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Psychotic Disorders In Alzheimer's Disease And Related Disorders: About A Study

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Abstract:
Background*: Psychotic disorders are highly prevalent in Alzheimer's disease and related dementias. According to studies, delusions can be present in up to 73% of patients, and hallucinations in over 30%. The average prevalence of identification disorders can reach 25.6% in Alzheimer's dementia, ranging from 38% to 78.3% in Lewy body and Parkinsonian dementias. The existence of these disorders significantly contributes to the reduction of the patient's well-being and places a burden on caregivers. Moreover, these disorders are associated with a faster progression of the dementia syndrome. The main objective of our article is to describe the characteristics of psychotic disorders in patients with Alzheimer's disease and related dementias attending the Algerian memory and psychogeriatric consultation.*
Materials and Methods*: **Materials and Methods**: We conducted a descriptive study involving 73 adult patients diagnosed with Alzheimer's disease and related dementias, with or without psychotic features, attending the specialized memory and psychogeriatric consultation at the DRID Hocine University Hospital specialized in psychiatry in Kouba, Algiers, Algeria, over a 12-month period. Case validation was performed using the DSM-5 criteria. Psychotic symptomatology was assessed by using the positive subscale of the PANSS (Positive and Negative Syndrome Scale). Brain MRI was performed for all patients. Outcome criteria focused on the clinical characteristics of delusions, hallucinations, and identification disorders, as well as their evolution within the dementia syndrome.*
Results: *Among the 73 patients, 52% were male and 48% were female, with a sex ratio of 1.01. The average age was 68.5 years. All patients were living with family members, with at least one caregiver. Diagnoses included 53.4% Alzheimer's dementia (AD), 20.5% vascular dementia (VD), 17.8% mixed dementia (MD), 4.1% Parkinsonian dementia (PD), and 4.1% Lewy body dementia (LBD). Over half had moderate to severe brain atrophy (Scheltens grades 2 and 3). Clinically, 64.4% of patients experienced psychotic disorders (PD), with persecutory and theft themes predominating in thematic associations. Hallucinations were present in 54.8%, with a predominance of visual hallucinations (23.3%). Identification disorders were observed in 43.8%, including 32.8% with self-recognition and false recognitions, and 2.7% with the Frigoli syndrome. These disorders appeared more frequently in the chronic phase for the majority of dementia clinical forms (59%), except for LBD, which occurred in the early phase of the disease. The recurrence duration of PD was mostly between 3 to 6 months for all dementia types, except for LBD, which had a chronic course (6.8%). Therapeutic management was based on combination therapy in the majority of cases, involving an anticholinesterase and an antipsychotic, notably risperidone.*
Conclusion*: Overall, our results align with the existing literature regarding the clinical and evolutionary characteristics of psychotic disorders in patients with Alzheimer's disease and related dementias. It is noteworthy that our study did not find a significant relationship between psychotic disorders and psycho-behavioral disturbances.*

Keywords: *Dementia, Delusion, Hallucination, Identification Disorders, Antipsychotic*

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I. Introduction

Established dementia pathologies are referred to as major neurocognitive disorders in the DSM-5, defined as acquired cognitive decline in one or more cognitive domains resulting in functional impairment in daily activities [1].

The prevalence of psychotic symptoms reaches one-third of Alzheimer's-type dementias and up to 50% of Lewy body dementias [2]. Indeed, in dementia cases, the prevalence of delusions ranges from 10 to 73% (Fischer et al., 2018) [3], and over 30% for hallucinations. It is noteworthy that visual hallucinations are more common (4-59%) than auditory hallucinations (1-29%). Other delusional syndromes, quite typically, can be found, such as identification disorders, with an average prevalence of up to 25.6% in Alzheimer's dementia [4-6]

and ranging from 38 to 78.3% in Lewy body and Parkinsonian dementias [3,7]. The evolution of these psychotic symptoms is characterized by relapse and chronicity [4,8] in 95% of cases.

According to hypotheses from certain literature studies, psychotic disorders are complex symptoms likely stemming from neurobiological changes in specific brain regions, associated with genetic predispositions and interactions with the environment [9]. Psychotic disorders (PD) in these pathologies have a specific clinical presentation, evolution, and prognosis different from psychotic disorders encountered in late-onset primary psychoses such as schizophrenia and other psychiatric disorders with psychotic features [10]. Delusions, hallucinations, and identification disorders significantly contribute to the reduction of patient well-being and the burden on caregivers [3]. Moreover, these disorders are associated with a faster progression of the dementia syndrome, including loss of autonomy, cognitive decline, early institutionalization, and death [3].

