

## Concern between medication non-adherence and diabetes associated depression

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### ABSTRACT

**Background:** Diabetes mellitus is one of the health disorders that acquire mankind immensely. An ominous twin of diabetes mellitus is diabetes associated depression which is often unrecognised in routine diabetic care. The objective of this study was to find the prevalence and correlation between medication adherence and diabetes associated depression.

**Methods:** It is a conducted as cross sectional study using Morisky medication adherence scale to evaluate treatment adherence of type II diabetes mellitus. Patient health questionnaire-9 was used to scale the level of depression among our study subjects. Correlation between measures of treatment non adherence and level of depression was elucidated.

**Results:** Out of 250 patients, 167 (66.8%) (Males -103, Females-64) and 83 (33.2%) (Males-31, Females-52) subjects has medium & low adherence to medication with an average score 6.8 and 4.2 respectively. Total prevalence of depression among diabetics in our study is 41.1% (males-19.2%, females 21.9%). Percentage of patients found to have minor depression was 22.3 % and 18.8 % of depressive subjects falls under major depression category according to PHQ-9 questionnaire with average score of 8.6 for minor depression and 11.9 for major depression. Positive correlation is seen between medication non adherence and diabetes associated depression (Low adherence & Major depression -0.85, Medium adherence & Minor depression -0.79).

**Conclusions:** Unnoticed depression among diabetic individuals reduces treatment adherence and must be addressed in any patient showing poor response to the treatment. Improving treatment adherence helps to combat diabetes as well as depression.

**Keywords:** Diabetes associated depression, Diabetes education, Medication adherence

### INTRODUCTION

In the era of epidemiologic transition, diabetes mellitus is one of the health disorders that acquire mankind immensely. There is no plummet in the prevalence of diabetes; India is expected to harbour seventy millions of diabetes patients by 2030. Considerable level of illiteracy, hindered access to health care, low socioeconomic status perpetuates the complexity seen with diabetes mellitus management.<sup>1,2</sup> Among various barriers that are studied to overcome the diabetes pandemic, non-adherence to medication is evident and

prevails widely in our population.<sup>3</sup> In General, medication adherence is defined as the patient's conformance with the provider's recommendation with respect to timing, dosage, and frequency of medication-taking during the prescribed length of time.<sup>4</sup> Longer duration of treatment, unaffordability, lack of awareness and poor self-care are some of the common, well known factors that culminates in medication non-adherence of diabetes mellitus.<sup>5</sup>

An ominous twin of diabetes mellitus is diabetes associated depression which is often unrecognised in routine diabetic care. The association is postulated as

'bidirectional', diabetes is having significant impact on determinants of depression and vice versa. There are few consensus that give us an input, diabetes patients with depression are reluctant to adhere with their treatment and hence has constant high blood glucose level. Biological plausibility is also explored between hyperglycaemia and accentuation of depression.<sup>6,7</sup> Studies has suggested that diabetes associated depressive patient's neglects not only their anti-diabetes medications, they tend to tend express less adherence to treatment of the co morbid conditions like hypertension and dyslipidemia.<sup>8,9</sup> Amidst other studies done individually on medication adherence and depression determinants on diabetes patients, we conducted a cross sectional study to correlate the level of medication adherence and depression with an eagle eye view.

## METHODS

### Study permission

This study was conducted by department of Pharmacology in collaboration with internal medicine of tertiary care teaching hospital. Study protocol was approved by our institutional ethics committee (ECR/724/Inst/TN/2015) and approved by Indian council of medical research (ICMR).

### Study questionnaire

Adherence to medication was assessed using Morisky medication adherence scale (MMAS-8). This is a validated tool and found to be satisfactory to assess treatment adherence. Depression assessment was done using patient health questionnaire<sup>9</sup> which is validated and standard questionnaire, used to assess diabetes associated depression by various research organisations including Indian council of medical research. This questionnaire has overall accuracy of 85%, sensitivity 75% and specificity 90%.

### Sample size determination

Sample size was determined by assuming the average prevalence of depression among diabetes patients, 0.28, power 80% and alpha error 5% and rounded off with respect to study duration. Consecutive two hundred and fifty patients were included for the study.

