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Pseudobulbar affect prevalence in Turkish multiple sclerosis patients

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Abstract

Objective: Pseudobulbar affect (PBA) is characterized by uncontrolled crying or laughing attacks which are usually socially inappropriate. The estimated prevalence in patients with multiple sclerosis (MS) ranges from 10% to 46.2%. We conducted a cross-sectional study to evaluate the prevalence of PBA in the Turkish MS population. Also, we aimed to estimate whether there was gender preference or coexistent depression.

Material and Methods: We used the Center for Neurologic Study - Lability Scale (CNS-LS) for this study. We included patients who were followed up at our outpatient clinic of Sultan Abdulhamid Han Education and Research Hospital with definitive diagnosis of MS at least for one year. The total number of patients was 328. 60.4% were women (198/328) and 39.6% were men (130/328). Descriptive statistical methods, student t test and chi-square tests were used for the analysis by using SPSS. The prevalence of PBA in the Turkish MS population was 39.6%. 34.6% of the men with MS had PBA; whereas 42.9% of the women with MS had PBA (p=0.132). The incidence of PBA was 48.1% in MS patients with depression and 38% in those without depression (p=0.175).

Results: As a result of t-test applied it was understood that depression did not significantly contribute to PBA frequency. The average depression test score was 13.28 in non-depressed, 17.85 in others. Furthermore, there was a difference between pathological laughing and pathological crying ($p<0.05$). Also, in both gender pathological laughing laughter was more and the difference was significant ($p<0.05$).

Conclusion: Our study revealed the increased frequency of PBA in MS patients. Gender and having depression did not make a significant difference on the PBA prevalence. However, depression significantly increased PBA test scores

Keywords: CNS-LS Scale, Gender, Multiple sclerosis, Pseudobulbar affect

Introduction

Sudden outbursts of involuntary, exaggerated laughter and/or crying have been described in patients with certain neurological disorders since the 19th century [1]. And, several different terms have been used for this clinical syndrome by clinicians such as “pathological laughing and weeping,” “emotional lability,” “pseudobulbar affect,” “emotional incontinence,” “pathologic emotionality” [2]. The term “pseudobulbar affect [PBA]” has generally been used more broadly, to refer to syndromes of exaggerated affective display which can be either mood incongruent or mood congruent [3,4]. Pseudobulbar affect [PBA] is characterized by uncontrolled crying or laughing which may be socially inappropriate to the social context. Thus, there is a disparity between the patient’s emotional expression and their emotional experience [5].

Despite the mechanisms are not fully understood, serotonergic and glutamatergic transmission is suggested to play major roles. Clinical improvements have been reported after treatment with SSRIs, TCAs or dextromethorphan/quinidine [5]. The underlying mechanism in PBA appears to be a lack of voluntary control, also termed cortical inhibition over brainstem centers that produced the facio-respiratory functions associated with laughing and crying. This loss of cerebral control results in a dissociation of affective displays from the subjectively experienced emotional states [6].

Detailed reviews of the widespread neuropathological and neurophysiological abnormalities found by neuroimaging and neurophysiological studies in patients with PBA have been published [7].

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PBA may coexist seen with amyotrophic lateral sclerosis [ALS], extrapyramidal and cerebellar disorders [Parkinson's disease, multiple system atrophy, progressive supranuclear palsy], multiple sclerosis [MS], traumatic brain injury, dementias like Alzheimer's disease, stroke, and brain tumors [8].

The patient's emotional response to a stimulant is often largely out of proportion . The crying or laughter may persist for a considerable period of time, and may not be suppressed by the patient. In addition, these episodes occasionally occur in situations that are not perceived by others as sad or being funny [5].

There is significant variability in reported prevalence rates, both between and within syndromes [1]. The range of estimates of prevalence in various neurological disorders is high, from 5% to well over 50%. This variability stems from the diagnostic criteria, methodologies, and patient populations studied [7-9]. Depending upon the scoring criteria used for the online instruments, prevalence rates ranged from 9.4%–37.5%, resulting in an estimated 1.8–7.1 million affected individuals in the USA [5]. PBA in MS patients is associated with severe intellectual deterioration, physical disability, and neurological disability [10].

The estimated prevalence of PBA in patients with MS ranges from 10% to 46.2% [11].Thus, we conducted this study to evaluate the prevalence of PBA in the Turkish MS population. In this direction, the prevalence of PBA in men and women was determined separately. Moreover, the prevalence of PBA with and without depression were investigated to determine whether depression is a vital factor of PBA.

Material and Methods

We included patients who were followed up at our outpatient clinic of Sultan Abdulhamid Han Education and Research Hospital with definitive diagnosis of MS at least for one year. The total number of participants was 328, 60.4% were women (198/328) and 39.6% were men (130/328). Depression was present in 15.85% (52/328) of MS patients participating in our study.

