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Research Article

Correlation of Obesity Type with Diabetic Retinopathy in an Indian Population

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Abstract

Purpose: Contradictory reports exist regarding protection against diabetic retinopathy (DR) by different obesity types. We assessed correlation of DR with obesity pattern in a population from eastern part of India.

Method: Institution based cross sectional study with 114 cases of DR and 114 patients with no retinopathy (NODR) from type 2 diabetes patients between 30-70 years of age. Body mass index (BMI), waist circumference (WC), hip circumference (HC), waist hip ratio (WHR) was measured and various types of obesity were defined based on these anthropometric indices. Axial length of globe was measured.

Result: Higher weight, BMI, and WC were observed in NODR. Waist circumference and HC were more among women in both groups. Significant difference in BMI was observed in DR below and above 60 years of age ($p < 0.05$). Waist hip ratio based obesity was the commonest obesity pattern in both groups. All obesity types except WHR based obesity and isolated generalized obesity was more prevalent among women in both groups. Isolated generalized obesity was present only among men in both groups. Among women 59.3% in NODR and 41.1% in DR had combined obesity ($p = 0.022$). Waist circumference based obesity was inversely associated with DR (Odds ratio: 0.46; 95% CI 0.24, 0.88; $p = 0.01$). This difference disappears after stratifying the data with respect to gender. Axial length was not correlated with any obesity type and > 22.6 mm was protective against DR.

Conclusion: No obesity pattern offers any protection against DR in population from Eastern India.

Keywords: *Diabetic Retinopathy; Body Mass Index; Obesity, Type 2 Diabetes Mellitus, Waist-Hip Ratio*

Introduction

Diabetic retinopathy (DR) occurs even with good blood pressure and glycemic control [1,2]. Risk factors for DR are many including obesity. In anthropometry, while body mass index (BMI) is the most commonly used measure of generalized obesity, circumferences are measures of central obesity. Prevalence of retinopathy was positively associated with BMI along with elevated blood pressure, serum cholesterol, and triglyceride levels in the Hoorn study [3]. However, several studies reported conflicting results regarding association of

DR with BMI. Few studies reported association between high BMI and the incidence of DR [4,5]. Some studies, on the other hand, have reported a decreased incidence of DR in patients with higher BMI [6]. We also previously reported lower incidence of DR with higher BMI in a small study population [7]. There are reports suggesting no correlation of DR with BMI [8] and obesity [9] in Asian population. Interestingly, studies from the Asia-Pacific region have reported conflicting findings regarding associations of DR with lipid levels and obesity, while consistently reporting positive association with hyperglycemia and systolic blood pressure [10]. Mean waist-hip ratios and trunk skin folds are reported higher in the South Asian population than in the European. Obesity in South Asians is mostly abdominal obesity and visceral fat [11]. In a survey in Southern part of India, isolated abdominal obesity and increased waist-to-hip ratio (WHR) were reported to be associated with DR in women [12]. In India differences in prevalence of diabetes and obesity are observed in different geographic regions [13]. Overweight and obesity when analyzed together, the prevalence ranged from a low (21%) in the East to a high (40%) in the Southern India. The prevalence of abdominal obesity was also high in the Southern region (39%), compared to Eastern regions (18·8%) [14]. These reports suggest that association of DR with patterns of obesity needs to be examined in different geographic regions in India. No such report is available from the Eastern part of India, except one small study reported by us earlier [7].

Neck circumference (NC) is a simple, easy to-use screening measure for obesity with reasonable accuracy [15]. This is marker of upper body subcutaneous adipose tissue distribution and thus can differentiate between normal and abnormal fat distribution [16]. NC was found significantly associated with any DR in Australian population [17]. Association of neck circumference with DR has not been studied in Asian population. Myopic refraction and longer axial length (AL) are associated with a lower risk of DR [18]. A pattern of a greater burden of myopia is observed in low to middle, compared to high income countries, a trend similar to cardio-metabolic disease like diabetes. Insulin resistance and hyperinsulinemia have been proposed in pathogenesis of myopia, thus providing a link between higher trends of both myopia and diabetes in these countries [19]. Protective effect of myopia on DR might be due to long axial length [20]. Axial length has not been taken into account in previous studies while assessing relationship of DR with obesity. In this study with a population from eastern part of India we assessed correlation of DR with obesity defined by several diverse criteria, taking axial length into consideration.

