# Correlation between Cardiometabolic Diseases and Depression in a Peruvian reference Hospital.

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***Introduction:*** *A correlation has been reported between presence of cardio metabolic diseases and mental health problems, specially depression.* ***Objectives:*** *To determine the correlation between cardio metabolic diseases and depressive symptomatology, evaluated by means of the PHQ-9 questionnaire, for patients attended in Internal Medicine Outpatient Clinics of the "Hospital Nacional Hipólito Unanue".* ***Methodology:*** *observational/analytic/cross sectional study. A cardio metabolic disease was defined as the presence of diabetes mellitus, arterial hypertension, dyslipidemia, and/or obesity. The PHQ-9 questionnaire was used for evaluating symptoms suggesting depression. The crude/adjusted association was evaluated to potential confounders. For the multivariate analysis a Poisson´s regression model was used, aimed to find prevalence reasons with their relevant confidence intervals, at 95%. A p<0,05 was deemed as statistically significant.* ***Results:*** *252 patients were included. 205 of them (81.4%) had cardio metabolic diseases; 181 of them (71.9%) had symptoms consistent with a degree of depression. Presence of cardio metabolic diseases was correlated with depressive symptoms, both in the crude analysis (CP 1.43; CI 95% 1.08-1.89; p=0.012), as well as in the adjusted analysis (AP 1.31; CI 95% 1.00-1.71; p=0.048). Additionally, a correlation between feminine sex and depressive symptomatology was reported (AP 1.35; CI 95% 1.11-1.63; p=0.002).* ***Conclusions:*** *Presence of cardio metabolic diseases was correlated with the presence of depressive symptoms in patients attended in the Internal Medicine Outpatient Clinic. Addressing mental health must be an integral part of multidisciplinary management of patients with cardio metabolic diseases.*

***Key words:*** *Depression, Diabetes Mellitus, Hypertension, Dyslipidemia, Obesity. (Source: DeCS BIREME).*

## INTRODUCTION

Non communicable diseases are the main cause of death all over the world. Every year nearly 41 million people die (equivalent to 71% of deaths, all over the world); mostly made up of cardiovascular diseases and diabetes (17.9 million and 1.6 million, respectively)[1].

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In Peru, cardio metabolic diseases have become one of the widest areas of research, thus becoming a national priority of research[2]. in Peruvian population, prevalence of diabetes mellitus, arterial hypertension, dyslipidemia and obesity are estimated in 7%[3], 23.7%[4], 11.6%[5], and 22.3%[6] respectively. These conditions are still being poorly diagnosed, treated and controlled, and have a strong correlation among themselves, thus favoring progression of complications[7].

A patient, when diagnosed with a chronic disease must face new situations in his/her life, such as take care of his/her health, avoid complications, and responsibly adapt himself/herself to a healthy life style he/she was not used to. Before this process of adjustments and changes, the patient may experience various reactions and feelings, and depression among them. This may be associated to self-care problems, functionality impairment, and difficulties in treatment adherence, thus leading to a poor control of the basal disease[8]. Additionally, from a physio pathological point of view, in patients with depressive disorders, some hormonal, inflammatory disturbances and autonomous nervous system problems have been reported, which could influence on physio pathological mechanisms of cardiovascular diseases, such as insulin resistance, hypertension and even obesity[9].

Despite the importance of mental health in patients with chronic diseases, studies regarding frequency of depression in patients with cardio metabolic diseases are relatively few in LatAm and especially in Peru. The objective of this study is to determine the correlation between cardio metabolic diseases and depressive symptoms in patients of Internal Medicine Outpatient Clinic of the "Hospital Nacional Hipólito Unanue", during a period from October to December, 2019.

