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Depression, anxiety and stress, comorbidity evaluation among a large sample of general adults: results from SEPAHAN study

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ABSTRACT. Depression, anxiety and stress are common psychological disorders (PDs). This study aimed to assess the odds of co-occurrence of mentioned PDs in total sample and different levels of socio-demographic characteristics, specifically among a large sample of general adults. In a cross-sectional, community-based study conducted among 4763 Iranian adults, depression and anxiety were assessed with Hospital Anxiety and Depression Scale (HADS) and stress with General Health Questionnaire (GHQ). The loglinear analysis was applied to investigate their comorbidities. Based on selected models with pair-comorbidity of anxiety with stress, depression with stress, and anxiety with depression, the results showed the odds of comorbidity between anxiety and depression (odds ratio (OR) =12.29, 95%CI: 9.58-15.80), depression and stress (OR = 7.80, 95%CI: 6.55-10.18), and stress and anxiety (OR = 4.62, 95%CI: 3.71-5.75). Also, ORs of pair-comorbidities were the same, except between stress and anxiety for men compared to women (adjusted-OR = 6.47, 95%CI: 4.44-9.49 versus 3.85, 95%CI: 2.95-5.00) and comorbidity between stress and depression for the participants with lower than 40 years compared to others (adjusted-OR = 9.03, 95%CI: 7.17-11.36 versus 6.41, 95%CI: 4.90-8.41), p< 0.05. Stress comorbidity with depression was higher level than other pair-comorbidities. Obvious discrepancies were also observed in terms of ORs of pair-comorbidities between three mentioned disorders in different levels of SDCs.

Keywords: depression; anxiety; stress; comorbidity; loglinear model.

Introduction

Psychological disorders (PDs) affect most cognitive and emotional actions, and gradually cause some mental, emotional, and cognitive imbalance in individuals. Anxiety (prevalence among Iranian population: 4.7-11.5% and over the world: 0.9-28.3%), stress (prevalence among Iranian population: 34.8-36% and over the world: 33%), and depression (prevalence among Iranian population: 9.3-11.75% and over the world: 4.4-12%) are considered as the most prevalent PDs through different decades of human life (Ahmadvand, Sepehrmanesh, Ghoreishi, & Afshinmajd, 2012; World Health Organization [WHO], 2017; Mirzaei, Ardekani, Mirzaei, & Dehghani, 2019). Results of a comprehensive study on Iranian population as a part of a larger sample enrolled by Iranian national health institute, indicated that psychological disorders' prevalence is 20.89% in rural areas and 24.55 % in urban areas (Noorbala et al., 2017).

The three disorders have had numerous consequences and usually has been followed by physiological responses including metabolism increase, endocrine system, immune deficiency, hypertension, heart diseases, cancer, gastrointestinal and skin diseases, PDs and chemical reaction such as oxidative stress (Cohen, Edmondson, & Kronish, 2015; Foyet et al., 2017; Gaber, 2016; Yancy et al., 2017).

Comorbidity and overlap between these disorders lead to significant physical consequences. In some studies, comorbidity between depression, anxiety, and stress caused patients to experience recurrence of mentioned PDs repeatedly (Hofmeijer-Sevink et al., 2012). In addition, patients suffering from comorbidity between these disorders experienced more severe psychosomatic symptoms, more physical and mental inability, and lower quality of life compared to those with one disorder; patients with comorbidity were also more likely to attempt suicide. Therefore, health care costs could increase in the patients with comorbidity between these PDs (Maes,

Kubera, Obuchowiczwa, Goehler, & Brzeszcz, 2011; Sun, Li, Buys, & Storch, 2015; Sweeney, Shui, Calder, & Duggan, 2016).

Majority of conducted studies have focused on only the overlap between two disorders (Ayazi, Lien, Eide, Ruom, & Hauff, 2012; Flory & Yehuda, 2015). However, some limited studies, on specific population such as college students, patients and remnants of war, comorbidity between three PDs has been evaluated (Ginzburg, Ein-Dor, & Solomon, 2010; Bener, Al-Kazaz, Ftouni, Al-Harthy, & Dafeeah, 2012; Beiter et al., 2015; Coplan, Aaronson, Panthangi, & Kim, 2015;); and hence their results could not be generalized to general population. In addition, there is no study available among developing countries as well as Iranian adults in this regard.

