



REVISTA COLOMBIANA DE PSIQUIATRÍA

www.elsevier.es/rcp



Original article

Frequency of depression and quality of life in patients with diabetes mellitus in public health facilities in Metropolitan Lima[☆]



Roberto A. Accinelli^{a,b,c,e,*}, Kevin Brian Arias^{b,c,f}, Juan Alonso Leon-Abarca^{b,c,g}, Lidia M. López^{b,h}, Javier E. Saavedra^{c,d,i}

^a Hospital Cayetano Heredia, Lima, Peru

^b Instituto de Investigaciones de la Altura, Universidad Peruana Cayetano Heredia, Lima, Peru

^c Facultad de Medicina Alberto Hurtado, Universidad Peruana Cayetano Heredia, Lima, Peru

^d Instituto Nacional de Salud Mental “Honorio Delgado – Hideyo Noguchi”, Lima, Peru

^e Médico Neumólogo, Magister en Salud Pública

^f Médico Cirujano

^g Estudiante de Medicina

^h Médico Cirujano

ⁱ Médico Psiquiatra, Doctor en Medicina

ARTICLE INFO

Article history:

Received 29 May 2019

Accepted 30 January 2020

Available online 4 November 2021

Keywords:

Diabetes mellitus

Depression

Quality of life

ABSTRACT

Introduction: Diabetes is one of the main pandemics in recent years. Its association with depression increases the risk of mortality and morbidity. The coexistence of both diseases leads to poor management of diabetes, which leads to a worse quality of life.

Objective: To determine the frequency of depression in patients with diabetes mellitus and the effect of both pathologies on the quality of life in patients who attend outpatient appointments at public health facilities in Lima and Callao.

Methodology: Secondary analysis of the Epidemiological Study of Mental Health of depression in diabetic adults. The instrument used to determine the depressive episode was the MINI (Mini-International Neuropsychiatric Interview) while quality of life was measured using the Mezzich Quality of Life Index. Diagnosis information of type 1 or 2 diabetes was obtained from the daily medical record (HIS) of care.

Results: The frequency of depression in the 471 patients with diabetes was 5.8% in the last two weeks. While the annual frequency was 8.6% and 31.8% at some point in life. Being a woman was associated with a greater frequency of depression. Quality of life was lower in patients with diabetes and depression ($p < 0.005$).

DOI of original article: <https://doi.org/10.1016/j.rcp.2020.01.006>.

[☆] Please cite this article as: Accinelli RA, Arias KB, Leon-Abarca JA, López LM, Saavedra JE. Frecuencia de depresión y calidad de vida en pacientes con diabetes mellitus en establecimientos de salud pública de Lima Metropolitana. Rev Colomb Psiquiat. 2021;50:243–251.

* Corresponding author.

E-mail address: roberto.accinelli@upch.pe (R.A. Accinelli).

2530-3120/© 2020 Asociación Colombiana de Psiquiatría. Published by Elsevier España, S.L.U. All rights reserved.

Conclusions: The frequency of depression in patients with diabetes who are treated on an outpatient basis in public health centres is higher than the general population and their quality of life is significantly reduced, which raises the need for considering depression as an additional factor to the burden of morbidity of this condition.

© 2020 Asociación Colombiana de Psiquiatría. Published by Elsevier España, S.L.U. All rights reserved.

Frecuencia de depresión y calidad de vida en pacientes con diabetes mellitus en establecimientos de salud pública de Lima Metropolitana

R E S U M E N

Palabras clave:
Diabetes mellitus
Depresión
Calidad de vida

Introducción: La diabetes es una de las principales pandemias en los últimos años. Su asociación con depresión incrementa el riesgo de mortalidad y morbilidad. La coexistencia de ambas patologías produce un mal manejo de la diabetes, lo que conlleva a una peor calidad de vida.

Objetivo: Determinar la frecuencia de depresión en pacientes con diabetes mellitus y el efecto que tienen ambas patologías sobre la calidad de vida en pacientes que acuden de forma ambulatoria a establecimientos de salud públicos de Lima y Callao.