## METHODOLOGY

This is an observational/analytic/cross sectional study. The population was made up of patients, older than 18 years who were attended in the Internal Medicine Outpatient Clinic of the "Hospital Nacional Hipólito Unanue" during a period from October to December, 2019. In order to find the sample size, the authors worked with the expected prevalences for depression, in general population, i.e. 16%[10]; for population with cardio metabolic diseases, 34%[11–13]. The latter was obtained from the combined prevalence of three relevant cardio metabolic diseases (diabetes mellitus, arterial hypertension and obesity). Considering a confidence level of 95%, and un statistical power of 80%, a sample size of 202 was obtained.

The inclusion criteria were: patients attended in the internal medicine outpatient and health cardio metabolic Clinics of the "Hospital Nacional Hipólito Unanue" who accepted to participate in this study, prior signature of an informed consent. The exclusion criteria were, denial to participate in this research, not understanding the questions of the questionnaire, to have some kind of cognitive disability hindering communication, and to have a psychiatric diagnosis/treatment, including depression.

The dependent variable was depression, defined with a score ≥5, according to the PHQ-9 questionnaire[14]. The independent variable was the presence of cardio metabolic diseases, defined as the presence of diabetes mellitus, arterial hypertension, dyslipidemia and/or obesity (BMI ≥ 30 kg/m2 )[15]. Non-controlled diabetes mellitus was considered for patients who did not have a basal diagnosis and reported a glucose level on empty stomach of >130mg/dL and an HbA1c > 7%, oran HbA1c > 8%, in elderly people[16]. In turn, non-controlled arterial hypertension to those who did not have a basal diagnosis and arterial pressure record of ≥ 140/90 mmHg, ≥ 140/80 mmHg in those patients who additionally had diabetes mellitus, PAS < 140 or > 150 mmHg in elderly people[17].

For collecting the data, prior to the questionnaire a record was applied. Age, gender, education level, and marital status of the patients were recorded. In turn, blood pressure was measured in millimeters of mercury, weight in kilograms, and size in meters for all patients. (The last two measurements were used to determine the Body Mass Index [BMI]). Presence of cardio metabolic diseases (diabetes mellitus, arterial hypertension, dyslipidemia, obesity) was confirmed in the diagnosis made by the attending physician on the clinical record. After the interview, the last laboratory values were collected (glu-

cose on empty stomach, glycosylated hemoglobin, total cholesterol and triglycerides) in their clinical record, within the previous six months to the day of the interview. The Patient Health Questionnarie-9 (PHQ-9) was used as a screening instrument for depression. It has an official version for Peru14, and it was validated by the Mental Health Department (Dirección de Salud Mental) of the Ministry of Health, in Peru and by the National Health Institute[18] (Instituto Nacional de Salud). Its Cronbach´s Alpha coefficient is 0.903[19].

The data collected was registered in a data base, based on Microsoft Excel 365. The analysis was made by using the statistical pack STATA, version[16]. For the descriptive analysis, the qualitative variables were presented as frequencies and percentages; the quantitative variables were presented with central tendency/dispersion measures, according to their distribution. For the bivariate analysis, in case of qualitative variables, the Chi square test was made. In case of quantitative variables, Student´s Test or Mann Whitney´s Test were used, according to the distribution of such variable. The multivariate analysis was made by means of the Poisson´s regression Model with robust variances. The reasons of crude prevalences (CP) and adjusted prevalence (AP) were obtained with their relevant confidence intervals, at 95%. A value of p, lower than 0.05 as statistically significant, was included.

The study was reviewed and approved by the Ethics Committee of the Faculty of Medicine, Universidad Ricardo Palma and by the Ethics Committee, of the Hospital Nacional Hipólito Unanue. The informed consent of all the participants was obtained, thus guaranteeing data confidentiality. This research meets all the ethical norms regarding the Declaration of Helsinki.