The aims of current study were to investigate the prevalence of depression, anxiety, stress and their overlap, and to evaluate of socio-demographic determinants on different combinations of co-occurrence using loglinear analysis, as an advanced statistical method, in a large sample of the Iranian population.

Methods

Study design and subjects

The present cross-sectional study was conducted within the framework of 'the Study on the Epidemiology of Psychological, Alimentary Health and Nutrition (SEPAHAN)', describing the epidemiological components of purposeful gastrointestinal problems and their association with life-style and psychological factors in 2010 (Adibi et al., 2012). The SEPAHAN project was performed in two phases among a large sample of Iranian adults in the Isfahan province. In the first phase of SEPAHAN project, different questionnaires on demographic characteristics, lifestyle and nutritional habits and intakes, were distributed among 10087 invited persons, and 8691 subjects finally returned the distributed questionnaires (response rate: 86.16%). At the second phase, others questionnaires, which were designed to collect information on psychological, somatoform symptoms and gastrointestinal variables, were distributed and 6239 questionnaires were completed (rate of responses: 64.64%). Then, national identification numbers of the subjects participated in two phases were used to link the questionnaires collected in study phases.

The study sample was selected amongst four million human beings in 20 counties throughout Isfahan province located in central rigion of Iran. Multi-stage cluster random sampling was performed by geographical region as main clusters to determine the number of sample participants needed in every area. The individuals have been selected from apparently healthy adultswho have been residing in Isfahan province. The questionnaires have been given to the participants in their home and workplace and that they replied to the questionnaires at their resting time. Then the questionnaires have been acquired as sealed envelopes. All data was collected anonymous and confidential. Participating to this study was completely optional. In this study, as a sub-study of SEPAHAN, we used data from 4763 adults who had completed records on demographic data, personality traits, stressful life events, social supportsand psychological problems including anxiety and depression and stress. More details about the design and setting of the SEPAHAN has already been published (Adibi et al., 2012).

Study instruments and assessed variables

To detect anxiety and depression we used Hospital Anxiety and Depression Scale (HADS). The HADS has been translated into many languages and since its development in 1983 (Zigmond & Snaith, 1983) it has been extensively used in different nations such as Iran and Brazil. A review of the literature to assess the validity of the HADS certainly suggested that it is a well-achieved questionnaire in assessing the symptom severity and case-ness of anxiety disorders and depression disorder within primary care patients and even within the general population (Bjelland, Dahl, Haug, & Neckelmann, 2002). The HADS incorporates 14 items and includes two sub-scales: anxiety and depression. Each item is rated on a four-factor scale (range 0-3), giving maximum scores of 21 for anxiety and depression. Scores of eleven or greater on both subscales are taken into consideration to be a significant 'case' of psychological morbidity, while scores of eight to ten represents 'borderline' and zero to seven 'normal' (Stern, 2014). We used Persian validated version of HADS with high internal consistency (Cronbach's α = 0.86) for depressionand with high internal consistency (Cronbach's α = 0.78) for anxiety. The convergent validation of Persian HADS questionnaire was assessed among 167 Iranian adults using the correlation of each item with its hypothesized scale. Pearson's correlation coefficients varied from 0.47 to 0.83 ($p < 0.0001$) for anxiety subscale and from 0.48 to 0.86 ($p < 0.0001$) for depression subscale,

indicating that the instrument provides relatively valid measures of psychological health (Montazeri, Vahdaninia, Ebrahimi, & Jarvandi, 2003a). Similarly, the internal consistency of the Brazilian validated version of HADS, assessed by Cronbach's alpha coefficient, was found to be 0.77 and 0.68 for depression and anxiety, respectively. The HADS instrument was used with a cut-off of 8/9 as previously validated among 78 consecutive admissions to a general medical ward in a Brazilian university general hospital. The sensitivity and specificity were found to be, respectively, 84.6 and 86.5 for depression, 93.7 and 54.8 for anxiety (Botega, Bio, Zomignani, Garcia Jr, & Pereira, 1995).

