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The Burden of Co-morbid Depression in Ambulatory Patients with Type 2 Diabetes Mellitus at Kenyatta National Hospital, Kenya

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Abstract

Background: Co-morbid depression is a serious condition in patients with diabetes that negatively affects their self-management, including drug adherence, consequently, the treatment outcomes and quality of life are also affected.

Objective: To determine the burden of co-morbid depression in ambulatory patients with type 2 diabetes at the Kenyatta National Hospital (KNH) and to document their socio-demographic and clinical characteristics and any associated risk factors.

Methods: This was a cross-sectional study done on patients living with type-2 diabetes on follow-up at the diabetes out-patient clinic (DOPC) at the KNH. Systematic sampling method was used to recruit 220 study subjects. The PHQ-9 questionnaire was used to assess for co-morbid depression. Socio-demographic and clinical details were obtained both from the subjects and their medical records. Physical examination was done, including blood pressure and BMI determined. Blood samples were collected from the cubital fossa to measure HbA1C in COBAS INTEGRA system with its reagent in the pre-dilution cuvette for automated analysis of glycated hemoglobin (HbA1c). Statistical associations of patients' characteristics and co-morbid depression were determined using Chi-square test and Odds Ratios.

Results: The prevalence of co-morbid depression in patients with type 2 diabetes at the DOPC of KNH using the PHQ-9 was 32.3% (95% CI 26.4-38.6%). Of these, depression was mild in 42.3%,moderate in 40.8% and severe in 16%. Subjects with co-morbid depression were: aged 65years and above (p = 0.006), over-weight/obese (p = 0.035), and had longer duration of diabetes of 5years and above. The presence of co-morbid depression was significantly associated with poor glycaemic control, (OR = 3.3, 95% CI, 1.6 - 6.8, p = 0.001).

Conclusion: About one-third (32.3%) of the study subjects with type 2 diabetes had co-morbid depression. Patients with type 2 diabetes who are at higher risk (older age of 65 years and above, long duration of diabetes, poor glycaemic control and presence of diabetes-related complications,) should be screened for co-morbid depression.

Background

Diabetes is a metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin utilization, or both [1]. The vast majority of diabetes is type 2 diabetes comprising about 90% of cases [1].

Diabetes is a chronic disease which affects virtually every organ in the human system. The global prevalence of diabetes is continuously rising and the World Health Organization (WHO) projected that 300 million people will suffer from diabetes by 2025 [2].

The prevalence of diabetes in sub-Saharan Africa is expected to triple by 2030, making it a cause for concern not only for health professionals but also policy makers as they initiate strategies to tackle it [3].

Kenya, like other developing countries, is experiencing this emerging diabetes epidemic. It is estimated that the prevalence of diabetes in the country is about 3.3%. This figure is projected to rise to 4.5% by 2025 if this trend continues, according to Kenya National Diabetes Strategy [4]. Diabetes-related co-morbidities and complications are expected to rise in parallel with the rising numbers of diabetes.

Depression is a chronic psychopathological state that involves a triad of symptoms with low or depressed mood, anhedonia, and low energy or fatigue. Other symptoms, such as sleep and psychomotor disturbances, feeling of guilt, low self- esteem, suicidal tendencies, as well as autonomic and gastrointestinal disturbances, are also present [5].

The lifetime prevalence of depression is as high as 20% in the general population worldwide with a female to male ratio of about 5:2 [5]. According to WHO, depression is ranked as the fourth global burden of disease, responsible for the greatest proportion of burden associated with non-fatal health outcomes and account for approximately 12% of total years lived with disability [6]. It is predicted to become second only to ischemic heart disease as a cause of morbidity worldwide [7].

Patients with type -2 diabetes have a rate of major depression 1.6-2 times higher than those in the general population affecting one in every 10 diabetic patients [8].