## RESULTS

268 patients were interviewed. From these, 16 were excluded, due to previous diagnosis of depression, or else because the patient did not understand the questions. The final amount was 252 participants. From all of them, 165 (65.5%) were women, with a median age of 57 (47.5 – 69) years old (Table 1). 205 (81.4%) patients who had a cardio metabolic disease were reported. Among them 100/252 (39,7%) patients had diabetes mellitus, 87/252 (34.5%) had arterial hypertension, 110/252 (43,7%) had dyslipidemia, and 88/252 (34,9%) had obesity. From the patients who had a diagnosis of diabetes mellitus and arterial hypertension, 49/91 (53,9%) and 44/87 (50,6%) were not under any control, respectively.

181/252 (71,9%) participants had symptoms consistent with some degree of depression, according to the PHQ-9 questionnaire. The most frequent grade presented was mild [101 (40,1%)] (Figure 1). Cardio metabolic disease was reported, along with depressive symptoms in 156/205 (76.1%) patients (Table 2). The bivariate analysis found correlation between the presence of depressive symptomatology and feminine sex (CP 1.34; CI 95% 1.11-1.63; p=0.003), higher BMI (CP 1.02; CI 95% 0.99-1.03; p=0.022), higher diastolic blood pressure (CP 1.00; CI 95% 1.00-1.01; p=0.138), higher glycosylated hemoglobin (CP 1.05; CI 95% 1.00-1.09; p=0.034), cardio metabolic disease (CP 1.43; CI 95% 1.08-1.89; p=0.012), dyslipidemia (CP 1.17; CI 95% 1.00-1.36, p=0.045), and obesity (CP 1.18; CI 95% 1.01-1.37; p=0.035) (Table 2).

Prevalence of depression was 30/42 (71.4%) and 40/49 (81.6%) in controlled and non controlled diabetes mellitus, respectively (CP 1.14; CI 95% 0.90-1.44; p=0.249); and 32/43 (74,4%) and 35/44 (79,5%) in controlled and non controlled arterial hypertension, respectively (CP 1.07; CI 95% 0.85-1.35; p=0.573).

In the multivariate analysis, both feminine sex (AP 1.35; CI 95% 1.11-1.63; p=0.002) as well as the presence of cardio metabolic disease (AP 1.31; CI 95% 1.00-1.71; p=0.048) were correlated with a higher prevalence of depression (Table 3).

## DISCUSSION

Our study reported a correlation between the presence of cardio metabolic diseases and depressive symptoms in patients attended in the Internal Medicine Outpatient Clinic of a Peruvian Reference Hospital. Prevalence of depressive symptoms in patients with cardio metabolic disease was 76.1% compared with 53.2%

**Table 1.** Descriptive Analysis of socio-demographic variables, vital functions, laboratory values, and cardiometabolic diseases in patients attended in the Internal Medicine Outpatient Clinic of the Hospital Nacional Hipólito Unanue, during the period from October to December, 2019

| Variable | Total (n = 252) | |
|---|---|---|
| Socio-demographic | | |
| Age | 57 | (47.5 - 69) |
| Feminine Sex | 165 | (65.5%) |
| Couple, Yes | 152 | (60.3%) |
| Marital Status | | |
| Single | 48 | (19.1%) |
| Married / Living together | 152 | (60.3%) |
| Widow(er) | 27 | (10.7%) |
| Divorced / Separated | 25 | (9.9%) |
| Education | | |
| None | 24 | (9.5%) |
| Primary | 63 | (25.0%) |
| Secondary | 116 | (46.1%) |
| College | 49 | (19.4%) |
| Vital Functions & Lab Values | | |
| BMI | 28,1 | (24,8 - 31,4) |
| Systolic Blood pressure | 120 | (100 - 125) |
| Diastolic blood pressure | 70 | (60 - 80) |
| Glucose On empty stomach | 101 | (91 - 123) |
| Glycosylated Hemoglobin | 6,4 | (5.7 – 8.5) |
| Total Cholesterol | 187,9 | ± 50.8 |
| Triglycerides | 139 | (104 - 184) |
| Cardio metabolic Disease | | |
| Cardio metabolic Disease | 205 | -81,40% |
| Diabetes Mellitus | 100 | -39,70% |
| Arterial Hypertension | 87 | -34,50% |
| Dyslipidemia | 110 | -43,70% |
| Obesity | 88 | -34,90% |

