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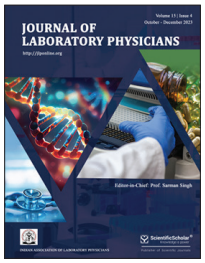

Original Article

Predictive value of adiposity index in identifying depression in individuals with type 2 diabetes mellitus in Indian population

Jiya Singh[1#], Praveen Kumar Singh[1#], Rashmi Nain[1], Ravi Kant[2], Anindya Das[3], Anissa Atif Mirza[1], Sarama Saha[1]

[1]Department of Biochemistry, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India, [2]Department of General Medicine, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India, [3]Department of Psychiatry, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India.
# These authors contributed equally.

***Corresponding author:**
Sarama Saha, MD, Dr Med. (Germany),
Additional Professor,
Department of Biochemistry,
All India Institute of Medical Sciences, Rishikesh 249203,
Uttarakhand, India

saramasaha@yahoo.co.in

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ABSTRACT

Objectives: Type 2 diabetes mellitus (T2DM) patients are four times more prone to develop depression. Common subjective tool to evaluate depression is Patient Health Questionnaire-9 (PHQ-9). Depression in T2DM remains unaddressed because of lack of objective tools resulting in poor treatment compliance. Both obesity and metabolic disturbances could influence mental health status. Therefore, this study was designed to determine the better adiposity index to predict depression in T2DM.

Materials and Methods: In this clinic-based cross-sectional study, 400 individuals (260 = T2DM and 140 = healthy) were recruited. Based on PHQ-9, T2DM patients were divided into T2DM + Dep (PHQ-9 ≤ 10) and T2DM-Dep (PHQ-9 < 10). The relationship between the PHQ-9 score and adiposity indices was examined by Pearson's/Spearman's correlation. The receiver-operating characteristic curve analysis was used to identify the cutoff value.

Statistical Analysis: Statistical analysis was performed using SPSS 22.0 version (IBM Corp., Armonk, New York, United States).

Results: Female diabetic patients showed significant correlation only in lipid accumulation product index (LAPI) and visceral adiposity index (VAI) (r = 0.206 and r = 0.0.237, respectively), while male diabetic patients did not show any significant association. Interestingly, T2DM + Dep group showed significant association between LAPI (r = 0.248) with PHQ-9 score, while T2DM-Dep group did not show significant association. VAI had maximum area under the curve in T2DM patients (0.619, p = 0.002) as well as in female diabetic patients (0.684, p = 0.002). The cutoff value for identifying depression among diabetic individuals was 5.60, with 70.3% sensitivity and 48.2% specificity, while in diabetic females, it was 6.612, with 70% sensitivity and 61.4% specificity.

Conclusions: VAI might be the best adiposity index to predict depression among diabetic individuals.

Keywords: type 2 diabetes mellitus, adiposity indices, Patient Health Questionnaire-9, receiver-operating characteristic curve, visceral adiposity index, lipid accumulation product index,

INTRODUCTION

Diabetes and depression are among the most prevalent disorders that significantly affect health outcomes. Worldwide, according to International Diabetes Federation (IDF 2022), 10.5% (~536.6 million) of people aged 20 to 79 years are suffering from diabetes. Globally, depression is one of the leading causes of morbidity and affects around 280 million people.[1] According to the Patient Health Questionnaire-9 (PHQ-9), used in subjective evaluation of mental disorders,

