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Clinical characteristics and socio-demographic features of psychotic major depression

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Abstract

Background

Psychotic major depression (PMD) is a special subtype of depression with a worse prognosis. Previous studies failed to find many differences among patients with PMD versus those with non-psychotic major depression (NMD) or schizophrenia(SZ). This study compared psychotic major depression with non-psychotic major depression and schizophrenia based on sociodemographic factors (including season of conception) and clinical characteristics. We aimed to provide data to inform clinical diagnoses and etiology research.

Methods

This case–control study used data for patients admitted to Shandong Mental Health Center from June 1, 2016 to December 31, 2017. We analyzed cases that had experienced a PMD episode (International Classification of Diseases, Tenth Revision codes F32.3, F33.3), NMD (F32.0–2/9, F33.0–2/9), and SZ (F20–20.9). Data were collected on sex, main discharge diagnosis, birth date, ethnicity, family history of psychiatric diagnoses, marital status, age at first onset, educational attainment, allergy history, and existence of trigger events.

Results

Patients with depression with a primary school/below education (odds ratio [OR] 0.397, CI: 0.18–0.874) and without a family history (OR 0.557, CI: 0.332–0.937) were less likely to have psychotic symptoms than other patients. Compared with patients with PMD, a primary school/below education (OR 3.646, CI: 1.65–8.053), no allergy history (OR 2.2, CI: 1.152–4.2), trigger events experienced before first onset (OR 2.428, CI: 1.528–3.859), being unmarried (OR 0.3, CI: 0.104–0.871), and an earlier age at first onset (OR 0.931, CI: 0.911–0.952) were features of SZ.

Conclusion

PMD and NMD are similar in terms of patients' demographic variables and clinical characteristics, whereas there are differences between PMD and SZ. The significant factors we identified may point to underlying heterogeneity of these diseases.

Background

Psychotic major depression (PMD) is a serious illness where patients suffer from a combination of depressed mood and psychosis. PMD accounts for about 14.7–18.5% of patients with major depressive disorder [1, 2]. In most guidelines, PMD remains a subtype of major depressive disorder [3]. However,

compared with major depression without psychotic symptoms, PMD is associated with longer duration of illness [4], greater morbidity and mortality [5], less response to antidepressants and psychotherapy [3, 6], a higher rate of current suicide risk [6], and more comorbid anxiety disorders [7], cognitive dysfunction [8], somatic disorders, and personality disorders [9, 10].

Psychotic symptoms are likely to be a risk factor for conversion from unipolar depression to bipolar disorder [11, 12] and schizophrenia (SZ) [13]. A longitudinal study showed that within 2 years of their first-hospitalization, 41% of patients initially diagnosed with PMD met the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria for bipolar or schizoaffective disorders [14]. Psychiatric comorbidity has also been reported to be common in PMD [15]. In addition, depression is common in different stages of SZ and may interplay in SZ progression, which has raised questions about the validity of a PMD diagnosis [16, 17]. Therefore, further work on the differential etiology of PMD from other psychoses is needed [18].

Few studies have been conducted to clarify the risk factors for PMD, especially early life risk factors [19]. In general, previous studies failed to find many demographic differences among patients with PMD versus those with non-psychotic major depression (NMD) [20]. However, there were some exceptions, with the main finding being that a family history [19, 21] of psychosis increased the risk for PMD. Other findings included that patients with PMD were less likely to be Caucasian [4, 14] and have lower educational attainment [4, 19] compared with those with NMD. One study observed more years of education in those with PMD compared with NMD [22]. In terms of early childhood and adolescent risk factors, patients with PMD were significantly more likely to report histories of physical or sexual abuse [24] and have lower sports grade in school [21] compared with patients with NMD.

Studies comparing PMD and SZ found a higher proportion of females in the PMD group than in the SZ group [19, 23]. Most studies that compared the mean onset age of PMD and SZ reported SZ had an earlier onset age [19, 23]. In one study, patients with PMD were less often single compared with those with SZ [25]. A number of psychosocial risk factors have also been associated with a follow-up diagnosis of PMD and SZ, including living alone, having a basic-level qualification, being unemployed, having less than monthly contact with friends, having no close confidants, and having experienced childhood adversity [18].

