

Chemical Liaison Between Diabetes and Hypertension, Depression and Socio-economic Deprivation Impact in Both

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Approaching two prevalent chronic conditions as Diabetes mellitus (DM) and High blood pressure/Hypertension (HTN) from a socio-economic and mental health perspectives using Beck Depression Inventory (BDI) and EPICES score simultaneously is a first for Arad County and for Romania. This research demonstrates the connection between the disease and the socio-economic pressures that lead to deprivation and depression and vice versa.

Keywords: diabetes, hipertension, depression, socio-economic deprivation

Diabetes mellitus (DM) and High blood pressure/Hypertension (HTN), apart of cancer [1], are at increased risk for anxiety, eating disorders and depression which can lead to serious complications, all of them altering quality of life. There are three monoamines known as neurotransmitters, playing an important role in mood regulation: serotonin, norepinephrine and dopamine, apart of others neurotransmitters that function as messengers in the brain, glutamate, GABA, and acetylcholine included [2]. Depression has been linked to imbalances in the brain with regard to these three neurotransmitters. Lower-than-normal levels of neurotransmitters produce symptoms such as: feelings of sadness, helplessness, worthlessness, overeating or loss of appetite, insomnia or sleeping too much, restlessness, irritability, lack of energy, distancing themselves from others, feeling numbness or lacking empathy, inability to concentrate, thoughts of hurting themselves or others and so on [3]. These symptoms could be screened with Beck Depression Inventory (BDI) which is a valuable substitute for the lack of reliable tests for brain chemical imbalance.

Previous studies have shown that coexistence of mental disorders such as anxiety and depression are considerably more frequent in people with DM and HTN than in the overall population [4,5], with a prevalence ranging from 15% to 24% and an incidence rate of depression during the first year after initiation of oral antidiabetic treatment of 12.61 per 1000 person-years [6] and 56% for HTN [5]. Depression occurrence is two to three times higher in people with DM, the majority of the cases being underdiagnosed, as it is in HTN.

In 2015, the prevalence of diabetes worldwide was of one in 11 adults and the estimated prevalence of the impaired glucose toleration was of one in 15 adults. These numbers are expected to further increase, especially in the urban population, leading to more medical and economic challenges, added on top of the 12% global

health expenditure currently spent on diabetes [7]. A recent study conducted in the Romanian population showed that diabetes is one of the major health care problems for our medical system, as its prevalence is of 11.6% and the prediabetes one is of 16.5% [8,9].

Evidences of the involvement of insulin signaling on brain mechanisms related to depression indicate that insulin resistance, a hallmark of Type 2 DM, could develop in the brains of depressive patients [10]. Some clinical reports and meta-analyses indicate a correlation between Type 2DM and depression with a bi-directional increased risk between both conditions [11]. Insulin has been implicated with diverse central roles, like modulating feeding behavior and energy maintenance by the hypothalamus, as well as memory-related processes by the hippocampus [12]. High-fat diet (HFD) impairs cell proliferation, insulin signaling and the Akt/glycogen synthase kinase 3 β (GSK3 β) activation promoted by serotonin in the dentate gyrus of the hippocampus [13].

Chronic psychological stress is associated with neuropsychiatric diseases, including depression and also with Type 2 DM [14,15]. Such a situation occurs with a notable magnitude when socio-economic deprivation elements exist, which can also be measured with EPICES score, a tool for detecting patients at high risk of diabetic complications (and not only) and poor quality of life [16]. Like patients with other chronic medical conditions, HTN patients experience many profound emotions which increase their risk for the development of mental health disorders particularly anxiety and depression [17] and even stroke and death [18]. There are also associations between cardiovascular disease (HTN) [19] and socio-economic deprivation [20,21].

We studied EPICES score in relation with BDI in apparently healthy population, (meaning that there were no known psychiatric documented disorders of the subjects) aged 20-90, in order to evaluate, by means of

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receiver operating characteristic (ROC) curves, whether cognitive vulnerabilities (CV) exist, and independently to discriminate between subjects with different severities of depression in relation with socio-economic deprivation [22]. Depression was classified to 0-13: minimal; 14-19: mild, 20-28: moderate, 29-63: severe depression. Deprivation cutoff was 30, no deprivation=EPICES score under 30, deprivation=EPICES score over 30.

Hypotheses

The alternative hypothesis: there is more risks for chronically ill individuals (i.e. DM and HTN) with socio-economic deprivation to develop depression. The null hypothesis: all individuals are at the same risks for depression.

