PANIC DISORDER AMONG PATIENTS WITH JOINT HYPERMOBILITY SYNDROME

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ABSTRACT

Panic disorder (P.D) is a common, chronic illness characterized by recurrent attacks of severe anxiety which are not restricted to any particular situation or set of circumstances and therefore unpredictable. Joint hypermobility syndrome (JHS) in an inherited connective tissue disorder characterized by increased distensibility of joint in passive movements and hypermobility in active movements. This study aims to measure the extent of association between panic disorder and JHS amongst a cohort of Iraqi patients. Fifty patients diagnosed as JHS cases according to Beighton's criteria by a rheumatologist, were collected from the rheumatic outpatient clinic of Baghdad Teaching Hospital. Those patients were screened by a DSM IV-based semistructural interview to detect panic disorder among them. The findings were compared with a control group of another (50) rheumatic patients who do not fulfill criteria of JHS. The results showed that the rate of panic disorder among patients with JHS is (32%) while in control sample is (8%). Also rate of panic disorder with agoraphobia found to be higher than control group (22%), (2%) respectively. Both the above results are statistically significant. The association of panic disorder with JHS is studied in relation to sociodemographic variables such sex, age, marital status, occupation and the results revealed that P.D is higher in females than in males, in younger age group, in unmarried than in married, in urban more than rural and more in house wives. But these results are non-significant statistically.

KEYWORDS: Panic disorder; patients; hypermobility Syndrome.

INTRODUCTION

In the nineteenth century there was a wide acceptance of the idea that psychological factors can play a part in the etiology of physical illness.[1] In the twentieth century psychoanalysts school suggested that Freud's theory of the conversion of mental disorder into physical symptoms could be applied to physical illness.[2]

Dunbar (1946) described specific personality types which were associated with specific disorders.[3] Several interviewing processes were proposed including psychophysiological mechanisms, behavioral processes and hormonal factors in support to the theory that nonspecific psychological stressors lead to physical illness in constitutionally proposed people.[2] Holmes and Rahe (1967) evaluated the effect of stressful events on occurrence of physical illness. They concluded that life events have a role in the etiology of physical illness, it is likely to act as triggers or precipitant rather than formative causes.[4] Engel (1980) developed the biopsychosocial model of disease which recognizes that all diseases have biological, psychological and social components.[5] Byrne (1988) studied the exogenous factors in panic disorder, he reviewed certain exogenous factors that seem capable of triggering attacks and/or

increasing their frequency and intensity.[6] Lumely et al (1994) studied the psychosocial functioning in Ehlers-Danlos syndrome which is one of joint hypermobility syndromes and found elevated levels of anxiety, depression, anger and interpersonal concerns, varying from 25% to 33%.[7] Grahame (2000) studied pain, distress and joint hyperlaxity and found that pain dominate the lives of patients with hyperlaxity syndrome and as a result they experience psychosocial problems.[8] The predisposition of some individuals to develop specific disorder may arise from genetic factors, environmental influences, learning or combination of these factors. The psychophysiological reaction which developed as a result of this predisposition if prolonged may act as precursor of or cause of disease. The process is interacting and not a one-way process. The biological variables are necessary but are not sufficient to explain the onset of disease. Thus the physician's knowledge and skills may span the biological, psychological and social aspects.[9] According to DSM IV panic disorder is classified as an anxiety disorder consisting of repeated and unexpected panic attacks, often more than one attack per week. A panic attack is characterized by the rapid onset of fear, terror or discomfort accompanied by at least four of the following: Such spontaneous panic