**Table 2.** Bivariate analysis between sociodemographic variables, vital functions, Lab values, and cardio metabolic diseases, with depression in patients attended in the Internal Medicine Outpatient Clinic, of the Hospital Nacional Hipólito Unanue, during the period from October to December, 2019.

| Variable | Depression | | Total | PR crude | CI 95% | Value of *p* |
|---|---|---|---|---|---|---|
| | Yes (n = 181) | Not (n = 71) | (n = 252) | | | |
| Sociodemographic | | | | | | |
| Age | 57 (48 - 65) | 59 (43 - 71) | 57 (47.5 - 69) | 0.99 | (0.99 – 1.00) | 0.525 |
| Sex | | | | | | |
| Masculine | 51 (58.6%) | 36 (41.4%) | 87 (100.0%) | Ref. | Ref. | |
| Feminine | 130 (78.8%) | 35 (21.2%) | 165 (100.0%) | 1.34 | (1.11 – 1.63) | 0.003 |
| Couple | | | | | | |
| No | 65 (65.0%) | 35 (35.0%) | 100 (100.0%) | Ref. | Ref. | |
| Yes | 116 (76.3%) | 36 (23.7%) | 152 (100.0%) | 1.17 | (0.99 - 1.39) | 0.063 |
| Marital Status | | | | | | |
| Single | 29 (60.4%) | 19 (39.6%) | 48 (100.0%) | Ref. | Ref. | |
| Married Living together | 116 (76.3%) | 36 (23.7%) | 152 (100.0%) | 1.26 | (0.99 - 1.62) | 0.063 |
| Widow(er) | 20 (74.1%) | 7 (25.9%) | 27 (100.0%) | 1.23 | (0.89 - 1.69) | 0.212 |
| Divorced or Separated | 16 (64.0%) | 9 (36.0%) | 25 (100.0%) | 1.06 | (0.73 - 1.54) | 0.762 |
| Education | | | | | | |
| None | 19 (79.2%) | 5 (20.8%) | 24 (100.0%) | Ref. | Ref. | |
| Primary | 51 (81.0%) | 12 (19.0%) | 63 (100.0%) | 1.02 | (0.81 - 1.30) | 0.854 |
| Secondary | 82 (70.7%) | 34 (29.3%) | 116 (100.0%) | 0.89 | (0.70 - 1.13) | 0.349 |
| College | 29 (59.2%) | 20 (40.8%) | 49 (100.0%) | 0.75 | (0.64 - 1.02) | 0.067 |
| Vital Functions & Lab Values | | | | | | |
| BMI | 28.7 (25.2 - 31.5) | 26.5 (24.1 - 30.6) | 28.1 (24.8 - 31.4) | 1.02 | (0.99 - 1.03) | 0.022 |
| Systolic Blood pressure | 115 (100 - 125) | 120 (95 - 120) | 120 (100 - 125) | 1.00 | (0.99 - 1.01) | 0.138 |
| Diastolic blood pressure | 70 (65 - 80) | 70 (60 - 80) | 70 (60 - 80) | 1.01 | (1.00 - 1.01) | 0.005 |
| Glucose on empty stomach | 101.5 (91 - 125) | 98.5 (90 - 117.5) | 101 (91 - 123) | 1.00 | (0.99 - 1.00) | 0.058 |
| Hemoglobin Glycosylated | 6.5 (5.7 - 9) | 6 (5.6 - 6.7) | 6.4 (5.7 - 8.5) | 1.05 | (1.00 - 1.09) | 0.034 |
| Cholesterol Total | 129.4 ± 49.4 | 174.8 ± 53.2 | 187.9 ± 50.8 | 1.00 | (1.00 - 1.00) | 0.046 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Triglycerides | 152 (108 - 197.5) | 122 (88 - 144) | 139 (104 - 184) | 1.00 | (1.00 - 1.00) | 0.000 |
| Cardio metabolic diseases | | | | | | |
| Cardio metabolic disease | | | | | | |
| No | 25 (53.2%) | 22 (46.8%) | 47 (100.0%) | Ref. | Ref. | |
| Yes | 156 (76.1%) | 49 (23.9%) | 205 (100.0%) | 1.43 | (1.08 - 1.89) | 0.012 |
| Diabetes Mellitus | | | | | | |
| No | 104 (68.4%) | 48 (31.6%) | 152 (100.0%) | Ref. | Ref. | |
| Yes | 77 (77.0%) | 23 (23.0%) | 100 (100.0%) | 1.13 | (0.97 - 1.31) | 0.129 |
| Arterial hypertension | | | | | | |
| No | 114 (69.0%) | 51 (31.0%) | 165 (100.0%) | Ref. | Ref. | |
| Yes | 67 (77.0%) | 20 (23.0%) | 87 (100.0%) | 1.11 | (0.96 - 1.30) | 0.167 |
| Dyslipidemia | | | | | | |
| No | 95 (66.9%) | 47 (33.1%) | 142 (100.0%) | Ref. | Ref. | |
| Yes | 86 (78.2%) | 24 (21.8%) | 110 (100.0%) | 1.17 | (1.00 - 1.36) | 0.045 |
| Obesity | | | | | | |
| No | 111 (67.7%) | 53 (32.3%) | 163 (100.0%) | Ref. | Ref. | |
| Yes | 70 (79.5%) | 18 (20.5%) | 88 (100.0%) | 1.18 | (1.01 - 1.37) | 0.035 |

