EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 3
Issue: 3
310-317
Year: 2016

EVALUATION OF THE INSULIN RESISTANCE IN DIABETIC PATIENTS WITH DEPRESSIVE DISORDERS

Vipul Kumar Garg[1], Santosh Kumar Yadav[1], Suchi Diwedi[2] and Kamlakar Tripathi[1*]

[1]Department of Medicine, Institute of Medical Science, Banaras Hindu University, Varanasi, Uttar Pradesh, India 221005.
[2]CHC Hospital Chunar Jamalpur, Mirzapur, UP, India 231001.

***Author for Correspondence: Prof. Kamlakar Tripathi**
Department of Medicine, Institute of Medical Science, Banaras Hindu University, Varanasi, Uttar Pradesh, India 221005.

Article Received on 30/12/2015 **Article Revised on 19/01/2016** **Article Accepted on 09/02/2016**

ABSTRACT

Aim: To examine the association between depression and insulin resistance in diabetic patients. **Objective:** The key objective of this study was to examine the relationship between depression and insulin resistance in Diabetic patients. Global prevalence of diabetes was 2.8% in 2000 and it will reach 4.4% in 2030 to be 366 million diabetics. Many epidemiologic studies have shown that patient with diabetes are more susceptible to depression. Diabetes and depression align in a non-accidental way and complicate one another. **Materials and methods:** Total 120 individuals were enrolled from S.S. Hospital BHU India in 2013-2015 with their written consent form and divided in to four groups. Group 1 considered as healthy control, Group 2 only diabetic, Group3 only depression and Group 4 both diabetic with depression which follows the inclusion criteria of WHO and Diabetes Data Group. Our aim was to evaluate the prevalence of depressive disorders in patients with diabetes and to describe their socio demographic and clinical profile. **Results:** Total 120 individuals (mean age 45±14 years) were equally divided in four groups with equal male and female proportion. BMI was higher in group2 only diabetic (43.3%) than group 3 only depressive (46.7%) which were under wight. Where as in Group 4 Depression with diabetes have maximum (46.7%) were obese ($p<0.015$). In Group 4 More than (60%) 18 patients have 10-20 Insulin Resistance code. Group 3 only depression have maximum (56.7%) 17 Patients with 2-10 Insulin Resistance code ($p<0.001$). **Conclusion:** Patient having both depression and diabetes were found to be having greater insulin resistance than patients who had only diabetes. Patients having more BMI were found to be having more insulin resistance. Obesity and depression may contribute in insulin resistance hence needs consideration while prescribing oral hypoglycemic drug.

KEYWORDS: Diabetes ▪ Depression ▪ Prevalence ▪ Dysthymia ▪.

INTRODUCTION

Insulin resistance is incidentally linked to the development of type 2 diabetes.[1] Clinical abnormalities, such as hypertension, increased triglyceride and low-density-lipoprotein cholesterol (LDL-C), or decreased high-density-lipoprotein cholesterol (HDL-C), that are directly associated with insulin resistance and its accompanying hyper insulinemia also contribute to an increased risk for cardiovascular disease.[2] Given advances in modernization and current sedentary lifestyles, the prevalence of insulin resistance has significantly increased.[3] The adverse effects of insulin resistance are latent but detrimental. Without intervention, insulin resistance can progress to type 2 diabetes and accompanying negative sequel, such as hypertension, dyslipidemia and other cardiovascular disease.[4]

Depression also is a major cause of morbidity and mortality in the United States. It has substantial depressing impact on patients' quality of life, physical and mental health and social functioning, which can lead to increased inability and reduced work productivity.[5] The economic burden of depression on society and individuals is monstrous. In 2000, the estimated total cost of depression in the United States was $83.1 billion.[6] This included $26.1 billion to $32 billion in 2008 for direct medical costs, $51.5 billion to $63 billion in 2008 for indirect costs and $5.4 billion for suicide-related mortality costs.[7] One study from Sweden, the total cost of depression for 2005 was 3.5 billion Euros, including 500 million Euros (16%) of direct medical costs, 3 billion Euros (86%) of indirect costs and 100 million Euros (3%) of drug cost.[8] At the individual level, other studies reported that patients with depression had 50-80% higher medical expenditures than comparable patients without depression.[9] Moreover,

workers and employee with depression were on short term inability an average of 1.5 to 3.2 days longer in monthly period than those without depression, translating into an average salary loss of $182 to $395 person/month.[10]

A positive bidirectional association between depression and type 2 diabetes also has been well established. Outcome from two meta-analyses studies demonstrated that individuals with depression had a 37% increased risk of expanding type 2 diabetes and patients with type 2 diabetes had a 24% increased risk of progressing depression.[11] Women with diabetes had significantly higher prevalence of depression than men (23.8% vs. 12.8%).[12] Although insulin resistance is the basic mechanism for type 2 diabetes, the relationship between depression and insulin resistance is very less studied and leftover indistinguishable with conflicting results reported from previous studies.

