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Sociodemographic, Clinical And Evolutionary Profile Of Bipolar Disorder With Or Without Psychotic Characteristics: About 144 Patients.

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Abstract:
Background*: Literature studies reveal that approximately half of the patients with bipolar disorder (BD) have experienced at least one episode with psychotic symptoms (PS), particularly during the manic phase. The presence of these symptoms has been associated with greater severity of the illness in terms of suicide attempts, frequent relapses, longer hospitalizations, and functional impairment between mood episodes. In addition to these findings, some studies have noted that a significant number of bipolar patients with psychotic symptoms are often misdiagnosed with other severe mental disorders, leading to delays in diagnostic and mood-stabilizing treatment. Objective: To determine the Sociodemographic, clinical, and therapeutic profile of BD with or without psychotic characteristics in the population of Algiers.*
Materials and Methods*: We conducted a descriptive cross-sectional study on 144 bipolar patients, selected according to the diagnostic criteria of BD in the DSM-5, over a period of 24 months, from January 2021 to December 2022. Sociodemographic, clinical, evolutionary, and therapeutic characteristics were collected using a structured questionnaire. Clinical assessment was performed using the Young Mania Rating Scale, Hamilton Depression Rating Scale, and Positive and Negative Syndrome Scale (PANSS) for psychotic symptoms.*
Results*: The mean age of our patients was 41.3±13 years. The majority of them were men, and over half were unmarried. The average age of onset of the illness was 22.7±4.8 years, with a mean duration of 16.5±11.5 years. The majority had an average of 4.6±4.3 hospitalizations. The mean diagnostic delay was 4.3±4.8 years. The average time between the first mood episode and initiation of mood stabilizer treatment was 3.6±4.5 years. There was an overrepresentation of bipolar disorder type I (92.4%). The mean number of psychotic episodes was 2.7±2.2. The dominant polarity was manic (83.3%). 77.1% had delusions with predominant themes of persecution and grandiosity. 29.9% had predominant auditory-verbal hallucinations. There was a significant relationship between psychotic symptoms and childhood trauma (p=0.007), prior diagnosis of schizophrenia and/or schizoaffective disorder (p=0.000), as well as a family history of mental illness (p=0.002), age at first episode (p=0.0001), delay in initiating mood stabilizer treatment (p=0.043), and comorbid addictive disorders (p=0.018). However, these symptoms showed no significant relationship with the mean diagnostic delay (p=0.224), number of hospitalizations (p=0.115), and intervals between hospitalizations (p=0.151).*
Conclusion*: Our data confirm a high incidence of psychotic symptoms among patients with bipolar disorders. These symptoms lead to diagnostic uncertainty and delays in early intervention. Early diagnosis and initiation of mood stabilizers can improve long-term outcomes. Keywords: Bipolar disorder, psychotic symptoms, diagnostic error, diagnostic delay.*

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I. Introduction

Psychotic disorders, particularly delusions and hallucinations, are common features of various psychiatric disorders, including schizophrenia and bipolar disorder (BD) [1-2]. In fact, literature studies have reported that nearly half of bipolar patients have experienced at least one episode with psychotic symptoms, congruent or incongruent with mood, during the course of their illness [3-5]. Among psychotic symptoms, delusions have been found to be more frequent than hallucinations (12-96% vs. 8-66%) [5]. Other studies have highlighted the higher frequency of psychotic

features in manic episodes (33-96%) compared to depressive episodes (9-66%) [3, 5-7]. Besides these results, some studies have mentioned that the psychotic symptoms accompanying mixed episodes are more common than in depressions and approach those of mania (about 40%) [5]. However, the results of some studies that have been conducted to assess the different clinical aspects of BD with psychotic features are inconclusive. From a clinical perspective, the presence of these symptoms has been associated with greater illness severity in terms of suicide attempts, frequent relapses, longer hospitalizations, and functional impairment between mood episodes [5-8]. It should also be pointed out that the results of studies carried out to assess the different clinical aspects of BD with or without psychotic features are contradictory [3, 7, 9]. Furthermore, a significant number of bipolar patients with psychotic characteristics are often misdiagnosed with other mental disorders such as schizophrenia or other psychotic disorders, leading to diagnostic uncertainty and delays in initiating mood stabilizers [10]. Based on the aforementioned findings, this study aimed to determine the socio-demographic, clinical, and evolutionary profile of bipolar patients with or without psychotic characteristics in the population of Algiers.