The main objective of our article is to describe the characteristics of psychotic disorders in patients suffering from Alzheimer's disease and related dementias attending the memory and psychogeriatric consultation at Drid Hocine, Kouba/Algiers.

II. Material And Methods

We conducted a descriptive study of 73 adult patients (the study had found extreme ages ranging from 34 to 103 years), suffering from Alzheimer's dementia and related dementias with or without psychotic features, followed up at the specialized memory and psychogeriatric consultation of the DRID Hocine university hospital specialized in psychiatry, Kouba Alger- Algeria, over a 12-month period, from September 2022 to September 2023. All patients suffering from late-onset psychotic disorders were excluded from the study, including schizophrenia, schizoaffective disorders, delusional disorders and melancholic depression with psychotic features in the elderly. Cases were validated by using the DSM-5 diagnostic criteria for neurocognitive impairment or delirium [1]. Cerebral MRI and neuropsychological tests were part of the systematic assessment of patients. The feasibility of neuropsychological testing depended on the patient's degree of clinical impairment. Sociodemographic, clinical, evolutionary and therapeutic data were collected by using a hetero-questionnaire.

Outcome criteria included:

- The clinical characteristics of delusions, hallucinations, and identification disorders.
- The evolution of psychotic disorders.

Statistical Analysis

All data collected on the pre-established questionnaire were entered into the SPSS software version 26. Qualitative variables were expressed as percentages or frequencies. Quantitative variables were expressed as means, standard deviations, and ranges. The comparison of qualitative variables was performed by using the Pearson chi-square test. The comparison between a qualitative variable and a quantitative variable was conducted by using the student's t-test. The significance threshold was set at 5% ($p \leq 0.05$). For better visualization, figures were created by using Excel spreadsheet software after transferring data from the SPSS software.

III. Result

Sociodemographic Characteristics

- **Age and Gender**: Our study included 73 dementia patients, comprising 52% men and 48% women, with a sex ratio of 1.01. The mean age was 68.5 years, ranging from 34 to 103 years.
- **Marital Status**: More than half of our patients were married, and 21.9% were widowed.
- **Lifestyle**: All patients were living with their families, with at least one caregiver.

Clinical, Evolutionary, and Therapeutic Characteristics

1. **Personal History** Over 72% (n=53) of the patients had one to four comorbidities, including hypertension, diabetes, prostate adenoma, blindness, and hearing problem
2. **Types of Dementias:**

More than half (53.4%) of our population was diagnosed with Alzheimer's dementia. Fifteen patients (20.50%) had vascular dementia, thirteen patients (17.80%) had mixed dementia, three patients (4.10%) had Lewy body dementia, and finally, three patients (4.1%) had Parkinsonian dementia (Fig. 1).

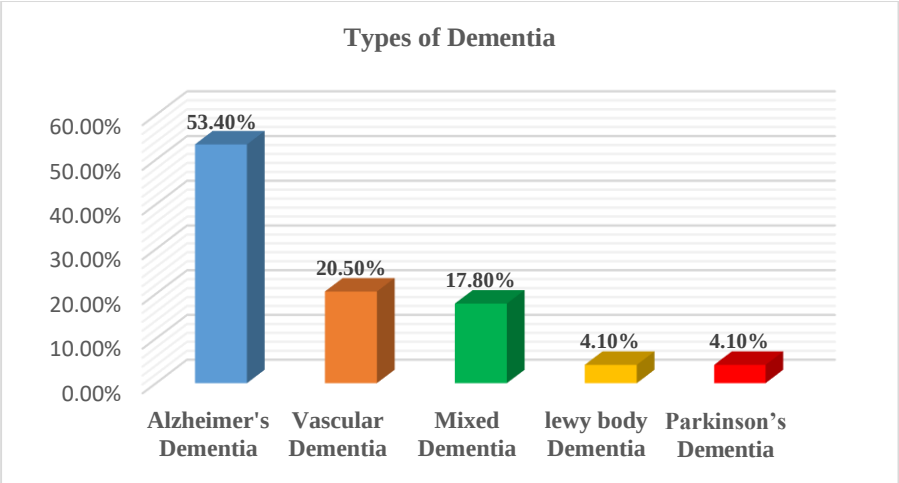

Figure. 1: distribution of the type of the Dementia

There was no gender difference in the distribution of clinical forms of dementia (Fig. 2).