To detect psychological stress level, we used 12-item General Health Questionnaire (GHQ-12). The GHQ has been translated into many languages, such as Persian and Portuguese, since its development by Goldberg in 1970 (Goldberg & Blackwell, 1970). The GHQ-12 contains 12 questions with a four-point rating scale as 'less than usual, no more than usual, rather more than usual, or much more than usual', and estimates distress level using a bimodal scoring method (0-0-1-1). Accordingly, two first answers were given a score of 0, and two-second answers were given a score of 1. Therefore, the possible score range would be 0-12, and higher scores indicate higher levels of psychological distress. Based on the mean of GHQ in Iranian population, psychological distress was defined as GHQ score ≥4. Persian validated version of GHQ-12 showed high internal consistency (Cronbach's α = 0.87). The convergent validity of Persian GHQ-12 was performed among 748 Iranian young people. The GHQ-12 was correlated significantly with global quality of life scores [r = − 0.56, p< 0.0001] (Montazeri et al., 2003b), Similarly, the Brazilian validated version of GHQ-12 where the internal consistency was assessed by Cronbach's alpha coefficient and it was found to be 0.72 for the clinical sample and 0.76 for the nonclinical sample. The factorial validity of a Brazilian–Portuguese version of the GHQ-12 among 228 chronic hemodialysis patients (as a clinical sample) and 350 university students (as a nonclinical sample). Pearson's correlation between the original and the reduced 8-item factor was found to be 0.96 for both clinical and nonclinical samples. Pearson's correlation between the original and the reduced 8-item factor was found to be 0.96 for both clinical and nonclinical samples. Standardized factor loading for one-factor model ranged from 0.48 to 0.71 for the chronic hemodialysis patients and from 0.50 to 0.75 for the university students, and all were statistically significant at p< 0.001 (Fernandes & Vasconcelos-Raposo, 2013). Criteria proposed by SATEPSI (a Brazilian evaluation system for psychological tests), and CFP's (Brazilian National Council for Psychologists) Resolution No: 009/2018 (Andrade & Valentini, 2018) on the value of reliability indices and large sample size indicting a favorable setting for evaluating psychological assessment in our current study based on GHQ-12 and HADS.

Assessment of other variables

Data on height (cm), weight (kg) had been acquired thru a self-reported questionnaire. Body mass index (BMI) became calculated as weight in kilograms divided by height in meters squared. Participants had been categorized into three classes based on their BMI: normal weight (range 18.5- 24.9 kg m^{-2}), overweight (range 25.0 - 29.9 kg m^{-2}) and obese (range greater than 30.0 kg m^{-2}). The validity of self-reported measures of weight and height was examined in a pilot study on 200 participants from the same population. In this validation examine, self-reported values of anthropometric characteristics were compared with measured values. We found that self-reported values of anthropometric measures provide a reasonable data of those characteristics. The correlation coefficients for self-reported weight, height versus measured corresponding values were r = 0.95 and 0.83 (p< 0.001) respectively. The correlation coefficient for computed BMI from self-reported values and the one from measured values was r = 0.70 (p< 0.001). Additional information about age (years), sex (male/female), marital status (single or non-married (never married, divorced, separated, and widowed) versus married), education (under diploma (12 years formal education) and diploma versus academic education (including bachelor, master and doctorate)) were obtained by the use of a questionnaire.

Ethics approval

The protocol of study was approved by the Regional Bioethics committee of Isfahan University of Medical Sciences (IUMS) with reference codes: IR.IUMS.REC.189069, IR.IUMS.REC.189082, and IR.IUMS.REC.189089, and the study objectives were clarified for all participants before participating in the study, and a written informed consent was obtained from all participants.

Statistical analysis

Data had been analyzed through SPSS version 15.0 (SPSS Inc, Chicago, Illinois, USA). A p-value < 0.05 was considered statistically significant. Results were reported as mean ± SD for the quantitative continuous data and percentages for the qualitative data as frequency. For investigating the prevalence of symptoms among the total sample and different categories of socio-demographic characteristics (SDC), contingency tables were constructed. Loglinear models were performed to evaluate the comorbidity of depression, anxiety and stress. Odds ratios (OR) with 95% confidence interval (95% CI) were estimated in the framework of loglinear model as an indicator of comorbidity of studied PDs both in total sample and different levels of SDCs of participants and BMI. During the models fitting, the hierarchical effect was considered and the best model was selected based on Chi-squared test as a goodness-of- fit criteria. The smaller values of Chi-square values had the larger p-values indicating better fits. Finally, between-group comparisons were conducted using independent Student's t-tests and one-way analysis of variances (ANOVA) for continuous parametric or in different levels of any SDCs.