Insulin resistance can be present in probably well appearing persons. The reported prevalence of insulin resistance in the general population ranges from 21.5% to 59% and varies by racial/ethnic groups.[13] Among adults aged 20 years and older aged 60 years with euglycemia, the prevalence of insulin resistance information was 32.2%.[14] The prevalence of insulin resistance was still higher among patients with metabolic syndrome and chronic diseases. In a recent study conducted among 1,453 United State adults those with highest quantity (20%) of the homeostasis model assessment for insulin resistance (HOMA-IR), a substitute of insulin resistance, were almost 20 times more likely to have metabolic syndrome than those with the lowest quintile of HOMA-IR.[15] A cross sectional study from Thailand adults estimated 21.5% of women with polycystic ovary syndrome had insulin resistance.[16] About 50% of patients with primary hypertension were insulin resistant, regardless of their treatment status (treated or untreated). Overall, the variations in reported prevalence rates may result from the methods used to measure insulin resistance and the cutoff value to identify the insulin resistance.[17]

Depression is a mood disorder. As defined by the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV) (American Psychiatric Association, 1994), depression can be further classified as major depressive disorder (MDD), also known as major depression, dysthymic disorder, and depressive disorder not otherwise specified or minor depression.[18] Investigation of the relationship between depression and insulin resistance among young adults is essential to understanding how insulin resistance may be influenced by depression among young which is generally considered a healthy population. With identification of persons who are at risk of developing insulin resistance in primary care clinics, preventive interventions can be developed to intervene at an early stage. Significant impact of depression on young adults' health will encourage health care professionals to recognize depression in the clinical settings and provide appropriate treatment. From patients intervention may help interruption or prevent the progression of insulin resistance to type 2 diabetes. Improving the state of insulin resistance at an early age can not only delay the onset of type 2 diabetes, but also may decrease the morbidity and mortality rate of chronic diseases associated with insulin resistance subsequently in life as well as health care costs.

We hypothesized that there would be a positive association between depression and insulin resistance and that this association would be explained by the embarrassing or interfering effects of clinical and behavioral factors and increasing with body mass index.

MATERIALS AND METHODS

The present cross sectional study was conducted in the Department of Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi during the period spread between April 2013 to Sep 2015. The approval of this study was obtained from Ethical Committee Institute of Medical Sciences, Banaras Hindu University, Varanasi. Total 120 individuals were enrolled (age groups 30-70 years) after containing their written consent form and divided in to four groups each group had 30 individuals. Group 1 was considering as healthy control, Group 2 was only diabetic, Group3 was only depression and Group 4 was both diabetic with depression which follows the inclusion criteria of WHO and Diabetes Data Group. Clinical examination was done by a registered physician using a predesigned questionnaire. Anthropometric measurements were taken using standard methods.

Inclusion and Exclusion Criteria

Diagnosis of diabetes was based on National Diabetes Data Group Study and World Health Organization criteria as given below: Symptoms of diabetes and random blood glucose concentration of 200mg/dl (11.1 mmol/l) and above or Fasting plasma glucose 126 mg/dL (7.0 mmol/L) and above or Two-hour plasma glucose of 200 mg/dL (11.1 mmol/L) and above during an oral glucose tolerance test.

A detailed history along with a detailed physical and mental status examination was undertaken. The patients were assessed for psychiatric morbidities as per the Diagnostic and Statistical Manual of Mental Disorders fifth edition (DSM-V 2013) criteria. Depressive patients have following symptoms for at least 2 week. One of the symptoms must be depressed mood or loss of interest. Depressed mood most of the day, nearly every day, as indicated by either subjective report or observed by others, insomnia or hyper insomnia nearly every day, psychomotor agitation or retardation nearly every day, fatigue or loss of energy nearly every day, feeling of worthlessness or inappropriate guilt nearly every day,

diminished concentration or indecisiveness nearly every day and recurrent thoughts of death or suicide.

Those patients age 30-70 years male/female that was not on any medication before and diagnosed drug naive depressive patient as per DSM V were included for the study. Patients below 30 and above 70 years of age with any other associated physical illnesses and taking any drug for longer period of time e.g. ATT, steroids etc were excluded from this study. All subjects were interviewed according to a proforma, which included socio-demographic details, duration of medical complaints, chief medical complaints, history of present illness, past history of medical and psychiatric illness, family history of medical and psychiatric illness, personal history, premorbid personality, physical and mental status mental status examination.