people with type 2 diabetes mellitus (T2DM) have 2.0 to 4.71 times higher risk of developing depression compared with nondiabetics.[2] Another study reported that depression affects one in four persons with T2DM.[3] However, depression is not taken care of during routine checkup of diabetes mellitus because of lack of objective tools to identify depression, giving rise to deterioration of mental health status that leads to poor treatment compliance and increased risk of development of various diabetes-related complications. Very recently, it was documented that the lipid ratio could be used as an objective indicator for mental health status in T2DM patients.[4] Moreover, it was postulated that aldosterone released by glycoxidized lipoproteins formed in the presence of hyperglycaemia[5] might induce cognitive impairment in T2DM patients.[6] Some adiposity indices like, lipid accumulation product index (LAPI) and visceral adiposity index (VAI), include triglyceride (TG) and high-density lipoprotein (HDL) as one of the metabolic parameters to assess obesity. A significant relation between adiposity index with reaction time has already been demonstrated.[7] Obesity was reported to be a high-risk factor for development of diabetes and depression[8-10] Hence, adiposity indices having combination of anthropometric and metabolic parameter such as (VAI and LAPI) could be hypothesized as a better indicator to predict depression in T2DM patients as compared with anthropometric parameters such as body mass index (BMI), waist hip ratio (WHR), or metabolic parameters (TG/HDL) alone. However, no study has been conducted to reveal which adiposity index would be better for prediction of mental health status in T2DM patients. Therefore, this study was designed to observe the association between adiposity indices, for example, BMI, body adiposity index (BAI), VAI, LAPI, abdominal volume index (AVI), and conicity index (CI), WHR with level of depression in the population attending tertiary care center of Uttarakhand.

MATERIALS AND METHODS

This clinic-based observational study was conducted in the department of biochemistry in collaboration with diabetes and psychiatric clinic at a tertiary care hospital in Uttarakhand. Total of 400 study participants were recruited in the study including 140 healthy and 260 T2DM patients. T2DM patients were more than 18 years of age, diagnosed on the basis of American Diabetes Association criteria. Level of depression was evaluated using PHQ-9. T2DM patients having PHQ-9 score more than or equal to 10 were recruited in T2DM + Dep category and having PHQ-9 score less than 10 were recruited in T2DM-Dep category. Patients having type 1 diabetes mellitus, malignant tumor, metabolic bone disease, or with any other disease such as thyroid disorder and autoimmune disorders were excluded from the study. Individuals having blood glucose level within reference range and PHQ-9 score less than 5 and devoid of any chronic illnesses were included in healthy group. After taking informed consent, study participants were subjected to anthropometric measurement, and 5 mL venous blood was collected after 8 to 10 hours fasting. Lipid profile and fasting blood sugar (FBS) were measured by enzymatic method, and hemoglobin A1c (HbA1c) was measured by using ion-exchange HPLC method (Tosoh G8 HPLC analyser).[11] BMI, BAI, VAI, LAPI, AVI, and CI were calculated as per formula.[12,13]

BMI: weight (kg)/ height(m)2; BAI: [hip circumference (cm)/ height (m)1.5]–18; VAI: for men: [Waist circumference/ (39.68 + (1.88 × BMI))] × (TG/1.03) × (1.31/HDL-C), and for women: [Waist circumference /(36.58 + (1.89 × BMI))] × (TG/0.81) × (1.52/HDL-C); LAPI: for men: (Waist circumference —65) × TG, and for women: (Waist circumference —58) × TG; AVI: [2× Waist circumference (cm)2 + 0.7× (Waist circumference (cm)— Hip circumference (cm))^2 /1000; CI:

Statistical Analysis

Results were expressed as mean T standard deviation and median (interquartile range) depending on normality test. Numerical values among three groups were compared using one-way analysis of variance or Kruskal–Wallis test. Pearson's/ Spearman's correlation test (whatever was applicable) was used for correlating PHQ-9 with different adiposity indices. Statistical analysis was performed using SPSS 22.0 version (IBM Corp., Armonk, New York, United States). The estimation of the predictive values for various adiposity indices for depression was performed by the receiver-operating characteristic (ROC) curves analysis. A *p*-value of less than 0.05 was considered as significant with a 95% confidence level.

RESULTS

Out of total 400 study participants, 236 were male and 164 were female. There was no age difference found between T2DM-Dep (n = 137; 50.21 ± 11.08 years) and T2DM + Dep group (n = 123; 49.95 ± 10.88 years). As expected, the T2DMDep group and T2DM + Dep group had significantly elevated FBS ($p < 0.001$) and HbA1c ($p < 0.001$). T2DM + Dep group had higher FBS, total cholesterol, and TG compared with the T2DM-Dep group; however, HDL showed a trend of significant decrease ($p < 0.001$) among the three groups (healthy, T2DM-Dep, and T2DM + Dep; Table 1).