In traditional Chinese medicine, the annual rhythm of the dominant seasons is believed to be an important force that maintains the stability of our living environment, with the structure and function of the human body adapting to this rhythm and changing regularly. Seasonal factors can potentially exert an influence before birth. Accumulating evidence suggests that environmental factors pertaining to early life are associated with alterations in gene expression regulated by epigenetic factors. These factors include placental dysfunction [26], maternal malnutrition during pregnancy [27], psychological distress during pregnancy [26], and infections during the gestational and postnatal periods [28, 29]. Therefore, it is possible that these factors also affect susceptibility to neuropsychiatric diseases in later life [26].

Previous studies have investigated potential associations between season of birth and major depression [30, 31]. However, few studies have investigated associations between season of birth/conception and psychotic features in patients with major depression. In the present study, inpatients with PMD were compared with those with NMD and SZ using measures of sociodemographic factors (including season of conception) and clinical characteristics. We examined the relative importance of various clinical features of PMD to identify characteristics reliably associated with this diagnosis.

Methods

Setting

This paper was based on data from patients admitted to Shandong Mental Health Center from June 1, 2016 to December 31, 2017. The database from which our data were acquired contained patients' admission number, age, sex, admission year, main discharge diagnosis, birth date, ethnicity, family history of psychiatric diagnoses, marital status, age at first onset, educational attainment, allergy history, and existence of trigger events.

Sample

Cases that had experienced an episode of PMD (International Classification of Diseases, Tenth Revision codes F32.3, F33.3), NMD (F32.0–2/9, F33.0–2/9), and SZ (F20–20.9) were included in our analysis. In total, 242 multiple admissions for the same patient were deleted from the included cases. Twenty cases with evidence of psychotic symptoms precipitated by an organic cause or developmental retardation were excluded. Patients who were not born in Shandong province were also excluded (78 patients with SZ, 27 patients with NMD, and five with PMD). This left, 98 patients with (PMD), 351 with NMD, and 967 with SZ for inclusion in our analysis.

Clinical characteristics

Family history of psychiatric diagnoses was defined as at least one family member with a mental disorder within the patient's first-, second-, and third-degree relatives. Age at onset was defined as the patient's age at the first episode of the disorder. Impactful negative life events within 1 year before the first diagnosis with the disorder were defined as trigger events. A positive allergy history was defined as having been allergic to something.

Sociodemographic factors

Marital status was determined according to the patient's situation at the time of treatment. For example, if a patient had been divorced but had remarried at the time of the medical record, they were classified as "married." Educational attainment was divided into four categories: primary school or below, junior high school or vocational school, senior high school or junior college, and university and above. Patients' ethnicity was classified as Chinese Han population and ethnic minorities.

The date of conception was calculated according to patients' date of birth. The expected delivery date is 280 days from the first day of the last menstrual period of a pregnant woman. We assumed that fertilization occurred during ovulation (i.e., the 14th day of the last menstrual period), meaning the date of birth minus 266 days would be the date of conception. The season of conception was classified according to the month of conception (spring: Feb–Apr, summer: May–Aug, autumn: Sep–Oct, winter: Nov–Jan). All factors were self-reported or reported by family members accompanying the patient.

Statistical analyses

Differences in missing data between diagnostic groups were compared using Fisher's exact test. The sociodemographic variables and clinical characteristics of the diagnostic groups (PMD vs. NMD and PMD vs. SZ) were compared using independent samples Mann-Whitney U tests or Pearson's chi-square tests. Variables with a P-value less than 0.15, family history of a psychiatric diagnosis, and season of conception were incorporated into the generalized linear model (GLM). Odds ratios (OR) were calculated using GLMs with binomial distribution and logit link. Cases with missing data were automatically dropped from each analysis by SPSS version 22. The findings were considered statistically significant when the two-tailed analysis resulted in a P-value <0.05. Categories of variables were transformed into serial numbers, including sex (1=male,2=female), marital status (1=umarried,2=married, 3=widowed,4=divorced), family and allergy history(1=yes,0=no),season of conception(1=spring, 2=summer,3=autumn,4=winter), educational attainment(1= Primary school or below,2= Junior high school or vocational school,3= Senior high school or junior college,4= University and above), ethnicity (1=Han,2=minority).