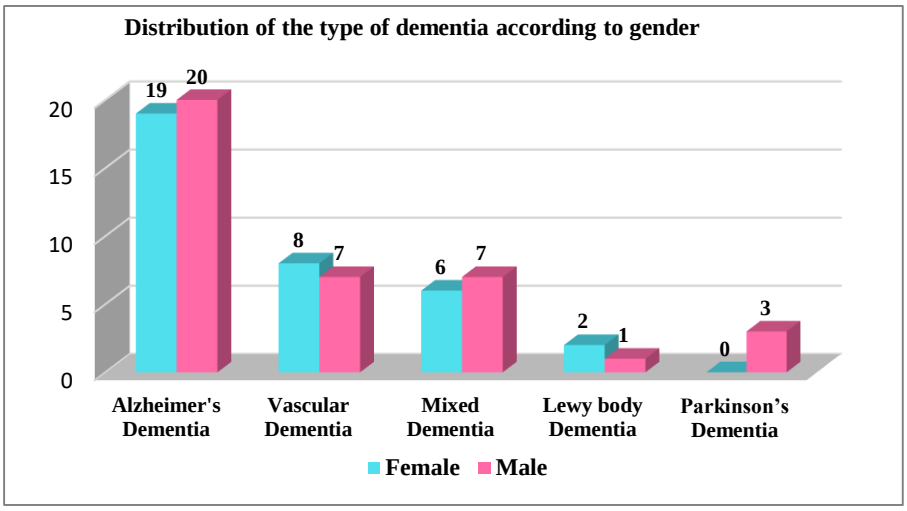

Figure. 2 : distribution of the type of the Dementia according to gender

Magnetic Resonance Imaging (MRI)

All the demented patients had benefited from a radiological exploration in particular, the MRI. Indeed, more than half (52.1%), had a grade 2 and 3 cerebral atrophy of Scheltens, which means, a moderate to severe impairment (Fig. 3)

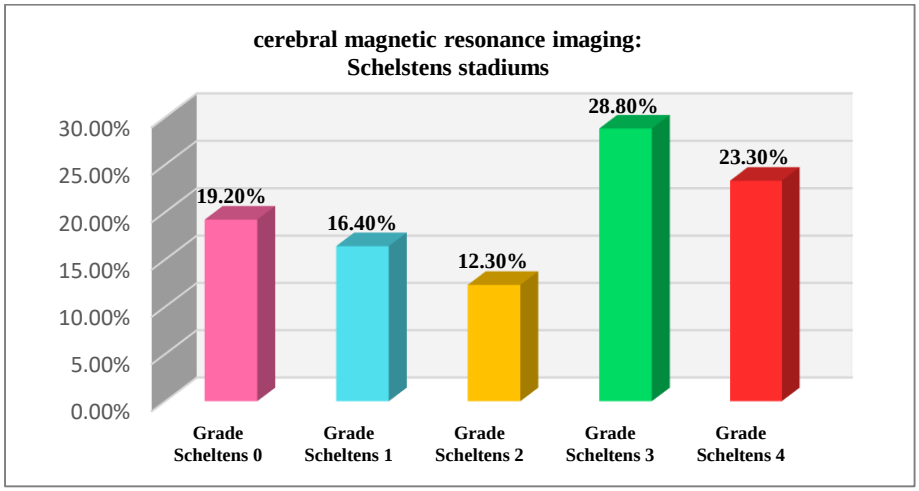

Figure. 3: distribution of the cerebral magnetic resonance imaging: Scheltens stadiums

IV. Psychotic Disorders:

More than half of our sample suffered from psychotic disorders, with 64.4% (n=47).

Hallucinations:

54.8% (n=33) of the patients suffered from hallucinatory activity, with 23.3% (n=17) experiencing visual hallucinations, 4.1% (n=3) reporting auditory hallucinations, and an association of at least two types of hallucinations in 27% (n=20). This included combinations such as visual and tactile hallucinations, or a combination of all three types of hallucinations (Fig. 4).