Abbreviations: RP, Reason of Prevalence; CI 95%, Confidence Interval to the 95%; Ref, Reference.

among those with no cardio metabolic diseases. Within specific cardio metabolic diseases, dyslipidemia and obesity were reported to be correlated with the presence of depressive symptomatology. On the other hand, no correlation was reported with diabetes mellitus (DM) and arterial hypertension (AH). A significant correlation was reported between dyslipidemia and depression, just as Sharif et. al.[20], Paredes-Arturo et. al.[21] and Jihoon et. al.[22] reported. The last study reported that these patients had a higher risk of cardiovascular disease (HRa 1.24; CI 95% 1,09-1,41), and cerebrovascular disorder (HRa 1.27; CI 95% 1,06-1,53). A correlation was also reported with high triglycerides, just as Dehesh et. al.[23], and Cardenas et. al.[24] reported. Likewise, a significant correlation was reported between obesity and depression; just like Paredes-Arturo et. al.[21] and Haregu et. al.[25] reported. The latter, additionally reported that these patients had 7,6 times more risk of DM (OR 7.62; CI 95% 4.51–12.87) and 6.7 times more risk of AH (OR 6.74; CI 95% 4.73–9.60). A correlation was also reported with a higher BMI, just as Dehesh et. al.[23] and Garg et. al.[26] reported.