Population and main outcome measures

Sample size: One thousand eighty-one (1,081) subjects responded to both EPICES and BDI questionnaires between January-June 2019, Confidence Level 95%, 300,000 total population aged 20-69, percentage 50, for Confidence Interval of 2.3. Socio-demographic data were: age, gender, residence, level of education, occupation, marital status in BDI, chronic illness if present and also items required by EPICES score (an individual index of deprivation, the Evaluation de la Precarite et des Inegalites de santé dans les Centres d'Examens de Sante (Evaluation of Precarity and Inequalities in Health Examination Centers [EPICES]) score computed on the basis of individual conditions of deprivation [23] (social worker contacts, private health insurance, home ownership, financial difficulties, practicing sports, attending a spectacle, taking a vacation, having social life, finding a place to stay or a help in need).

Experimental part

Methods

The EPICES score was used as a quantitative or as a dichotomous variable with the EPICES median considered as the cutoff value to divide the population into two subgroups: less deprived with a score ≤ 30 and more deprived with a score ≥ 30 . Correlations among the EPICES score, subjects characteristics, and BDI scores as variables were calculated by Pearson coefficients. Comparisons of less deprived with more deprived subjects for their socio-demographic characteristics and depression scores as variables, were analyzed by *chi-squared* tests and *t* tests as appropriate. Associations were first considered statistically significant at two-tailed 0.05. Cronbach's Alpha was performed for both BDI and EPICES scores.

Results and discussions

The socio-demographic and clinical characteristics of the 1,081 responders are reported in table 1. The mean age was 42.27 (SD 14.666) and 56.8% were female. The BDI score mean value was 16.31, Standard deviation SD (SD 12.925), with extreme values 0-56. The EPICES score mean value was 50.12 (SD 17.09273) with extreme values 7.10-100. DM was present in 11.47% (n=124) and HTN in 26.27% (n=284) of the responders. Depression was prevalent in 40.76% (n=505) of our sample, which is worrying; chronic illness was prevalent in 37.74% (n=408) and 64.95% of them were depressed (n=265) compared to 35.66% (n=240) of non chronically ill subjects.

The EPICES score was strongly correlated to BDI score (positive correlation, $r = 0.578$, $P < 0.001$) and to chronic illness (positive correlation, $r = 0.280$; $P < 0.000$). The result of the simple ANOVA F test (3.1077) = 261.690; $p < 0.001$ is consistent with these results and confirms that there are

significant differences between the four classes of depression in terms of EPICES scores, table 2. The average of EPICES scores is significantly higher in those with severe depression compared to all other classes and significantly lower in those with minimal depression than those with mild, moderate and severe depression.

Table 1
BDI AND EPICES SUBJECTS CHARACTERISTICS

item	category	Number	%
residence	rural	529	48.94
	urban	552	51.06
maritalstatus	cohabitation	188	17.39
	divorced	83	7.68
	married	509	47.09
	not married	270	24.98
	widower	31	2.87
occupation	employee	562	51.99
	no occupation	172	15.91
	retired	156	14.43
	student	73	6.75
	unemployed	118	10.92
education	no education	28	2.59
	4grade	14	1.30
	8grade	200	18.50
	10grade	10	0.93
	12grade	336	31.08
	college	237	21.92
	university	234	21.65
	postuniversity	22	2.04
depression	DM	265	24.51
	no DM	240	22.20
no depression	DM	143	13.23
	no DM	433	40.06
deprivation	DM	393	36.36
	no DM	564	52.17
no deprivation	DM	15	1.39
	no DM	393	36.36

By comparing chronically ill patients with others, we observed an average of EPICES score significantly higher in chronically ill patients, $t(1,079) = 9.568$; $p < 0.001$, mean EPICES = 46.40 versus 56.25. The mean BDI score is also significantly higher in chronically ill patients, $t(1,079) = 15.276$; $p < 0.001$, mean BDI = 23.30 versus 12.07. In terms of gender differences, there is a significant difference between men and women in the Beck Depression score, with men achieving higher mean scores than women $t(1,079) = 28.895$; $p < 0.001$ (mean M=18.14, mean F=14.92). There were no significant differences between the two groups in the EPICES score.

The psychometric properties of the BDI and EPICES score in the study sample were assessed by Cronbach's Alpha. Internal consistency for BDI shows an excellent Cronbach's Alpha of 0.941; Cronbach's Alpha Based on Standardized Items of 0.944, for 21 items, table 3, meaning that depression symptoms were accurately recognized and described by the subjects.