Results

The data obtained from 4763 subjects with a mean ± SD age of 36.58 ± 8.09 years participated. SDCs of study participants were as follows, 44.22% male, 81.2% married, and 57.2% academic educated. About 3.5% of participants were underweight, 36.7% were overweight, and 9.8% were obese. The prevalence of depression, anxiety and stress observed in total sample was 28.1, 13.7 and 22.2%, respectively. Table 1 shows the prevalence of depression, anxiety and stress in total sample and in different study levels of SDCs of participants. According to Table 1 the prevalence of anxiety and stress was significantly higher in the participants under 40 years old compared with those over 40 years old (p< 0.05). Although the prevalence of depression was higher in participants under 40 years old than those over 40 years old (16.8% vs. 12%), it was not statistically significant. In addition, the prevalence of three disorders was significantly higher in women than men (p< 0.05). The prevalence of depression and stress were significantly higher in married participants than single ones and for stress (p< 0.05). Significant differences were observed in terms of prevalence of depression, anxiety and stress among participants with different levels of educational attainments (p< 0.05). Furthermore, the disorders' prevalence was not statistically significant difference between participants in different categories of BMI.

Table 1. The prevalence of psychological disorders at levels of socio-demographic characteristics of the studied subjects (n = 4763).

	Depression		Anxiety		Stress	
	Case	No case	Case	No case	Case	No case
	n = 1338	n = 3315	n = 654	n = 4003	n = 1067	n = 3561
Variable	n (% of Total)	n (% of Total)	n (% of Total)	n (% of Total)	n (% of Total)	n (% of Total)
Age group(years)						
< 40	780 (16.8)	1871 (40.2)	406 (8.7)	2247 (48.2)	655 (14.2)	1991 (43)
> 40	558 (12.0)	1444 (31.0)	248 (5.3)	1756 (37.7)*	412 (8.9)	1570 (33.9)*
Gender						
Male	454 (9.8)	1590 (34.2)	204 (4.4)	1841 (39.5)	367 (7.9)	1657 (35.8)
Female	884 (19.0)	1725 (37.1)*	450 (9.7)	2162 (46.4)*	700 (15.1)	1904 (41.1)*
Marital status						
Single	277 (6.1)	582 (12.8)	116 (2.6)	744 (16.4)	219 (4.8)	643 (14.2)
Married	1030 (22.7)	2656 (58.4)*	521 (11.5)	3168 (69.6)	822 (18.2)	2836 (62.7)*
Level of education						
Under diploma& Diploma	650 (14.3)	1283 (28.3)	347 (7.7)	1587 (35.0)	484 (10.7)	1439 (31.9)
Academic	648 (14.3)	1950 (43.0)*	288 (6.4)	2313 (51.0)*	549 (12.2)	2036 (45.2)*
BMI (kg m^{-2})						
< 25 (normal weight)	686 (15.4)	1707 (38.3)	320 (7.2)	2077 (46.6)	562 (12.7)	1833 (41.3)
25-30 (overweight)	448 (10.1)	1184 (26.6)	230 (5.2)	1401 (31.4)	354 (8.0)	1264 (28.5)
> 35 (obes)	140 (3.1)	292 (6.6)	68 (1.5)	365 (8.2)	99 (2.2)	322 (7.3)

*p-value resulted from Chi-square test < 0.05.

Table 2 indicates the prevalence of comorbidity between three PDs in total sample and different levels of participants' SDCs. The prevalence of triple-comorbidity of three disorders was 9.14%, as well as the prevalence of pair-comorbidity of depression with stress (16.5%) was higher than pair-comorbidity of depression with anxiety (12.04%) and pair-comorbidity of anxiety with stress (10.23%) in total samples.

Table 2. The overlap of depression, anxiety and stress in total sample and in different categories of socio-demographic variables.