Diabetes distress (concerns and worries of diabetes and its management) is associated with depressive symptoms [9]. Co-morbid depression is associated with poor self-care [10], poor adherence to

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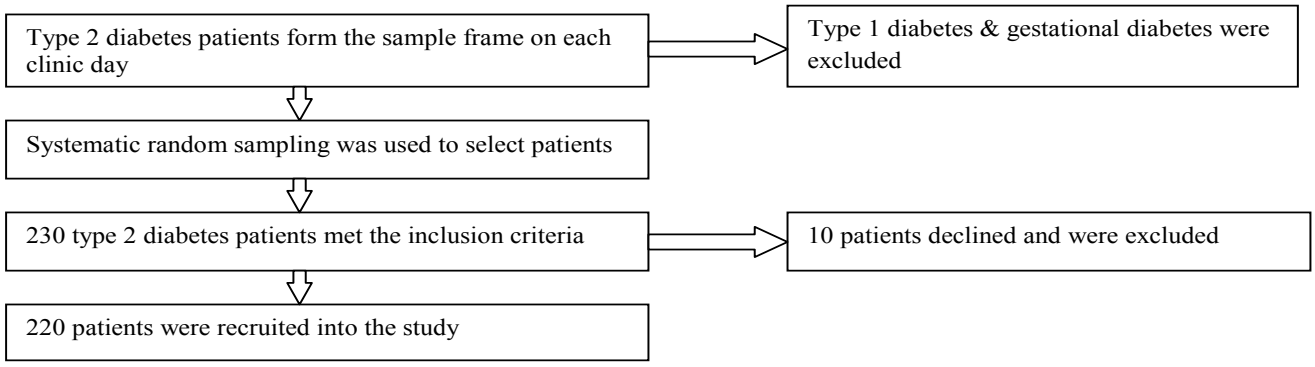

Figure 1: showing a flow chart of subject recruitment.

Table 1: Socio - demographic characteristics of the study subjects.

Variable	Categories	Frequency, N	Percentage (%)
Age (years)	35 - 44	19	8.6
	45 - 54	68	30.9
	55 - 64	78	35.5
	≥ 65	55	25.0
Gender	Male	89	40.5
	Female	131	59.5
Marital Status	Single, unmarried	18	8.2
	Married	188	85.5
	Separated/Divorced	4	1.8
	Widowed	10	4.5
Formal employment status	Employed	78	35.5
	Unemployed	142	64.5
Level of Education	None	20	9.1
	Primary	86	39.1
	Secondary	84	38.2
	Tertiary	30	13.6
Duration of diabetes (years)	< 5	99	45.0
	5 - 10	63	28.6
	>10	58	26.4
Diabetes treatment	Oral glucose - loweringagents (OGLA) alone (n =118):		
	Metformin	60	27.3
	Glibenclamide	2	0.9
	Metformin + other OGLA	56	25.5
	Insulin only	22	10.0
	OGLA + Insulin	80	36.4
BMI (Kg/m²)	Underweight (< 19	4	1.8
	Normal (20.0 - 24.9)	80	36.4
	Over - weight (25.0 - 29.9)	81	36.8
	Obese (≥ 30.0).	54	24.5
Hypertension, Known and/or BP ≥ 140/90 mmHg	Yes	157	71.4
	No	63	28.6

medication [11], chronic complications [12-14] and higher mortality rates [15].

Significance of the Study

Depression is a serious co-morbid condition in diabetes patients that negatively affects self-management, drug adherence, treatment outcomes and quality of life. Knowing the burden of the clinical condition heralds the first step to managing it. There are scarce published data on depression in ambulatory type 2 diabetes in this region. Therefore the study was done to determine the prevalence and severity of co-morbid depression in ambulatory type 2 diabetes patients at KNH and to document their socio-demographic and clinical characteristics.

Methods

This was a descriptive cross-sectional study that we conducted at the diabetes out-patient clinics in KNH. The study population consisted of patients of age ≥ 30 yrs with a diagnosis of type 2 diabetes for ≥ 1 year and followed up at the diabetes clinic. We used a systematic sampling method to recruit the subjects wherein every 2nd

patient on the minor clinic day and every 4th on the major clinic day that met the inclusion criteria was selected (Figure 1).

To collect socio-demographic and clinical data standard questionnaire was used. Patient Health Questionnaire 9 (PHQ-9), was used to assess symptoms of depression [16] (Table 1) (Appendix). PHQ-9 assesses the extent of bother by symptoms of Depressive illness in the previous two (2) weeks on a Likert scale (not-at-all to nearly-every-day). The symptoms range from interest or pleasure in doing tasks, feeling of hopelessness, trouble falling asleep, feeling tired, feeling bad about self, trouble with concentration, slow speaking or restlessness and a feeling of being better dead. The last, tenth, question on the PHQ-9 tool used performs Functional Health Assessment by seeking to know the psycho-social functioning of the study subjects is affected by the emotional difficulties. PHQ-9 has been validated locally and there is a Kiswahili translation available. The standard mercury sphygmomanometer was used to measure Blood Pressure (mmHg), weighing scale for weight (kilograms) and a stadiometer to measure height (meters).