Patients with depression were identified by applying the Beck Depression Scale. The cut-off score for depression was 17 points. The Center for Neurologic Study - Lability Scale (CNS-LS) was used to determine the prevalence of pseudobulbar affectation (PBA). The Center for Neurologic Study – Lability Scale (CNS-LS) is a seven-item self-administered questionnaire that has questions regarding the control of laughter and crying, and has been validated in patients with ALS and MS.12 The responses are graded from 1 to 5 for each question, with the total score range from 7 (no excess emotional lability) to 35 (severe excess emotional lability). Patients whose scores were 15 or more score were considered to have PBA [11].

In order to determine the PBA prevalence and test results, descriptive statistical methods such as mean, standard deviation and percentage were used. Student t test and chi-square test were also used by SPSS in comparison between sex and depression. The findings were evaluated at 95% confidence interval and p <0.05 significance level. P values less than 0.05 were considered to have significant differences.

Results

PBA Prevalence in MS Population

Of the 328 MS patients participated in our study, 39.6% had PBA. The frequency of PBA was 34.6% (45) in men and 42.9% in women (85). There was no statistically significant difference between gender groups (p=0.132) (Table 1).

Table 1: PBA prevalence in MS population

Group	n	n%	Chi-square	df	p
Female	85	42.9	2.267	1	0.132
Male	45	34.6			

PBA Prevalence in Patients with and without Depression

PBA frequency was 48.1% (25) in those with depression and 38% (105) in those without depression. there was no difference between these groups (p=0.175). In addition, as a result of detailed analysis according to gender, PBA frequency was similar between male patients' groups whether they have depression or not (p=0.969). Women with depression seemed to have PBA more 56.3% than men. However, PBA frequency did not differ among women regarding depression (p=0.096) (Table 2).

Table 2: PBA prevalence in patients with and without depression

Group	n	n%	Chi-square	df	p
Depressed	25	48.10	1.841	1	0.175
Non-depressive	105	38.00			
Depressed Male	7	35.00	0.002	1	0.969
Non-Depressive Male	38	34.50			
Depressed Female	18	56.30	2.764	1	0.096
Non-depressive Female	67	40.40			

Test Scores in MS Patients with and without Depression

In patients with depression, the independent samples t-test total score was 17.85±8.06. In patients without depression, the mean test score was 13.28±4.88.(p<0.001). Therefore, PBA scores of patients with depression were significantly higher (Table 3).

In addition, the mean PBA score was 16.15±8.20 in men with depression and 13.14±5.11 in men without depression. (t = -1,588, p = 0.127). In women, PBA score was 18.91±7.91 in those with depression and 13.37±4.74 in those without depression (t = -3.826, p = 0.001) (Table 3). It is possible to demonstrate the rates of PBA frequency according to gender and depression (Figure 1).

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Table 3. Test scores in MS patients with and without depression

Group	Min	Max.	±ss	t	df	p
Depressed	7	35	17.85±8.06	-3.952	58242	0.000
Non-depressive	7	33	13.28±4.88			
Depressed Male	7	35	16.15±8.20	-1.588	21759	0.127
Non-depressive Male	7	33	13.14±5.11			
Depressed Female	8	35	18.91±7.91	-3.826	35398	0.001
Non-depressive Female	7	31	13.37±4.74			

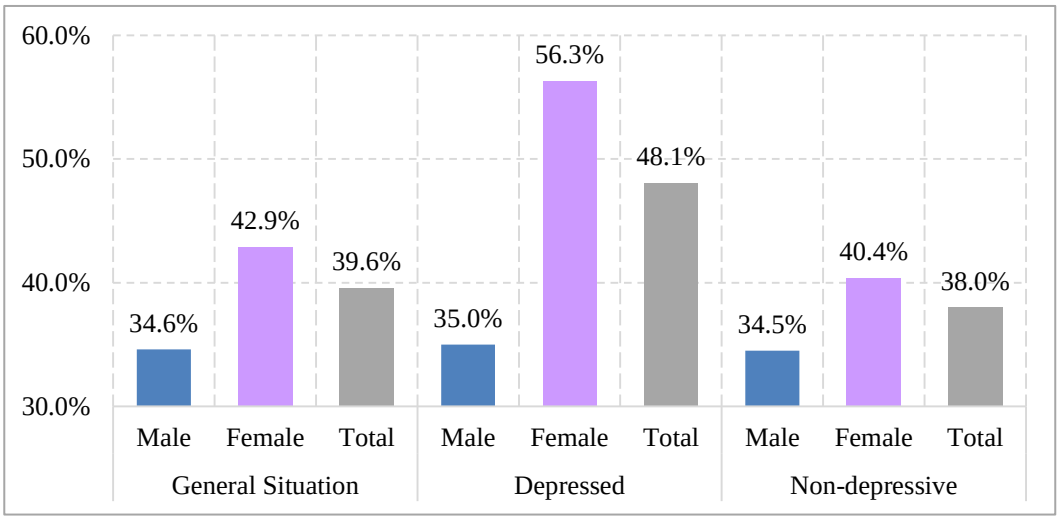

Figure 1. The rates of PBA prevalence

Item Levels

The item with the highest average among the CNS-LS scale items was "I find myself crying very easily" ($\bar{x}$=2.28). The item with the least average was "others have told me that I seem to become amused very easily or that I seem to become amused about things that aren't really funny", with $\bar{x}$=1.76. Accordingly, all items were at the "rarely agree" level (Table 4).