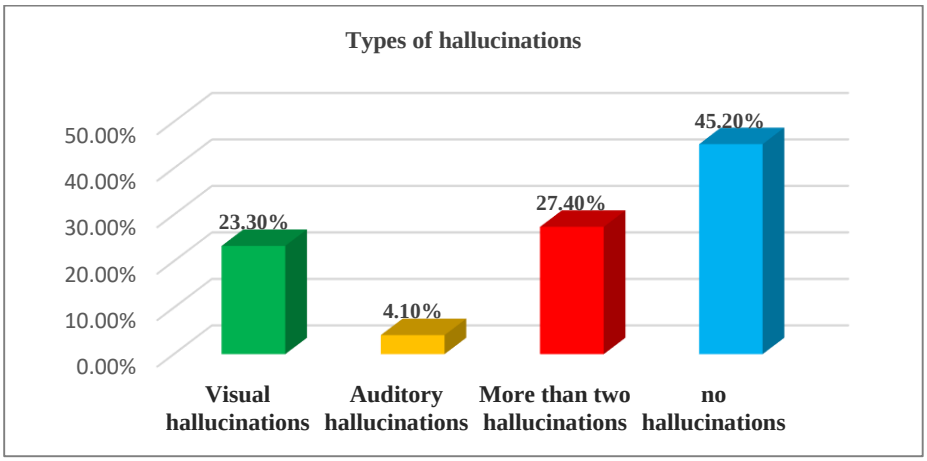

Figure. 4 : distribution of the types of hallucinations

Overall, there was a noted association of two to three types of hallucinations (visual, auditory, and tactile), especially in Alzheimer's disease, vascular dementia, and Lewy body dementia (Fig. 5).

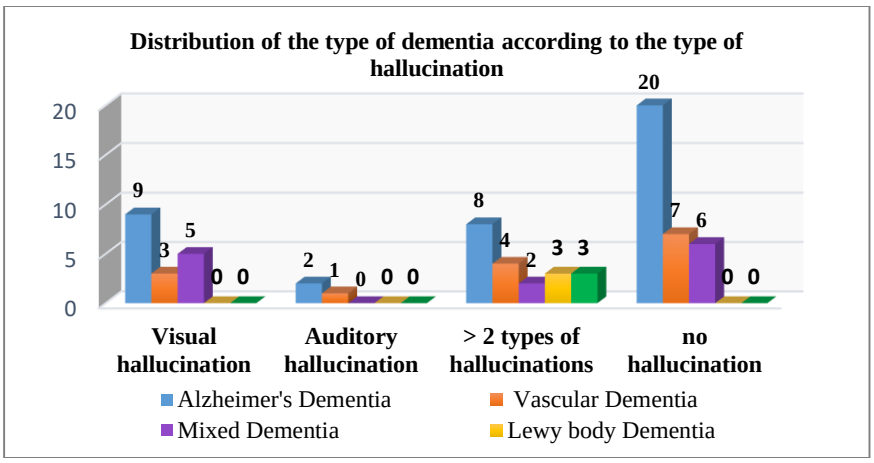

Figure. 5: distribution of the type of Dementia according to the type of hallucination

Delusion:

In your series, 27.4% (n=20) of dementia patients had at least two delusional themes (persecution + theft). The persecution theme was predominant in 54.8% (n=40), taking into account associations. Regarding the theme of theft, it was present in nearly 30.1% (n=22), also considering thematic associations. Finally, the theme of infidelity was a minority at 6.8% (n=5) (Fig. 6).

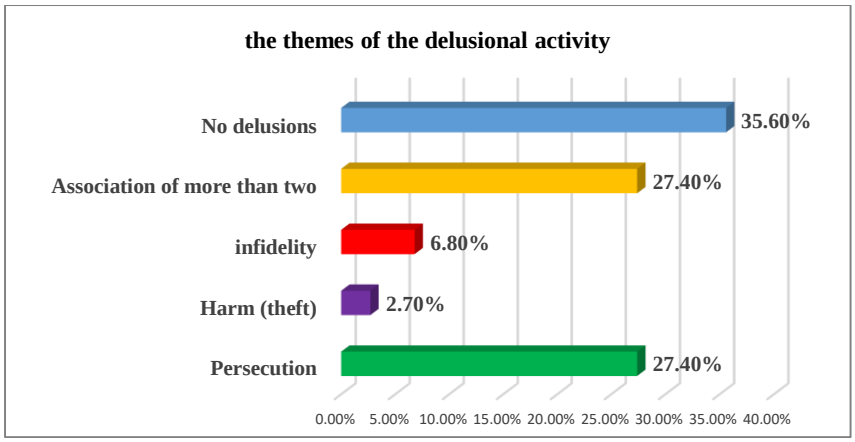

Figure. 6: distribution of themes of the delusional activity

Identification Disorders:

Concerning identification delusions, it was present in 43.8% of our patients. Among the themes, nearly 32.8% of patients experienced self-recognition disorders and false recognitions of people, and only 2.7% had the Frégoli syndrome (Fig. 7-8).

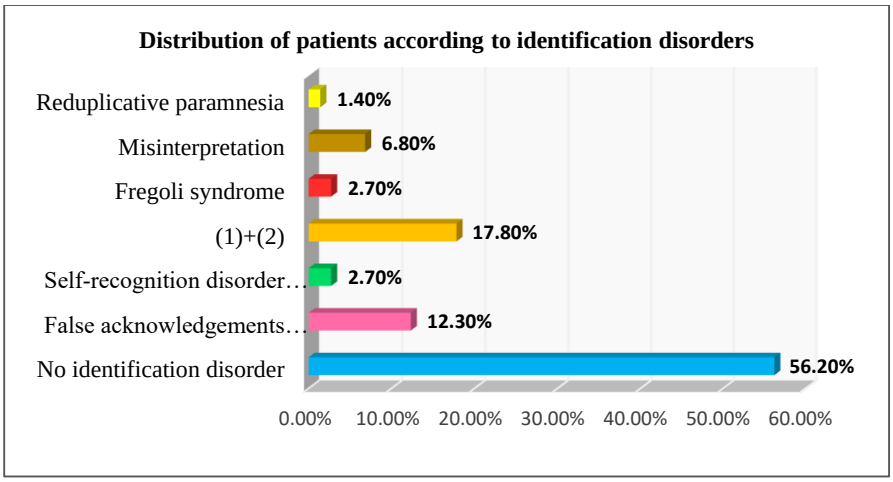

Figure. 7 : distribution of patients according to identification disorders

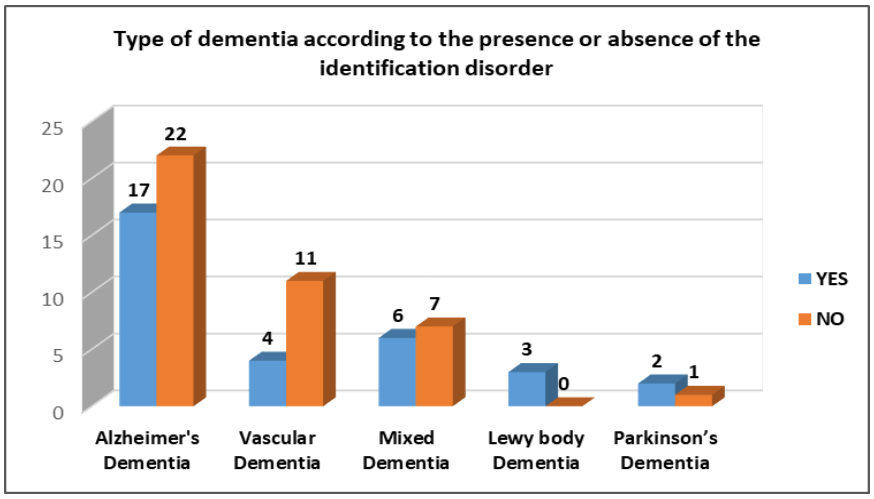

Figure. 8: distribution of type of Dementia to the presence or absence of the identification disorder

Onset Phase of Psychotic Disorders in the Dementia Process:

Psychotic disorders appeared much more in the chronic phase of the disease for the majority of clinical forms of dementia (59%), after the onset of cognitive impairments. However, in Lewy body dementia, delusions, hallucinations, and identification disorders appeared at the early stage (5%) and became chronic in different phases of the disease (Fig. 9).

