	37	44	48	45	51	56
Tribal	39	45	50	37	44	48	45	51	56
Total	78	90	100	74	88	96	90	102	112

Accordingly, 73 and 56 were the sample sizes calculated for the male and the female groups respectively within the non tribal and the tribal populations, of the final study

Measurement of Biocemical parameters: All the Biochemical Parameters were analysed in the Clinical Biochemistry Laboratory of the Midnapur Medical College.

Fasting and Post Prandial Blood glucose was estimated in every patient to assess the status of the patient. The Blood glucose analysis was done from the plasma of the subjects using Autoanalyser XL 600, Transasia Biomedicals.

HbA_{1c}: HbA_{1c} was measured from EDTA blood sample of the subjects using the HPLC technique. DS-5 HPLC instrument manufactured by Transasia Biomedicals, India was used for this analysis.

Data processing & analysis: Data analysis was done at Department of Pharmacology by Excel™, StatCalc™ and SPSS-15 ™ for the Windows™.

Result and Discussion

Among these 129 subjects (50%) were of non-tribal ethnic origin and 129 (50%) were of tribal origin, each group containing 73 adult males (56.59% of each ethnic group) and 56 adult females (43.41% of each ethnic group). The subjects had no co-morbid condition that could influence the study outcome. The results are tabulated in Table 3.

Table 3: Results of the study

		Non tribal males (n = 73)	**Tribal males (n = 73)**	**Nontribal females (n = 56)**	**Tribal females (n = 56)**
FPG	Mean±SD	146.8±49.02	126.12±33.76	136.27±62.12	113.48±41.27
	Median±IQR	135±78	120±37	112±54	102±51.75
	Kolmogorov – Smirnov *p* (2 tailed)	0.001	0.01	0.042	0.125
PPPG	Mean±SD	233±85.06	196.92±67.01	239.37±96.27	167.21±82.56
	Median±IQR	246±129	190±116	199.5±131.5	130.5±87.75
	Kolmogorov – Smirnov *p* (2 tailed)	0.430	0.302	0.078	0.019

HbA_{1c}	Mean±SD	7.53±2.32	6.35±1.42	7.73±2.57	6.15±2.31
	Median ± IQR	6.9±3.3	6.2±1.3	7.45±3.55	5.35±2.05
	Kolmogorov – Smirnov *p* (2 tailed)	0.001	0.026	0.471	0.009
eGDR	Mean±SD	6.83±2.82	7.83±2.6	6.89±2.42	9.51±2.77
	Median ± IQR	7.03±4	7.38±4.42	6.42±3.04	9.05±4.14
	Kolmogorov – Smirnov *p* (2 tailed)	0.648	0.111	0.29	0.406

The following proportions of subjects showed unsatisfactory results so far as treatment goals are concerned (Table 4)

Table 4: Comparison of proportions of the subjects not achieving treatment goals

	Subjects not achieveing treatment goals	**Non tribal male (n = 73**	**Tribal male (n = 73)**	**X^2**	**2 tailed p**	**Odds ratio**	**Nontribal female (n = 56)**	**Tribal female (n = 56)**	**X^2**	**2 tailed p**	**Odds ratio**
BP	>140/90 mm Hg or Anti-hypertensive medication	47	44	0.2625	0.6083822190 (not significant difference in proportions)	1.1914	33	24	2.8938	0.0889220758 (not significant difference in proportions)	1.9130
	%	64.38 %	60.27 %				58.93%	42.86 %			
FPG	>130 mg/dl	39	23	7.1767	0.0073858435 (significant difference in proportions)	2.4936	23	16	1.9276	0.1650165289 (not significant difference in proportions)	1.7424
	%	53.42 %	31.51 %				41.07%	28.57 %			
PPPG	≥180 mg/dl	52	42	2.9869	0.0839403727 (not significant difference in proportions)	1.8277	36	20	9.1429	0.0024969089 (significant difference in proportions)	3.2400
	%	71.23 %	57.53 %				64.29%	35.71 %			
HbA_{1c}	≥8.5%	21	6	10.2241	0.0013861815 (significant difference in proportions)	4.5096	20	4	13.5758	0.0005518329 (after Yate's correction) (significant difference in proportions)	7.2222
	%	28.77 %	8.22%				35.71%	7.14%			
	≥ 7%	34	13	13.8375	0.0001993157 (significant difference in proportions)	4.0237	30	12	12.3429	0.0004426770 (significant difference in proportions)	4.2308
	%	46.58 %	17.81 %				53.57%	21.43 %			
eGDR	<9 mg/kg/min	60	44	8.5568	0.0034423840 (significant difference in proportions)	3.0420	45	28	11.3692	0.0007467362 (significant difference in proportions)	4.0909
	%	82.19 %	60.27 %				80.36%	50.00 %			