Table 4. CNS-LS scale item averages

Items	n		ss
• I find myself crying very easily	328	2.28	1.28
• There are times when I feel fine one minute, and then I'll become tearful the next over something small or for no reason at all	328	2.20	1.22
• There are times when I won't be thinking of anything happy or funny at all, but then I'll suddenly be overcome by funny or happy thoughts	328	2.11	1.15
• I find that even when I try to control my crying I am often unable to do so	328	1.97	1.17
• I find that even when I try to control my laughter I am often unable to do so	328	1.85	1.20
• I find that I am easily overcome by laughter	328	1.83	1.10
• Others have told me that I seem to become amused very easily or that I seem to become amused about things that aren't really funny	328	1.76	1.08

Table 5. Pathological crying and laughing scores

Score	Min	Max.	±ss	t	df	p
Pathological crying	3	15	6.45±3.11	-4.199	638943	0.000
Pathological laugh	4	20	7.55±3.62			
Pathological crying in Male	3	15	7.45±3.27	-3.228	248457	0.001
Pathological laugh in Male	4	20	8.92±3.99			
Pathological crying in Female	3	15	5.79±2.81	-2.960	394	0.003
Pathological laugh in Female	4	16	6.67±3.06			

Pathological Crying and Laughing Scores

The mean total score describing pathological crying (items 1, 3, 6) was 6.45±3.11; and the mean total score describing pathological laughing (items 2, 4, 5 and 7) was 7.55±3.62. The difference between the mean scores was statistically significant (t = -4.199, p < 0.001). (Table 5).

The mean pathological crying score in men was 7.45±3.27; and the average score of laughing was 8.92±3.99 (t = -3.228; p = 0.001). On the other hand, in women, the mean pathological crying score was 5.79±2.81; and the average score of crying was 6.67±3.06. (t = -2.960, p = 0.003) (Table 5).

Discussion

PBA can be accompanied by many neurological disorders. Previous research shows that it can be seen in ALS, Alzheimer's disease, Parkinson's disease, especially healing stages of stroke and following traumatic brain injury [14,16]. The number of patients in the US is estimated to be around 2 million [18,19]. Several clinical trials have reported that PBA incidence in MS patients is 10- 42.6% [15]. Vidovic et al. found this rate to be 41.8%. The PRISM trial results showed that 46% of MS patients had PBA [14]. However, in our study, the frequency of PBA in the Turkish MS population was 39.6%. We hereby showed that PBA prevalence among MS patients in Turkey is higher than that in the US. The geographical locations of the countries in the world may be affecting this. Furthermore, the prevalence of PBA was 34.6% in men; 42.9% in females. However, there was no gender preference for PBA among MS patients.. The incidence of PBA was 48.10% in MS patients with depression and 38.0% in those without depression. The co-existence of depression was not associated with PBA frequency in our MS cohort.

Our study supports the existing literature on increased PBA in MS. Moreover, we demonstrate the higher PBA co-occurrence with depression, and its potential consequences. The disease may be confused with mood disorders such as depression and bipolar disorder. However, the differential diagnosis can be straightforward with improved scales. Thus, proper patient management could be achieved..

The PBA incidence in men with and without depression was 35% and 34.5%, respectively. On the other hand, the PBA prevalence in women with and without depression was 56.3% and 40.4%, respectively. The co-existence of depression did not affect PBA frequency in neither men nor women. However, it is noteworthy that PBA frequency in women with depression was significantly higher than men with depression, reaching up to 60%.

Although accompanying depression did not affect PBA frequency, it significantly increased test scores. The average PBA was 13.28 in non-depressed, 17.85 in others. The average PBA in women without depression was 13.37 and in women with depression was 18.91.. However, depression in men did not make a significant difference. For men without depression, the mean score was 13.14, for men with depression was 16.15. Furthermore, both laughing and crying scores were higher in men.

Amongst the drugs that have been tried for PBA treatment, dextromethorphan or quinidine has been the first drug to be approved by the FDA in 2008, with limited previous clinical data. No study has shown antidepressant drug effectiveness [20-23].

We evaluated the PBA frequency and depression among MS patients. But we did not gather information about patients' ongoing medical treatment including antidepressants or sedatives., We were unable to demonstrate an association between clinical parameters and underlying psychiatric disease or localization of demyelinated plaques. This may have been a confounding factor. .

Further studies investigating the clinical and radiological associations in MS patients with PBA would highlight the mechanisms of PBA pathology.

Conclusion

In conclusion, our study revealed the increased frequency of PBA in MS patients. PBA can cause anxiety and social inhibition which can effect patients' quality of life. Recognizing this challenging disorder may help clinicians improve patients' social functions.

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Ethical issues: All Authors declare originality and ethical approval of research. Responsibilities of research, responsibilities against local ethics commission are under the Authors responsibilities. The study was conducted under defined rules by the Local Ethics Commission guidelines and audits.

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