Variable (n in group)	Depression	Anxiety	Stress	
			n (%)	n (%)
			Case	No case
Total sample (n = 4553)				
	Case	Case	416(9.14)	132(2.9)
		No case	335(7.36)	428(9.40)
	No case	Case	38(0.83)	57(1.25)
		No case	266(5.84)	2881(63.38)
Gender				
Male (n = 1983)	Case	Case	126(6.35)	37(1.87)
		No case	111(5.60)	169(8.52)
	No case	Case	17(0.86)	20(1.01)
		No case	108(5.45)	1395(70.35)
Female (n = 2570)	Case	Case	290(11.28)	95(3.70)
		No case	224(8.72)	259(10.08)
	No case	Case	21(0.82)	37(1.44)
		No case	158(6.15)	1486(57.82)[*]
Age (years)				
< 40 (n = 2620)	Case	Case	271(10.34)	75(2.86)
		No case	206(7.86)	222(8.47)
	No case	Case	24(0.92)	32(1.22)
		No case	151(5.76)	1639(62.56)
> 40 (n = 1933)	Case	Case	145(7.50)	57(2.95)
		No case	129(6.67)	206(10.66)
	No case	Case	14(0.72)	25(1.29)
		No case	115(5.95)	1242(64.25)
BMI (kg m^{-2})				
< 25 (n = 2443)	Case	Case	218(9.25)	61(2.59)
		No case	181(7.68)	221(9.38)
	No case	Case	16(0.68)	23(0.98)
		No case	141(5.98)	1495(63.46)
25-30 (n = 1672)	Case	Case	139(8.75)	50(3.15)
		No case	106(6.67)	140(8.81)
	No case	Case	14(0.88)	23(1.45)
		No case	89(5.60)	1024(64.69)
> 30 (n = 445)	Case	Case	35(8.41)	17(4.09)
		No case	33(7.93)	47(11.30)
	No case	Case	5(1.20)	7(1.68)
		No case	26(6.25)	246(59.13)
Level of education				
Under diploma & Diploma (n = 1894)	Case	Case	221(34.70)	71(11.10)
		No case	141(22.10)	204(32.00)
	No case	Case	19(1.50)	-29(2.30)
		No case	99(7.90)	1110(88.30)
Academic (n = 2540)	Case	Case	182(28.70)	57(9.00)
		No case	179(28.20)	217(34.20)
	No case	Case	18(0.90)	27(1.60)
		No case	162(8.50)	1698(89.10)[*]
Marital Status				
Single (n = 3596)	Case	Case	329(9.15)	105(2.92)
		No case	244(6.79)	328(9.12)
	No case	Case	32(0.89)	44(1.22)
		No case	208(5.78)	2306(64.13)
Married (n = 851)	Case	Case	80(9.40)	20(2.35)
		No case	83(9.75)	92(10.81)
	No case	Case	5(0.59)	11(1.29)
		No case	48(5.64)	512(60.16)[*]

[*]p-value's resulted from Chi-square test < 0.05, related to triple-comorbidity between depression, anxiety and stress.

In Table 2**,** the prevalence of triple comorbidity of depression, anxiety and stress was significantly higher in women than men (p< 0.05), in addition, a significantly higher overlap was seen in the participants with under diploma & diploma education compared to those participants with academic education (p< 0.05); also significantly association was observed between marital status and PDs overlap (p< 0.05). However non-significantly higher in under 40-year-old participants compared to participants older than 40 years old, as well as in the participants with normal BMI than those with BMI > 30 kg m^{-2}.

Figure 1, presents the overlap between three disorders. 57.3% of depressed (D) cases had stress (S) and 41.8% had anxiety (A), on the other hand, 71.2% of participants with stress had depression and 43.0% had anxiety, in addition 70.6% of anxious cases had stress and 85.2% had depression.
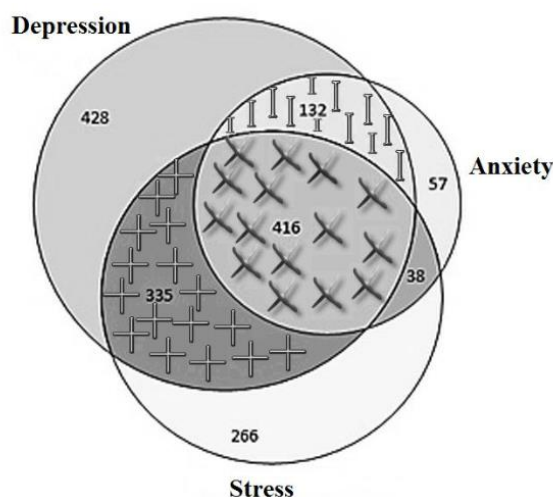
Figure 1. Overlap between anxiety, depression and stress as a frequency of the identified sample: stress = 1055; anxiety =643; depression =1311. *Total number of cases in diagram = 3009.