Depression	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
minimal	576	39.87	12.83770	0.53490	38.8222	40.9234	7.10	89.94
mild	92	58.04	14.96341	1.56004	54.9418	61.1395	28.40	100.00
moderate	233	60.77	13.00233	0.85181	59.0974	62.4540	20.11	100.00
severe	180	65.08	12.53825	0.93455	63.2430	66.9313	29.58	91.72
Total	1081	50.12	17.09273	0.51987	49.1029	51.1430	7.10	100.00

Table 2
DEPRESSION TYPES
AND EPICES SCORES

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Cronbach's Alpha if Item Deleted
Sadness	15.71	154.337	.938
Pessimism	15.60	147.449	.936
Past failure	15.50	152.261	.937
Loss pleasure	15.55	153.223	.937
Guilt feelings	15.70	152.165	.937
Punishment feel	15.26	151.276	.942
Self dislike	15.67	151.870	.937
Self criticalness	15.44	157.235	.940
Suicidal	15.81	152.813	.938
Crying	15.45	147.468	.938
Agitation	15.25	153.470	.941
Loss interest	15.50	151.506	.937
Indecisiveness	15.51	151.759	.937
Worthlessness	15.53	147.160	.935
Loss energy	15.62	151.427	.937
Sleep	15.30	149.018	.938
Irritable	15.49	152.802	.937
Appetite	15.68	152.681	.938
Concentration	15.65	162.424	.945
Tiredness	15.50	152.948	.938
Sex interest	15.61	150.083	.938

Table 3
BDI ITEM-TOTAL STATISTICS

Internal consistency for EPICES score shows a modest but acceptable Cronbach's Alpha of 0.526; Cronbach's Alpha Based on Standardized Items of 0.521, for 11 items, table 4.

As an explanation for all AUC values under 0.5 of Cronbach's Alpha for EPICES score we could try to understand the role of cultural and traditional way of life in Romania, where sports is not an adult habit, attending a spectacle has a different meaning from that of Western Europe, taking a vacation is an opportunity for renovation, cleaning, or preparation for winter/autumn reserves and so forth. Finding a shelter when needed might mean spending a few days with relatives and borrowing money from them or from friend and so on, as a patriarchal society is functioning.

The ROC curve was used to determine an appropriate cutoff, affecting the sensitivity and specificity of both BDI and EPICES score in relation with chronic illness. The area under the ROC curve (AUC) is a global measure of the ability of a test to discriminate whether a specific condition is present or not present. An Area Under the Curve (AUC) of 0.5 represents a test with no discriminating ability, while an AUC of 1.0 represents a test with perfect discrimination, Figure 1. For depression in relation with chronic illness AUC

was 0.646, $P < 0.000$ and for deprivation was 0.563, $P = 0.001$, meaning that both are appropriate tools, in terms of sensitivity and specificity for detecting chronic illness-deprivation-depression significance in a sample. For EPICES scores in relation to chronic illness AUC is 0.881, $P < 0.000$.

Chronic condition is associated with depression in men, $P = 0.0240$ and with deprivation in both gender, $P < 0.0001$. Relative Risk for depression in men is RR 1.1627 times higher than in women (95% CI 1.0243 to 1.3198, $P = 0.0197$) and chance Odds Ratio (OR) for detecting their depression is 1.3303 times higher (95% CI 1.0449 to 1.6938, $P = 0.0206$) compared to women.

Relative Risk RR for depression in chronic condition is 2.1137 times higher than in healthy subjects (95% CI 1.7929 to 2.4918, $P < 0.000$) and chance Odds Ratio (OR) for detecting their depression is 3.3434 times higher (95% CI 2.5847 to 4.3248, $P < 0.000$). RR for deprivation in chronic condition is 3.3948 times higher than in healthy subjects (95% CI 2.0996 to 5.4890, $P < 0.0001$) and chance OR for detecting their deprivation is 5.0635 times higher (95% CI 2.9070 to 8.8196, $P < 0.0001$).