In this study, the PHQ-9 score was significantly higher ($p < 0.001$) in the T2DM + Dep group than the T2DM-Dep group and the healthy controls. However, no significant difference ($p = 0.418$) was found between the T2DM-Dep group and healthy controls.

Table 1 also shows that VAI, LAPI, AVI, WHR, and CI were found to have tendency of significant increase among three groups (healthy, T2DM-Dep and T2DM + Dep). However, BMI and BAI were found to have no significant difference among the groups.

To identify the association of PHQ-9 with adiposity indices, Pearson's/ Spearman's correlation test was performed. When all participants (400 participants) were considered, PHQ-9 showed significant positive correlation with BAI, VAI, LAPI, AVI, WHR, and CI whereas BMI did not show significant association. Interestingly, PHQ-9 did not show significant association with adiposity indices in T2DM-Dep group patients, whereas PHQ-9 had significant association with BAI (r= 0.266, p = 0.007) and LAPI (r= 0.248, p = 0.012) in case of T2DM + Dep group (Table 2). Moreover, when all participants in T2DM group (n = 260) were categorized based on gender, there was no significant association found in male T2DM patients (n = 162), but PHQ-9 showed significant positive correlation with VAI (female: r =0.0.237, p = 0.022 vs. male: r = 0.083, p = 0.318), LAPI (female: r = 0.206, p = 0.047 vs. male: r = 0.071, p = 0.392, and CI (female: r = 0.219, p = 0.034 vs. male: r = 0.120, p = 0.147) in female T2DM patients (n = 98) (Table 3).

The ROC curves of all T2DM patients (n = 260), male T2DM patients (n = 162), and female T2DM patients (n = 98) are sequentially presented in Figure 1A–C. The ROC curve showed that VAI had the highest area under the curve (AUC = 0.619, p = 0.036) followed by CI (AUC = 0.611, p = 0.037) and LAPI (AUC = 0.592, p = 0.037) (Table 4A). In case of male T2DM patients, AUC of ROC curve did not show any significance (Table 4B), whereas in female T2DM patients (n = 98), there was significant AUC in case of VAI (AUC = 0.684,

Table 1: Comparison of various parameters among total study participants (n = 400)

Parameters	Healthy (n = 140) (male = 74; female = 66)	Diabetes without depression (n = 137) (male = 93; female = 44)	Diabetes with depression (n = 123) (male = 69; female = 54)	p-Value
Age	45.20 ± 10.79	50.21 ± 11.08	49.95 ± 10.88	0.000
FBS	93 (13)	168 (85.25)	175 (126)	0.000
TC	192.43 ± 37.58	190.25 ± 47.23	192.17 ± 59.74	0.919
TG	111.50 (65)	152 (115.50)	178 (108.50)	0.000
LDL	116.34 ± 25.21	115.66 ± 34.95	115.46 ± 40.44	0.976
HDL	47.99 ± 10.78	45.23 ± 13.29	43.00 ± 11.09	0.004
HbA1c	5.4 (0.40)	8.8 (3.93)	8.4 (4.65)	0.000
PHQ-9	2 (3)	3 (6)	15 (6)	0.000
Body mass index	26.31 ± 4.65	25.92 ± 4.37	25.53 ± 4.59	0.403
Body adiposity index	29.69 ± 6.17	28.97 ± 5.87	30.18 ± 7.09	0.321
Visceral adiposity index	4.55 ± 2.71	7.09 ± 5.47	8.42 ± 4.68	0.000
Lipid accumulation product index	41.15 ± 27.71	64.63 ± 46.01	75.49 ± 47.30	0.000
Abdominal volume index	16.14 ± 4.27	17.80 ± 4.09	18.57 ± 5.22	0.000
Waist/hip ratio	0.91 ± 0.07	0.97 ± 0.08	0.97 ± 0.11	0.000
Conicity index	1.26 ± 0.14	1.33 ± 0.10	1.37 ± 0.12	0.000

Abbreviations: FBS, fasting blood sugar; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PHQ-9, Patient Health Questionnaire-9; TG, triglyceride; TC, total cholesterol.