Materials and Methods

Cross sectional case control study was carried out in the Ophthalmology department of a tertiary care hospital. Sample size was calculated using P and S software version 3.0.43, assuming that the probability of exposure among controls is 0.5 and the true odds ratio for DR in obese subjects relative to non obese subjects is 0.45 to reject the null hypothesis that this odds ratio equals 1 with power 0.8. The Type I error probability of this null hypothesis was 0.05. The total calculated sample size was 228. Consecutive 114 cases with DR in at least one eye and 114 controls with no diabetic retinopathy (NODR) were selected from patients with type 2 diabetes mellitus above 30 years of age attending retina clinic of our institute for DR screening. Only patients from Eastern states of India (with self reported ethnicity) were included. Diagnosis of type 2 diabetes mellitus was based on standard diagnostic criteria of American Diabetic Association [21]. In cases with DR in both eyes more severely affected eye was selected as study eye. In controls and in cases with DR of equal severity in both eyes the study eye was selected randomly using tossing of a coin. Patients with history of cataract surgery, refractive surgery, intravitreal injection, significant media opacity and corneal condition not suitable for biometry were excluded. Subjects from other part of the country, with > 70 years of age, thyroid disorder, Cushing's disease, and pregnant or lactating women were excluded. Dilated fundoscopy was carried out in all cases and controls by a single experienced observer and DR was graded as per modified Early Treatment Diabetic Retinopathy Study (ETDRS) guidelines [22].

Axial length and anterior chamber depth were measured by USG A scan (Appasamy Assoc India). Average of eight readings was taken. Central corneal thickness was measured (CT-1P, Topcon, Japan). BMI was calculated by formula (weight in kg) /(height in meter) [2]. Waist circumference (WC) was measured at the midpoint between lower margin of the least palpable rib and the top of the iliac crest. Hip circumference (HC) was measured at the widest portion of the buttock, with the tape parallel to the floor. Neck circumference was measured in the midway of the neck, between mid-cervical spine and mid anterior neck. All these measurements were taken using nonstretchable tape at the end of expiration with subjects standing both feet close together looking straight ahead, arms at the side, shoulders down but not hunched. Each measurement was repeated twice and average was calculated only if two values were within 1 cm. All these measurements on every subject were done by a single observer on the same day and within seven days of recruitment. Each subject's refraction was obtained by auto refraction, after which subjective refraction was done by a single optometrist. The final subjective refraction result was used in the analysis. In our study, various types of obesity based on anthropometric indices were defined using the WHO Expert Consultation guidelines [23] as follows:

- BMI based obesity: BMI ≥ 23
- WC based obesity: WC (male) ≥ 90 cm or WC (female) ≥ 80cm
- WHR based obesity: WHR ≥ 0.9 (M) or ≥ 0.85(F)
- Combined obesity: BMI ≥ 23 + WC ≥ 90cm (M) or ≥ 80 cm (F)
- Isolated abdominal obesity: BMI < 23 + WC ≥ 90 cm (M) or ≥ 80 cm (F)
- Isolated generalized obesity: BMI ≥ 23 + WC < 90cm (M) or < 80 cm (F)
- Normal WHR obesity: BMI≥23 + WHR <0.9 (M) or < 0.85 (F)
- Normal WC WHR obesity: BMI≥23 + [WC < 90cm (M), < 80 cm (F) and WHR <0.9 (M), < 0.85 (F)].