Inclusion criteria

1. The patients of age ≥ 30 years with a documented diagnosis of type 2 diabetes of ≥ 1 year attending the diabetes clinic and gave informed consent.

2. Participants who were able to speak and understand Kiswahili and/or English.

Exclusion criteria

The patients with psychiatric illness other than depression and patients who did not consent to participate were excluded.

Sample size determination

Using the Cochran formula [17], a sample size of 220 diabetic mellitus patients was calculated to estimate prevalence of co-morbid depression at 95% confidence interval within 6.2% precision error.

Definition of study variables

Depression: PHQ-9 score of ≥ 10 was described as presence of clinical depression, a level of score at which there was optimal discriminatory power to make diagnosis of Major Depressive illness [16].

Severity of depression: Clinical depression was categorized into Moderate (10-14), moderately severe (15-19) and Severe (20-27) based on the PHQ-9 scores in the brackets.

Body mass index (BMI): This was calculated and expressed in kg/m^2 and classified as: Underweight (< 19 kg/m$^{2)}$, Normal (20-24.9 kg/m^2), Pre-obese/overweight (25-29.9 kg/m^2) and Obese (≥ 30 kg/m^2) as per The International Obesity Task Force of WHO 2000 [18].

Blood pressure: A subject was considered to have arterial hypertension if he/she was a on blood pressure lowering drugs

Table 2: Factors associated with co - morbid depression in the study patients.

Variable	Co - morbid Depression	No co - morbid depression	OR (95% CI)	P value
Age group (years)				
35 - 44	3 (15.8%)	16 (84.2)	1.0	
45 - 54	21 (30.9%)	47 (69.1)	2.4 (0.6 - 9.0)	0.203
55 - 64	22 (28.2%)	56 (71.8)	2.0 (0.6 - 7.9)	0.210
≥ 65	25 (45.5%)	30 (54.5)	4.4 (1.2 - 17.0)	***0.029****
Gender				
Male	34 (38.2%)	57 (61.8%)	1.6 (0.9 - 2.8)	0.130
Female	37 (28.5%)	94 (71.5%)	1.0	
Employment				
Employed	35 (27.8%)	91 (72.2%)	1.0	
Not employed	36 (38.3%)	58 (61.7%)	0.6 (0.4 - 1.1)	0.110
Education				
None	6 (30.0%)	14 (70.0%)	1.4 (0.4 - 5.0)	0.599
Primary	29 (33.7%)	57 (66.3%)	1.7 (0.6 - 4.4)	0.293
Secondary	29 (34.5%)	55 (65.5%)	1.7 (0.7 - 4.5)	0.261
Tertiary	7 (23.3%)	23 (76.7%)	1.0	
Marital status				
Married	60 (31.9%)	128 (68.1%)	1.0	
Single #	11 (34.4%)	21 (65.6%)	1.1 (0.5 - 2.5)	0.783
Diabetes treatment				
OGLAs only	31 (26.3%)	79 (73.7%)	0.6 (0.4 - 1.1)	0.135
OGLAs + Insulin	32 (37.9%)	48 (62.1%)	1.5 (0.9 - 2.7)	0.147
Insulin only	8 (33.3%)	14 (66.7%)	1.1 (0.4 - 2.6)	0.906
Hypertension BP ≥ 140/90mmHg				
Yes	54 (34.4%)	103 (65.6%)	1.4 (0.7 - 2.7)	0.288
No	17 (27.0%)	46 (73.0%)	1.0	
Duration of diabetes (years)				
< 5	25 (25.3%)	74 (74.7%)	1.0	
≥ 5	46 (38.0%)	75 (62.0%)	1.8 (1.0 - 3.3)	***0.044****
BMI (kg/m^2)				
Underweight	0 (0.0%)	4 (100.0%)	-	0.999
Normal	19 (23.8%)	61 (76.3%)	1.0	
Overweight/Obese	51 (37.8%)	84 (62.2%)	1.9 (1.0 - 3.6)	***0.035****
Glycemic control				
Good HbA_{1C} ≤ 7%	11 (16.4%)	56 (83.6%)	1.0	
Poor HbA_{1C} > 7%	60 (39.2%)	93 (60.8%)	3.3 (1.6 - 6.8)	***0.001****

*Statistically significant, p < 0.05;

#Single(widowed, divorced, separated, unmarried).

from the hospital records. For subjects with no prior history of hypertension, a blood pressure ≥ 140/90 mmHg was considered to have hypertension. (JNC 8 Guidelines 2014) [19].