Table 2: Correlations of adiposity indices with PHQ-9 in the study participants

Variables	Parameter	Total study participants (n = 400)		Diabetes without depression (n = 137)		Diabetes with depression (n = 123)	
		Coeff.	p-Value	Coeff.	p-Value	Coeff.	p-Value
Body mass index	PHQ-9	—0.032	0.535	0.012	0.884	0.083	0.409
Body adiposity index		0.109*	0.033	0.106	0.214	0.266**	0.007
Visceral adiposity index		0.273**	0.000	0.130	0.126	0.192	0.053
Lipid accumulation product index		0.273**	0.000	0.052	0.543	0.248**	0.012
Abdominal volume index		0.182**	0.000	–0.007	0.930	0.119	0.233
Waist/hip ratio		0.144*	0.004	–0.061	0.474	–0.041	0.684
Conicity index		0.273**	0.000	0.026	0.761	0.159	0.111

Abbreviation: PHQ-9, Patient Health Questionnaire 9.
*denotes p<0.05; ** denotes p<0.001

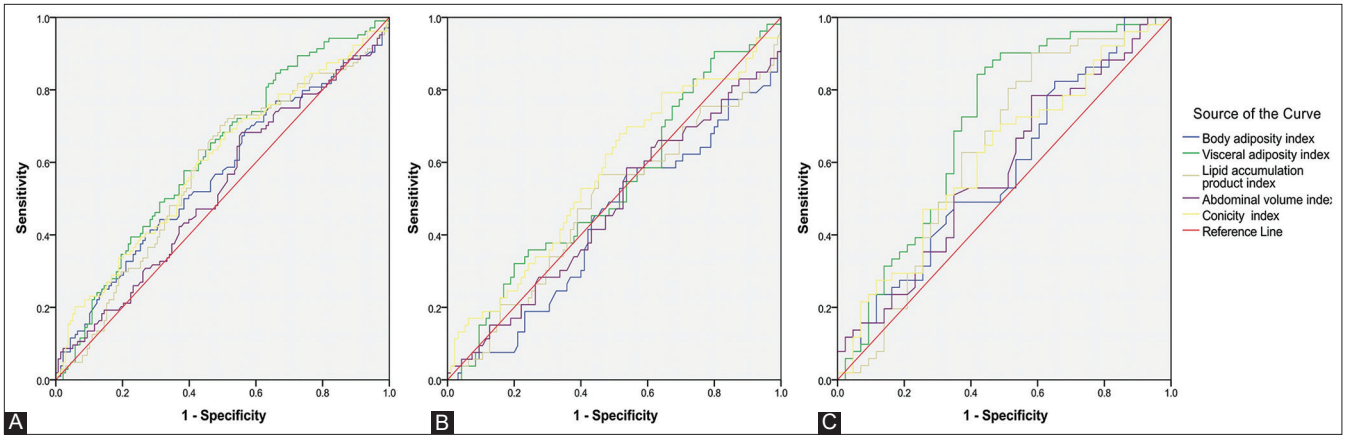

Figure 1: Receiver operating characteristics curve to estimate the predictive values of various adiposity indices for depression in type 2 diabetes mellitus (T2DM) group (n = 260); (A) all T2DM participants (n = 260), (B) male T2DM patients (n = 162), and (C) female T2DM patients (n = 98).

Table 3: Correlations of adiposity indices with PHQ-9 in male and female study participants (n = 260) of T2DM group

Variables	Parameter	Male diabetes patients (n = 162)		Female diabetes patients (n = 98)	
		Coeff.	p-Value	Coeff.	p-Value
Body mass index	PHQ-9	—0.147	0.075	—0.010	0.672
Body adiposity index		—0.106	0.198	0.161	0.122
Visceral adiposity index		0.083	0318	0.237*	0.022
Lipid accumulation product index		0.071	0.392	0.206*	0.047
Abdominal volume index		—0.035	0.610	0.128	0.218
Waist/hip ratio		0.101	0.220	—0.080	0.446
Conicity index		0.120	0.147	0.219*	0.034

Abbreviations: PHQ-9, Patient Health Questionnaire-9; T2DM, type 2 diabetes mellitus.