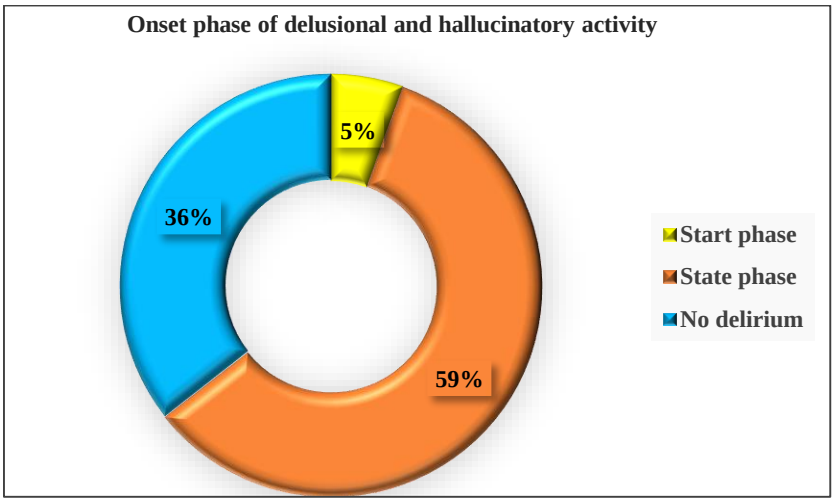

Figure 9: Distribution of the onset phase of delusional and hallucinatory

Duration of Relapses of Psychotic Disorders (PD)

In our series, more than half of our patients had different relapse patterns. The predominant recurrence duration was between 3 to 6 months in 19.3% of cases, more than 9 months in 12.3%, between 6 to 9 months in 9.6%, and only 6.8% became chronic (Fig. 10).

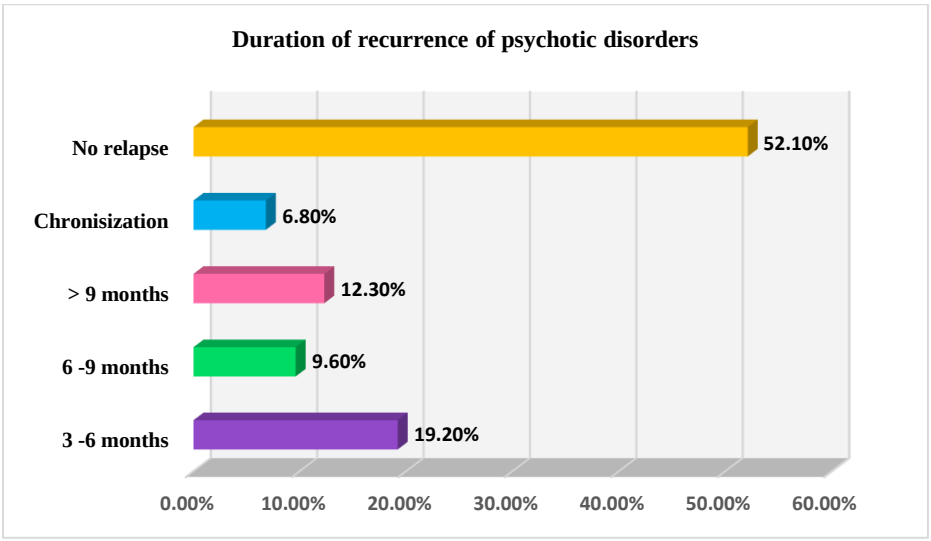

Figure 10: Distribution of the duration of recurrences of psychotic disorders

We also observed a significant difference in the distribution of episodic durations of psychotic relapses (p=0.000). Indeed, relapses occurred in cyclical episodes, between 3 to 9 months, averaging two episodes per year in Alzheimer's disease and related conditions, except for Lewy body dementia, where psychotic disorders progressed in a chronic manner (Fig. 11).