Métodos: Análisis secundario de la base de datos del Estudio Epidemiológico de Salud Mental de depresión en adultos diabéticos. El instrumento empleado para determinar el episodio depresivo fue el MINI (Entrevista Neuropsiquiátrica Internacional) mientras que la calidad de vida fue medida empleando el Índice de Calidad de Vida de Mezzich. Se obtuvo información de diagnóstico de diabetes tipo 1 ó 2 del registro médico diario (HIS) de atención.

Resultados: La frecuencia de depresión en los 471 pacientes con diabetes fue 5.8% en las últimas dos semanas. Mientras que la frecuencia anual fue 8.6% y en algún momento de la vida 31.8%. Ser mujer se asoció con mayor frecuencia de depresión. La calidad de vida fue menor en los pacientes con diabetes y depresión ($p < 0.005$).

Conclusiones: La frecuencia de depresión en pacientes con diabetes que son atendidos en forma ambulatoria en centros de salud públicos es mayor a la población general y su calidad de vida se ve reducida significativamente, lo que plantea la necesidad de considerar la depresión como un factor aditivo a la carga de morbilidad de esta condición.

© 2020 Asociación Colombiana de Psiquiatría. Publicado por Elsevier España, S.L.U. Todos los derechos reservados.

Introduction

Diabetes is one of the most prevalent diseases in the world, and it is on the rise worldwide, especially in middle-income countries like Peru. It is becoming one of the main pandemics today, with more than 420 million people suffering from it per year.¹ In addition, diabetes presents a high degree of comorbidity, not only with cardiovascular problems derived from the pathophysiological complications of the disease itself, but also with other problems such as Parkinson's disease, schizophrenia and depression.² Moreover, the risk of mortality and morbidity increases as it is associated with other pathologies, depression being one of them,³ affecting adherence, functioning, and treatment costs.⁴ The relationship between depression and chronic diseases, including diabetes, has been established in a two-way relationship where psychosocial factors associated with depression affect medical conditions and, in turn, the impact of chronic diseases can predispose to depression. Depression is one of the illnesses with the highest burden of morbidity in the world and is a priority public health problem.

Various studies in developed countries have shown that patients with diabetes have twice the risk of developing depression compared to non-diabetic groups.⁵ Moreover, the course of depression is longer in those with diabetes mellitus than in the general population.⁶ In all, 64% of people with diabetes have depression with a relapsing-remitting course, 15% never recover from their depression and only about 20% fully recover.^{7,8} The Medical Outcomes Study showed that the coexistence of chronic diseases with depression has an added impact on the functioning of the person who suffers from it.⁹ There are few studies on the frequency and prevalence of depression in patients with diabetes in developing countries.

Methods

This study was a cross-sectional study based on the secondary analysis of the database of the "Estudio de Salud Integral en Hospitales Generales y Centros de Salud de Lima Metropolitana y el Callao-2015" [Comprehensive Health Study in General Hospitals and Health Centres of Metropolitan Lima and Callao-

2015] carried out by the Honorio Delgado-Hideyo Noguchi Instituto Nacional de Salud Mental (INSM) [Honorio Delgado-Hideyo Noguchi National Institute of Mental Health]. This original research was approved by the INSM's Ethics Committee and the present research by the Ethics Committee of the Universidad Peruana Cayetano Heredia [Cayetano Heredia Peruvian University].

Data

The information was collected in 24 public health facilities in the city of Lima and Callao, dependent on the Ministry of Health of Peru. These included eight general hospitals with a large movement of patients, and their corresponding primary health centres, two for each hospital. The sample of the original study conducted between July and November 2015, was 10,885 adults aged 18 years or older. The subjects were selected from among the people waiting to be seen in different specialties. For the present study, only those patients with a diagnosis of type 1 or 2 diabetes mellitus and whose information was complete were considered.