Table 4A: AUC of different adiposity indices of ROC curve of study participants (n = 260) from T2DM group

Variable(s)	AUC	Standard error	Significance	95% Confidence interval	
				Lower bound	Upper bound
BMI	0.470	0.038	0.424	0.395	0.544
BAI	0.564	0.038	0.092	0.489	0.638
VAI	0.619*	0.036	0.002	0.548	0.690
LAPI	0.592*	0.037	0.014	0.519	0.665
AVI	0.533	0.038	0.388	0.458	0.607
WHR	0.493	0.038	0.860	0.419	0.568
CI	0.611*	0.037	0.003	0.539	0.683
TG/HDL	0.574	0.037	0.050	0.502	0.646

Abbreviations: AUC, area under curve; AVI, abdominal volume index; BAI, body adiposity index; BMI, body mass index; CI, conicity index; HDL, high density lipoprotein; LAPI, lipid accumulation product index; ROC, receiver-operating characteristic; TG, triglycerides; T2DM, type 2 diabetes mellitus; VAI, visceral adiposity index; WHR, waist/hip ratio.

p = 0.002), and LAPI (AUC = 0.562, p = 0.011), where VAI had the maximum AUC (Table 4C). The cutoff value for identifying depression among individuals with T2DM group independent of gender was 5.60, with 70.3% sensitivity and 48.2% specificity. Similarly, the cutoff value for identifying depression in female T2DM individuals was 6.612, with 70% sensitivity and 61.4% specificity.

DISCUSSION

The aim of this study was to verify if there was a relation between depression and adiposity indices in patients with T2DM. Several studies have showed a positive correlation between depression and T2DM as well as poor glycemic control.[4,14]

Table 4B: AUC of different adiposity indices of ROC curve of male participants (n = 162) from T2DM group

Variable(s)	AUC	Standard error	Significance	95% Confidence interval	
				Lower bound	Upper bound
BMI	0.401	0.049	0.427	0.305	0.496
BAI	0.433	0.050	0.183	0.335	0.532
VAI	0.540	0.050	0.423	0.442	0.639
LAPI	0.501	0.052	0.990	0.399	0.602
AVI	0.476	0.051	0.637	0.377	0.576
WHR	0.521	0.053	0.669	0.417	0.626
CI	0.578	0.050	0.119	0.480	0.676

Abbreviations: AUC, area under curve; AVI, abdominal volume index; BAI, body adiposity index; BMI, body mass index; CI, conicity index; LAPI, lipid accumulation product index; ROC, receiver-operating characteristic; T2DM, type 2 diabetes mellitus; VAI, visceral adiposity index; WHR, waist/hip ratio.

Table 4C: AUC of different adiposity indices of ROC curve of Female participants (n = 98) from T2DM group

Variable(s)	AUC	Standard error	Significance	95% Confidence interval	
				Lower bound	Upper bound
BMI	0.498	0.061	0.967	0.379	0.616
BAI	0.559	0.060	0.323	0.442	0.677
VAI	0.684*	0.057	0.002	0.572	0.796
LAPI	0.652*	0.059	0.011	0.536	0.768
AVI	0.580	0.059	0.182	0.464	0.696
WHR	0.506	0.061	0.922	0.386	0.626
CI	0.625*	0.058	0.036	0.512	0.739

Abbreviations: AUC, area under curve; AVI, abdominal volume index; BAI, body adiposity index; BMI, body mass index; CI, conicity index; LAPI, lipid accumulation product index; ROC, receiver-operating characteristic; T2DM, type 2 diabetes mellitus; VAI, visceral adiposity index; WHR, waist/hip ratio.