Statistical Analysis

Statistical analysis for Comparisons of group differences was analyzed by Chi $\chi 2$ test for normal, non-normal, and categorical variables, respectively. Means ± SD, medians and percentages are reported where appropriate. Data analysis was performed using SPSS 16.0 and a value $p<0.05$ was considered as significant.

LABORATORY INVESTIGATION

Hematological

These include hemoglobin, total leukocytes count, differential leucocytes count, platelet count and general blood picture (GBP). Hemoglobin was estimated by acid-hematin method employing Sahli's hemoglobin meter. Total Leucocytes Count was done by hemocytometer method using Thomas pipette and white blood cells counting Chamber. Differential Leucocytes Count and Platelet count were done by standard laboratory method. Liver function tests including aspartate aminotransferase, alanine aminotransferase, Alkaline phosphates, Gamma glutamyl trans peptidase were done using Synchron CX5 (Clinical Auto analyzer, USA) Fasting plasma glucose was done after a fasting of 8-10 hours, by auto analyzer (Synchorn CX5, clinical system autoanalyser, USA) using enzymatic glucose oxidase peroxides technique. Blood urea was estimated by the GLDH urease method by autoanlyzer. Serum creatinine was done by alkaline picrate method of Jaffe reaction by auto analyzer. 24 hour urine was measured by ESABACH'S method. Total cholesterol, triglycerides and HDL was measured by autoanalyzer (Beckman-US-Synchron Cx5 system) using cholesterol reagent for cholesterol, TG, GPO reagent for triglycerides and HDL cholesterol reagent for HDL estimation. VLDL cholesterol was estimated by the formula, triglyceride divided by five. LDL cholesterol was calculated using the Friedewald formula.

Plasma Insulin Assay

Plasma samples were separated from blood by centrifuging at 1500 *g* for 15 minutes. Samples for insulin were taken under fasting condition with duration of 8-10 hours no any caloric intake. Simultaneously sample for blood sugar was drawn. Radioimmunoassay of insulin was done using the kit supplied by the Radiopharmaceutical Division of the Bhabha Atomic Research Centre (BARC), Mumbai. The assay was conducted as per the manual supplied with the kit and its intra and inter assay variation was found to be <5% and <7% respectively.

Calculation of Insulin Resistance

Insulin resistance was calculated using the homeostasis model assessment R (HOMA), which is a mathematical model, and gives a quantitative estimation based upon the basal insulin level multiplied by the basal plasma glucose concentration divided by 22.5 in human. This is based on the interaction between various organs, especially the liver, pancreas and the peripheral tissues. HOMA estimates of insulin resistance (HOMA-R) have also been validated by comparison with euglycemic hyper insulinemic clamp studies (Matthews et al, 1985; Bonoras et al, 2000) as well as with the intravenous glucose tolerance tests (IVGTF) and continuous infusion of glucose with model assessment (Hermans et al, 1999). HOMA-R has been found to have a better correlation with clamp studies than the insulin resistance obtained by the first insulin response (Ikeda et al, 2001).

HOMA-R is a useful mode to assess insulin resistance and has been used in several studies (Kastuski et al, 2001, Albraeda et al, 2000, Emoto et al, 1999, Chiu et al, 2000) and epidemiological studies (Haffner et al, 1996).

$$\text{HOMA-R} = \frac{\text{Fasting plasma insulin (µU/ml) x Fasting glucose (mmol/L)}}{22.5}$$

HOMA-R = level >2 were taken as significant and predictive of insulin resistance.

Test Principle

The insulin Quantitative Test Kit is based on a solid phase enzyme linked immunosorbent assay. The assay system utilizes one anti insulin antibody for solid phase (micro titer wells) immobilization and another anti-Insulin antibody in the antibody-enzyme (horseradish peroxidase) conjugate solution. The standards and test specimen (serum) are added to the Insulin antibody coated wells. Then anti-Insulin antibody labeled with horseradish peroxidase (conjugate) is added. If human Insulin is present in the specimen it will combine with the antibody on the well and the enzyme conjugate resulting in the Insulin molecules being sandwiched between the solid phase and enzyme-linked antibodies. After 1 hour incubation at room temperature, the wells are washed to remove unbound labeled antibodies. A solution of tetramethylbenzidine (TMB) is added and incubated for 20 minutes, resulting in the development of a blue color. The color development is stopped with the addition of stop solution. The color is changed to yellow and measured spectrophotometrically at 450 nm. The

concentration of Insulin is directly proportional to the color intensity of the test sample.