attacks typically reach an apex of intensity within 10 minutes.[10] The attacks are accompanied by one month or more of persistent concern about having additional attacks, worry about the significance of the attack (e.g. heart disease or fear of losing control) or significant changes in behavior. The individual experience intense fear and feels that he or she may die, lose control or go crazy. A strong urge to flee or escape the situation is usually reported.[11] When panic attacks have occurred in certain situations in some persons it becomes associated with these situations. Examples of such situations include the use of public transportation, crossing bridge, being in crowed or in a line, and leaving familiar settings alone. Because they do not want to have more attacks, the solution is to avoid such situations. Hence patients become phobic and begin to avoid situations in which they expect to get panic attack or escape may be difficult or help cannot rapidly have obtained. The person might insist on being accompanied by a friend or relative when getting out, a person with this form of panic disorder is said to have a panic disorder with agoraphobia. Some persons have agoraphobia without a history of panic disorder. In those persons the fears and avoidance are associated with the possibility of developing a panic-like symptoms in the situations exampled above.[12] Because panic disorder has an underlying biologic and probably genetic basis, the role of factors outside the organism in initiating and sustaining panic is often overlooked. Certain exogenous factors were studied that seem capable of triggering attacks and/or increasing their frequency and intensity; self-administered pharmacologic agents (caffeine, alcohol, nicotine, over-the counter cold preparations, cannabis, cocaine), habits (sleep deprivation, diet, exercise, hyperventilation); and aspects of the environment (fluorescent lighting, life stressors).[6] It has been proved that infusion of sodium lactate into panic patients can induce an attack. This is not applicable into non panic subjects. The explanation of this effect is unclear. The same effect can be induced by breathing carbon dioxide. Both lactate and carbon dioxide increase cerebral blood flow and it has been suggested that these may be a hypersensitivity of the "suffocation alarm mechanism" to rising levels of carbon dioxide and by lactate.[13] Reiman et al 1986 using brain imaging studies in panic disorder especially positron emission tomography (PET) have found structural changes in the right parahippocompal area of panic disorder patients vulnerable to lactate induced panic. There is asymmetry in blood flow, blood volume and oxygen metabolism suggestive of abnormal increase in the right side. This may indicate increase in neuronal activity or a relative increase in permeability of the blood-brain in that area.[14] Panic disorder has also been found to be associated with medical illness like cardiomyopathy, chronic obstructive airway disease and Parkinson's disease. The significance of specific organ pathologies in panic disorder is unclear although it has been considered in many studies. Joint Hypermobility Syndrome (JHS) was found in a preliminary study by Bulbena et al (1998) to be highly associated with anxiety

disorders and specifically with panic disorder.[15] The Hypermobility Syndrome also known as congenital laxity of ligaments and joints occurs as an isolated condition. The genetic background is distinct from that found in other connective tissue disorders. Although joint hypermobility is relatively common in general population, reports of muscloskeletal complaints are infrequent.[16] JHS is characterized by an increased distensibility of joints in passive movements and hypermobility in active movements. JHS is first described by Rotes and Argancy (1957) and was later extensively studied by Beighton et al (1973, 1989). Generalized ligaments laxity, the feature of JHS, may be seen in a proportion of healthy individuals and is a common feature to a variety of connective tissue disease of heritable etiology. Hypermobility diminishes markedly throughout childhood and then more slowly during adult life, showing no fluctuations.[15] Inherited connective tissue disorders which are characterized by generalized joint hypermobility include Ehlers-Danlos syndrome, osteogenesis imperfecta, marfan syndrome and Larsen syndrome. Others like Morquio syndrome or achondroplasia, have hypermobility in a more limited distribution.[18] Prevalence of JHS in the general population ranges between 10% and 20% and is more common in women than in men. The assessment of JHS patients depends on clinical measures such as the five Beighton criteria and was recently studied by Bulbena.[17] Psychosocial problems which affect JHS patients and may affect their healthy functioning is attributed to their complaint of their chronic pain in joints, muscle and ligaments which arises from an inherent predisposition to the effect of everyday trauma, but other factors may play a role like associated osteoarthritis or fibromyalgia are also important. Laxity of connective tissues within or providing support for the abdominal, thoracic or pelvic vescera may cause pain and distress of vesceral origin and may lead to hernias, uterine or rectal prolapse, mitral valve prolapses or spontaneous pneumothorax.[8] In a recent study by collier (2002) a genetic relation was found between panic disorder and joint hypermobility. The study was to conform a genomic linkage of panic disorder to chromosome 15. This study was supported by the fact that patients with panic disorder are upto 16-fold more likely to have joint laxity.[19] Some geneticist noticed that the chromosomes of patient with panic disorder, had a slightly longer arm of chromosome 15. These patients come from families with multiple incidences of panic disorder and joint laxity.[20]

MATERIALS AND METHODS

This study was conducted at Baghdad Teaching Hospital-Rheumatology outpatient clinic for the period from 1st of January 2015 to 30th of October 2015. A sample of fifty patients attending the rheumatology outpatient clinic diagnosed by rheumatologist as cases of Joint Hypermobility Syndrome. Patients were diagnosed as having JHS if they fulfilled ≥ 3 of Beighton's criteria or who scored ≥ 5 in Beighton's diagnosis scheme. The Control sample of 50 patients was randomly selected

from the patients seen at the same clinic but did not met criteria for JHS. After detailed rheumatology assessment, psychiatric assessment for panic disorder was undertaken from the patient and control samples in the same visit using semi structured DSM IV based schedule after fulfilling the sociodemographic data. A signed consent was taken from individuals in both groups for inclusion in the study.[21]

RESULTS AND DISCUSSION

It is well known that there is a significant association between physical and psychiatric disorder, also it is well known that studies conducted in medical settings yield higher psychiatric prevalence rates than studies in the general population.[22,15] The component of this association is either increased risk of psychiatric morbidity in physical illness or vice versa or as recently proved there is genetic relationship between many psychiatric illnesses and physical illness.[20] The present study revealed that the prevalence rate of panic disorder, among patients with Joint hypermobility syndrome (JHS) is significantly higher than in the control sample (32% and 8% respectively) (Table 1) which shows that the rate of panic disorder among patient and control samples is 32% and 8% respectively.