In this study, T2DM patients had higher PHQ-9 score than the healthy individuals. This finding was supported by an earlier study showing that T2DM had higher chance of developing depression as compared with nondiabetic individuals.[2] In previous research, it was stated that relief of depression is noted to be associated with improved glycemic control.[14] In this study, the T2DM + Dep group had also higher blood glucose level compared with T2DM-Dep group. Many previous studies reported an association between obesity with increased risk of diabetes and depression.[8-10] BMI was widely used as a simple indicator of adiposity. However, it has been demonstrated in many studies that BMI is not a reliable indicator of obesity since it cannot differentiate between visceral fat and fat mass.[15-17] Therefore, in this study, various adiposity indices were used to correlate with depression in diabetic people to see the impact of BMI, WHR, BAI, AVI, CI, which are based on anthropometric (height, waist, hip circumference) parameters and VAI, LAPI, which are based on combination of anthropometric measurements and metabolic (TG or HDL or both) parameters.

In this study, non-significant correlation was found between PHQ-9 and BMI. On the contrary, numerous studies have linked BMI to an increased risk of anxiety and depression in adults, particularly in women.[18,19] This discrepancy in findings may be because BMI does not take into consideration of the metabolic parameters that may be influenced by the cultural difference of the recruited study participants. This also indicates the importance of inclusion of metabolic parameters such as TG and HDL in adiposity indices to predict the development of depression.

Interestingly, in this study LAPI and BAI had significant positive correlation with PHQ-9 only in T2DM + Dep patients. However, only female T2DM patients showed positive correlation between PHQ-9 with VAI, LAPI, and CI which were partially in agreement with a very recent study conducted by Lei et al in United states on apparently healthy individuals since they investigated only VAI but not other adiposity indices.[20] Moreover, they did not mention if there was any difference in findings with respect to gender.

Furthermore, with respect to the ROC curve, VAI (AUC = 0.684, p = 0.002) had highest followed by LAPI (AUC = 0.592, p = 0.014) compared with other commonly used adiposity indices (BMI AUC = 0.470, p = 0.424) and metabolic parameter (TG/HDL: AUC = 0.574, p = 0.050) inT2DM patients. Thus, these findings emphasize that adiposity indices having combination of anthropometric and metabolic parameters (VAI and LAPI) provide more information regarding prediction of depression in diabetic individuals compared with only anthropometric based (BMI) or only metabolic parameter based (TG/HDL) indices.

Strength and Limitations

Our study has some strengths as well as limitations. To the best of our knowledge, the results of this study are the first to demonstrate which adiposity index would be a better predictor for the mental health of the Indian diabetic population. However, since it is a cross-sectional study, cause–effect relationship between depression, T2DM, and adiposity could not be established. The small sample size in each group warrants the necessity of conducting a study on larger sample size. Since metabolic parameters are influenced by race, ethnicity, and cultural habits, these data limit its generalizability.

CONCLUSIONS

This clinic-based observational study revealed that diabetes patients had higher PHQ-9 scores than controls. In people with diabetes, VAI and LAPI are better indicators of mental health condition than BMI or waist circumference or TG/HDL alone. VAI having the highest AUC could be considered as a screening tool for the diagnosis of depression in T2DM individuals that would help in preventing diabetes-related complication through early identification and initiation of personalized therapy.

Authors' Contributions

PKS and JS wrote manuscript, collected samples, and performed tests; RN was involved in literature review; RK and AD helped in selection of patients; AAM was involved in editing of manuscript; SS was involved in conceptualization, data collection, statistics, and editing of the manuscript. All authors have read and approved the manuscript.

Ethics Approval

The study was approved by the Institutional Research Ethics Committee (IEC approval letter no: AIIMS/IEC/ 19/1169, dated 29/11/2019), All India Institute of Medical Sciences, Rishikesh. The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Consent to Participate

Informed consent was obtained from all participants. Consent for Publication: Not applicable.

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Conflicts of Interest

Dr Sarama Saha reported Funding received from Science and Engineering Research Board (SERB), sanction letter no. EEQQ/2019/000040, dated 31/12/2019.

All other authors reported no conflict of interest.

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