RESULTS

Total 120 subjects were equally divided in four groups and the base line characteristics of all groups are shown in Table 1. Each group had taken in only 30 subjects equal proportion of male and female. Group 1 considered as healthy control with maximum age group (16) 50-70 year. Group 2 diabetic group maximum patient were in the age group (28) 30-70 years, while in the Group 3 containing only depressive patient, maximum patient were in (18) 30 to 50 yr age group. Whereas in Group 4 containing patient both diabetes and depression, maximum patient were in the age group (15) 50-70year Maximum number of patient suffering from diabetes were found to be older, where as patient having only depressive disorder were found to be younger (p=0.015). Male and female patient were equally distributed in all four group. The Body mass index of Group 1 healthy control was normal weight (53.3%) BMI 18.5-24.9, Group 2 diabetic patients maximum (43.3%) were overweight (BMI 25-29.9), while in the third group containing only depressive patient, maximum were in the range of normal (46.7%) BMI 18.5-24.9, But in the fourth group containing patient having both depression and diabetes, maximum patients (46.7%) were obese (BMI>30). In the diabetic group, maximum patient (43.3%) had insulin resistance between 2 to 10. while in the third group containing only depressive patient, maximum patients were in the range of having insulin resistance 2 to 10. While in the fourth group having both depression and diabetes maximum patient had insulin resistance more than 10.

Figure 1 shows the correlation between body mass indexes with insulin resistance and fasting blood sugar in all four groups. Group 4 have both depressions with diabetes showing higher Insulin resistance, with higher Body mass index and fasting blood sugar in comparisons with other three groups.

Table 1. Anthropometric and characteristic details of all four Group of Patients.

Parameter		Control		Only Diabetic		Only Depression		Both Diabetic +Depression		*p*-value
		No.	%	No.	%	No.	%	No.	%	
Age code	30-50yr	12	36.7	14	46.7	18	60	13	43.3	0.739
	50-70yr	16	56.7	14	46.7	11	36.7	15	50	
	>70yr	2	6.6	2	6.7	1	3.3	2	6.7	
Gender	Male	15	50	15	50	15	50	15	50	1.000
	Female	15	50	15	50	15	50	15	50	
BMI	18.5-24.9	16	53.3	6	20	14	46.7	6	20	0.015
	25-29.9	13	43.3	13	43.3	13	43.3	10	33.3	
	30-39.9	1	3.4	11	36.7	3	10	14	46.7	
IR code	<2	-	-	3	10	12	40	2	6.7	0.001
	2-10	-	-	13	43.3	17	56.7	10	33.3	
	10-20	-	-	10	33.3	1	3.3	12	40	
	>20	-	-	4	13.3	0	0	6	20	
Total		30	100	30	100	30	100	30	100	

The Characteristic details of Biochemical analysis of all four groups of Patients are shown in Table 2. Group 1 healthy control have mean age was 45.35±5.77. The mean age in patient in diabetic group was 52.87± 9.19years and 49.90±11.90 in those having only depression group third and in the fourth group, patient having both depression and diabetes, mean age was 53.10±11.75. Group 1 healthy control have normal value of Creatinine mean 0.58±0.101. The mean Creatinine level in patient in diabetic group 2 was 0.92± 0.32 and 0.89±0.34 in those having only depression patients in group 3 and in the fourth group, patient having both depression and diabetes, mean Creatinine level was 0.94±0.33. Group 1 healthy control have normal value of urea mean 18.25±0.75. The mean urea level in patient in diabetic group2 was 25.97±8.16 and 25.33±9.01 in those having only depression group 3 and in the fourth group patient having both depression and diabetes, mean urea level was 26.97±8.19. Group 1 healthy control have normal body mass index mean 19.81±1.56.The mean BMI in patient in diabetic group2 was 28.430±43.03 and 25.63±3.50 in those having only depression group 3 but in the fourth group patient having both depression and diabetes mean BMI was overweight 29.313±4.63. It suggested that body mass index is directly related to insulin resistance. Patient having more body mass index were found to have more insulin resistance. Group 1 healthy control have normal value of cholesterol level mean 130.90±10.78. Mean cholesterol level in diabetic group2 was 239.23±20.61. and in group third containing patient having only depression mean cholesterol level was 239.23±20.61, but in the fourth group patient having both depression and diabetes mean cholesterol level was 286.57±57.00. Group 1 healthy control have normal value of HDL mean 33.62±1.26. Mean HDL level in diabetic group2 was 40.77±9.44 .and in third group containing patient having only depression mean HDL

level was 41.13±9.58, but in the fourth group patient having both depression and diabetes mean HDL level was 39.30±10.10. Group 1 healthy control has normal value of LDL mean 54.295±0.919. Mean LDL level in diabetic group2 was 156.8±9.17. and in third group containing patient having only depression mean LDL level was 156.93±9.34, but in the fourth group patient having both depression and diabetes mean LDL was 172.80±24.02. Group 1 healthy controls have normal value of triglyceride mean 123.60±0.548. Mean triglyceride level in diabetic group 2 was 229.39±44.60 and in third group containing patient having only depression mean triglyceride level was 227.70±46.58, but in the fourth group patient having both depression and diabetes mean triglyceride level was 231.63±42.64.