Table (1): The association of panic disorder and JHS among patient and control samples.

Sample	With Panic Disorder	Without Panic Disorder	Total
	No. (%)	No. (%)	No. (%)
JHS (cases)	16 (32%)	34 (68%)	50 (100%)
Control	4 (8%)	46 (92%)	50 (100%)

$X^2=7.56$ P=0.006.

This result is concomitant with Bulbena et al study (1993) who found that a higher prevalence of anxiety disorders especially panic disorder and agoraphobia among patients with JHS than controls (34% and 6.8% respectively).[15] Clinical and genetic studies tend to produce similar clustering.[23] This study also revealed a prevalence rate of panic disorder with agoraphobia in patient sample (22%) higher than control sample (2%) and prevalence rate of agoraphobia in patient sample (14%) higher than control sample (4%). The rate of P.D, with agoraphobia in JHS pts (22%) is higher than that of P.D without agoraphobia in those pts (10%). The rate of agoraphobia is more (14%) in JHS patients than with control group (4%). These findings are statistically significant (Table 2).

Table (2): Panic disorder with or without agoraphobia in JHS patients and control samples.

Agora-phobia	Patient Sample (JHS) n=50			Control Sample n=50		
	P.D	No P.D	Total	P.D	No P.D	Total
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
With	11(22%)	7(14%)	18(36%)	1(2%)	2(4%)	3(6%)
Without	5(10%)	27(54%)	32(64%)	3(6%)	44(88%)	47(94%)
Total	16(32%)	34(68%)	50(100%)	4(8%)	46(92%)	50(100%)

$X^2=8.96$ $x^2=0.326$
P=0.003 P=0.57

In Bulbena et al study they found prevalence of panic and agoraphobia in JHS patients was also significantly different between patients and controls.[15] In a study by Biro et al among 262 patients with JHS, he found only 15(5.7%) consult a rheumatology clinic within 6 months in spite of their rheumatic complaint.[25] In this work diagnosis was done in two levels: the diagnosis of JHS by Beighton's criteria, which performed by a rheumatologist which is clinical method of diagnosis yet it is not only way of diagnosis.[17] The other level is the diagnosis of panic disorder and/or agoraphobia using semi structural interview which based on DSM IV criteria. This was not designed to be an epidemiological instrument, although it has been used in a number of general hospital surveys the diagnostic criteria are insufficiently precise for acceptable reliability.[24] This study shows that the prevalence of panic disorder among patients' sample is higher in younger age group than controls (Table 3) which shows that the rate of panic disorder is higher in the age group (≤30yrs) of the patient sample, than with control group while it is higher in the age group (≤40yrs) of control group (26%) and (58%) respectively.

Table (3): Rate of panic disorder among patients and control samples in relation to age group.

Age Group (yrs)	Patient Sample (JHS) n=50			Control Sample (No JHS) n=50		
	P.D	No P.D	Total	P.D	No P.D	Total
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
≤30	13(26%)	27(54%)	40(80%)	1(2%)	17(34V)	18(36%)
≤40	3(6%)	7(14%)	10(20%)	3(6%)	29(58%)	32(64%)
Total	16(32%)	34(68%)	50(100%)	4(8%)	46(92%)	50(100%)

$X^2=0.02$ P>0.05.

This is understandable by the fact that JHS a disease of young age group and prevalence of joint hypermobility decreases with aging.[25,15] The JHS patients sample is generally younger than control group: (80%) of age group (18-30) and (20%) of age group (31-40) while in control sample (30%) of age group (18-30) and (64%) of age group (31-40) and since both JHS and panic disorder are more common in young women this might lead to a bias which should be considered. This finding is consistent with other studies.[26,27] The study revealed that the prevalence of panic disorder is higher among females than males in patient's sample (30% and 2% respectively) and also in control sample (8%, 0% respectively). But it is not statistically significant which may be due to small sample size (Table 4) which shows that the rate of panic disorder is higher in females than in males in both patient (30%, 2%) and control (8%, 0%) samples respectively.

Table (4): Rate of panic disorder among patient and control samples in relation to sex.

Sex	Patient Sample (jhs) n=50			Control Sample (no jhs) n=50		
	P.D	No P.D	Total	P.D	No P.D	Total
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
Female	15(30%)	27(54%)	42(84%)	4(8%)	38(76%)	42(84%)
Male	1(2%)	7(14%)	8(16%)	0(0%)	8(16%)	8(16%)
Total	16(32%)	34(68%)	50(100%)	4(8%)	46(92%)	50(100%)

Fisher exact test $x^2=0.09$
P>0.05   P=0.842

A high prevalence of panic disorder is found among intermediate school education level of both patients and control samples. (12% and 4% respectively) (Table 5) which shows that the rate of panic disorder is higher in those with intermediate school education in both samples.