Measurements

The presence was determined of a current depressive episode (in the last two weeks), an episode in the last 12 months, or at some point in life. For this, the module that evaluates the depressive episode according to the ICD-10 of the Mini International Neuropsychiatric Interview (Spanish version ICD-10¹⁰) was used, modified to obtain the annual and lifetime frequency, and linguistically adapted in previous studies conducted by the INSM. The psychometric analysis of depressive symptoms reached a Cronbach's alpha coefficient of 0.665.¹¹

Quality of life was measured using the Mezzich Quality of Life Index (Spanish version).¹² This consists of 10 items that include physical well-being, psychological or emotional well-being, self-care and independent functioning, occupational functioning, interpersonal functioning, social-emotional support, community and service support, personal fulfilment, spiritual satisfaction, and overall quality of life. Each item is rated by the subject on an ordinal scale of 1–10 points. This instrument was linguistically adapted and validated for the Peruvian population, with a Cronbach's alpha coefficient of 0.867.¹³

The diagnosis of diabetes mellitus was obtained from the daily statistical report of care provided by the treating physician, regardless of whether it was type 1 or type 2. The covariates include age group in years (18–30, 30–45, 45–60 and over 60), gender, level of education (primary, secondary, non-university higher, university) and marital status (single, married, cohabiting, and grouping together those who were separated, divorced or widowed).

Statistical analysis

The database was analysed with the statistical software Stata 14 (Stata Corporation, College Station, Texas, USA). A significance level of 0.05 was considered in all the statistical tests. An exploratory analysis was made of the variables that could

Table 1 – Characteristics of the population.

Variable	n (%)
Gender	
Female	311 (66)
Male	160 (34)
Age group	
20–46	103 (21.9)
47–54	94 (19.9)
55–59	89 (18.9)
60–66	96 (20.4)
67–88	89 (18.9)
Marital status	
Married (a)	157 (33.4)
Cohabiting	117 (24.9)
Separated (a), divorced (b) or widowed (c)	155 (32.8)
Single (a)	42 (8.9)
Level of education	
None	24 (5.1)
Primary*	135 (28.7)
Secondary+	244 (51.8)
Non-university higher	43 (9.1)
University**	25 (5.3)
*Includes pre-primary education.	
+Includes baccalaureate (A-level equivalent).	
** Includes postgraduate.	

be associated with depression. For this, a chi square test was performed first and only those variables with a p value <0.05 (gender, age, educational level and marital status) were included in the logistic regression models.

The quality of life analysis was carried out in each of the 10 areas in the Mezzich quality of life index and for this the T test was used. The results are shown as mean and standard deviation. To obtain the minimum clinically important difference (MCID), the mean standard deviation value of the quality of life variable was determined,^{14,15} which was equivalent to 0.74. Then it was determined if the difference between patients with DM and depression and those with DM but without depression in each area of the quality of life is greater than 0.74. In the areas where this occurred, an MCID was established.

Results

Of 471 patients with diabetes mellitus registered in the database, 468 were included for the study. The average age of these patients was 55 + 12.2 years. The rate of current depression was 5.9%, the annual 8.6% and the lifetime 31.8%. Most of the participants were female and were married or cohabiting. As regards their educational level, the majority had reached at least the secondary level (Table 1).

Table 2 shows that women had a higher rate of depression, whether it was current, in last 12 months, or at some point in their life (8.44%, 11.69% and 37.01% respectively, $p < 0.0001$). With regard to age, there were no differences in depression between groups in the current, annual and lifetime categories, except for the higher rate of depression in adults aged 45–60 years (36.57%) compared to adults older than 60 years (26.99%). In the case of marital status, it was found that cohabiting dia-

Table 2 – Sociodemographic variables of diabetic patients with depressive episode who were treated at public health centres in Metropolitan Lima.

Socio-demographic variables	Current n = 27	%	p	Annual n = 40	%	p	Lifetime n = 149	%	p
<i>Gender</i>									
Female	26	8.4	<0.001	36	11.7	<0.001	114	37.0	<0.001
Male	1	0.6		4	2.5		35	21.9	
<i>Age</i>									
18–30	1	6.7	>0.05	2	13.3	>0.05	5	33.3	>0.05*
30–45	4	5.4		9	12.2		21	28.4	
45–60	14	6.5		19	8.8		79	36.6	
60+	8	4.9		10	6.1		44	27.0	
<i>Marital status</i>									
Married	7	4.5	>0.05	11	7.0	>0.05	45	28.7	>0.05
Cohabiting	10	8.8		13	11.4		30	26.3	
Separated/Divorced/Widowed	10	6.5		15	9.7		63	40.9	
Single	0	0.0		1	2.4		11	26.2	
<i>Level of education</i>									
Primary	9	5.7	>0.05	12	7.6	>0.05	46	29.1	>0.05
Secondary	14	5.8		19	7.9		78	32.2	
Non-university higher	3	7.0		7	16.3		16	37.2	
University	1	4.0		2	8.0		9	36.0	

NS: Not significant ($p > 0.05$, unless otherwise indicated).