Group 1 healthy controls have normal value of fasting blood sugar mean 119.20±8.78. Mean fasting blood sugar in diabetic group2 was 143.73±9.39 and in third group containing patient having only depression mean FBS was 99.63±9.25 but in fourth groups having patient diabetes and depression both, mean FBS was 146.90±8.81. Group 1 healthy controls have normal value of insulin level mean 54.86±10.45. Mean insulin level in diabetic group2 was 30.50±20.48 and in third group containing patient having only depression mean insulin level was 16.836±12.65, but in the fourth group patient having both depression and diabetes mean insulin level was 35.060±20.13. Group 1 healthy controls have normal value of insulin resistance mean 2.86±0.12. Mean insulin resistance level in diabetic group second was 11.0333±7.74 and in third group containing patient having only depression mean insulin resistance level was 4.0533±2.97, but in the fourth group patient having both depression and diabetes mean insulin resistance level was 13.0263±7.85.

Group 1 healthy controls have normal value of systolic blood pressure mean 118.60±11.56. Mean systolic blood pressure in diabetic group2 was 138.93±15.79 and in group 3 containing patient having only depression mean SBP was 128.93±10.63, but in the fourth group patient having both depression and diabetes mean SBP was 138.93±15.79 mm Hg. Group 1 healthy controls have normal value of diastolic blood pressure mean 68.50±6.220. Mean diastolic blood pressure in diabetic group2 was 88.40±13.30 and in third group containing patient having only depression mean DBP was 80.80±5.35, but in the fourth group patient having both depression and diabetes mean DBP was 88.40±13.30.

Table 2. Details characteristic of Biochemical analysis of all four groups of Patients.

Parameter	Control N=30	Only Diabetic N=30	Only Depression N=30	BOTH (Diabetic +Depression) N=30	p-value
Age (Year)	45.35±5.77	52.87±9.19	49.90±11.90	53.10±11.75	0.459
Creatinine (mg/dl)	0.58±0.101	0.92±0.32	0.89±0.34	0.94±0.33	0.857
Urea (mg/dl)	18.25±0.75	25.97±8.16	25.33±9.01	26.97±8.19	0.945
BMI(Wt./m^2)	19.81±1.56	28.430±4.03	25.633±3.50	29.316±4.63	0.002
cholesterol (mg/dl)	130.90±10.78	239.23±20.61	239.23±20.61	286.57±57.00	0.001
HDL(mg/dl)	33.62±1.26	40.77±9.44	41.13±9.58	39.30±10.10	0.742
LDL(mg/dl)	54.295±0.919	156.80±9.17	156.63±9.34	172.80±24.02	0.001
Triglyceride (mg/dl)	123.60±0.548	229.30±44.60	227.70±46.58	231.63±42.64	0.943
FBS (mg/dl)	119.20±8.78	143.73±9.39	99.63±9.25	146.90±8.81	0.001
Insulin(ml U/L)	54.86±10.45	30.5043±20.48	16.8363±12.65	35.060±20.13	0.001
Insulin resistance	2.86±0.12	11.0333±7.74	4.0533±2.97	13.0263±7.85	0.001
Systolic BP (mmHg)	118.60±11.56	138.93±15.79	128.93±10.63	138.93±15.79	0.010
Diastolic BP(mmHg)	68.50±6.220	88.40±13.30	80.80±5.35	88.40±13.30	0.013

The difference is statistically significant as compared to controls groups, $p < 0.05$ considered as significant. The values are expressed as mean ± SD (Standard Deviation).

