



A Study on the Role of Glycosylated Hemoglobin In Type 2 Diabetes Mellitus Associated with Risk Factors (Obesity)

KEYWORDS

Obesity, Diabetes mellitus, Glycosylated hemoglobin and HbA1c.

Dr.M.Venkateshwarlu

Professor and Head, Department of Biochemistry, Rajiv Gandhi Institute of Medical Sciences, Adilabad.

Dr.Chelmakuri Gayathri

Assistant Professor, Department of Biochemistry, Rajiv Gandhi Institute of Medical Sciences, Kadapa.

ABSTRACT

The role of Glycosylated hemoglobin in diabetes with obesity is studied. 160 diabetic patients have participated in our study and it was completed the period of 2012-2013 in Government general Hospital, Rajiv Gandhi Institute of Medical Sciences, Adilabad, India. The overall mean values have been determined for 20 diabetic patients in the period of two years including 20 control patients values were subjected for statistical analysis. The blood samples were collected from both male and female subjects belonging to different economic groups, different dwellings, and different professions. Estimation of various biochemical parameters were done in the samples collected. Efforts were made to establish a correlation between the above and glycosylated hemoglobin on the basis of the results obtained. The present study of the diabetes associated obesity leads to conclusion that a good glycemic control would be the useful tool to prevent the possibilities of development of diabetes associated obesity. In conclusion, monitoring HbA1c level is an easy, cost effectiveness and less time consuming method for assessing diabetes as well as diabetes associated obesity.

INTRODUCTION

Diabetes is a syndrome characterized by chronic hyperglycemia and disturbances in carbohydrate, fat and protein metabolism due to absolute or relative deficiency of insulin secretion or action. Life threatening complications may result, from acute metabolic decompensation. In Type 2 Diabetes Mellitus, the risk for the development of complications is greatly increased. Obesity is one of the risk factors for complications of Diabetes Mellitus.

Diabetes is strongly associated with obesity. The risk of developing the disease increases progressively as Body Mass Index (BMI) increases. Recently, the BMI is widely used as a parameter for the progression of diabetes associated obesity and is calculated as $\text{weight (in kg)/[height(in meters)}^2]$. It has been described that people with BMI of $>35 \text{ kg/m}^2$ may have a 40 fold higher risk than those with a BMI $<23 \text{ kg/m}^2$. It has been assumed that BMI of $20\text{-}25 \text{ kg/m}^2$ is considered as normal and the ideal BMI is 23 kg/m^2 . Further, overweight (grade-1 obesity) is defined as a BMI of $25\text{-}29.9 \text{ kg/m}^2$; obesity (grade-2) as BMI $30\text{-}40 \text{ kg/m}^2$; and morbid obesity (grade-3) as BMI $30\text{-}40 \text{ kg/m}^2$. It has been postulated that the syndrome of diabetes with obesity is caused by variable interactions between genetic and environmental factors, which result in lack of insulin resistance and defective β -cell function. It has been evidenced that obesity in human populations is partially inherited. The genetic component probably accounts for 25-40% of susceptibility in most populations. Other risk factors include a high-fat diet that is poor in complex carbohydrates and fibers, Cigarette smoking and reduced level of physical activity. The prevalence of obesity appears to be even higher in the diabetic populations. Obesity is an important threat to health and life expectancy in the general population [1]. A BMI of $>25 \text{ kg/m}^2$ has been associated with increased morbidity in diabetes and cardiovascular disease, while a BMI of $>30 \text{ kg/m}^2$ carries increase in both morbidity and mortality leads to diabetes, coronary artery disease and stroke [2]. According to world health organization (WHO) guidelines, being overweight for a longer period of time and exceeding certain threshold values leads to disease [3]. Numerous diseases arise from being

overweight and obese, and these lead to infirmities, limit of quality of life and lower life expectancy [4, 5].