* Regarding lifetime frequency, it was found that patients between 45 and 60 years of age had more severe depression than those 60 and older ($p < 0.05$) +. In current frequency, those cohabiting presented a higher percentage of depression than single people ($p < 0.05$)°. In lifetime frequency, married people had a lower percentage of depression than those separated/divorced/widowed ($p < 0.05$).

betics had a higher frequency of depression than those who were single (8.77% vs 0%, $p < 0.05$). In addition, in the lifetime rate, married people presented less depression than those who were separated, widowed or divorced (28.66% vs 40.91%, $p < 0.05$). By educational level, no differences were found for current, annual or lifetime depression.

The logistic regression showed that gender was the only factor associated with depression, in the current, annual and lifetime frequencies. Moreover, the annual frequency of a depressive episode was associated with having a non-university higher education level (Table 3).

The quality of life in diabetic patients was lower when they had current depression (6.7 vs. 7.6 $p < 0.0001$) (Table 4). When the differences in each of the parameters that make up this Mezzich scale were analysed, the same difference was observed with the exception of the areas of psychological or emotional well-being and in the area of community and service support ($p > 0.05$). Comparing the same, but using the minimum clinically important difference (MCID), it was found that both physical well-being and community and service support did not have a clinically important difference.

Discussion

Our results indicate that DM patients from Metropolitan Lima attending public health centres present more depression than the general population. In the present study, the current rate of depression in diabetic patients was 5.77%, the annual rate was 8.55% and the lifetime was 31.84%, while in the general population of Metropolitan Lima the prevalence of current depression was found to be 2.8%, the annual, 6.2% and life-

time, 17.2%.¹⁶ In 1993, it was found that people with DM had a prevalence of depression three times higher than the general population.¹⁷ In another meta-analysis of 42 studies that included 20,218 patients with DM, it was found that depression is twice as common in people with DM compared to the general population.¹⁸ In a meta-analysis of 10 controlled studies, Ali et al. obtained a rate of depression among those with type 2 DM that was almost twice as high.¹⁹ We believe that it is important to examine the course of depression in patients with a long-standing diagnosis of diabetes.

It has been suggested that depressive symptoms could be a consequence of the burden of DM. The number of chronic diseases seems to explain part of the association between DM and depressive symptoms.²⁰ Depression in DM would thus be a multi-determined phenomenon resulting from the interaction between biological and psychosocial factors.²¹ But the higher incidence of depression in patients with diabetes may be a consequence of central insulin resistance. Insulin resistance in the brain can cause alterations in mitochondrial function, increased levels of monoamine oxidases, and increased clearance of dopamine.²² It has been suggested that mitochondrial dysfunction may contribute to depression.²³ Insulin resistance is directly related to the severity of depression symptoms in individuals without DM.²⁴ But it is one of several mechanisms associated with depression, such as decreased dopamine neurotransmission.²⁵ These alterations can also interact with other factors that may contribute to depression and anxiety, including genetic susceptibility, alterations in circadian rhythms, or changes in the content of monoamines such as serotonin, norepinephrine and dopamine.²⁶ People newly diagnosed with DM have fewer symptoms of depression

Table 3 – Logistic regression: Shows the significance of the selected variables versus the final status of the depressive patient by categories.