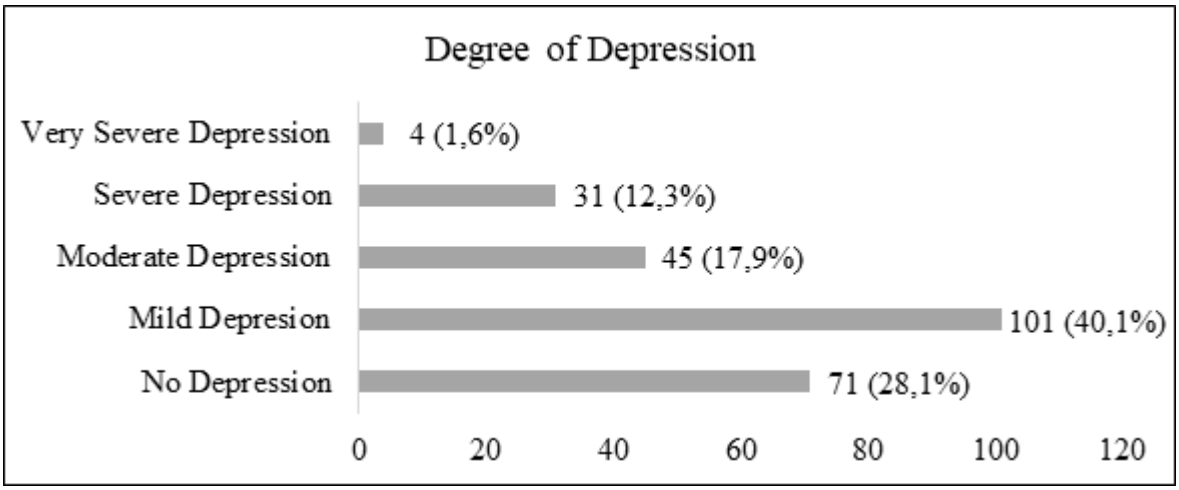
No correlation was found between DM and depression, unlike other studies[25,27,28]. It is important to mention that, Cardenas et. al.[24], found that in patients with DM, depression is a risk factor to suffer metabolic syndrome (OR 5.79; CI 95% 1.32-25.42; $p<0.05$). Although our study did not find any correlation between DM control and depression, a higher level of HbA1c was reported in patients with depressive symptoms. The correlation between glycemic control and depression have been reported to be uneven[13,29]. Regarding the correlation of higher

**Table 3.** Multivariate analysis among the aforementioned Variables, with depression in patients attended in the Internal Medicine Outpatient Clinic, of the Hospital Nacional Hipólito Unanue, during the period from October to December, 2019.

| Variable | RP adjusted | CI 95% | Value of *p* |
|---|---|---|---|
| Sex feminine | 1.35 | (1.11 - 1.63) | 0.002 |
| Cardio metabolic disease | 1.31 | (1.00 - 1.71) | 0.048 |
| Couple | 1.12 | (0.96 - 1.32) | 0.156 |
| Education | | | |
| Primary | 1.11 | (0.87 - 1.39) | 0.395 |
| Secondary | 0.98 | (0.78 - 1.23) | 0.869 |
| College | 0.85 | (0.63 - 1.14) | 0.284 |

Abbreviations: RP, Reason of prevalence; CI 95%, Confidence Interval, at 95%; Ref, Reference

**Figure 1**. Degree of depression in patients attended in the Internal Medicine Outpatient Clinic, of the Hospital Nacional Hipólito Unanue, during the period of October to December, 2019December, 2019.



HbA1c levels with depression, our results are consistent with the reviewed literature[20,23,28]. We did not find any correlation between AH diagnosis and depression, in accordance with other publications[13,24]. However, there are other studies where this correlation does exist[23,27]; Dehesh et. al.[23], reported that lack of physical activities is a risk factor for depression (ORa 1.64; CI 95% 1.18-2.22; p=0.01). Likewise, we did not find any correlation between the non controlled AH and depression.