The data was entered in a Microsoft excel worksheet. All mean values were compared using independent t-test and ANOVA using SPSS IBM PC v20.0. Institutional ethics committee permitted the study. The work described has been carried out in accordance with the code of ethics of the world medical association (Declaration of Helsinki) for experiments involving humans with informed consent. No funding was involved. Any supplemental information is available with authors.

Results

There was preponderance of women compared to men in both groups, although difference was not significant (p = 0.07). Distribution of cases with respect to severity of DR was as follows: moderate NPDR (38.5%), mild NPDR (36%), PDR (13.2%) and severe NPDR (12.3%).

Obesity parameters like weight, BMI and WC were significantly more prevalent among controls while there was no difference in NC and WHR between cases and controls (Table 1). When stratified gender wise, significant difference (p = 0.005) in BMI between cases and controls was maintained among women and not in men. Among cases, WC in women (87.9 ± 7.9cm) was significantly more (p = 0.037) than in men (84.6 ± 8.2 cm); HC in women (91.7 ± 8.1cm) was more (p = 0.003) than that in men (87.2 ± 7.0 cm). In controls, WC in women (93.4 ± 9.6 cm) was significantly more (p = 0.001) than in men (86.9 ± 6.2); HC in women (97.9 ± 8.0 cm) was more (p < 0.001) than in men (90.9 ± .6.7 cm). BMI and neck circumference were significantly correlated with each other (r = 0.655, p = .001) in the study population independent of gender. Various anthropometric parameters were used for assessing the relationship of obesity with DR. WHR based obesity was the commonest obesity pattern in both groups followed by WC based obesity, combined obesity, BMI based obesity, isolated abdominal obesity, isolated generalized obesity, normal WHR obesity in that order. WC based obesity was found to be inversely associated with DR, patients with DR being 54% less likely to have WC based obesity as compared to the controls (Table 2). However, the difference disappears after stratifying the data with respect to gender, suggesting that the relationship is confounded by gender. Further examination of data showed that by no criteria of obesity, could any relationship be established between obesity and presence of diabetic retinopathy.

	NODR	DR	p value
Age (years)	49.7 ± 8	50.9 ± 7.05	.267
Duration DM (month)	48.9 ± 51.4	98.6 ± 62.12	<.001
Systolic blood pressure	130.4 ± 14.6	133 ± 13.5	.150
Diastolic blood pressure	79.9 ± 7.9	81.9 ± 7.6	.070
Height (cm)	153.7 ± 8.6	153.9 ± 8.8	.897
Weight	59 ± 10.2	54.3 ± 9.8	<.001*
Body mass index	25.1 ± 4.5	22.9 ± 3.9	<.001*
Waist circumference(cm)	91.8 ± 9.3	86.7 ± 8.2	<.001*
Hip circumference(cm)	96.2 ± 8.9	90.1 ± 8	<.001*
Waist hip ratio (WHR)	0.95 ±0.05	0.96 ± 0.03	.102
Neck circumference(cm)	34.1 ± 2.8	33.4 ± 3.1	.085
Visual acuity (LogMAR)	0.2 ± 0.2	0.7 ± 0.4	<.001*
Intraocular pressure (mm Hg)	16.2 ± 3.4	16.1 ± 3.2	.794
Central corneal thickness(μ)	508.2 ± 30.1	510.9 ± 31.7	.546
Anterior chamber depth(mm)	2.9 ± 0.4	2.8 ± 0.4	.057
Axial length (mm)	22.7± 0.8	22.3 ± 0.8	<.001*
Spherical equivalent(dioptre)	-0.11 ± 1.38	0.42 ± 1.03	.001*
HbA1c (%)	6.4 ± 0.4	6.5 ± 0.7	.267
Total cholesterol (mg/dl)	188.65 ± 43.01	190.73 ± 55.15	.751
Triglyceride(mg/dl)	190.1 ± 91.7	166.4 ± 57.6	.020*
High density lipoprotein(mg/dl)	46.7 ± 10.5	44.5 ± 11.5	.136