II. Material And Methods

We conducted a prospective cross-sectional descriptive study involving 144 hospitalized bipolar patients at the DRID Hocine Psychiatric Hospital in Kouba-Algiers, Algeria. The inclusion criteria were based on the diagnostic criteria for bipolar disorder outlined in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) [11]. The study was conducted over a period of 24 months, from January 2021 to December 2022. Patients were required to be 18 years old. Patients diagnosed with schizophrenia, schizoaffective disorder, schizophreniform disorder, and recurrent depressive disorders were excluded from the study. Prior to their participation, patients were informed about the purpose of the study, the importance of anonymity, and the confidentiality of their data; in order to obtain their free and informed consent to participate in the study.

Data Collection and Measurement Instruments:

Sociodemographic data: Age, gender, marital status, level of education, occupation, family history of mental illness, personal history of suicide attempts and childhood trauma, comorbidities (anxiety disorders, personality disorders, and addictions).

Instruments used for data collection may include standardized questionnaires or interviews specifically designed to gather information on these variables.

Clinical and Evolutionary Data: Age at first episode, current mood episode, dominant polarity (calculated according to the proposal of Barcelona, defined as at least two-thirds of the total number of past episodes being of the same polarity: Colom et al., 2015) [12], duration of illness, length of hospitalization, interval between hospitalizations, and number of mood episodes with psychotic symptoms. We also examined the duration of diagnostic delay (which in our study corresponds to the period of untreated symptoms between the onset of the illness and the confirmed diagnosis of bipolar disorder), the duration of delay in initiating mood stabilizer treatment, the first diagnoses assigned to patients before the diagnosis of TB and past and current therapy.

Concerning the evaluation of the clinical severity, we opted for three scales: the Young Mania scale [13], the Hamilton depression scale [14] and the positive sub-score scale of PANSS [15] for psychotic symptoms. This latter scale was originally designed to assess symptoms in patients with schizophrenia (Kay and al, 1987), but currently it is frequently used to assess psychotic symptoms in patients with other disorders, including TB (Vieta and al. 2004) [16].

Statistical Analysis

All data were collected by using the predefined questionnaire and were entered into SPSS software, version 22. Qualitative variables were expressed as percentages or frequencies, while quantitative variables were presented as means, standard deviations, and ranges. The Pearson chi-square test was used to compare qualitative variables, and the Student's t-test was used for comparing quantitative variables between groups. The significance level was set at 5% ($p \leq 0.05$).

III. Result

Prevalence

The study sample consisted of 144 patients. One hundred and thirteen patients (78.5%) experienced more thymic episodes with psychotic characteristics. The average number of psychotic episodes was 2.7 ± 2.2 episodes, with a maximum of nine episodes. Nearly half of these psychotic symptoms were mood-congruent (n=70; 48.6%). These symptoms were more frequent in bipolar disorder type I than in type II. They were significantly present during manic episodes. One hundred and eleven (77.1%) patients had delusional ideas, with a predominance of

grandiose and persecutory themes in 56.2% of cases (n=81). Forty-three patients (29.9%) experienced hallucinations, primarily auditory-verbal hallucinations.