Our study reported that feminine sex was correlated to the presence of depressive symptoms; other studies[23,27,28] reported similar results. It is important to highlight that Haregu et. al.[25] reported that being married (OR 0.48; CI 95% 0.31-0.75, p=0.001) would be a protecting factor before depression; while Paredes-Arturo et. al.21 reported that widowhood (OR 3.00; CI 95% 1.3–7.1) is reported as a risk factor for depression, unlike the findings reported in our study. Among others potentially correlated factors, Alzahrani et. al.[28] found that a protecting factor for depression is compliance of control measures (life style modifications, along with use of medicaments) (OR 0.47; CI 95% 0.28-0.81; p=0.006); while Haregu et. al.25 found that a protecting factor for depression is to have a high socio economic level (OR 0.54; CI 95% 0.32-0.93; p=0.03) and to perform physical activities (OR 0.27; CI 95% 0.17-0.41; p<0.001). On the contrary, Alzahrani et. al.28 found that a risk factor for depression is the presence of comorbilities (OR 1.94; CI 95% 1.08-3.46; p=0.026); while Haregu et. al.25 found that a risk factor for depression is not to have a job (OR 3.33; CI 95% 2.25-4.93; p<0.001); Paredes-Arturo et. al.21 found that a risk factor for depression is not to have an income (OR 3.7; CI 95% 1.5-8.9). Finally, Sharif et. al.20 found that a risk factor for depression is diabetic retinopathy (OR 3.83; CI 95% 1.11-10.4; p<0.000). However, these factors were not evaluated in our study.

Management of cardio metabolic diseases is a significant challenge, due to its complex physiopathology and the high cost involved in its care, disorders and complications. If this is added to depression as an associated comorbility, patients are negatively affected by two factors; on the one hand, factors associated to their behavior; and, on the other hand, physiological factors. Regarding conduct, when depression is neither diagnosed nor treated properly, that affects self-care, thus leading to a sedentary life style, high fat diets, and even, it involves constraints in adherence to medical treatment, and causing a poor control of the basal disease 8. On the other hand, depressed patients present physio pathological disturbances affecting and intensifying the basal disease. Depression has been correlated to with metabolic anomalies, such as abdominal obesity, AH and insulin resistance[9]. All of these anomalies have been interrelated by means of various mechanisms. The list is ranked by chronic emotional stress suffered by depressed people. Such stress would activate the sympathoadrenal system, thus leading to a decreasing blood flow and left ventricular hypertrophy. It has also been correlated with deregulation of the hypothalamic-pituitary-adrenal axis, evidenced by hypercortisolemia, and causing a higher risk of metabolic syndrome. These patients have been even reported to have an increase of platelet activation, which could lead to atherosclerosis; as well as inflammatory hyperactivity of the immune system (high marker levels, such as C-reactive protein, interleukins 1- 2 and 6, and the tumor necrosis factor alpha)[9].

This correlation is also important from a public health point of view, as cardio metabolic diseases have become the main causes of mortality[1]; while depression, has become the main cause of disability, thus significantly contributing to the world burden of morbility[30]. Because of this, it is important to address this malignant synergy from a preventive standpoint, by proposing measures aimed to minimize diagnostic constraints, to interventions aimed to improve life style and healthy habits, in order to reduce the burden of these diseases.

Among the constraints, this study is not capable to diagnose depression, but it rather evaluates symptoms compatible with such diagnosis. The Patient Health Questionnarie-9 (PHQ-9) was the instrument used for evaluating depression. This tool has been widely used for screening depressive symptoms in patients with cardio metabolic diseases, such as AH and DM, at a local[13] and international[20,24–26]level. It a specific version for Peru 14, with national

validation studies[18], and high reliability[19]. As this is a cross-sectional study, neither diagnosis time of cardio metabolic diseases nor the duration of depressive symptoms could be measured; therefore, only correlation, but no causality was found. Additionally, the reverse causality principle should be taken into account (maybe cardio metabolic disease causes depression, or else depression causes cardio metabolic disease). Likewise, as a non probabilistic sampling was made, our findings could not be extrapolated to others institutions or health systems. However, despite the aforementioned constraints, we consider that our study provides valuable information to be taken in to account for clinical management of patients with cardio metabolic disease.

As a conclusion, diagnosis of cardio metabolic diseases was correlated with the presence of depressive symptoms, in patients attended in an Internal Medicine Outpatient Clinic. Therefore, we believe management of patients with cardio metabolic disease must be integrally addressed, beyond pharmacotherapy, including evaluation and management of aspects related with mental health, and specially depression.

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