Results

Missing data (Table 1)

Table 1 shows the comparison of missing data between the PMD, SZ, and NMD groups. There were no statistically significant differences between the diagnostic groups in terms of missing data.

stribution of missing data

gnose	NMD	PMD	SZ	X^2	P
	0/351	0/98	0/967		
	3/351	2/98	14/967	1.296	0.493
tus	7/351	0/98	8/967	3.496	0.174
tory	0/351	0/98	0/967		
ents	2/351	0/98	1/967	2.724	0.335
l attainment	14/351	0/98	41/967	5.080	0.080
et	2/349	0/98	21/967	5.148	0.058
conception	0/351	0/98	0/967		

Distribution of sociodemographic factors and clinical characteristics (Table 2)

Patients with PMD were better educated compared with those with NMD and SZ (Mantel-Haenszel chi-square test χ^2=11.631, P<0.001 for NMD; χ^2=40.888, P<0.001 for SZ). Patients in the SZ group were significantly younger (Mann-Whitney U=31244.50, P<0.001) than those with PMD at the first psychotic episode, whereas no statistically significant differences were observed between the PMD and NMD groups (Mann-Whitney U=15969.5, P=0.317). The percentage of unmarried patients in the PMD group was significantly lower than that in the SZ group (χ^2=16.253, Fisher's exact test P<0.001), but comparable with the NMD group (χ^2=2.118, Fisher's exact test P=0.555). There were fewer patients with an allergy history in the SZ group (χ^2=7.545, P=0.006) compared with the PMD group. There were no statistically significant differences in allergy history between the PMD and NMD groups (χ^2=2.463, P=0.155).

We found that more patients with PMD had trigger events within 1 year before the first episode of psychosis (χ^2=14.939, P<0.001) compared with the SZ group, but there were no differences between the PMD and NMD groups (χ^2=0.734, P=0.379). Compared with the NMD group, those with PMD were significantly more likely to have a relative/relatives with a psychiatric diagnosis (χ^2=4.567, P=0.033), but this finding was comparable between the PMD and SZ groups (χ^2=0.833, P=0.362). There were fewer patients with autumn conception in the PMD group (16.3%, n=6) than in the NMD (24.6%, n=86) and SZ (21.6%, n=209) groups. However, these differences were not statistically significant. In addition, there were no significant differences between the groups in sex and ethnicity, although there were more female patients in the PMD group than in the SZ group (χ^2=2.556, P=0.11).

Table 2 Distribution of social-demographic factors and clinical characteristics

x	Family history		Marital status #			
Woman	No	Yes	Unmarried	Married	Widowed	Divorced
198(56.4%)	274(78.7%)*	74(21.3%)	93(27%)	222(64.5%)	13(3.8%)	16(4.7%)
54(55.1%)	67(68.4%)	31(31.6%)	33(33.7%)	58(59.2%)	2(2.0%)	5(5.1%)
451(46.6%)	695(72.7%)	261(27.3%)	474(49.4%) *	368(38.4%)	17(1.8%)	100(10.4%)

history	Trigger events		Educational attainment			
YES	NO	YES	Primary school or below	Junior high orvocational school	Senior high or junior college	University and above
37(10.5%)	161(46.1%)	188(53.9%)	136(40.4%)*	93(27.6%)	66(19.6%)	42(12.5%)
16(16.3%)	50(51.0%)	48(49.0%)	18(18.4%)	32(32.7%)	34(34.7%)	14(14.3%)
78(8.1%)	677(70.1%)*	289(29.9%)	458(49.5%)*	236(25.5%)	144(15.6%)	88(9.5%)

Ethnicty #		Season of conception			
Han	Minority	Spring	Summer	Autumn	Winter
341(98%)	7(2%)	84(24.0%)	90(25.7%)	86(24.6%)	90(25.7%)
94(97.9%)	2(2.1%)	27(27.6%)	25(25.5%)	16(16.3%)	30(30.6%)
932(97.8%)	21(2.2%)	241(24.9%)	278(28.7%)	209(21.6%)	239(24.1%)

ınge, PMD psychotic major depression, NMD none psychotic major depression, SZ schizophrenia.
d with PMD patients. # Fisher's exact test.

Model for relative utility of clinical and demographic variables between groups

In the GLM comparing PMD with NMD, we included variables with a P-value <0.15 and season of conception. As shown in **Table 3**, fewer patients with PMD had a primary school or below education compared with the NMD group (P=0.022, OR 0.397, 95% confidence interval [CI]: 0.18–0.874). Not having a family history of a psychiatric diagnosis was a protective factor for PMD (P=0.027, OR 0.557, 95% CI: 0.332–0.937). Season of conception showed no statistically significant difference between the groups.