Diabetes control: This was assessed by measuring HbA_{1c}, using COBAS INTEGRA machine, in an automated platform. $HbA_{1c} \leq 7\%$ was categorized as good/optimal metabolic control and $HbA_{1c} > 7\%$ as poor/sub-optimal control (ADA 2015 Recommendations) [20].

Data analysis

Statistical analysis was done using IBM SPSS statistics v21 (2012). Prevalence of co-morbid depression was calculated and presented as a percentage of the total study subjects, at 95% confidence interval. In addition, the proportion with co-morbid depression was presented as percentages. Factors associated with depression were analyzed using Chi square tests and odds ratios (OR). Statistically significant factors in the univariate associations were put in binary logistic regression model to determine factors independently associated with co-morbid depression while controlling for confounding effects. The statistical tests were performed at 5% level of significance (p value less or equal to 0.05 will be interpreted as significant) (Table 2 and Table 3).

Table 3: Independent factors associated with Co - morbid Depression in the study subjects.

Variable	Adjusted OR (95% CI)	P value
Age group (years)		
35 - 44	1.0	
45 - 54	2.3 (0.6 - 9.2)	0.230
55 - 64	2.2 (0.6 - 8.7)	0.259
≥ 65	3.9 (0.9 - 15.7)	**0.060**
Duration of diabetes (years)		
< 5	1.0	
≥ 5	1.3 (0.7 - 2.4)	0.462
BMI (kg/m²)		
Underweight	-	0.999
Normal	1.0	
Overweight/Obese	1.4 (0.7 - 2.8)	0.279
Glycemic control		
Good $HbA_{1C} \leq 7\%$	1.0	
Poor $HbA_{1C} > 7\%$	2.9 (1.4 - 6.1)	**0.006**

*Hosmer and Lemeshow goodness of fit p value = 0.985;

The parameters of age, duration of diabetes and obesity that were previously, in univariate analysis, significantly associated with Co - morbid Depression cease to be, except for quality of glycaemic control, in the regression model.

Ethical Considerations

Permission and approval was obtained from the Department of Clinical Medicine and Therapeutics of the University of Nairobi and the Institution's Ethical Review Committee for research, before data collection.

We obtained consent from the study subjects after providing them with adequate information about the study. Blood pressure, BMI and HBA_{1C} results were communicated to patients as well as their primary physicians for clinical decision-making. Those who were found to have depression were referred to the mental health department for further care. Blood samples were used only for the intended purpose and were discarded after the study.

Results

A total of 220 participants with type 2 diabetes mellitus were recruited into the study. Below is a summary of their characteristics.

Discussion

The study was set to determine the burden of co-morbid depression in ambulatory patients living with type 2 diabetes at the diabetes out-patient clinic of KNH using the PHQ-9 questionnaire.

The prevalence of co-morbid depression in the study subjects in the out-patient clinic of this hospital was found to be 32.3%, 95% CI 26.4-38.6%, and more than half (18.7%) of them had moderate to severe depression. This is a significant proportion of people already afflicted by a chronic disease (Figure 2).

This prevalence of co-morbid depression is lower than that reported in a cross-sectional study by Ndetei DM et al. [21], also done in Kenya which included 2,770 general medical out-patients across 10 different health facilities. They reported that 42.3% of their study patients had clinical depression using BDI [21]. The cohort of patients in the study of Ndetei et al. had various diagnostic labels that included, but not limited to, cancers, respiratory diseases, cardiovascular diseases, diabetes, and HIV disease. More than half of the patients suffering from cancer (59.6%) and HIV/AIDS (52.2%) had co-morbid depression. The heterogeneous diagnostic labels and data collection tool would probably explain the observed differences in prevalence of depression compared to our study.