### Study procedure

Questionnaire was read out by the investigator to the diabetic patients who read the information sheet and gave consent to participate in our study. Demographic details, treatment profile of diabetes and other co morbid conditions were noted. Anthropometry assessment was carried out on the study day. Body height was measured using stadiometer, height (to the nearest 0.1 cm) was taken. A digital scale, with an accuracy of  $\pm 100$  g, was used to measure body weight (BW). The readings were repeated three times and the mean was calculated. The waist circumference (WC) was measured in a horizontal plane, midway between the inferior margin of the ribs and the superior border of the iliac crest. Body mass index (BMI) ( $\text{kg/m}^2$ ) was calculated by dividing weight (in kilograms) by the square of height (in meters). In the end, all our participants were informed the significance of treatment adherence by the investigator.

## RESULTS

Data entry and analysis was done MS Excel Macro and SPSS (Statistical package for Social Sciences) Version 17. Chi square test and Spearman correlation test were employed to elucidate significance and correlation between variables respectively. Out of 250 patients enrolled for our study, number of males were 113 (45.2%) and 137 (54.8%) females. Mean duration of diabetes is 11.6 years and HbA1c 8.9. The most common co morbidity present in our study population was hypertension 54%, followed by dyslipidemia 48.2%. Baseline characteristics of the study subjects are depicted in table 1.

**Table 1: Baseline characteristics of our study subjects.**

Baseline Characteristics	Overall ( Mean $\pm$ SD)	Number of males (n-113)	Number of females (n-137)
Age (in years )	66.2 $\pm$ 9.8	59.01 $\pm$ 4.5	64.02 $\pm$ 3.4
Duration of diabetes (in years)	11.6 $\pm$ 2.1	10.8 $\pm$ 3.4	9.8 $\pm$ 2.3
Body mass index ( $\text{Kg/m}^2$ )	25.1 $\pm$ 1.4	25.7 $\pm$ 1.78	24.3 $\pm$ 0.76
Literacy rate	63.00%	66.26%	60.01%
Income	Rs .8815/-INR	Rs. 10.031/-INR	Rs. 7600/-INR
Residence, urban vs. rural	Urban 54.4 %	52.10%	50.98%
	Rural 45.6%	47.90%	49.02%
HbA1c value	8.9 $\pm$ 0.9	8.2 $\pm$ 1.2	9.7 $\pm$ 1.1
Using oral hypoglycaemic agents alone	165 (66%)	73	92
Using oral hypoglycaemic with insulin	85 (34%)	48	37
Diagnosed with coexisting hypertension	135 (54%)	61	74
Diagnosed with coexisting dyslipidemia	123 (48.2%)	67	66

**Table 2: Variables showing significant association with medication non adherence and diabetes associated depression.**

Variables	MMAS score	Odds ratio (95% CI)	PHQ-9 score	Odds ratio (95% CI)
Gender (Male vs. Females)	3.7	p- 0.041, 1.17 (1.11-1.63)	9.12	p-0.05, 1.14 (1.02-1.34)
Duration of diabetes (< 5 years Vs. >5 years)	4.6	p-0.002, 1.89 (1.11- 1.92)		
Literacy (Illiterate Vs literate)	4.1	p-0.028, 2.3 (1.76-2.59)	7.95	p-0.032, 1.67 (1.21-1.89)
Income (< 5000 or >5000) per month	5.9	p-0.015, 1.54 (1.33-1.75)	8.32	p-0.021, 1.33 (1.11-1.78)
BMI (< 25 or >25kg /m <sup>2</sup> )	6.8	p-0.052, 1.76 (1.32-1.92)	7.81	p-0.05, 1.32 (1.02-1.56)
Use of oral drugs only	6.7	p-0.031, 1.13 (1.02-1.45)	6.81	p-0.05, 1.12 (1.09-1.38)
HbA1c (< 7or >7)	3.7	p-0.033, 1.43 (1.21-1.63)	9.61	p-0.023, 1.12 (1.01-1.24)
Use of Insulin plus oral agents	4.6	p-0.027, 1.13 (1.09-1.45)	10.09	p-0.001, 1.22 (1.12 -1.42)
Co morbidity (present vs absent)	4.3	p-0.022, 1.78 (1.44-1.98)	10.79	p-0.001, 1.44 (1.14 -1.78)

MMAS -8 Score 8 - High Adherence; 6-8 –Medium adherence; <6 -Low adherence; PHQ- 9 Score 5-9 Minor depression; PHQ-9 Score 10-14 major depression