Table 3 Model for relative utility of variables between PMD and NMD

		B	Std.Error	95% Wald C.I.		Hypothesis Test			Exp (B)	95% Wald C.I. for Exp(B)	
:r				lower	upper	Wald X2	df	Sig.		lower	upper
t		-0.454	0.416	-1.269	0.362	1.189	1	0.275	0.635	0.281	1.436
:eption	Spring	-0.082	0.3187	-0.707	0.543	0.066	1	0.797	0.921	0.493	1.72
	Summer	-0.158	0.322	-0.789	0.473	0.24	1	0.624	0.854	0.454	1.605
	Autumn	-0.602	0.3559	-1.299	0.096	2.86	1	0.091	0.548	0.273	1.1
	Winter	0[a]							1		
ainment	Primary school or below	-0.923	0.4027	-1.713	-0.134	5.259	1	0.022	0.397	0.18	0.874
	Junior high orvocational school	0.024	0.3768	-0.715	0.762	0.004	1	0.949	1.024	0.489	2.143
	Senior high or junior college	0.385	0.3807	-0.361	1.132	1.024	1	0.312	1.47	0.697	3.101
	University and above	0[a]							1		
ory	No	-0.584	0.2651	-1.104	-0.065	4.861	1	0.027	0.557	0.332	0.937
	Yes	0[a]							1		

able: Diagnose(PMD VS NMD)
pt), educational attainment, family history, season of conception.

A GLM was conducted to examine the relative utility of various clinical and demographic variables in differentiating patients with PMD versus SZ. Demographic and clinical variables that had a P-value <0.15, family history of a psychiatric diagnosis, and season of conception were tested. This included sex (male, female), marital status (unmarried, married, widowed, divorced), family and allergy histories (yes, no), season of conception (spring, summer, autumn, winter), and educational attainment (primary school or below, junior high school or vocational school, senior high school or college, university or above).

Results from the model are presented in **Table 4**. Educational attainment, existence of trigger events, age at first onset, and allergy history significantly differentiated the diagnostic groups when other variables were controlled in the model (P<0.01). Patients with a primary school or below education and that were unmarried (P<0.05) were less likely to have PMD compared with SZ. Patients with PMD were more likely to have trigger events, be allergic to something, and be older at the age at first onset compared with those with SZ.

Table 4 Model for relative utility of clinical and demographic variables between SZ and PMD

		B	Std.Error	95% Wald C. I.		Hypothesis Test			Exp (B)	95% Wald C.I. for Exp(B)	
				lower	upper	Wald X^2	df	Sig.		lower	upper
		3.507	0.8186	1.903	5.112	18.355	1	0	33.355	6.704	165.955
nt	Primary school or below	1.294	0.4044	0.501	2.086	10.234	1	<0.01	3.646	1.65	8.053
	Junior high or vocational school	-0.171	0.377	-0.91	0.568	0.206	1	0.65	0.843	0.403	1.764
	Senior high or junior college	-0.523	0.3779	-1.264	0.218	1.916	1	0.166	0.593	0.283	1.243
	University and above	0[a]							1		
	No	0.789	0.3299	0.142	1.435	5.711	1	0.017	2.2	1.152	4.2
	Yes	0[a]							1		
	No	0.887	0.2363	0.424	1.35	14.088	1	<0.01	2.428	1.528	3.859
	Yes	0[a]							1		
	Unmarried	-1.203	0.543	-2.267	-0.139	4.907	1	0.027	0.3	0.104	0.871
	Married	-0.995	0.5244	-2.022	0.033	3.598	1	0.058	0.37	0.132	1.034
	Widowed	-0.024	0.9812	-1.947	1.899	0.001	1	0.981	0.976	0.143	6.681
	Divorced	0[a]							1		
	No	0.434	0.2561	-0.068	0.935	2.865	1	0.091	1.543	0.934	2.548
	Yes	0[a]							1		
		-0.071	0.0113	-0.093	-0.049	39.891	1	<0.01	0.931	0.911	0.952
	Male	-0.039	0.2494	-0.527	0.45	0.024	1	0.877	0.962	0.59	1.568
	Female	0[a]							1		
n	Spring	0.055	0.3131	-0.558	0.669	0.031	1	0.86	1.057	0.572	1.952
	Summer	0.102	0.3175	-0.52	0.724	0.103	1	0.748	1.108	0.594	2.063
	Autumn	0.417	0.3584	-0.286	1.119	1.352	1	0.245	1.517	0.751	3.062
	Winter	0[a]							1		

iagnose(SZ vs PMD)

cational attainment, allergic history, trigger events, marital status, family history, age of first onset, sex, season of

Discussion

Although season of conception was not a factor that differentiated PMD from NMD and SZ in the present study, we did observe interesting findings. Patients with PMD appeared to be better educated than those with SZ and NMD, which was partly inconsistent with previous studies that reported no significant difference (or the opposite) in education between NMD and PMD [4, 19, 32]. A reason for this could be that previous studies mainly considered college degree versus no college degree [4, 32], whereas we divided educational attainment into four groups; only patients with primary school and below education showed a statistically significant difference between groups.