On analysis of the biochemical results, fasting plasma glucose, post prandial plasma glucose and HbA_{1c} were significantly lower in the tribal diabetics than in the non-tribals in both the sexes. Estimated glucose disposal rate was marginally (mildly significantly) higher in the tribals than in the non-tribals in the males; but significantly higher in the female tribals compared to the female non-tribals. A significantly larger proportion of male non-tribals had uncontrolled FPG (> 130 mg/dl), HbA_{1c} (both ≥ 8.5% and ≥ 7%), estimated glucose disposal rate less than lower limit (i.e. < 9 mg/kg/min) of the normal range, compared to the male tribals. Compared to the male tribals, a larger proportion of the male non-tribals had

PPPG ≥180 mg/dl. A significantly larger proportion of female non-tribals had uncontrolled PPPG, HbA_{1c} and estimated glucose disposal rate less than lower limit of the normal range, compared to the female tribals. Compared to the female tribals, a larger proportion of the female non-tribals had uncontrolled FPG.

Limitations of the present study

Effect of the medications prescribed on the important treatment outcomes, were not measured because of the cross sectional study design, and limited sample size (as the difference in effects of different combinations of antidiabetic drugs is small and dependent on various patient factors; it would have required a much larger sample size to demonstrate the differences).

Estimated glucose disposal rate is validated in the type 1 diabetics. Due to financial and infrastructural constraints [*Wallace et al, 2004*]) at Midnapore Medical College, validating the same in the type 2 diabetics, using serum C peptide measurements could not be done.

Summary & Conclusion

Average fasting and post prandial serum glucose and HbA_1C were significantly lower in the tribal diabetics than the non-tribal in both sexes. Estimated glucose disposal rate was higher in the tribal than in the non-tribal in both the sexes, but the difference was of mild significance in the males.

Conflict of Interest: There has been no conflict of interest at any stage of the study.

Acknowledgement: We express our Gratitude to Dr. Anup Sharma for his contribution in editing the Research article. We extend our thanks to the Medical Laboratory Technicians of the Department of Pharmacology and Biochemistry for their technical support throughout the study.

References

1. Banerji M.A., Chaiken R.L., Gordon D. Does intra-abdominal adipose tissue in black men determine whether NIDDM is insulin-resistant or insulin-sensitive? *Diabetes*. 1995. 44:141–146.
2. Bonora E., Targher G., Alberichie M. Homeostasis model assessment closely mirrors the glucose clamp technique in the assessment of insulin sensitivity. *Diabetes Care*. 2000.23:57–63.
3. Das R., Das P.N. Systematic Random Sampling in *Biomedical Research Methodology* 1st Ed. 2011. p 96.
4. Ehtisham S., Crabtree N., Clark P. Ethnic differences in insulin resistance and body composition in United Kingdom adolescents. *J Clin Endocrinol Metab*. 2005. 90(7):3963-9.
1. IDF Diabetes Atlas, the International Diabetes Federation 2013.
5. Misra A., Chaudhary D., Vikram N.K. Insulin resistance and clustering of atherogenic risk factors in women belonging to low socio-economic strata in urban slums of North India. *Diabetes Res Clin Pract*. 2002.56(1):73-5.
6. Misra A., Sharma R., Pandey R.M. Adverse profile of dietary nutrients, anthropometry and lipids in urban slum dwellers of northern India. *Eur J Clin Nutr*. 2001;55(9):727-34.
7. National high blood pressure education program (NHBEP) .Working group on high blood pressure in children and adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics* 2004.114:555–576.
8. Reaven G.M. Role of insulin resistance in human disease.*Diabetes*.1988.37:1595–1607.
9. Wallace T.M., Levy J., Matthews D.R. Use and Abuse of HOMA Modeling. *Diabetes Care*. 2004.27:1487-1495.
10. Whincup P.H., Gilg J.A., Papacosta O. Early evidence of ethnic differences in cardiovascular risk: Cross-sectional comparison of British South Asian and white children. *BMJ*. 2002. 324(7338):635.
11. Williams K.V., Erbey J.R., Becker D. Can clinical factors estimate insulin resistance in type 1 diabetes? *Diabetes* 2000.49:626–63.
12. World Health Organization 2014, Global status report on noncommunicable diseases 2014. World Health Organization, Geneva. Report of a WHO Study Group.