**Table 3: Correlation between medication adherence and diabetes associated depression.**

No	Adherence Range	Average depression score	Correlation coefficient
1	<6	11.7	0.85
2	6-8	9.3	0.79
3	8	5.2	0.72

MMAS -8 Score 8 –High Adherence; 6-8 –Medium adherence; <6 -Low adherence; PHQ- 9 Score 5-9 Minor depression; PHQ- 9 Score 10-14 major depression

Number of subjects with medium adherence is 167 (66.8%) (males-103, females-64) and 83 (33.2%) (males-31, females-52) subjects has low adherence to medication with an average score 6.8 and 4.2 respectively. Total prevalence of depression among diabetics in our study is 41.1% (males-19.2%, females 21.9%). The percentage of patients found to have minor depression was 22.3% and 18.8% of depressive subjects falls under major depression category according to PHQ-9 questionnaire with average score of 8.6 for minor depression and 11.9 for major depression. Binary logistic regression values between variables and average adherence score & depression score is shown in Table 2.

## DISCUSSION

Escalating number of chronic illness mandates the daily intake one or more medicines by global population. Medication not continued as prescribed in about 50% of cases and never filled in 20-30% of cases. Medication non adherence results in poor quality of life, decreased life expectancy and affects health economy, direct cost expenditure rise up to 300 million US dollars. Non-adherence causes ~30% to 50% of treatment failures and 125,000 deaths annually.<sup>10,11</sup>

In our study, about sixty six percent of subjects has medium to low adherence towards their anti-diabetes medicines. A study conducted by Arulmozhi et al showed fifty percent of diabetic population has low adherence which is slightly less than our findings.<sup>12</sup> Rates of medication adherence drops as years pass on, our study subjects exhibit poor adherence with increase in mean duration of diabetes and similar trend is reported by Mukherjee et al in 2013. In our study females subjects were found to be less compliant with their treatment when compared with males which is in contrast to the aforesaid studies.<sup>13</sup> Low literacy rate, less income, insulin intake, high BMI and presence of co morbid conditions affects medication adherence considerably.<sup>14</sup>

Findings focussed regarding presence of coexisting diabetes associated depression revealed about forty one percent of diabetic population is affected with depression. In a report by Indian council of medical research showed similar values of prevalence, however the results are discordant with respect to mean duration and use of insulin with respect to us. In our study, longer the duration of diabetes, higher HbA1c values and intake of insulin associated with more score on depression scale.<sup>15,16</sup>

In our study, positive correlation is established between levels of medication adherence and scale of depression in diabetic population. The correlation is also supported by experimental and clinical studies which are discussed here. Diabetes associated depression contributes significantly in medication non adherence and poor diabetic control increases the risk of depression , this vicious relationship is supported by biological certain recent biological findings. Serotonergic system is affected by uncontrolled hyperglycaemias, the levels of free tryptophan decreases and tryptophan hydroxylase enzyme which is responsible for conversion tryptophan to 5-Hydroxytryptamine (5-HT) is found dysfunctional among diabetes population. Low levels of serotonergic system

function pave the possible link between diabetes and depression.<sup>17,18</sup> In an experimental study, streptozocin induced diabetic rats express less number of 5-HT1A receptors in prefrontal cortex which increases risk of depression. Genetic links are also established between diabetes associated depressions, the polymorphisms in the lower expressing allele of the 5-HTT gene 5' promoter region increases depression risk. Down regulation of insulin receptors in and worsening of insulin resistance is implicated in patients with significant depression.<sup>19-26</sup> There are well documented clinical studies that proved diabetes associated depressive patients do not adhere with their treatment and succumb to higher macrovascular complication and higher mortality rate. Psychological well-being and health outcome improves when treatment given for hidden depression among diabetes population.<sup>27-29</sup>

From our study we suggest along with the steps taken to improve medication adherence so far, patients with poor control of diabetes must be assessed for treatment adherence and presence of unsaid depression. Empathy and good communication from physician increases confidence and medication adherence among patients. We suggest also screening for depression is a must need in routine diabetic care. Diabetic counselling by trained educators improves treatment adherence as well as depression.<sup>30,31</sup>

## CONCLUSION

Unnoticed depression among diabetic individuals reduces treatment adherence and must be addressed in any patient showing poor response to the treatment. Improving treatment adherence helps to combat diabetes as well as depression.

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