Table1: *Baseline characteristics of the study population.*

** Significance at 0.05 level, DR: diabetic retinopathy.*

	DR n(%)	No DR n(%)	Odds ratio(95%CI)	p
BMI based Obesity	58 (50.9)	71 (55.0)	0.62 (0.35-1.09)	.08
WC based Obesity	74 (64.9)	91 (79.8)	0.46 (0.24-0.88)	.01*
WHR based Obesity	110 (96.5)	107 (93.8)	1.79 (0.44-8.60)	.35
Combined obesity	58 (50.9)	71 (62.3)	0.62 (0.36-1.09)	.08
Isolated abdominal obesity	22 (19.3)	23 (20.2)	0.94 (0.47-1.91)	.86
Isolated generalized obesity	6 (5.3)	3 (2.6)	2.05 (0.42-12.98)	.30
Normal WHR Obesity	2 (1.7)	1 (0.9)	2.01 (0.10-120.7)	.56

Table 2: *Distribution of different obesity types among the study population.*
** Significance at 0.05 level, DR: diabetic retinopathy.*

Among women 59.3% in controls and 41.1% in cases had combined obesity (p = 0.022). Among men 57.1% in controls and 56.1% in cases had combined obesity (p = 0.931). Among cases and controls, prevalence of obesity based on all types of anthropometric parameters was similarly distributed among men and women. Normal WC WHR obesity was present in only one patient in controls and none among cases.

Intra group gender wise comparison was made in respect to various obesity types (Table 3). All obesity types except WHR based obesity and isolated generalized obesity was more prevalent among women in both cases and controls. Isolated generalized obesity was seen only among men in both groups. The relationship between isolated abdominal obesity and DR was not affected by gender when examined by Mantel Haenszel chi square test. Intra group analysis was carried out with patients below 60 years and ≥ 60 years in respect of BMI. BMI was significantly different among cases below and above 60 years (p < 0.05) but not so in controls (p > 0.5). Further analysis with respect to gender of the subjects showed that among controls, isolated abdominal obesity was more common in women above 60 years than in women below sixty years and this difference was statistically significant (p = 0.035). But no such difference was observed between two genders in the two age groups with respect to any other obesity type.

	DR			NODR		
	F	M	p	F	M	p
BMI based obesity	63	29.3	0.001*	67.4	46.4	0.046*
WC based obesity	87.7	24.4	<0.001*	91.9	42.9	0.001*
WHR based obesity	98.6	95.1	0.261	94.2	92.9	0.799
Combined obesity	63	14.6	<0.001*	67.4	35.7	0.003*
Isolated abdominal obesity	24.7	9.7	0.053	24.4	7.1	0.048*
Isolated generalized obesity	0	14.63	NA	0	10.71	NA
Normal WHR Obesity	9	9	NA	9	0	NA

Table 3: *Gender wise prevalence of different obesity types in the study population*
** Significance at 0.05 level, DR: diabetic retinopathy.*

Axial length was more ($p < 0.001$) in controls than cases. A value of > 22.6 mm for axial length was found using ROC curve which gives significant protection against DR. However no association could be established between various types of obesity and axial length of the eye ball irrespective of presence or absence of DR. Difference in spherical equivalent between cases and controls ($p = 0.001$) did not persist after adjusting for axial length. Of all types of obesity significant difference between two groups in axial length ($p < 0.001$) was seen only with WHR based obesity.

Discussion

The objective of the study was to find association of obesity with DR. Being a case control study, we compared the obesity status of cases (DR) and controls. We considered several anthropometry based criteria, as described in detail in the methodology section. In order to establish such association, if any, obesity status of cases and controls were assessed and compared.

Our finding of lower BMI associated with DR is in agreement with previous studies with Asian population [6-8] and from South India [12]. However this difference was not observed among males in our study. There are conflicting reports regarding this in Asian population as well. While reports from South Korea [24] and Singapore [25] observed an inverse relationship between BMI and the presence of DR; studies from China [26] reported no significant association between them. It is possible that lower BMI found in various studies including ours may reflect more poorly controlled diabetes in patients with DR which results in both unintentional weight loss as well as DR. Another possible explanation could be that persons with DR adopted positive behavioral modifications resulting in lower BMI. However this cannot explain higher BMI among controls in our study as the cases were more poorly controlled with higher HbA1C level.