Sociodemographic Characteristics and Family and Personal History

The average age of the patients was 41.3 ± 13 years, with a minimum of 18 years and a maximum of 77 years. The majority were males (sex ratio = 1.5). More than half were unmarried (n=81; 56.3%), and 68.1% (n=98) had an educational level ranging from secondary school to university. 40.3% (n=58) were unemployed. A history of psychiatric family history was found in 57.9% (n=82) of cases, with 22.2% (n=32) having a diagnosis of schizophrenia, 25.7% (n=37) with bipolar disorder, and 0.7% (n=1) having both diagnoses. 40.3% (n=58) of cases had a history of childhood trauma, which showed a statistically significant relationship with psychotic symptoms (p=0.007) (Figure n 1).

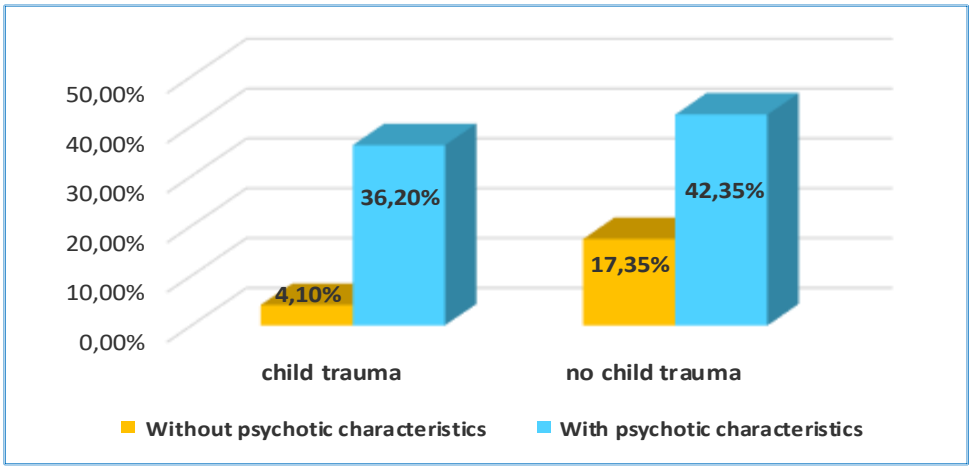

Figure 1: Distribution of 144 bipolar patients with or without psychotic characteristics by history of childhood trauma

39.6% (n=57) of cases had made at least one suicide attempt in their history. Psychiatric comorbidities were observed in 88% (n=90) of cases, with a rate of 9% (n=13) for anxiety disorders, 31.9% (n=16) for personality disorders (with a predominance of histrionic personality), and 47.9% (n=69) of cases had a substance use disorder (psychoactive substances, alcohol, and cannabis). Concurrent alcohol and substance use disorders were significantly associated with psychotic symptoms (p=0.018).

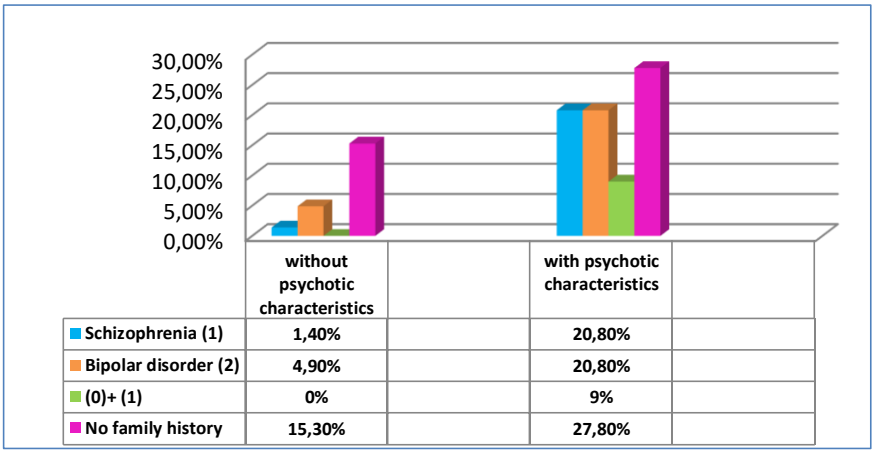

Figure 2: Distribution of 144 bipolar patients by family history of mental illness

Our results also revealed a significant relationship between psychotic symptoms and family history of mental illness (p=0.002) (Figure n 2). However, these symptoms showed no correlation with gender and had no influence on suicidal behavior (p=0.473).