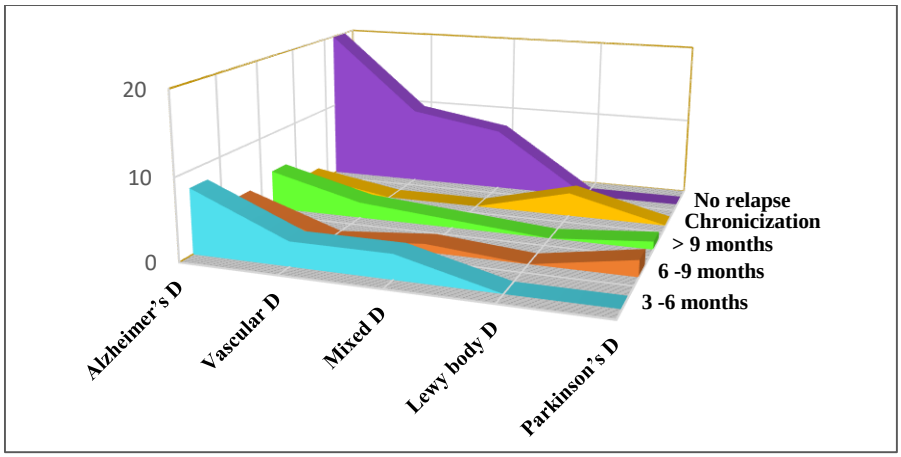

Figure. 11: distribution of type of Dementia according to the duration of recurrence of psychotic disorders

Impact of Psychotic Disorders on the Behavior of Dementia Patients:

In our population, there was no significant relationship between the intensity of behavioral disturbances and the presence or absence of psychotic disorders (p=0.153).

V. Recommended Therapeutics:

The prescription of therapeutic approaches was primarily based on anticholinesterases and antipsychotics either as monotherapy or in combination, as shown in the table below (Table 1).

Tableau. 1: Therapeutic prescription

Drugs	Frequency	Percentage %
Anticholinesterase (1)	21	28,8
Antipsychotic (2)	16	21,9
Antidepressant (3)	8	11,0
(1)+(2)	17	23,3
(1)+(3)	11	15,1
Total	73	100,0

VI. Discussion

In our series, sociodemographic characteristics showed little notable difference compared to studies in the literature addressing psychotic disorders in patients with Alzheimer's disease and related conditions [11, 12, 3-4]. Regarding clinical and evolutionary characteristics, our results are consistent with the literature, particularly concerning psychotic disorders such as delusions, hallucinations, and identification disorders [12-13]. Psychotic disorders (PD) were prevalent in all studied clinical forms.

VII. Hallucinations:

Hallucinations are mainly visual hallucinations in 59.8%, and auditory hallucinations in 54.4% [10], which is in line with our results, as visual and acoustico-verbal hallucinatory activity combined was over 50.7%. Visual hallucinations were primarily related to deceased relatives.

Auditory hallucinations mainly involved voices of relatives or strangers in the second or third person, conveying threats, mockery, or issuing commands [14]. Hallucinations in other modalities were exceptional [8]. According to studies, hallucinations typically occur later than delusional ideas [15]. These symptoms persist throughout the course of the disease in Lewy body dementia (LBD) [15-16].

VIII. Delusional Ideas:

The prevalence of delusional ideas in Alzheimer's disease (AD) is higher than that of hallucinations (22% versus 3%, with a concurrent occurrence of 9%) [3, 10].

This result has been subsequently confirmed (32% versus 7%) [17-18]. Delusional ideas tend to occur earlier than hallucinations and identification disorders.

Indeed, the literature reports a majority of persecutory themes, followed by ideas of theft and reference, mainly in Alzheimer's disease and related conditions [19]. The prevalence of delusional ideas in these patients can range from 10% to 97.1% [20], which is in perfect agreement with our results (63%) (Table 3). The prevalence of persecutory ideas in this population has been estimated to reach up to 40% in a literature review of 35 studies [8]. Our result aligns with literature findings as the persecution theme alone or in association was predominant at

54.8%. As for ideas of theft, its prevalence varies in literature studies and represents up to 75% of persecutory ideas in Alzheimer's dementia [10], which is consistent with our results. It's worth noting that the designated persecutors are usually people known to the patient (neighbors, family, caregivers).

Indeed, delusional themes are generally connected to the real experiences of the individual, which is not completely detached from reality [10]. The systematization of these delusions is less structured compared to those encountered in psychiatric clinics and tends to fluctuate, often modulated by the immediate physical and social environment, stressful life events, emotions, severe somatic illnesses, and other factors. In dementia patients, delusional ideas may fill the void induced by memory loss and temporal-spatial disorientation [17].