The Glycosylated haemoglobin (HbA1c) is widely accepted and used as the most reliable test for assessing chronic glycaemic condition [6]. It is one of the most important advances in the assessment diabetes mellitus management The HbA1c reflects overall blood glucose levels over a period of 2-3 months and further, used to monitor diabetic treatment. It has been recognized that the HbA1c as an essential adjunct to regular self-blood glucose measurement assisting in the achievement of the best possible glycaemic control. The major use of the HbA1c assay is to assess changes in metabolic control that follow an alteration in treatment. The HbA1c does not require fasting blood sample and it is not affected by recent meals [7].

Therefore in the present investigation the effect of HbA1c is estimated in Diabetes associated obesity.

MATERIALS AND METHODS

2.1. Subjects:

The present study was carried out in the Department of Biochemistry, Rajiv Gandhi Institute of Medical Sciences, Adilabad, India. Subjects with both sex were belonging to different age groups (35 to 75 years), different economic groups (upper, middle and lower), different dwellings (urban, semi-urban, rural), different occupations (professionals, farmers, businessmen and students), those who are suffering from the Type-2 Diabetes mellitus. Sample collection was normally carried out during the working hours i.e. in between 8.00 am to 5.30 pm. every day. A consent letter has been taken from all the subjects and the experiment is approved by Institution Ethics Review Board, Rajiv Gandhi Institute of Medical Science, Adilabad, India.

2.2. Chemicals and Reagents:

All chemicals and reagents of Excellent quality of Roche diagnosis Ltd., (Germany and USA), Randox (UK), Bayer & Accurex (India) have been used for various chemical analyses and estimations.

2.3. Experimental Design:

The study was undertaken in 160 diabetic patients during 2012-13. The experiment was carried out in four different groups and was divided into control (CON), diabetes (DM), obesity (OB) and diabetes associated obesity (DM+OB) groups. The overall mean values have been determined for 20 diabetic patients in the period of two years including 20 control patients values were subjected for statistical analysis.

2.4. Sample Collection:

The blood samples were collected in the morning on fasting (8-12 hrs fasting after their dinner the previous night) and post-prandial (1.5 hrs. to 2 hrs after lunch). The same procedure was followed for each patient on his/her every visit. The Hb1Ac was estimated in EDTA anti-coagulated specimen, as it has to be done in the whole blood with preparation of haemolysate sample, while other parameters were estimated in serum or plasma samples. Special care was taken during sample collection from different patients to maintain and keep up time.

2.5. Biochemical estimation:

The fasting and post prandial blood sugar, Blood urea, Serum creatinine, Lipid profiles and other Biochemical parameters were estimated by following end point colorimetric assay method [8] and the Hb1Ac was estimated by following Ion Exchange Resin method [9].

2.6. Statistical analysis:

The results are expressed as Mean \pm S.E.M. The statistical significance was determined by One-Way Analysis of Variance (ANOVA) followed by Post-hoc Student Newman Keuls test. $P < 0.05$ was considered to be statistically significant.

RESULT

3.1. Effect on fasting, post-prandial blood sugar and HbA1c levels:

The effect of fasting blood sugar level is illustrated in Fig-1 (A). Statistical analysis by One way ANOVA revealed that there was significant difference among groups [F (3, 76) = 21.32, $P < 0.05$]. Post hoc analysis by Student Newman keuls test revealed that diabetes (DM) and diabetes associated obesity (DM+OB) groups were significantly increased fasting blood sugar levels and no significant change in fasting blood sugar levels was observed in obesity (OB) group compared to control. Further, there was significant decrease in fasting blood sugar level in OB and was found to be no significant change in fasting blood sugar levels in DM+OB compared to DM, indicating that obesity alone has no role in the levels of fasting blood sugar level. Furthermore, DM+OB showed significant increase in fasting blood sugar levels compared to OB group. The similar effect was observed in both post-prandial blood sugar [Fig-1 (B); F (3, 76) = 33.59, $P < 0.05$] and HbA1c levels [Fig-1 (C); F (3, 76) = 13.89, $P < 0.05$].