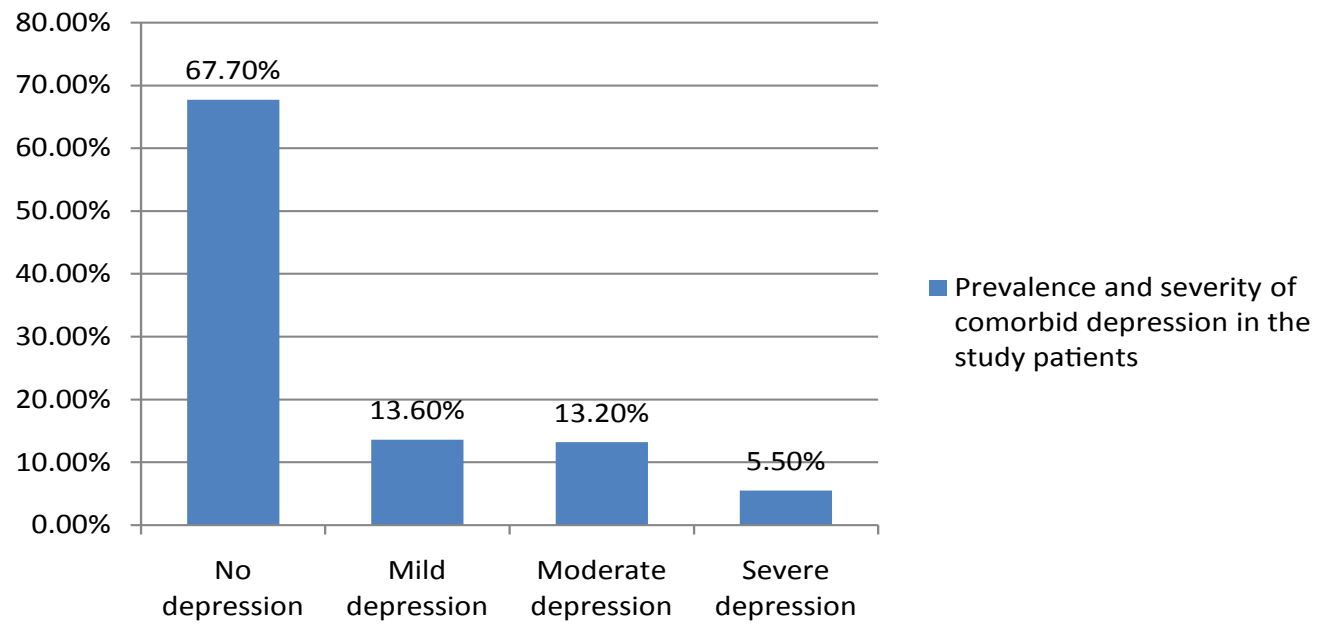

Figure 2: Prevalence and severity of co-morbid depression in the study patients.