Logistic variables		Rate of current depressive episode (p = 0.0323)				Rate of annual depressive episode (p = 0.0082)				Rate of lifetime depressive episode (p = 0.0099)			
		OR	p	[95% CI]		OR	p	[95% CI]		OR	p	[95% CI]	
Gender	(0 = F, 1 = M)	0.07	<0.001	0.01	0.51	0.20	<0.01	0.07	0.59	0.53	<0.01	0.33	0.84
Age	30–45 years	0.63	NS	0.06	7.10	0.83	NS	0.14	4.99	0.84	NS	0.25	2.90
	45–60 years	0.81	NS	0.08	8.16	0.57	NS	0.10	3.37	1.23	NS	0.37	4.01
	>60 years	0.86	NS	0.08	9.72	0.48	NS	0.07	3.15	0.84	NS	0.24	2.90
Level of education	Secondary and baccalaureate	1.31	NS	0.51	3.35	1.08	NS	0.47	2.44	1.28	NS	0.79	2.05
	Non-university higher	2.11	NS	0.49	9.09	3.13	<0.05	1.02	9.63	1.83	NS	0.84	4.02
	University, including postgraduate	0.79	NS	0.09	7.02	0.94	NS	0.18	4.79	1.28	NS	0.51	3.22
Marital status	Cohabiting	1.99	NS	0.69	5.74	1.53	NS	0.62	3.74	0.84	NS	0.48	1.48
	Separated, divorced, widowed	1.17	NS	0.42	3.22	1.27	NS	0.55	2.96	1.61	NS	0.98	2.62
	Single	1.00	NS	–	–	0.21	NS	0.02	1.94	0.84	NS	0.37	1.90

95% CI: 95% confidence interval; OR: odds ratio; NS = p > 0.05.

Table 4 – Quality of life in diabetic patients with and without depression.

Areas	Total (n = 467)		Diabetic patients with current depression (n = 27)		Diabetic patients without depression (n = 440)		T test
	Median	IQR	Average score	SD	Average score	SD	p
Physical well-being, i.e., feeling energetic, without pain or physical problems	7	2	6.1	1.9	6.8	1.5	>0.05
Psychological or emotional well-being, i.e., feeling good and satisfied with yourself	8	1	6.0	1.8	7.6	1.5	<0.0001
Self-care and independent functioning, i.e., taking good care of yourself (e.g., being able to feed and clean yourself), making your own decisions	8	2	7.3	1.9	8.2	1.5	<0.01
Occupational functioning, i.e., being able to carry out paid work, study activities and/or household activities	8	2	6.9	1.9	7.8	1.5	<0.01
Interpersonal functioning, i.e., being able to interact and get on well with family, friends and groups	8	2	6.7	2.1	8.0	1.4	<0.0001
Social-emotional support, i.e., having people you can trust and who provide you with help and emotional support	8	2	6.8	2.1	7.7	1.6	<0.01
Community and service support, that is, having good neighbours, having financial help and other services available, e.g., helping in difficult situations by group loans, collections, etc.	7	3	6.1	2.2	6.6	2.1	p> 0.05
Personal fulfilment, i.e., be doing what you have set yourself in your life. Sense of personal fulfilment and of meeting your most important goals	8	2	6.6	1.8	7.6	1.5	<0.001
Spiritual satisfaction, i.e., having developed a spiritual attitude towards life beyond material things and being at inner peace with yourself and with other people **** 439	8	2	7.1	1.8	8.2	1.4	<0.001
Overall quality of life, i.e., feeling satisfied, happy and content with your life in general	8	2	6.9	1.7	8.0	1.4	<0.001
Average total quality of life	7.7	1.5	6.7	1.6	7.6	1.1	<0.0001

IQR: interquartile range.

SD: standard deviation.

than those already diagnosed.²⁷ With ageing, brain-specific insulin receptor knockout mice show signs equivalent to depression.²⁴

These biochemical variations would explain the abnormal brain imaging findings in people with DM, which include altered brain activity and connectivity by functional magnetic resonance imaging,²⁸ altered microstructure by diffusion tensor imaging²⁹ and altered neuronal circuits in the corpus striatum.³⁰

In other studies carried out in Peru in patients with DM, high prevalences of depression have been found. In Metropolitan Lima, the current prevalence of depression was 73.3%³¹, in Chiclayo it was 57.78%³², and in Trujillo it was 38.21%³³. This dissimilarity in the results can be attributed to methodological differences. In the case of our study, a categorical diagnostic instrument was used, based on the presence or absence of a depressive episode according to the operational criteria of the ICD-10, while in the other studies, dimensional instruments such as the Beck Depression Inventory were used. It is also possible that ethnocultural factors could have caused measurement biases,³⁴ or because the study was conducted among hospitalised or more seriously ill patients, who will have higher percentages of depression.