DISCUSSION

In the present investigation, diabetes associated obesity (DM+OB) showed significant elevated levels of HbA1c in blood. The present study gains critical importance as HbA1c is an important tool in clinical investigation and would guide in the pathogenesis of diabetes associated obesity. The prevalence of obesity is higher in diabetic population especially in type2 diabetes. Obesity is a great threat to the general population. A BMI of >25 kg/m² has been associated with diabetes and cardiovascular disease. The effect of obesity apparently is synergized with poor

early growth.

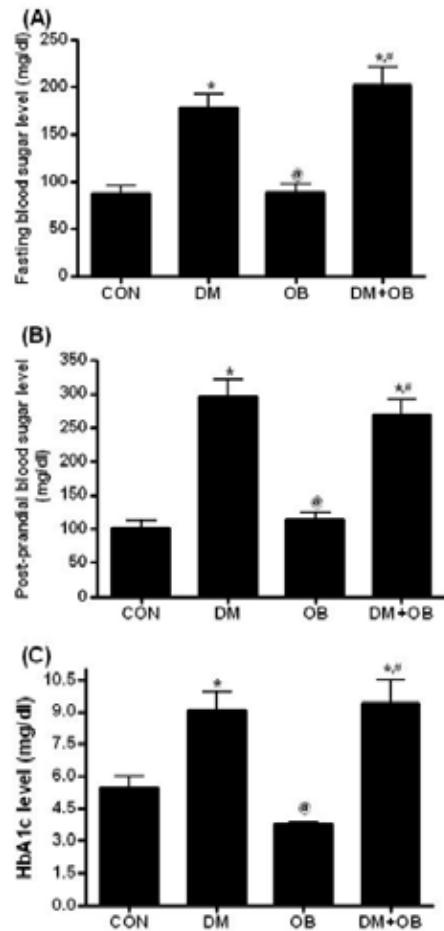


Fig. 1. The effect on level of fasting blood sugar (A), post-prandial blood sugar (B) and glycosylated haemoglobin (C) in control, diabetes (DM), obesity (OB) and diabetes associated obesity (DM+OB) are depicted. All values are Mean \pm SEM. * $P < 0.05$ compared to control, # $P < 0.05$ compared to DM and # $P < 0.05$ compared to OB [One-way ANOVA followed by Student Newman keuls test].

It has been suggested that the key diabetogenic factors may be reduced with dietary availability of protein and amino acids as these are essential for beta cell growth and development for insulin secretion until late fetal life. Insulin is a key regulator of fetal growth and impaired insulin secretion would further exacerbate fetal growth failure [10]. Studies have shown that a high carbohydrate intake in early pregnancy can impair fetal and placenta growth. In lean individuals, an increase fat intake produces a corresponding increase in fat oxidation that maintains constant weight. If this process fails to increase the fat oxidation sufficiently, this could favor for fat storage initiating obesity [11].

Insulin resistance stimulates insulin secretion and hyperinsulinemia to maintain normoglycemia. But individuals who have defective beta cell function will develop hyperglycemia with impaired glucose tolerance and ultimately develop diabetic complications. Defects in beta cell development and its function is due to protein deficiency [12]. The major diabetogenic dietary factor is an excessive total

energy intake especially, if combined with lack of physical activity, which pre-dispose to obesity. High fat and low dietary intake may also independently pre-dispose to type-2 diabetes [13].