IX. Identification Disorders

Other delusional syndromes can be found in dementia, particularly in Alzheimer's disease and Lewy body dementia, somewhat typically but less frequently than the previously mentioned typical themes – these are identification disorders. They are characterized by the delusional belief that a person, place, or object has transformed or duplicated (Table 2). They frequently appear in neurodegenerative conditions [20-21].

The hypothesis involves a disconnection between the temporal visual image of the person or object, on the one hand, and the associated limbic affective mental representation, derived from the amygdala, on the other hand.In our study, identification disorders approached 44%, with a predominance of self-recognition disorders and false recognitions of people. Their onset was late in Alzheimer's disease and related conditions, except for Lewy body dementia (LBD), where the disease began with these disorders. Generally, their presence was associated with a deteriorated state. These results align with the literature [7, 19].

Table 2: Examples of identification disorders

Examples of identification disorders	
Recognition Disorders of one's own image	The individual does not recognize their reflection in the mirror
False recognitions	Recognition of unknown individuals by the patient and systematic misrecognition of their close ones
Identity errors (Fregoli syndrome)	The individual feels persecuted by another person who regularly changes appearance (disorder of person identification)
Interpretation errors	The individual is convinced of being secretly the object of someone's desire
Capgras syndrome	Identification of a doppelgänger (delusional denial of a person)

Onset Phase of Psychotic Symptoms in the Dementia Process:

In our series, psychotic symptoms appear to be most active during the moderate stage of dementia (Alzheimer's, Parkinsonian, Vascular) and early in Lewy body dementia. Our results align with those of the literature, notably the study by Tsunoda N, et al in 2018 [22].

Recurrence of Psychotic Symptoms

The progression of psychotic symptoms is characterized by recurrence and chronicization in 95% of cases, according to certain studies in the literature [4,19]. A longitudinal study [15] reports variable durations of evolution ranging from three to six months, extending to more than a year in some cases, which is consistent with the results of our series. On average, patients experienced two to three episodes per year in Alzheimer's disease and related conditions, except for Lewy body dementia, where a chronicization of symptoms was observed.

Impact of Psychotic Symptoms on the Behavior of the Demented Individual

It is worth noting that our study did not find a significant relationship between psychotic symptoms and psycho-behavioral disorder. The majority of patients, across all forms of dementia with or without psychotic characteristics, had psycho-behavioral disorders of the same severity. This is likely due to the degree of cerebral impairment in our patients, who were already in the advanced stage with significant cognitive decline.

Magnetic Resonance Imaging (MRI)

Half of our patients had moderate to severe cerebral atrophy, explaining the onset of psychotic symptoms that were proportional to cognitive impairment, consistent with most studies in the literature [10]. However, in our results, we noted that a proportion of dementia patients (19.2%) were at Scheltens grade 0, indicating no radiological cerebral abnormality, but clinically, psychotic symptoms were highly pronounced.

This suggests that the mechanism of occurrence of these symptoms is very complex and likely multifactorial. In this regard, three explanatory hypotheses have been put forward by some authors in the literature regarding the mechanisms underlying psychotic symptoms and their expression [9-10]:

– The symptoms in affected individuals result from dementia-related cognitive impairments.

- Psychotic symptoms are an adaptive psychogenic phenomenon to the environment.
- Psychotic symptoms result from a neurological impairment, distinct from the cognitive impairment of dementia, superimposed on it.

Therapeutic Prescription

In terms of therapy, our prescriptions depended on the risk/benefit balance [23]. The majority of our patients underwent combination therapy with a new-generation antipsychotic (risperidone) and an anticholinesterase, in line with the new recommendations of the international expert consensus on therapeutic prescription practices for geriatric subjects with dementia and psychotic disorders [24], advocating for risperidone and anticholinesterase. In case of antipsychotic intolerance, the anticholinesterase alone sufficed according to the American Psychological Association (APA) 2016 recommendation.

Regarding future treatments for psychotic disorders in dementia patients, Citalopram and Pimavancerin have demonstrated efficacy in clinical trials.

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

X. Conclusion

Psychotic symptoms in dementia patients represent a distinct semiological entity within the psychiatric manifestations of the elderly. Therefore, their in-depth study constitutes a significant research approach, potentially marking a major turn in patient management. It allows for an explanation of the underlying pathophysiological processes and, consequently, the implementation of appropriate medication aimed at achieving better prognosis and comfort for both patients and their caregivers.

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