Women had a higher frequency of depression, which is what was found in similar studies.^{11,35} In the general population, being a woman is associated with higher rates of depression.³⁶ One reason to explain this higher frequency in the female gender could be that women perform less physical activity (which is a protective factor of depression) than men, which would predispose them to have depression.³⁷ In their study, Khuwaja et al. reported that the social role that women have (passivity, dependence, emotional expression) allows them to better express their emotions and thus identify when they feel depressed.³⁴ But we consider that the main reason is that women have greater insulin resistance than men,³⁸ which would explain why they have a higher percentage of depression.³⁰

Meanwhile, we did not find that age, marital status or educational level were related to depression. But, in the analysis, we found that those cohabiting presented a higher percentage of depression than single people, and that, in those who were married, the percentage of depression was lower than in those separated/divorced/widowed. Chew also found a higher percentage of depression among separated/divorced.³⁹

Our diabetics with depression had a lower quality of life. In patients with diabetes, depression seems to be a determining factor of a poor quality of life.⁴⁰ High levels of depression have been reported to have a negative impact on quality of life. Eren et al. classify depression as a pervasive condition and assert that its impact on the quality of life of diabetics is directly proportional to the severity of the depression.⁴¹ The simultaneous presence of DM and depression causes poorer self-care⁴² than when each disease presents separately, and also decreases adherence to treatment and the quality of life, and increases complications⁴³ and mortality⁴⁴, all of which translates into an increase in health costs.⁴⁵

When we separately analysed the ten areas that make up the quality of life questionnaire that we used, we found that the scores were lower in DM patients with depression in all

areas except in psychological and emotional well-being, and in community and service support. The physical, social and emotional condition of diabetic patients is diminished.⁴⁶ In DM, there is a loss of muscle mass and polyneuropathy, which causes a reduction in muscle strength, leading to a decrease in physical well-being that is greater when the person is in a depressed state.⁴⁷ The self-care of most people with DM is not so good. This is because at diagnosis DM patients are adults, and thus teaching control measures is a challenge. This learning process is hampered even more if they have depression, since depression intervenes negatively in the cognitive processes of learning.⁴⁸

As this is a cross-sectional study, the first limitation is that we were only able to observe one moment in the life of DM patients treated at health facilities in Lima. Being a survey-only study, we do not know the true level of their DM or if its treatment was carried out adequately or not. Another limitation is the selection bias of the participants, since only those attending public sector hospitals were selected. However, this was taken into account when making the conclusions.

Conclusion

The rate of depression in patients with diabetes who are treated on an outpatient basis at public health centres is higher than in the general population and their quality of life is significantly reduced, which raises the need to consider depression as an additive factor to the burden of morbidity of this condition.

Funding source

None.

Academic thesis for the qualification of Physician

Prevalence of depression and its associated factors in patients with diabetes mellitus attending the outpatient clinic of general hospitals and health centres in Metropolitan Lima and Callao -2015, 2018, Universidad Peruana Cayetano Heredia

Conflicts of interest

The authors have no conflicts of interest to declare.

REFERENCES

1. World Health Organization. Global report on diabetes. WHO: Geneva; 2016.
2. Klimek P, Kautzky-Willer A, Chmiel A, Schiller-Frühwirth I, Thurner S. Quantification of diabetes comorbidity risks across life using nation-wide big claims data. *PLoS Comput Biol*. 2015;11:e1004125.
3. Luijckx H, Biermans M, Bor H, van Weel C, Lagro-Janssen T, de Grauw W, Schermer T. The effect of comorbidity on glycemic control and systolic blood pressure in type 2 diabetes: a

