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Original article

Effect of obesity and glycated hemoglobin on oxygen saturation in ambulatory type 2 diabetic individuals: A pilot study

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ABSTRACT

Aims: Tissue hypoxia is an important contributor to diabetic complications. Glycation of hemoglobin (Hb) and obesity are major determinant of oxygen saturation (SpO2) in blood. Hence, the present study was planned to evaluate the effect of obesity on SpO2 in a wide range of glycated hemoglobin (HbA1c) levels in ambulatory type 2 diabetic patients.

Material and methods: A cohort of 60 subjects irrespective of diabetic status were recruited and clustered in group I (HbA1c <6.5) and group II (HbA1c ≥ 6.5) depending on HbA1c. Anthropometry and routine biochemical parameters were measured. HbA1c (%) were estimated by high performance liquid chromatography (HPLC) respectively. SpO2 (%) levels were measured by pulse oximetry. Pearson correlation, bivariate regression and student 't' test were used for statistical analysis.

Results: Blood concentration of HbA1c was <6.5 in 29 participants and ≥ 6.5 in 31 participants. Plasma fasting and post prandial glucose, HbA1c as well as Hb levels were significantly ($p < 0.50$) higher in diabetics as compared to non diabetics. Waist circumference (WC) ($r = -400$; $p = 0.026$) and body mass index (BMI) ($r = -381$; $p = 0.034$) showed a significant negative correlation with SpO2 in diabetic patients. On adjusting HbA1c in group II, SpO2 was found to independently and inversely associated with WC ($p = 0.042$) and BMI ($p = 0.049$).

Conclusions: Obesity was found to be a strong independent contributor to reduction in oxygen carrying capacity in ambulatory type 2 diabetic subjects. However there is no effect of glycated Hb on SpO2 in the same population.

1. Introduction

Type 2 diabetes mellitus (T2DM) is a major cause of morbidity and mortality worldwide. The worldwide prevalence of diabetes among adults (aged 20–79) was about 285 million in 2010 and is predicted to become 439 million by 2030 and this increase will be most notable in the developing countries [1]. Diabetes is strongly associated with both microvascular and macrovascular complications, including retinopathy, nephropathy, and neuropathy (microvascular) and ischemic heart disease, peripheral vascular disease, and cerebrovascular disease (macrovascular), resulting in tissue and organ hypoxia and damage in approximately one third to one half of people with diabetes [2]. Of these Myocardial infraction (MI) is the leading cause (~70%) of death in diabetic patients [3].

Hemoglobin is the principal carrier of oxygen in the body. HbA1c measures the percentage of HbA that has been irreversibly glycated at the N-terminal amino group of the β-chain. The value is determined by the level of plasma glucose and the life span of red blood cells. Thus HbA1c is commonly used as an indicator to assess the glycemic control over the preceding 2–3 months [4]. Previous studies have shown that glycation alters the structure and function of hemoglobin [5,6] and tends to shift the oxygen dissociation

Abbreviations: T2DM, type 2 diabetes mellitus; MI, myocardial infarction; Hb, hemoglobin; HbA1c, glycated hemoglobin; SpO2, oxygen saturation; HbA, hemoglobin A; ADA, American Diabetic Association; BMI, body mass index; WC, waist circumference; ELISA, enzyme linked immunosorbent assay; HPLC, high performance liquid chromatography; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; VLDL-C, very low density lipoprotein cholesterol; 2,3-DPG, 2,3-diphosphoglycerate.

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curve to the left, leading to an increase in hemoglobin-oxygen affinity and a reduction in oxygen delivery to tissues [5,7,8]. It has been reported that glycation of hemoglobin may be acting as a contributory factor in tissue hypoxia [5]. However, the involvement of obesity with the resting level of SpO2 has not been reported in ambulatory T2DM population. Since diabetes in associated with obesity, such information would be useful for clinicians to gauge whether decreased SpO2 readings can be explained by increased weight. Our study is the first to explore the association of obesity with SpO2 with in ambulatory diabetic individuals in a wide range of HbA1c levels.

2. Subject material and methods

2.1. Subjects and setting

In present study we recruited total 60 subjects above 30 years of age, irrespective of gender, glycemic index of patients from Medicine OPD/Diabetic Outpatient Clinic of our Hospital. To include wide range of HbA1c levels, non diabetic individuals who were relatives/friends of patients and staff members of the hospital were also included in the study. To avoid any potential confounding factors, smokers, patients with respiratory disorder and patients on insulin were excluded from the study. Later the study population was divided into two groups based on their HbA1c levels as per ADA guidelines [9]. The subjects with HbA1c $<$6.5% were grouped as group I and subjects with HbA1c $\geq$6.5% were categorized as group II. The protocol of this study was approved by the Institutional Ethics Committee for Human Research and informed written consent was taken from all the participants.

2.2. Anthropometry and clinical examination

Weight was measured using a digital scale with sensitivity of 0.1 kg. Height was measured to the nearest 0.1 cm using wall mounted scale. Body mass index (BMI) was calculated as weight (kilogram) divided by squared height (meter^2). Waist to hip ratio (WHR) was calculated as ratio of waist circumference (WC), measured at the level of umbilicus after expiration, to hip circumference (HC), measured as maximal horizontal circumference at the level of the buttocks. Blood pressure was measured using mercury sphygmomanometer using auscultatory method.