The findings reported in this paper highlighted that people with PMD were more likely to have a family history of a psychiatric diagnosis compared with people with NMD, which was consistent with previous studies [20]. Similar to other studies [19], we found no differences in family history between PMD and SZ. Our findings concerning onset age in PMD versus SZ were consistent with earlier studies [19, 23]. Previous studies comparing the onset age of PMD with NMD were not explicit. In some studies, patients

with PMD had an earlier onset age [22], whereas in others, the onset age showed no statistically significant differences [33]. In our study, patients with PMD were younger than those with NMD patients at the first episode of the disorder, but this difference was not statistically significant.

Despite differences in onset age and marital status [25] that were previously reported in other studies, we found no statistically significant sex differences between the PMD and SZ groups, although there were more female patients in the PMD group (55.1%) than in the SZ group (46.6%). However, differences in the sample size may explain the discrepancies between the studies [19, 23].

The analysis of differences between Chinese ethnic minorities and Han population received little attention in past epidemiological research that compared PMD with NMD and SZ. Our finding of no statistically significant differences in ethnicity was not surprising as there were few patients recorded as ethnic minorities. A previous study found that experiencing a major life event in the year before illness onset had a substantial effect size, but did not meet statistical significance compared PMD (P = 0.058) and SZ (P = 0.056) to a population-based sample of controls without a history of psychosis [18]. In the present study, more patients with PMD reported impactful negative life events within 1 year before the first onset of the mental disorder compared with those with SZ, indicating a difference in pathological mechanisms between the two disorders. However, it is important to note that patients with SZ may be more likely to have underreported trigger events because the nature of their disease.

To our knowledge, this is the first study that included allergy history in the analysis. Surprisingly, we found statistically significant differences when comparing SZ with PMD. This result requires further verification, but may offer some enlightenment for pathological studies focused on PMD.

Limitations

The classification of some influencing factors in this study was a little unclear. For example, family history could have been divided more specifically according to parents or other relatives and different kinds of psychiatric diseases. The presence of trigger events was mainly determined by patients, and was not assessed and defined using evaluation tools such as the Life Events and Difficulties Schedule. Another limitation was that we failed to investigate the potential role of comorbid disorders, which probably resulted in bias.

Conclusion

Our results suggest that patients with PMD are similar to those with NMD in terms of demographic variables and clinical characteristics, although they are more likely to have a family history of a psychiatric diagnosis in their first-, second-, and third-degree relatives and to have obtained a primary school degree. The small number of significant factors may point to underlying heterogeneity. There were more differences between patients with PMD and those with SZ, with the difference in allergy history suggesting a direction for further research. In general, major depression is a highly heterogeneous

disorder [34]. It is known that there are clinical differences between PMD that has its onset in early adulthood and PMD in old age [19, 35]. Therefore, further refinements in screening and treatment are needed for this clinical population.

Abbreviations

Psychotic major depression (PMD); Non-psychotic major depression (NMD); Schizophrenia (SZ); Generalized linear model (GLM); Odds ratios (OR).

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the tenets of the Declaration of Helsinki and was approved by the ethical committee of the National Natural Science Foundation of China. The research did not directly involve any human body. Patient data were extracted from monthly reports maintained by Shandong Mental Health Center. All individual-level data were anonymous.

Consent for publication

This manuscript is approved by all authors for publication.

Availability of data and materials

Research data has been uploaded with the paper in supplementary file “data.xlsx” and can be requested from doramaia@sina.com.

Competing Interests

The authors have declared that no competing interests exist.

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Author Contributions

MW: Methodology, Formal analysis, Writing-Original Draft, Visualization

RW: Investigation, Writing - Review & Editing

YH: Writing - Review & Editing

WX: Investigation

JH: Conceptualization, Supervision, Funding acquisition, Project administration, Validation

DQ: Supervision, Resources, Data Curation, Validation

All authors have read and approved the manuscript.

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