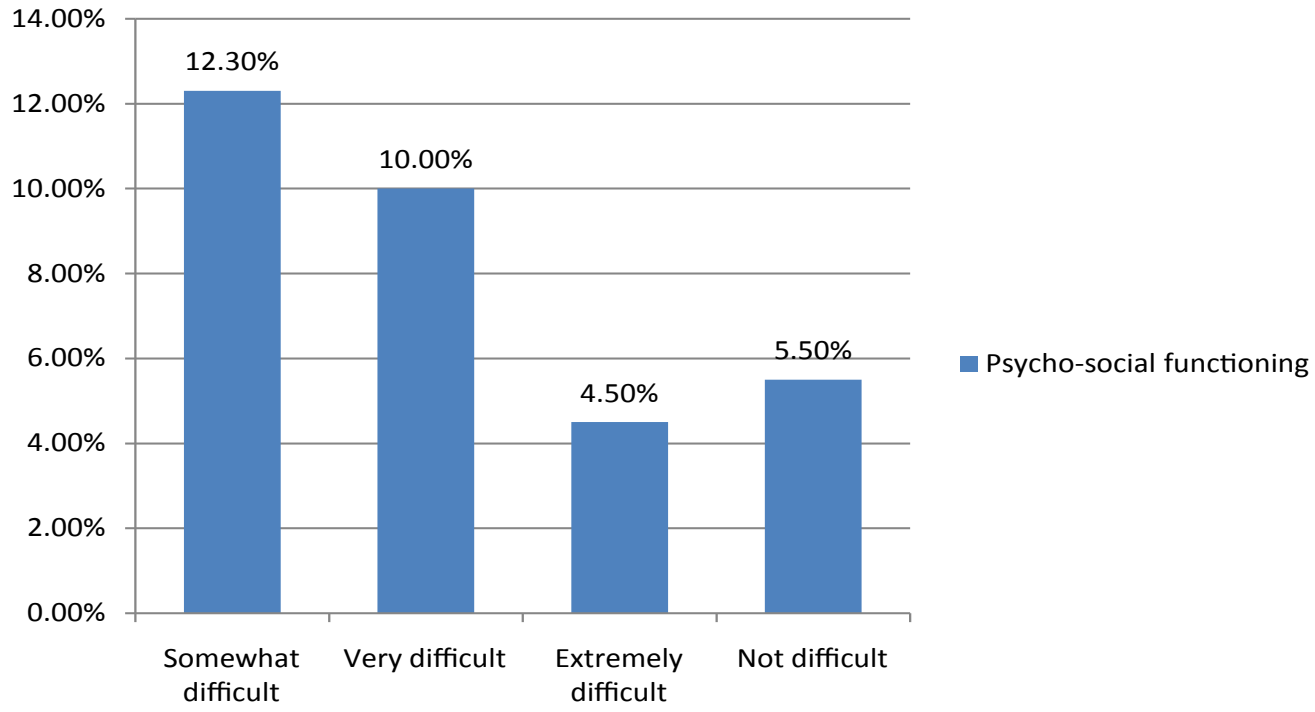

Figure 3: Psycho-social functioning of the study patients with co-morbid depression.

The overall prevalence of co-morbid depression in our study was comparable to other studies done in sub-Saharan Africa on patients with type 2 diabetes in the out-patient setting. Teklay et al. in Ethiopia found a prevalence of 33% using PHQ-9, in their cross-sectional, hospital-based study of 267 diabetic out-patients, 2011 [22], Camara A. et al. in Guinea found a prevalence of 34.4%, using HADS tool in a cross-sectional, hospital-based study, 2014 [23], and Akena D. et al. in Uganda, in their cross-sectional survey used PHQ-9 on patients with type 2 diabetes and found a prevalence of co-morbid depression of 34.8% [24]. This similarity in the prevalence of co-morbid depression in patients with type 2 diabetes may be due to shared psycho-social stressors among sub-Saharan Africans. The countries in sub-Saharan Africa share health system challenges and comparable poverty indices of their populations that may help explain part of this similarity in prevalence. However the prevalence of depression in our study was lower than that reported by Amit R et al. in India [25], of 41%, using PHQ-9 in a cross-sectional hospital-based study, 2009. It was relatively higher than the prevalence reported by studies in the developed world on patients with type2 diabetes. Ali S. et al. in the UK [26] reported a prevalence of 9.3%, using CESD tool in their cross-sectional study, 2009 and Chaoyang Li et al. in the USA [27] found a prevalence of 8.3%, using PHQ-9 in their population-based survey, 2008.

The prevalence reported in these studies differ, probably due to variation in characteristics of study participants coming from populations of multiple social and cross-cultural backgrounds, level of income of countries [28] use of different psychometric tools in studies with varying definitions of depression [29], and the diversity in psycho-social stressors from one community to another in the many countries where the studies were conducted.

In our study, the mean age of subjects with co-morbid depression was 59.1 ± 8.5 years, similar to that of the overall study population of 57.1 ± 8.6 years. Forty five (45.5%) percent of the study patients aged above 65years had co-morbid depression compared to 15.8% of the younger age group of 35-44 years. Old age above 65yrs was significantly associated with presence of co-morbid depression. ($p = 0.006$) in univariate analysis. This age is associated with diabetes-related complications, co-morbidities and therefore added hurdle in coping with diabetes care. Other investigators like Nitin J et al. in India in a cross-sectional study, 2010 [30] and Camara A. et al. in Guinea [22], had similar finding, but Akena D et al. [23]. In their cross-sectional study in Uganda, reported that their study subjects with co-morbid depression were younger, and they were also poorer and suicidal.