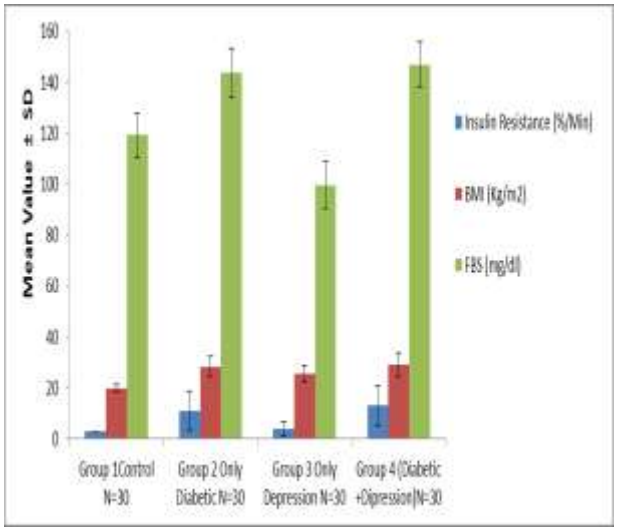

Fig. 1: Bar Diagram showing relation between HOMA Insulin Resistance, Body mass index and Fasting Blood Sugar in all subjects groups.

DISCUSSION

The present study supports previous several cross sectional studies which have been done earlier on insulin resistance with depression (Adriaaness et al., 2006) and have showed positive correlation between depressive symptoms and insulin level in diabetic patients. In our study group patient's having both depression and diabetes mean Body mass index was 29.313±4.63. Whereas those with depression had BMI lower side (25.633±3.50) than those with diabetes without depression (28.430±4.03). Patients having higher BMI more than 25 had high insulin resistance among diabetics only where as those with depression only 53.3% patients had higher BMI more than 25 and insulin resistance more than 10 was found in 3.3% only. On contrary patients having depression and diabetes both with BMI of more than 25. Total 66.7% patients had insulin resistance more than10 among all patients. Thus when depression is a comorbid condition with diabetes there is more insulin resistance. All the observation was statistically significant. Higher value of lipid was seen amongst patients having diabetes and depression both than depression and diabetic only. The HDL values were identical in all three groups. Similarly higher insulin resistance was observed amongst diabetics than the depressive patients and greater resistance was seen in those who had diabetes and depression both.

It suggests that body mass index is directly related to insulin resistance. Patient having more body mass index were found to have more insulin resistance. Patients having depressive disorders were found to have more insulin level compared to normal person. In the diabetic group, maximum patient (43.3%) had insulin resistance between 2 to 10 insulin resistance codes. While in the depressive group, maximum patients (56.7%) were found to have insulin resistance codes 2 to 10. In group four, patient having both depression and diabetes, maximum patient (60%) had insulin resistance more than 10 insulin resistance codes. If the patients having insulin resistance have not clinically manifested as diabetes it remains a potential threat in future to develop diabetes, however those with diabetes and depression both treatment with oral hypoglycemic drug may have impaired insulin resistance. A positive relationship between depressive symptoms and insulin resistance has been found in several cross-sectional population based studies.[19] Three of the studies focused on young adults (Pearson, et al., 2010, Timonen, et al., 2006, Timonen, et al., 2007), while the other four investigated the association among middle- or older-aged adults.[20] Contradictory to these studies, depression was found to be negatively associated with insulin resistance in one cross-sectional study conducted among a randomly selected sample of 4,286 British women aged 60-79 years. In this study, depression was assessed via three methods: use of antidepressant medications, self-report of having a clinical diagnosis of depression and the EQ5D mood question of the EuroQol group 2009. Two studies have reported no significant association between depression and insulin resistance. In a prospective 4-phase cohort study (phase I: 1979-1983; phase II: 1984-1988; phase III: 1989-1993; Phase IV: 1993-1997), found no significant association between depression and insulin resistance among Wales men aged 45-59 years.[21] Similarly, Roos et al. (2007) found no association between insulin resistance and depressive symptoms in a retrospective study among 1,047 Swedish women with risk factors for diabetes aged 50- 64 years old.[22]

All of the above studies were correlation studies; therefore, no causation between depression and insulin resistance was established. Previous six studies were based on limited to middle and older-aged adults and often failed to examine the effect of gender on the relationship between depression and insulin resistance. Moreover, all were conducted in China, Australia and Finland.[23,24,25] None of these previous studies had investigated the role of race/ethnicity in the relationship between depression and insulin resistance. Few examined the role of gender in this relationship in young adults. In addition, measures of depression and insulin resistance varied across the studies. Depression was primarily measured by self-report depression questionnaires or inventory, such as use of antidepressant medicine, self-report of being diagnosed with depression and response to Euro Qol mood questions (Lawlor, et al., 2003), with the Beck's depression inventory (Timonen, et al., 2005; Timonen, et al., 2007), with the Centre for Epidemiological Studies Depression (CESD) (Adriaanse, et al., 2006; Pan, et al., 2008), with the 30-item General Health Questionnaire (GHQ) (Lawlor, et al., 2005), with Hopkins Symptoms Checklist (Timonen, et al., 2006), or with self-rated symptoms of depression from the Gothenburg Quality of Life Instrument.[26] There was only one study that used the Composite International Diagnostic Interview (CIDI) to make a clinical diagnosis of depression.[27] A study found that depression is inversely associated with insulin resistance, but

positively associated with diabetes.[28]

In present study, it has been observed that depression also contributes significantly to insulin resistance. In other words, we can say that depression is also a risk factor for insulin resistance. In our study a significant association has been found between depression with diabetes and insulin resistance. Probably in other studies the antidepressant drugs have also been taken in to considerations which have not been taken account and therefore the variations occur in two studies.