Table 3 shows the result of loglinear model selection process. The smallest value of chi-square goodness-of-fit (χ^2 = 3.38 and p = 0.02) was observed for the model containing pair-comorbidity of the three PDs i.e. (anxiety*stress [A&S]; depression & stress [D&S]; and anxiety*depression [A&D]) in total sample. Therefore, models with pair-comorbidity of A&S, D&S and A&D were selected in total sample and different levels of SDCs.

Table 3. Goodness-of-fit test for loglinear models evaluating the comorbidity of depression, anxiety and stress.

Model df		Total sample	Gender		Age (years)		BMI (kgm^{-2})			Level of education		Marital status	
			Male	Female	<40	>40	<25	25-30	>30	Under diploma & Diploma	Academic	Single	Married
(D,A,S)	4	2036.8*	2036.8*	2208.1*	2648.5*	1575.2*	2317.1*	1506.5*	269.2*	1756.1*	2330.8*	725.7*	3522.1*
(A,D&S)	3	618.1*	618.1*	813.9*	886.3*	559.4*	782.5*	510.5*	105.1*	651.9 *	746.0*	235.5*	1208.8*
(S,D&A)	3	609.1*	609.1*	803.5*	921.1*	512.1*	772.8*	491.6*	100.2*	628.3 *	749.2*	286.4*	1145.1*
(D,A&S)	3	637.5*	637.5*	963.1*	1048.4*	599.0*	879.6*	582.7*	123.6*	690.7 *	875.2*	301.4*	1315.0*
(D&S,A&D)	2	131.5*	131.5*	116.4*	148.7*	89.8*	121.5*	79.6*	20.8*	131.6*	108.5*	37.5*	211.0*
(D&A,A&S)	2	245.3*	245.3*	379.4*	434.1*	215.1*	345.7*	220.9*	47.2*	245.4 *	362.6*	154.1*	476.2*
(D&S,A&S)	2	198.7*	198.7*	368.9*	363.1*	231.6*	307.6*	224.0*	52.4*	254.5*	301.6*	75.6*	494.5*
(D&S,A&S,D&A)	1	3.4(0.02)	3.4	1.6	5.2	1.01	1.9	2.5	1.3	1.9	2.6	0.02	5.4
(D&A&S)	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

After adopting the model (A&S, D&S, A&D), we compared odds ratio (OR) of comorbidity between each pair of PDs in total sample and different levels of SDCs.*p-value resulted from Pearson Chi-square statistics < 0.001.D, Depression; A, Anxiety; S, Stress; D&S, Comorbidity between depression and stress; A&S, Comorbidity between anxiety and stress; D&A, Comorbidity between depression and anxiety.

Table 4 indicates that comorbidity between anxiety and depression in total samples and different levels of SDCs has the highest OR (95%CI: 9.16- 14.42) and comorbidity between stress and anxiety in total samples and different levels of SDCs has the lowest OR (95%CI: 3.63-6.47).

Table 4. Results of loglinear model for association of depression (D), anxiety (A) and stress (S) based on best model, according to their socio-demographic characteristics.