We found no significant association between gender and co-morbid depression ($p = 0.130$), apparently fewer females (28.5%) had depressive symptoms than the males (38.2%) in this study. We did not specifically interrogate the obtaining psycho-social support systems of our study subjects beyond knowing their marital and employment status. Even then, the marital status, employment and the level of formal education were not significantly associated with presence of co-morbid depression ($p = 0.783$, $p = 0.110$ and $p = 0.261$ respectively) in this study.

The study of Nitin J et al. in India [18] and a multicenter cross-sectional study of Ali Khan et al. in Pakistan, 2010 [19], both found female gender, among other risk factors, to be associated with co-morbid depression. Katon WJ et al. [11], in a longitudinal study, Tellez-Zenteno JF et al. [31], in a cross-sectional study of 189 subjects in Mexico, found female gender, young age, poor psycho-social support, low formal education and socio-economic status, amongst other risk factors, were associated with presence of co-morbid Depression in their patients with type 2 diabetes.

Thirty nine, (39.3%) percent, of the study subjects who were either on combination (OGLAs + insulin) or insulin-only therapy, had co-morbid depression compared to 26.3% on OGLAs-only but there was no significant association between treatment groups and Co-morbid Depression. However, medication burden as well as daily insulin injections are potential stressors in the group of patients who are on injections.

We observed that high BMI ≥ 25 kg/m² (overweight and obese) was significantly associated with co-morbid depression ($p = 0.035$) in univariate, but collapsed in multivariate analysis. Obesity in some patients with diabetes: can be a consequence of reduced physical activities, an observation in those with co-morbid depression, as reported by Lin EH et al. [32], and unhealthy diets, as reported by Dipnal JF et al. [33]. The tenth item on PHQ-9 tool assesses physical and psycho-social function. In this study, over 80% of the subjects with Co-morbid Depression reported difficulty with physical and psycho-social function of varying proportions. We did not explore

the dietary discretions and physical activity status of our study patients (Figure 3).

There was a significant association between longer duration of diabetes (5yrs and above) and co-morbid depression. (p = 0.044). Other workers, Tapash et al. in a cross-sectional study, 2011, in Bangladesh [34], Nitin J et al. in India [29], Ali Khan et al. in Pakistan [35] also reported that longer duration of diabetes was significantly associated with co-morbid depression. The patients with longer duration of diabetes are more likely to have co-existing complications of diabetes and high disease burden with additional health care challenges. These factors are potential stressors sufficient to drive depression (or distress) in such patients with diabetes.

There was a significant association between presence of co-morbid depression and poor glycemic control (p = 0.006). Many studies, for example, Bot et al. in a multicenter cross-sectional study in Netherlands [36] and Marcello et al. in a cross-sectional study in Brazil [37], have reported the association of Depression with poor glycemic control in their study patients. This is an important observation that puts these patients at higher risk of complications associated with poor glycaemic control.

Conclusions

Co-morbid Depression occurred in 1 in 3 of the study subjects with type 2 diabetes, which is a fairly high prevalence. Poor glycaemic control was consistently associated with Co-morbid depression therefore, patients with type 2 diabetes should be screened for Co-morbid depression. However, other potential risk factors, (older age of 65 yrs and above, long duration of diabetes and presence of diabetes-related complications) should be screened for the same and treated.

Study Limitations

1. This study is a cross-sectional study, of a small sample size per formed at a single center, a tertiary hospital, therefore not representative of the general population in Kenya.

2. Cross-sectional design of this study limits one to infer causality between Depression and Diabetes.

3. We did not determine the medication adherence, diets, psycho-social support levels and systems nor actively searched diabetes-related complications in the patients.

Author contributions

Kanu Joseph E, *josephkanu17@yahoo.com*: Design of study, data collection, major financing, read the drafts and made in-put. Corresponding author.

Otieno Frederick CF, *cfotieno@gmail.com*: Design of the study, part financing, wrote all the drafts.

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Okech-Helu, Violet, Design of the study, read the drafts.

MutaiKenn, *mutaikk@gmail.com*: Participated in the design, sample size calculation and statistical analysis

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APPENDIX (PHQ-9 –English version)

Patient Health Questionnaire - 9 (PHQ - 9)				
Over last 2 weeks, how often have you been bothered by any of the following problems? (Use "✔" to indicate your answer)	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself - or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3
For Office Coding 0 + ---------- + ---------- + --------- = Total Score: ---------				
If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people? Not Difficult at all ☐ Somewhat difficult ☐ Very difficult ☐ Extremely difficult ☐				

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