- cohort study with 5 year follow-up in primary care. *PLoS One*. 2015;10:e0138662.
4. Ciechanowski PS, Katon WJ, Russo JE. Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. *Arch Intern Med*. 2000;160:3278–85.
 5. Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes Care*. 2001;24:1069–78.
 6. Simon GE. Long-term prognosis of depression in primary care. *Bull World Health Organ*. 2000;78:439–45.
 7. Lustman PJ, Griffith LS, Freedland KE, Clouse RE. The course of major depression in diabetes. *Gen Hosp Psychiatry*. 1997;19:138–43.
 8. Peyrot M, Rubin RR. Persistence of depressive symptoms in diabetic adults. *Diabetes Care*. 1999;22:448–52.
 9. Wells KB, Steward A, Hays RD, Burnam MA, Rogers W, Daniels M, et al. The functioning and well-being of depressed patients. Results from the Medical Outcomes Study. *JAMA*. 1989;262:914–9.
 10. Lecrubier Y, Weiller E, Hergueta T, Amorim P, Bonora LI, Lépine JP, et al. Mini International Neuropsychiatric Interview. Versión en Español 5.0.0; 2001, documento proporcionado por el autor.
 11. Instituto Nacional de Salud Mental. Confiabilidad y Validez de los Cuestionarios de los Estudios Epidemiológicos de Salud Mental de Lima y de la Selva Peruana. *Anales de Salud Mental*. 2009;25 Supl. 1.
 12. Mezzich JE, Ruipérez MA, Pérez C, Ion G, Liu J, Mamad S. The Spanish version of the quality of life index: presentation and validation. *J Nerv Ment Dis*. 2000;188:301–5.
 13. Robles Y, Saavedra JE, Mezzich JE, Sanéz Y, Padilla M, Mejía O. Índice de Calidad de Vida: validación en una muestra peruana. *Anales de Salud Mental*. 2010;26:33–43.
 14. Copay AG, Subach BR, Glassman SD, Polly DW Jr, Schuler TC. Understanding the minimum clinically important difference: a review of concepts and methods. *Spine J*. 2007;7:541–6.
 15. Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. *Med Care*. 2003;41:582–92.
 16. Instituto Nacional de Salud Mental. “Honorio Delgado-Hideyo Noguchi”. Estudio Epidemiológico de Salud Mental en Lima Metropolitana y Callao – Replicación 2012. Informe General. *Anales de Salud Mental*. 2013;29:1–392.
 17. Gavard JA, Lustman PJ, Clouse RE. Prevalence of depression in adults with diabetes. An epidemiological evaluation. *Diabetes Care*. 1993;16:1167–78.
 18. Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. The prevalence of comorbid depression in adults with diabetes. *Diabetes Care*. 2001;6:1069–78.
 19. Ali S, Stone MA, Peters JL, Davies MJ, Khunti K. The prevalence of comorbid depression in adults with Type 2 diabetes: a systematic review and meta-analysis. *Diabet Med*. 2006;23:1165–73.
 20. Knol MJ, Heerdink ER, Egberts AC, Geerlings MI, Gorter KJ, Numans ME, et al. Depressive symptoms in subjects with diagnosed and undiagnosed type 2 diabetes. *Psychosom Med*. 2007;69:300–5.
 21. Talbot F, Nouwen A. A review of the relationship between depression and diabetes in adults: is there a link? *Diabetes Care*. 2000;23:1556–62.
 22. Kleinridders A, Cai W, Cappellucci L, Ghazarian A, Collins WR, Vienberg SG, et al. Insulin resistance in brain alters dopamine turnover and causes behavioral disorders. *Proc Natl Acad Sci U S A*. 2015;112:3463–8.
 23. Rezin GT, Amboni G, Zugno AI, Quevedo J, Streck EL. Mitochondrial dysfunction and psychiatric disorders. *Neurochem Res*. 2009;34:1021–9.
 24. Timonen M, Laakso M, Jokelainen J, Rajala U, Meyer-Rochow VB, Keinänen-Kiukaanniemi S. Insulin resistance and depression: cross sectional study. *BMJ*. 2005;330:17–8.
 25. Dunlop BW, Nemeroff CB. The role of dopamine in the pathophysiology of depression. *Arch Gen Psychiatry*. 2007;64:327–37.
 26. Perona MT, Waters S, Hall FS, Sora I, Lesch KP, Murphy DL, et al. Animal models of depression in dopamine, serotonin, and norepinephrine transporter knockout mice: prominent effects of dopamine transporter deletions. *Behav Pharmacol*. 2008;19:566–74.
 27. Palinkas LA, Barrett-Connor E, Wingard DL. Type 2 diabetes and depressive symptoms in older adults: a population-based study. *Diabet Med*. 1991;8:532–9.