Parameter	Total sample	Gender		Age (years)		BMI (kg m⁻²)			Level of education		Marital status	
		Male	Female	< 40	> 40	< 25	25-30	> 30	Diploma & under diploma	Academic	Single	Married
S&A	4.62 (3.71,5.75)	6.47 (4.44,9.49)	3.85* (2.95,5.00)	4.66 (3.49,6.17)	4.45 (3.19,6.23)	4.87 (3.56,6.69)	4.31 (3.00,6.23)	3.63 (1.90,6.96)	5.05 (3.71,6.82)	4.47 (3.25,6.17)	4.94 (3.86,6.30)	4.52 (2.72,7.54)
S&D	7.80 (6.55,10.18)	7.62 (5.70,10.18)	7.67 (6.11,9.58)	9.03 (7.17,11.36)	6.41* (4.90,8.41)	8.16 (6.36,10.38)	7.88 (5.81,10.70)	5.76 (3.32,9.97)	7.12 (5.42,9.3)	8.04 (6.36,10.17)	7.48 (6.11,9.12)	9.52 (6.42,14.15)
A&D	12.29 (9.58,15.80)	10.78 (6.28,7.10)	12.59 (9.22,17.29)	12.64 (9.12,17.46)	11.83 (8.00,17.46)	14.42 (9.87,21.11)	12.43 (8.25,18.73)	9.16 (4.48,18.73)	10.97 (7.69,15.64)	12.91 (8.93,18.54)	12.79 (9.68,16.94)	9.78 (5.37,17.99)

D: Depression, A: Anxiety, S: Stress, S&A: pair-comorbidity between stress and anxiety, S&D: pair-comorbidity between stress and depression, and A&D: pair-comorbidity between anxiety and depression. Values in table are OR (95% CI). *p-value resulted from independent t-student test < 0.05.

According to final selected model (Table 4), in total sample, participants suffering from stress suffered from anxiety 4.62 times as much as those without stress (OR = 4.62, 95%CI: 3.71-5.75), significantly higher ORs were observed for men than women; adjusted OR = 6.47, (95%CI: 4.44-9.49) vs. OR = 3.85, (95%CI: 2.95-5.00); p< 0.05) however no statistically significant ORs were observed between categories of other SDCs. Furthermore, the odds of suffering from depression in participants with stress is 7.8 times as much as in those without stress participants of total sample (OR = 7.80, 95%CI: 6.55-10.18), and the adjusted OR of comorbidity between stress and depression in the age group of under 40 years old higher than participants in the age group of upper 40 years old (adjusted OR = 9.03, 95%CI: 7.17-11.36 versus OR = 6.41, 95%CI: 4.90-8.41; p< 0.05), however, no significantly higher in women compared to men, participants with normal BMI compared with those in other levels of BMI, participants with academic education compared with participants in other educational attainments, and married participants compared with singles. On the other hand, odds of being depressed in anxious participants are 12.29 times more than people without anxiety (OR = 12.29, 95%CI: 9.58-15.80) in total sample, however, adjusted ORs of comorbidity between anxiety and depression were not statistically significant different between categories of SDCs of study participants.

Discussion

This study examined the prevalence rate and comorbidity between depression, anxiety and stress in total and at different levels of SDCs in a large sample of Iranian adults.

Our results showed that the prevalence of the studied PDs is higher in the participants under 40 years old than who were over 40 years old (Table 1). In a previous study also younger participants were more predisposed to depression and anxiety (Klapow et al., 2002). The possible explanation for this finding is that the majorities of young people in Iran, after graduation, are faced with social and job related challenges (Seyedan & Abdolsamadi, 2012).

In the present study the prevalence of the three disorders and triple comorbidity in women were significantly higher than men (Table 1 and 2). This is in agreement with a previous study which conducted without considering comorbidity between depression, anxiety and stress (Gorman, 2006; Gonçalves et al., 2014). The mentioned gender differences might be associated with many factors including socio-cultural and biological factors (Kaur, Tee, Ariaratnam, Krishnapillai, & China, 2013).

Married participants had higher prevalence of the three disorders and their triple comorbidity compared with non-married participants (Table 1 and 2). This finding could be attributed to quality and duration of married life, which is in agreement with some previous studies (Scheid & Wright, 2017). However in those studies, comorbidities between depression, stress and anxiety were not considered.

The prevalence of depression and its comorbidity with both anxiety and stress was higher in less educated participants compared to participants with academic education (Table 1 and 2). This supports the results of the previous study which showed depression was more prevalent in illiterate participants (Kessler & Greenberg, 2002), although there is no study on evaluating the comorbidity between three PDs in levels of educational attainments. Furthermore, the prevalence of anxiety and stress was higher in less educated participants compared with the participants with academic education (Table 1). Our findings regarding to anxiety and stress could be justified by socio-economic challenges particularly job insecurity in society of Iran.