Table (5): Rate of panic disorder in patients and control samples in relation to education.

Education	Patient Sample (cases) N=50			Control Sample n=50		
	P.D (%)	No P.D (%)	Total	P.D (%)	No P.D (%)	Total
Illiterate	1(2%)	2(4%)	3	0(0%)	3(6%)	3
Primary school	4(8%)	3(6%)	7	1(2%)	10(20%)	11
Intermediate school	6(12%)	15(30%)	21	2(4%)	17(34%)	19
Secondary school	3(6%)	2(4%)	5	1(2%)	7(14%)	8
College	2(4%)	12(24%)	14	0(0%)	9(18%)	9
Total	16(32%)	34(68%)	50	4(8%)	46(92%)	50

$X^2=0.937$ P=0.919

Housewives found to be more panic than those with other occupations in both patients and controls (18% and 4% respectively) but this result is statistically not significant (Table 6) which show that the rate of panic disorder is higher in housewives in both patient and control samples 18% and 4% respectively.

Table (6): Rate of panic disorder among patients and control samples in relation to occupation.

Occupation	Patient Sample N=50			Control Sample n=50		
	P.D (%)	No P.D (%)	Total	P.D (%)	No P.D (%)	Total
Student	3(6%)	12(6%)	15	0(0%)	5(10%)	5
House wife	9(18%)	17(34%)	26	3(6%)	27(54%)	30
Employed	4(8%)	5(10%)	9	1(2%)	10(20%)	11
Unemployed	0(0%)	0(0%)	0	0(0%)	4(8%)	4
Total	16(32%)	34(68%)	50	4(8%)	46(92%)	50

$X^2=4.773$ P=0.1892

It has been found also that panic disorder is more prevalent among those with intermediate financial income of both patients and control samples (24% and 4% respectively). This result is not statistically significant (Table 7) which shows that the rate of panic disorder is higher in those with moderate financial income of both patient and control samples (24% and 4%) respectively.

Table (7): Rate of panic disorder among patients (JHS) and control sample in relation to financial income.

*Financial Income	Patient Sample (P.D) No. (%)	Control Sample (p.D) No. (%)	Total No. (%)
Low	3 (6%)	1 (2%)	4 (8%)
Moderate	12 (24%)	2 (4%)	14 (28%)
High	1 (2%)	1 (%)2	2 (4%)
Total	16 (32%)	4 (%)8	20 (80%)

$X^2=1.473$ P=0.4787

*Low income: the income of the patient and his family doesn't occur this daily requirement.
*Moderate income: the income of the patient and his family just cover his daily requirements.
*High income: the income of the patient and his family covers more than his daily requirements.

The study revealed a higher prevalence rate of panic disorder in unmarried than in married patients (20%, 10% respectively), while equal prevalence in control sample (4%). This might be explained regarding the patients sample on the basis of the age since JHS and panic disorder more common in young age group. This result is statistically not significant (Table 8) which shows higher rate of panic disorder in the unmarried group in both patients (20%) and control (4%) samples.

Table (8): Rate of panic disorder in patient and control samples in relation to marital status.

Marital status	Patient Sample N=50			Control Sample N=50		
	P.D (%)	No P.D (%)	Total	P.D (%)	No P.D (%)	Total
Unmarried	10(20%)	23(26%)	23	2(4%)	18(36%)	20
Married	5(10%)	10(20%)	15	1(2%)	25(50%)	26
Divorced	1(2%)	0(0%)	1	1(2%)	1(2%)	2
Widow	0(0%)	1(2%)	1	0(0%)	2(4%)	2
Total	16(32%)	34(68%)	50	4(8%)	46(92%)	50

$X^2=0.655$ P=0.7208

Prevalence of panic disorder is found to be higher among urban (24%) than rural. For both patients and control samples, but this result is statistically not significant (Table 9) which shows that the rate of panic disorder is higher in urban than rural for both patients and control samples (24% and 6%) respectively.

Table (9): Rate of panic disorder in patients (JHS) and control samples in relation to residential area.

Residence	Patient Sample (P.D) No. (%)	Control Sample (P.D) No. (%)	Total No. (%)
Urban	12(24%)	3(6%)	15(30%)
Rural	4(8%)	1(2%)	5(10%)
Total	16(32%)	4(8%)	20(40%)

Fisher exact test   P>0.05.

CONCLUSION
There is a strong association between joint hypermobility syndrome and panic disorder and there is a significant association between panic disorder with agoraphobia and JHS. And also there is a significant association between agoraphobia and JHS.

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