In the present study, we found that there was significant elevation in fasting, post-prandial and HbA1c levels in both diabetes and diabetes associated obesity. The result was found to be similar with the previous published report [14]. According to the World Health Organization, being over-weight for a longer period and exceeding certain threshold values would lead to diabetes. Numerous diseases arise due to overweight or obesity and these lead to infirmities limit affecting quality of life and lower life expectancy. Obesity is frequently accompanied with hypertension. High blood pressure is a risk factor for coronary heart disease, pre-mature development of arteriosclerosis and stroke. Obesity in human is partially inherited and the genetic components probably account for 25% to 40% of susceptibility in most population is because of genetic related obesity [15]. Other risk factors include a high fat diet e.g. complex carbohydrate and fiber and reduced physical activity. It affects more than one third of many developed societies and rapidly becoming more common in India. Although the oral glucose tolerance test (OGTT) is the "gold standard" for diagnosing diabetes, it is known to be poorly reproducible and is often not performed. The use of HbA1c is not only more convenient for diagnosis of diabetes, but also therapeutic decision is based on this value.

The clinical utility of HbA1c is a tool to detect the risk of various diabetes complications. Glycosylated hemoglobin reflects retrospective time averaged glycemic status of an individual and thus it becomes useful screening test in assessing the long term control of diabetes mellitus. It is a powerful predictor and plays a crucial role in the prevention of diabetes hyperlipidemia, diabetes nephropathy, diabetes neuropathy, diabetes hypertension. The HbA1c test is exclusively used for diabetes mellitus to assess the treatment efficacy and patients compliance.

CONCLUSION

In conclusion, monitoring HbA1c level is an easy, cost effectiveness and less time consuming method for assessing diabetes as well as diabetes associated obesity and also for assessment for management. Glycosylated hemoglobin assay has high specificity when compared to oral GTT which has low specificity in the Diabetes Mellitus.

Acknowledgement

The authors thankful to Principal, Rajiv Gandhi Institute of Medical Sciences, Adilabad and to the Faculty of Biochemistry and General medicine for providing facilities and permitting us to carry out this research work.

REFERENCE

- [1] Manson J.E., Willett W.E., Stampfer M.J. *N Engl J Med* 1995, 333:677-685. || [2] Iribarren C., Sharp D.S., Burchfiel C.M., Petrovich H. *N Engl J Med* 1995, 333:686-692. || [3] Fontaine K.R., Redden D.T., Wang C., Westfall A.O., Allison D.B. *JAMA* 2003, 289:187-193. || [4] Manson J.E., Willett W.C., Stampfer M.J., Colditz G.A., Hunter D.J., Hankinson S.E., Hennekens C.H., Speizer F.E. *NEJM* 1995, 333:677-685. || [5] Manson J.E., Willett W.C., Stampfer M.J., Colditz G.A., Hunter D.J., Hankinson S.E., Hennekens C.H., Speizer F.E. *Lancet* 1991, 338:774-778. || [6] Saudek C.D., Derr R.L., Kalvani R.R. *JAMA* 2006, 295:1688-1697. || [7] Pfab T., Slowinski T., Godes M., Halle H., Priem F., Hoher B. *Circulation* 2006, 114:1687-1692. || [8] Tietz, N.W. (ed) *Clinical Guide to Laboratory Test* 3rd edition, Philadelphia, Pa: WB Saunders Company 1995, 518-522. || [9] Abell L. *Standard Methods in Clinical Chemistry* 1958, 26:2. || [10] Kissebah A.M., Vydlingum N., Murray R. *J. Clin. Invest.* 1982, 54:254-260. || [11] Connacher A.A., Bennet W.M. Jung R.T. et al. *Clin Sc* 1991, 81: 635-644. || [12] Borkman U., Storlein L.H., Pan D.A. *N Engl J Med* 1993, 328: 238-244. || [13] Vinik A.L., Jenkins D.J.A. *Diabetic Care* 1988, 11: 160-173. || [14] Zarger A.H., Wandroo F.A., Wadhwa M.B. *Int J Diabetes Care* 1995, 15: 9-13. || [15] Williamson D.F., Pamuke, Thun M., Flanders D., Byers T. *Am J Epidemiol* 1995, 141: 1128- 1141.