In current study for evaluating of comorbidity between PDs, we studied all possible two and triple comorbidity diagnosis using loglinear analysis, and finally based on goodness-of-fit criterion, models with pair-comorbidity of A&S, D&S and A&D were selected in total sample and different levels of SDCs. Limited

studies about comorbidity and/or correlation between these three major PDs have been conducted in the world (Ginzburg et al., 2010; Bener et al., 2012; Beiter et al., 2015) and most of them have not been done in a population-based setting and/or, the studied sample size is considerably lower than our study as well as with less focus on controlling of confounder variables (Shamsuddin et al., 2013; Yusoff, Rahim, Baba, Ismail, & Pa, 2013; Iqbal, Gupta, & Venkatarao, 2015; Kulsoom & Afsar, 2015). On the other hand, majority of previous studies have focused on comorbidity and/or connection between two disorders only, for example comorbidity between anxiety and depression (Ameringen, 2016), stress and anxiety (Leuner & Shors, 2013), and depression and stress (Ayazi et al., 2012; Flory & Yehuda, 2015). In a comprehensive search on the referred studies about comorbidity between stress and anxiety and comorbidity between anxiety and depression, we could not find any similar study on mentioned pair comorbidities in different levels of SDCs.

Our study demonstrated a higher rates of comorbidities than pure prevalence of anxiety, stress and depression (Figure 1). This was in agreement with parallel result for comorbidity of depressive disorder on Iranian population (Mohammadi et al., 2019). Our findings were also in agreement with the cross-sectional study from a sample of civilians from South Lebanon, showing the prevalence of co-occurring posttraumatic stress disorder (PTSD) and depression was higher than that of PTSD or depression alone (Farhood, Fares, Sabbagh, & Hamady, 2016). However, in the mentioned studies, all possible two way comorbidity between depression, anxiety and stress were not considered. In our study, the highest prevalence of comorbidity in total sample was obtained for stress and depression and similar findings were obtained in different levels of SDCs (Table 2 and Figure 1). In parallel, the cross-sectional study based on the primary healthcare clinics of Qatar reported that the overlap of stress and depression was higher compared to the overlap of stress and anxiety, and overlap of depression and anxiety (Bener et al., 2012). Nevertheless, the reason for the differences between these rate of pair comorbidities is yet to be established. Furthermore, our results showed that a high percentage of anxious cases in total sample suffer from depression (Figure 1). In consistent with our findings, the previous studies have pointed out high prevalence of comorbidity between depression and anxiety (Bener et al., 2012; Coplan et al., 2015).

The odds of comorbidity between stress and anxiety was higher in men compared to women, as well as comorbidity between anxiety and depression was significantly higher in age group under 40 years old. Interpretation of these findings in the context of existing literature is difficult because previous studies on psychological disorder comorbidities have tended to focus on total sample and they did not pair-comorbidities in levels of SDCs.

Study strengths

Compared to similar previously studies in the world (Ginzburg et al., 2010; Bener et al., 2012; Beiter et al., 2015), the present study was performed in a community based setting among a large sample of population in a developing country with relatively specific socio-eco demographic structure on evaluating prevalence and triple and all possible two way comorbidity between three common PDs using a comprehensive and sophisticated statistical model not only in total sample but also in levels of important SDCs.

Study limitations

Results of our study could not be extended to all Iran's general population due to diversity of socio-cultural and economic background of different ethnics living in Iran, however because we studied a large sample in central region of Iran, its results are extendable to people living in this region. Another limitation of this study was its observational cross-sectional in nature that precludes the assumption of cause and effect relationship.

Conclusion

We found a higher rates of pair and triple comorbidity than pure prevalence of anxiety, stress and depression among a large sample of adults in Iran. Also, pair-comorbidity between stress and depression was higher than pair-comorbidity between stress and anxiety, and anxiety and depression. On the other hand, a high percentage of anxious cases in total sample suffer from depression. Obvious discrepancies were observed in terms of prevalence and the risk (ORs) of pair and/or triple comorbidities between three mentioned disorders among participants with different levels of SDCs. Accordingly, management strategies for three mentioned PDs, pair and/or triple comorbidities between them need to contribute the potential impacts of some SDCs including age, gender, marital status and level of education.

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