 28. Musen G, Jacobson AM, Bolo NR, Simonson DC, Shenton ME, McCartney RL, et al. Resting-state brain functional connectivity is altered in type 2 diabetes. *Diabetes*. 2012;61:2375–9.
 29. Hoogenboom WS, Marder TJ, Flores VL, Huisman S, Eaton HP, Schneiderman JS, et al. Cerebral whitematter integrity and resting-state functional connectivity in middle-aged patients with type 2 diabetes. *Diabetes*. 2014;63:728–38.
 30. Ryan JP, Sheu LK, Critchley HD, Gianaros PJ. A neural circuitry linking insulin resistance to depressed mood. *Psychosom Med*. 2012;74:476–82.
 31. Lopez M, Mariluz M, Pereda M. Asociación entre el control glicémico en pacientes con Diabetes Mellitus tipo 2 y grado de depresión según Escala de Beck II en el Hospital Edgardo Rebagliati Martins en octubre del 2014. [Tesis para obtener el título de médico cirujano]. Lima: Universidad Peruana de Ciencias Aplicadas. Escuela de Medicina; 2016.
 32. Constantino A, Bocanegra M, León F, Díaz C. Frecuencia de depresión y ansiedad en pacientes con diabetes tipo 2 atendidos en un hospital general de Chiclayo. *Rev Med Hered*. 2014;25:196–203.
 33. Bobadilla R. Asociación entre depresión y control glicémico en pacientes con diabetes mellitus tipo 2. [Tesis para obtener el título de médico cirujano]. Trujillo: Universidad Nacional de Trujillo. Facultad de Medicina; 2013.
 34. Kirmayer L. Culture, context and experience in psychiatric diagnosis. *Psychopathology*. 2005;38:192–6.
 35. Collins MM, Corcoran P, Perry JJ. Anxiety and depression symptoms in patients with diabetes. *Diabet Med*. 2009;26:153–61.
 36. Khuwaja AK, Kadir MM. Gender differences and clustering patterns of behavioral risk factors for chronic non-communicable diseases: community-based study from a developing country. *Chronic Illn*. 2010;6:163–70.
 37. Craft LL, Freund KM, Culpepper L, Perna FM. Intervention study of exercise for depressive symptoms in women. *J Women Health (Larchmt)*. 2007;16:1499–509.
 38. Chen S, Chen Y, Liu X, Li M, Wu B, Li Y, et al. Insulin resistance and metabolic syndrome in normal-weight individuals. *Endocrine*. 2014;46:496–504.
 39. Chew BH, Vos R, Mohd-Sidik S, Rutten GE. Diabetes-related distress, depression and distress-depression among adults with type 2 diabetes mellitus in Malaysia. *PLoS One*. 2016;11:e0152095.
 40. Eren I, Erdi O, Sahin M. The effect of depression on quality of life of patients with type II diabetes mellitus. *Depress Anxiety*. 2008;25:98–106.
 41. Eren I, Erdi O, Sahin M. The effect of depression on quality of life of patients with diabetes type II. *Depress Anxiety*. 2008;25:98–106.
 42. Lloyd CE, Pambianco G, Orchard TJ. Does diabetes-related distress explain the presence of depressive symptoms and/or poor self-care in individuals with Type 1 diabetes? *Diabet Med*. 2010;27:234–7.

43. Egede LE, Nietert PJ, Zheng D. Depression and all-cause and coronary heart disease mortality among adults with and without diabetes. *Diabetes Care*. 2005;28:1339–45.
44. Lin EH, Heckbert SR, Rutter CM, Katon WJ, Ciechanowski P, Ludman EJ, et al. Depression and increased mortality in diabetes: unexpected causes of death. *Ann Fam Med*. 2009;7:414–21.
45. Katon WJ. Clinical and health services relationships between major depression, depressive symptoms, and general medical illness. *Biol Psychiatry*. 2003;54:216–26.
46. Hervás A, Zabaleta A, De Miguel G, Beldarrain O, Díez J. Calidad de vida relacionada con la salud en pacientes con diabetes mellitus tipo 2. *An Sist Sanit Navar*. 2007;30:45–52.
47. Cadore EL, Izquierdo M. Exercise interventions in polypathological aging patients that coexist with diabetes mellitus: improving functional status and quality of life. *Age (Dordr)*. 2015;37:64.
48. Hernan Gómez L. Vulnerabilidad cognitiva a la depresión: relación entre sesgos atencionales, auto-representación y síntomas depresivos [Tesis para obtener el título de doctor]. Madrid: Universidad Complutense de Madrid; 2012.