Clinical and evolutionary characteristics

The mean age at first episode was 22.7±4.8 years, with the most representative age groups between 18 and 27 years. The mean duration of the disorders was 16.1±11.2 years. In our series, there were significantly more type I than type II bipolar patients (92.4% vs. 7.6%, p=0.000). The majority of thymic episodes were manic. The dominant polarity was manic in 120 patients (83.3%). The mean number of hospitalizations was 4.6 ± 4.3, with a minimum of one and a maximum of 25. The mean interval between hospitalizations was 2.8 ± 1.5 years. Almost half of the patients (n=49.3) were initially diagnosed with something other than bipolar disorder, including schizophrenia (n=37; 25.7%), schizoaffective disorder (n=18; 12.5%) and 7.3% (n=14) with both diagnoses. The average delay in diagnosis was 4.3 ± 4.8 years, with a minimum of one year and a maximum of 32 years. The mean time from first thymic episode to initiation of thymoregulator was 3.6 ± 4.5 years. Inclusion assessment scales showed mean scores of moderate to severe severity for Young's mania (24.4±10.6), HDRS depression (13.4±8.2) and PANSS positive subscore (23.5±14.5).

Statistical analysis revealed that psychotic symptoms were significantly related to younger age of onset (p=0.0001), previous diagnosis of schizophrenia and/or schizoaffective disorder (p=0.000) (Figure n 3) and time to initiation of thymoregulatory therapy (p=0.043). On the other hand, these symptoms had no significant relationship with mean delay in diagnosis (p=0.224), number of hospitalizations (p=0.115), therapeutic intake (of antipsychotics, antidepressants and thymoregulators) and intervals between hospitalizations (p=0.151).

Finally, the majority of past prescriptions were combinations of first-generation antipsychotics (n=32; 22.2% - n= 31; 21.5%) or second-generation antipsychotics with an anticonvulsant. In terms of current therapeutic prescription, most patients were either on a 2nd-generation antipsychotic monotherapy (n=64; 44.4%), or a combination of a 2nd-generation antipsychotic and an anticonvulsant (n=43; 29, 9%).

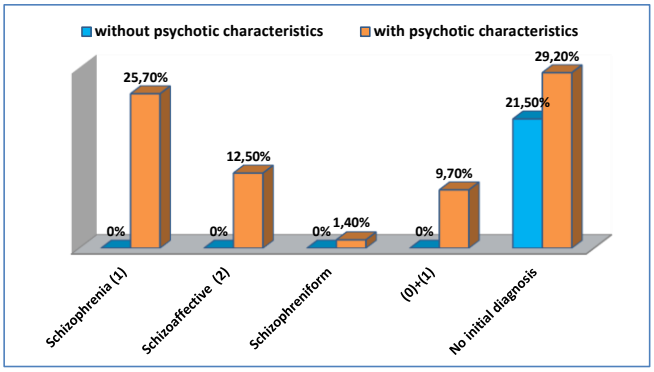

Figure 3: Distribution of 144 bipolar patients by previous diagnosis to bipolar disorder

IV. Discussion

The reported prevalence in this study regarding the psychotic symptomatology accompanying mood episodes was consistent with the literature [17-18]. The present study revealed a high prevalence of psychotic symptoms during mood episodes, particularly manic episodes. The analysis of sociodemographic, clinical, and evolutionary variables based on the presence or absence of psychotic symptoms revealed the following profiles:

Sociodemographic Profile, Family, and Personal History

The sociodemographic variables in our study were comparable to some literature studies involving bipolar patients enrolled in mood disorder research studies [10, 17], with a slight male predominance. However, the influence of the patient's gender on the presence or absence of psychotic symptoms is not unanimous. Our study did not find a significant relationship concerning gender, but the literature data remain divided on this point. Indeed, some authors, such as Annet et al. and Upthegrave et al. [1, 18], found that women were more likely to experience hallucinations compared to men. On the contrary, several other studies did not find a gender difference in the presence or absence of psychotic symptoms [3, 19], as in our study. Regarding occupation, education level, and marital status, our results did not show a significant relationship with psychotic symptomatology. Regarding family history, bipolar disorder (BD) is one of the psychiatric disorders with the highest level of familial heritability (ten times more common among first-degree relatives of bipolar patients than among the general population [17]. However, the results of some studies in the literature on the association between psychotic symptoms in BD and family history of mood disorders are contradictory. Some studies have shown that family members of bipolar patients without psychotic symptoms are more frequently affected by BD [3, 18] compared to family members of bipolar patients with psychotic features. Other studies have reported that the presence of psychotic disorders in BD is not associated with a family history of depression and BD [7]. Finally, the results of the study by Renda et al. [20] indicated that BD and depression are frequently encountered among family members of patients with BD with psychotic features or schizophrenia. Consistent with these findings, we observed in our study a history of first-degree family members with BD and schizophrenia in almost half of our patients. These findings are consistent with partially shared genetic factors between BD and schizophrenia [17, 21]. Furthermore, our study showed a correlation between the prevalence of family history of mental illness and the risk of developing psychotic symptoms, especially in the context of mania. Our results are in line with those of the Lebanese study by Nehme et al. in 2018 [22].

Regarding a history of suicidal behavior, some authors [7, 18, 23-24] have indicated that one of the risk factors for suicide attempts is the presence of hallucinations accompanying the mood episode, especially in women. Contrary to these studies, our results did not find a significant relationship between a history of suicide attempts and hallucinations, which is consistent with recent publications [25-27]. However, this hypothesis remains to be verified, as our sample had a sex ratio of 1.5.

The results also revealed that delusions and auditory-verbal hallucinations were considered the psychotic symptoms most correlated with a history of childhood trauma, especially child abuse and sexual assault in both sexes. Our findings are consistent with the results of several studies [3, 19, 28]. Indeed, a meta-analysis of 19 studies found a 2.63-fold risk (95% CI: 2.00-3.47) of developing a mood disorder in cases of early traumatic exposure outside of post-traumatic stress disorder [28]. Moreover, a large majority of authors have found more severe positive symptoms, particularly auditory hallucinations and delusions, in patients with a history of childhood abuse [27, 28], as observed in our study. Regarding the causal link between a traumatic history and the emergence of a mood disorder with psychotic features, some authors have hypothesized that specific gene-environment interactions may play a mediating role in this association [27, 28], which is shared with schizophrenia.

Clinical and Evolutionary Profile of Bipolar Disorder with or without Psychotic Features

Our study revealed an overrepresentation of bipolar disorder type I, significantly more frequent in the manic phase than the depressive phase. These findings are consistent with some studies in the literature [2, 7, 17]. Our results also confirm that nearly half of bipolar patients with psychotic symptomatology were mood-congruent. However, among psychotic symptoms, delusions (persecutory and grandiose) were more common than hallucinations, with frequencies of 77.1% vs 29.9%, respectively. These results are similar to findings from other studies demonstrating that a significant number of patients with bipolar disorder experience at least one psychotic symptom during a mood episode, particularly during manic episodes [3, 8]. For instance, a cross-sectional cohort study of 1342 type I bipolar patients by Annet et al. [1] observed a high frequency of psychotic symptoms, with delusions present in 68.9% and hallucinations in 42.6% of patients. Other studies [5, 23, 29] found a prevalence of over 50% of psychotic symptoms in their samples, with nearly half of bipolar patients exhibiting delusional activity, predominantly with themes of grandiosity and persecution.