CONCLUSION

In this study we have found that prevalence of diabetes directly associated with depression and insulin resistance which is very high in older diabetic patients than depressive patient. The Patients having higher body mass index were found to be having more insulin resistance. Obesity directly contributes to insulin resistance in diabetic depressive patients. Lipid parameter was also found to be deranged amongst diabetic patient. The patient having more insulin resistance were found to have greater decline in high density cholesterol, while total cholesterol, Low Density Lipid and triglycerides level were found to be greater in these patient. Depression also contributes to insulin resistance. Out of 30 (60%) 18 depressive patient had insulin resistance more than twice. Thus we can say depression is directly correlated with insulin resistance. Patient having both depression and diabetes were found to be having greater insulin resistance than patients who had only diabetes. It suggests that depression contributes to insulin resistance.

ACKNOWLEDGMENT

We are grateful to the Diabetic patients and Depressive patients without whose invaluable information for this study could not have been analyzed**.** We acknowledge the author Mr. Santosh Kumar Yadav for helped in design of the study, manuscript preparation, interpretation, statistical analysis, and literature search, Dr. Vipul Kumar Garg for Concept and Design of the study, analysis and interpretation, data collection, statistical analysis, and literature search and Dr. Suchi Tripathi for revision of the manuscript and draft literature. The Author acknowledges the help rendered by Prof. Kamlakar Tripathi for advising the Concept and manuscript design, critical revision of the manuscript.

Conflict of Interest

None Declared.

REFERENCES

1. Fonseca, V. Early identification and treatment of insulin resistance: impact on subsequent prediabetes and type 2 diabetes. Clinical Cornerstone, 2007; suppliment7: S7-18.
2. Reaven G.M. Insulin resistance, type 2 diabetes mellitus and cardiovascular disease: the end of the beginning. Circulation, 2005; 112(20): 3030-3032.
3. Lloyd-Jones, D, Adams, R.J. Brown, T.M. Carnethon, M., Dia, S, De Simone, G., Wylie-Rosett, J. Heart disease and stroke statistics-2010 update: a report from the American Heart Association. Circulation, 2010; 12197: e46-e215.
4. Jellinger, P.S. Metabolic consequences of hyperglycemia and insulin resistance. Clinical Cornerstone, 2007; 8(supplement7): S30-S42.
5. Halfin, A. Depression: the benefits of early and appropriate treatment. American Journal of Managed Care, 2007, 13(4Suppliment), S92-97.
6. Greenberg, P.E., Kessler, R.C. Birnbaum, H.G., Leong, S.A. Lowe, S.W. Berglund, P.A. Corey Lisle, P.K. The economic burden of depression in the united states: how did it change between 1990 and 2000.Journal of clinical Psychiatry, 2003; 64(12): 1465-1475.
7. Wade, A.G. and Haring, J.: A review of the cost associated with depressions and treatment noncompliance: the potential benefits of online support. International Clinical Psychopharmacology, 2010; 25(5): 288-296.
8. Sobocki, P. Lekander, I., Borgstrom, F, Strom, O., Runeson, B.: The economic burden of depression in Sweden from 1997 to 2005.European Psychiatry., 2007; 22(3): 146-152.
9. Kessler, R.C. Barber, C. Birnbaum, H.G., Frank, R.G., Greenberg, P.E., Rose, R.M. Wang, P. Depression in the workplace: effect on short-term disability. Health affairs, 1999; 18(5): 163-171.
10. Chapman, D.P., Perry, G.S. Strine, T.W. The vital link between chronic disease and depressive disorders. Preventing Chronic Disease, 2005; 2(1).
11. Di Marco, F. Santus, P. Centanni, S.: Anxiety and depression in asthma. Current opinion in pulmonary Medicine.2010.Doi:10.1097/MCP.0b013e328341005f.
12. Rougulies, R.: Depression as a predictor for coronary heart disease. A review and meta-analysis. American Journal of Preventive Medicine, 2002; 23(1): 51-61.
13. Nabi, H., Kivimaki, M., Suominen, S. Koskenvuo, M. Singh Manoux, A. Vahtera, J.: Does depression predict coronary heart disease and cerebrovascular disease equally well? The Health and Social support Prospective cohort Study. International Journal of Epidemiology, 2010; 39(4): 1016-1024.
14. Nouwen, A., Winkley, K. Twisk, J. Lloyd, C.E. Peyrot, M. Ismail, K. Pouwer, F. Type 2 diabetes mellitus as risk factor for the onset of depression: a systematic review and meta-analysis. Diabeteologia, 2010; 53(12): 2480-2486.
15. Ali, S. Stone, M.A., Peters. J., Davies, M.J. Khunti, K. The prevalence of co-morbid depression in adults with type 2 diabetes: a synthetic review and Meta analysis. Diabetic Medicine, 2006; 2391(1): 11, 1165-1173.
16. Do H.D., Lohsoonthorn, V., Jiamjarasrangsi, W., Lertmaharit, S., Williams, M.A. Prevalence of insulin resistance and its relationship with