2.3. Biochemical analysis

Fasting blood sample was withdrawn from ante-cubital vein under aseptic precautions and collected in fluoride, EDTA and plain vacutainers. For HbA1c 1 mL whole blood was kept in EDTA as aliquot at 4–8 °C and its concentration was assayed using high performance liquid chromatography (HPLC) (Bio-Rad D-10 Hemoglobin Testing System). Serum insulin was estimated by sandwich ELISA by commercially available kit (Diametra, Italy) according to manufacturer's protocol. SpO2 was monitored in the seating position with a pulse-oximeter which detects oxygen saturation (SpO2) by measuring transdermal light absorption in the blood flow through a fingertip. The probe was applied to the index finger of left hand after ensuring that nail polish is not applied. Mean of the two reading taken 10 min apart was recorded.

Routine biochemical investigation such as fasting and postprandial plasma glucose [10], serum creatinine [11], total cholesterol [12], high density lipoprotein-cholesterol (HDL-C) [13], low density lipoprotein-cholesterol (LDL-C) by Friedwald's and Fredrickson's formula [14], triglycerides [15] were carried out using Olympus AU-400, Japan. Serum electrolytes were estimated by ion selective electrodes (AVL 9181, Roche diagnostics India Pvt. Ltd.). Hemoglobin was estimated by automated fivepart differential hematology analyser (Melet Schloesing MS 95, USA).

2.4. Statistical analysis

All statistical tests were performed using SPSS version 20. For comparisons of different variables student's t-test was used. The statistical analysis was carried out using Pearson coefficient of correlation for assessment of relationship between variables. Bivariate regression analysis was carried out to assess the effect of WC on SpO2. A p value <0.05 was considered statistically significant (two-tailed).

3. Results

A total of 60 individuals participated in the study. The mean age of all participants was 49.52 ± 7.81 years (range 30–65 years). The baseline demographic, clinical findings and routine biochemical investigations are given in Table 1. Participants had a wide range of HbA1c (4.5–13.8%). Considering the cut off limits for obesity [16] as $\geq$80 cm for females and $\geq$90 cm for males, 35 individuals were found to be obese. According to the cut off values given by eight report of the Joint National Committee [17] on prevention, detection, evaluation and treatment of high blood pressure, 26 participants were hypertensive. A total of 13 individuals were anemic when assessed for Hb concentration according to WHO criteria [18]. Correlation between SpO2 and different measured variables are shown in Table 2. It is evident from Table 2 that SpO2 does not have correlation with HbA1c, Hb, fasting glucose, serum insulin, weight, and WHR. However, a significant negative association of SpO2 was observed with WC ($r = -0.290$, $p = 0.025$) and BMI ($r = -0.263$, $p = 0.042$).

To further elucidate the effect of glycation of Hb on SpO2, the participants were grouped on the basis of HbA1c values [9]. There were 29 participants with HbA1c $<$6.5% (Group I) and 31 participants with HbA1c $\geq$6.5% (Group II). The comparison of clinical, anthropometric and biochemical parameters were shown in Table 3. All the variables were similar in both groups, except plasma fasting and postprandial glucose, HbA1c and hemoglobin which were significantly ($p < 0.050$) higher in group II. Correlation between SpO2 and different measured variables in individual

Table 1
The baseline demographic characteristic and biochemical parameters (all subjects together).

Variables	All participants (n = 60)	Range
Age (years)	49.52 ± 7.81	30–65
Weight (kg)	68.6 ± 10.8	46–95
WC (cm)	93.3 ± 14.2	57–115
BMI (kg/m^2)	26.6 ± 4.7	19.8–39.3
SBP (mm Hg)	127.4 ± 19.2	88–193
DBP (mm Hg)	81.9 ± 10.6	54–110
Hb (gm%)	12.5 ± 2.0	6.4–16.9
Fasting glucose (mmol/L)	7.45 ± 3.57	3.60–17.26
Postprandial glucose (mmol/L)	11.10 ± 4.02	5.05–23.70
Total cholesterol (mmol/L)	4.97 ± 1.80	2.48–11.37
HDL-C (mmol/L)	1.01 ± 0.27	0.57–1.50
TAG (mmol/L)	1.90 ± 1.06	0.59–5.18
LDL-C (mmol/L)	3.19 ± 1.56	1.63–8.97
Serum creatinine (μmol/L)	72.49 ± 22.98	35.36–132.6
Serum sodium (mmol/L)	139.8 ± 4.2	133–149
Serum potassium (mmol/L)	4.48 ± 0.4	3.5–5.3
HbA1c (%)	7.7 ± 2.2	4.5–13.8
Serum insulin (μIU/mL)	5.02 ± 5.0	0.89–15.33
SpO2 (%)	97.0 ± 1.1	94.1–98.9

Values are expressed in mean ± S.D.
WC: waist circumference; BMI: body mass index; SBP and DBP: systolic and diastolic blood pressure; Hb: hemoglobin; HDL-C: high density lipoprotein cholesterol; TAG: triacylglycerol; LDL-C: low density lipoprotein cholesterol; HbA1c: glycated hemoglobin; SpO2: oxygen saturation.