It is also worth noting that several results have indicated that mood episodes with psychotic features tend to recur during the course of bipolar disorder [5, 10]. Which is in line with the present study, as the majority of bipolar patients experienced an average of two bipolar episodes with psychotic symptomatology and a maximum of nine episodes throughout the course of their illness. Other emerging results from this study include:

Several studies [7, 23, 28] have highlighted the link between early onset of the illness and psychotic symptoms, which is in line with the results of our study. However, the findings of some previous studies suggest that early onset

of bipolar disorder is not associated with the presence of psychotic symptoms during the course of the illness [30-31]. Currently, the young age of onset of bipolar disorder is a clinical marker of poor prognosis for the disorder. However, this clinical characteristic has not yet been clarified as a biological vulnerability factor in bipolar patients with psychotic symptoms [32].

On the other hand, bipolar patients with psychotic features were victims of misdiagnosis. This finding is shared by several research studies [33]. However, the first diagnosis before TB was different in each study [9, 36]. Our results were consistent, since the majority of bipolar patients with psychotic features were initially diagnosed with schizophrenia followed by schizoaffective disorder, or both. Indeed, recent data in the literature have shown that 40% of bipolar patients initially received a diagnosis other than bipolar disorder at varying rates [9, 37], with major depressive episode being the most common, followed by schizophrenia. In other studies, such as that by Altamura et al [33], schizophrenia was reported as the first diagnosis, followed by schizophreniform disorders. These results confirm that making a correct diagnosis of TB is not easy when psychotic symptoms are present. Indeed, TB with psychotic features can present clinically in several forms, where the clinician's attention is focused on psychotic symptoms rather than mood symptoms [3].

The results of some studies also suggest that the presence of such symptoms in bipolar patients leads to longer hospital stays and shorter intervals between episodes compared to bipolar patients without psychotic features [23, 31, 34]. In contrast to these studies, our results demonstrated that the number of hospitalizations and the intervals between hospitalizations did not have a significant relationship with the psychotic symptomatology accompanying mood episodes, which is in line with the results of the Italian study by Caldieraro et al. (2017) [7].

Furthermore, the average delay in diagnosing bipolar disorder has been reported in several studies. Some studies [35-38] found that the delay between the first mood episode and the diagnosis of bipolar disorder was at least five years. Other studies reported an even longer delay of around ten years on average [37, 38]. In our subjects, the diagnosis was delayed by an average of ten years if we take into account the standard deviation in nearly 40% of our patients, which is consistent with the results of the aforementioned studies. These differences in the duration of untreated illness may be due to a higher presence of psychotic symptoms, according to several other authors [1, 38], which can lead to diagnostic confusion. However, our results did not demonstrate a correlation between the delay in diagnosis and psychotic symptoms.

The results of this study also revealed an average delay in initiating mood stabilizer treatment of over six years. This delay is mainly due to diagnostic errors in the early stages of the illness. This finding aligns with some studies in the literature, notably the study by Azorin et al. [39], which reported a delay between the first mood episode and the initiation of the first mood stabilizer of nine years, which is consistent with our findings.

Finally, this study did not find any significant difference between psychotic symptoms and the prescription of pharmacological treatments (atypical antipsychotics and anticonvulsants), past or current. Given that atypical antipsychotics are often used as mood stabilizers, their prescription is high in bipolar patients with or without psychotic features, which is in line with the results of the Italian study by Dell'Osso et al. (2017) [2].

Limitations of the Study and Perspectives

The results of the present study should be considered preliminary. Prospective comparative studies between bipolar disorder with psychotic features and bipolar disorder without psychotic features will likely provide more precise results and are necessary to confirm the findings presented in this document.

Declaration of Interests

The authors declare no conflicts of interest related to this article.

V. Conclusion

Overall, the results of this study did not show any differences in the profile of bipolar disorder with or without psychotic features in terms of sociodemographic variables. However, some emerging findings regarding the clinical and evolutionary profile are worth noting. Psychotic symptoms seem to punctuate the course of the illness, particularly during the manic phase. Unfortunately, the presence of these symptoms often leads to misdiagnosis, resulting in delayed intervention at the early stages of the disease due to the lack of recognition by clinicians of these clinical presentations.

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