RR for depression in DZ is 1.8583 times higher than in healthy subjects (95% CI 1.6535 to 2.0886, $P < 0.0001$) and OR for detecting their depression is 5.0936 times higher

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Cronbach's Alpha if Item Deleted
Social worker	48.7346	313.009	.538
Private health insurance	49.0900	318.363	.539
Living in couple	44.1124	310.035	.565
Home ownership	44.8324	292.451	.536
Financial difficulties	37.9507	264.946	.565
Practicing sports	46.9640	281.393	.486
Attending a spectacle	46.2000	283.848	.502
Taking a vacation	44.3018	275.511	.473
Having social life	43.7919	227.861	.396
Finding a place to stay	43.2663	235.712	.414
Finding a help in need	45.2673	264.671	.456

Table 4
EPICES SCORE ITEM-TOTAL STATISTICS

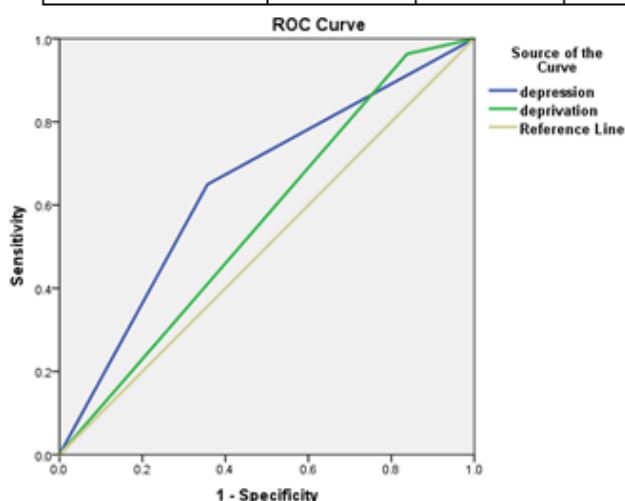


Fig. 1. ROC curve for depression in chronically ill patients depending on depression and deprivation score

(95% CI 3.2446 to 7.9961, $P < 0.0001$). RR for depression in HTN is 1.3742 times higher than in healthy subjects (95% CI 1.2103 to 1.5603, $P < 0.0001$) and OR for detecting their depression is 1.9006 times higher (95% CI 1.4442 to 2.5013, $P < 0.0001$).

RR for deprivation in DM is 1.1448 times higher than in healthy subjects (95% CI 1.1144 to 1.1760, $P < 0.0001$) and OR for detecting their deprivation is 37.1932 times higher (95% CI 22.2987 to 601.7976, $P = 0.0109$). RR for deprivation in HTN is slightly increased 1.0579 times higher than in healthy subjects (95% CI 1.0135 to 1.1043, $P = 0.0101$) and OR for detecting their deprivation is 1.7478 times higher (95% CI 1.0792 to 2.8307, $P = 0.0232$) (Figure 2).

Conclusions

DM and deprivation is, no doubt, a twin problem in Arad County. The association between DM and HTN with depression has been well known for at least three decades [24,25,26,27]. DM and HTN frequently occur together; there is substantial overlap between diabetes and hypertension in etiology and disease mechanisms because obesity, inflammation, oxidative stress, and insulin resistance are thought to be the common pathways [28-31]. The prevalence of depression in people with DM or HTN varies widely. We analyzed the depression in a cohort of patients with DM and HTN from Arad County based on Beck Depression Inventory as the screening tool in correlation

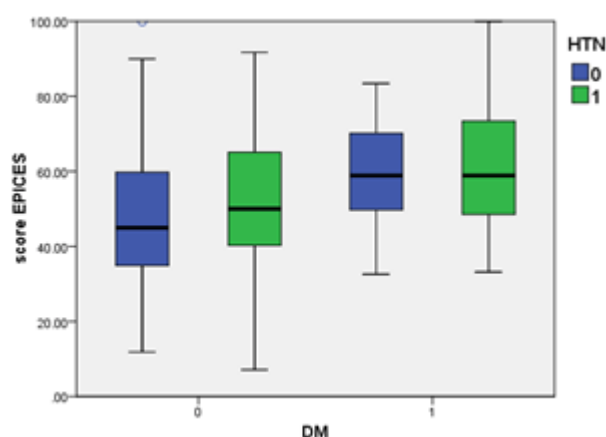


Fig. 2. Diabetes mellitus and Hypertension in relation with EPICES score

with deprivation scores established with EPICES index to measure individual deprivation.

Half of Romania's population (50%) suffered from material and social deprivation in 2016, this being the highest rate registered in the European Union (EU), according to data from the European statistics office Eurostat [32]. Only Bulgaria had a rate close to that of Romania, namely 48%. Other EU Member States with high rates were Greece (36%), Hungary (32%) and Lithuania (29%) [32].

The improvement of these parameters depends very much on the health policies and the practice of each state [33-41].

The socio-economic deprivation is a powerful predictor of the prevalence and persistence of depressive symptoms.

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Manuscript received: 22.01.2019