cardiovascular disease risk factor among Thai adults over 35 years old. Diabetes Research and Clinical Practice, 2010; 89(3): 303-308.
17. Jago, R., Baranowski, T., Buse, J., Edelstein, S., Galassetti, P., Harrell, J., Pham, T. Prevelence of the metabolic syndrome among a racially/ethnically diverse group of U.S. eighth grade adolescents and associations with fasting insulin and homeostasis model assessment of insulin resistance level. Diabetes Care, 2008; 31(10): 2020-2025. doi:10.2337/dc08-0411dc08-0411.
18. American Psychiatric Association. Diagnostic manual of mental disorder, Washington, DC., 1994; 4th Edition.
19. Ioannou, G.N., Bryson, C.L. Boyko, EJ: Prevalence and trends of insulin resistance impaired fasting glucose and diabetes. Journal of diabetes and its complications, 2007; 21(6): 363-370.
20. Vrbikova, J. Dvorakova, K. Grimmichova, T, Hill, M, Stanicka, S, Cibula, D. Vondra, K. Prevalence of insulin resistance and prediction of glucose intolerance and type 2 diabetes mellitus in women with polycystic ovary syndrome. Clinical chemistry and Laboratory Medicine, 2007; 459(5): 639-644.
21. Lima, N.K., Abbasi, F., Lamendola, C., Reaven, G.M.: Prevalence of insulin resistance and related risk factor for cardiovascular disease in patients with essential hypertension. American Journal of Hypertension, 2009; 22(1): 106-111.
22. Adriaanse, M.C. Dekker, J. M, Nijpels, G., Heine, R.J. Snoek, F.J. Pouwer, F. Associations between depressive symptoms and insulin resistance: the Hoorn study. Diabeteologia, 2006; 49(12): 2874-2877.doi:10.1007/s00125-006-0500-4.
23. Pan, A., Ye, X., Franco, O.H., Li, H., Yu, Z., Zou, S. Lin, X. Insulin resistance and depressive symptoms in middle aged and elderly Chinese: finding from the Nutrition and Health of Ageing population in China Study. Journal of affective disorders, 2008; 109(1-20): 75-82.
24. Pearson, S. Schmidt, M. Patton, G. Dwyer, T. Blizzard, L. Otahal, P. Venn, A. Depression and insulin resistance: Cross-Sectional Association in Young Adults. Diabetes care., 2010.
25. Timonen, M., Salmenkaita, I., Jokelainen, J. Laakso, M., Harkonen, P. Koskela, P. Keinanen Kiukaanniem I, S: Insulin resistance and depressive symptoms in young adult males: finding from Finnish military conscripatientss. Psychosomatic Medicine, 2007; 69(8): 727-728.
26. Lawlor, D.A. BenShlomo, Y., Ebrahim, S., Davey Smith, G., Stansfeld, S.A., Yarnell, J.W., Gallacher, J.E. Insulin resistance and depressive symptoms in middle aged men: findings from the Caerphilly prospective cohort study. British Medical Journal, 2005; 330(7493): 705-706.
27. Roos, C., Lidfeldt, J., Agardh, C.D., Nyberg, P., Nerbrand, C, Samsioe, G., Westrin, A. Insulin resistance and self rated symptoms' of depression in Swedish women with risk factors for diabetes: the women's Health in the Lund Area Study. Metabolism: Clinical and Experimental, 2007; 56(6): 825-829.
28. Markku Timonen, Mauri Laakso, Jari Jokelainen, Ulla Rajala, V Benno Meyer-Rochow, Sirkka Keinänen-Kiukaanniemi : Insulin resistance and depression: cross sectional study *BMJ*, 2005; 330: 17–18.