WC based obesity in our study was found to be inversely associated with DR, patients with DR being 54% less likely to be obese as compared to the controls. We did not find any difference between two groups in respect of other criteria of obesities. This differs with report from South India12 where prevalence of DR was more in the isolated abdominal obesity group. It may be explained by the occurrence of different obesity pattern in Eastern Indian population, abdominal obesity being less prevalent in this part of the country compared to South India [14]. While WC was significantly more in female in both groups, absence of difference in WHR may be explained by significantly more hip circumference in female.

Among DR patients we observed that BMI based obesity, WC based obesity and combined obesity was more in women than in men but such difference was not seen with respect to other types of obesity. In women with and without DR, prevalence of combined obesity was 41.1% and 59.3% respectively and the difference was significant ($p = 0.022$). No such difference was observed in men. This is exactly in agreement with what was reported in South Indian population. 12 Like us they also did not observe any gender difference with regard to isolated generalized obesity or isolated abdominal obesity. They did not study low WHR obesity. CURES study from South India also reported similar trends in respect of BMI based obesity, WC based obesity and isolated abdominal obesity [27]. Data from the 2007 national family health survey demonstrated that overweight/obesity was higher for Indian women than men [28]. Isolated generalized obesity was more common in men in that report.

Obesity pattern changes with age. Previous studies from South India have shown that abdominal obesity increases in women till the sixth decade and declines after seventh decade. In men abdominal obesity is maintained till sixth decade and then rises in the seventh decade before it starts to decline [12,27]. As obesity declines in both genders after seventh decade, we excluded patients above 70 years of age to reduce this bias.

When we made intra group analysis with patients below 60 years and ≥ 60 years, we observed significant difference in BMI in cases but not so in controls. As far as obesities are concerned, only isolated abdominal obesity was found significantly more among females of < 60 years compared to those with ≥ 60 years in controls. However no conclusive evidence could be drawn about the role of gender in establishing relationship of obesity with diabetic retinopathy because the selection criteria in our case control design was presence or absence of retinopathy and not the gender of the patients.

In difference with observation in Australian population17, in our study mean NC was not different between cases and controls and NC was well below the cut off value of >36 cm found in Chinese diabetics [29]. The report from South India12 did not include information on NC. Neck circumference is a marker of upper body subcutaneous adipose tissue distribution. Our finding again highlights less upper body fat distribution among Eastern Indian population. Asian Indian phenotype is characterized by less of generalized obesity measured by BMI and greater central obesity (measured by WC and WHR) [30].

Limitations of the study were that it was cross sectional in nature, failure to use optical biometry, failure to measure visceral fat, failure to include treatment history, rural urban difference and socio economic profile of study subjects. However no significant difference in prevalence of DR in different socioeconomic groups was reported in the study from South India [12]. As it was an observational study design, temporality of diseases cannot be ascertained. The strengths of the present study are that we excluded patients above 70 years of age to exclude the effect of natural decline of obesity after seventh decade and inclusion of axial length in the analysis. Obesity was examined on all possible criteria.

Our study emphasizes that it is important to define obesity by central obesity parameters in Indian population and not only by BMI. Contrary to observations in some studies including the one with South Indian population regarding protection against DR by different obesity types, we found that no obesity pattern offers any protection against DR in population from Eastern India.

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Conflict of Interest

None.

Declarations

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Conflicts of Interest/Competing Interests

None to declare.

Availability of Data and Material

With first author.

Authors' Contributions

Each author qualifies for authorship as per defined criteria.

Ethics Approval

Approved by Institutional Ethics committee.

Consent to Participate

All study participants were included with informed consent.

Consent for Publication

Manuscript has been read and approved by all the authors. All authors mutually agree to publish the article in the present form.

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