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#### RESEARCH ARTICLE

# SCHIZOPHRENIA AND EPILEPSY: WHAT LINKS BETWEEN? ARRAZI HOSPITAL EXPERIENCE ABOUT 56 CASES

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# Manuscript Info

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# Abstract

**Background:** Given the higher incidence of psychotic disorders in patients with epilepsy, several neurologists and psychiatrists have attempted to explain this controversial comorbidity. Thus, several hypotheses have been put forward but no link has been established with certainty until today.

**Objectives**: The aim of our work is to draw up a socio-demographic and psychopathological profile of patients with schizophrenia-epilepsy comorbidity as well as to assess the risk of suicide, the management, the reasons for admission and the length of hospitalization.

**Methodology**: we conducted a retrospective cross-sectional study on medical records of patients with schizophrenia and epilepsy who were hospitalized at the Ar-Razi University Psychiatric Hospital in Salé between January 01, 2017 and March 31, 2021.

**Results**: Our study included 56 patients. The average age was 33 + / 9.83, 55% male. 50% of patients had attempted suicide in the past and 25% had a history of depressive episode, 41.1% had substance use disorder and 26.8% had a family history of psychosis. 85.7% of our patients developed schizophrenia from pre-existing epilepsy; the time to onset of schizophrenia compared to epilepsy was 11.08 years +/-7.71. The mean age of onset of schizophrenia is 23.3 years with a mean duration of progression of 9.18 years, 55.4% of patients were on monotherapy and 8.9% had resistant schizophrenia on clozapine. The average age of onset of epilepsy is 14.73 years, with generalized epilepsy in 84% of cases. The average length of stay is 42 days. The reasons for admission were as follows: hetero-aggression 78.6%, delusional verbalization 85.7% and suicide attempt 23.2%. The majority of our patients have been treated with atypical antipsychotics: Risperidone 30.4%, Amisulpride 21.4% and Aripiprazole 12.5%.

Conclusion: The co-occurrence of schizophrenia epilepsy suggests the existence of possible common etiopathogenic factors. The management of this comorbidity requires a multidisciplinary collaboration between neurologist and psychiatrist, in order to confirm the diagnosis, establish a good therapeutic approach and propose a management algorithm taking into account the two pathologies.

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## Introduction:-

Epilepsy is one of the most common neurological conditions and affects approximately 70 million people worldwide [1]. It is a chronic condition of various origins characterized by the repetition of epileptic seizures, which represent all the clinical manifestations of a paroxysmal hypersynchronous hyperactivity of a more or less extensive group of neurons and its possible spread to the Cerebral cortex. It can be generalized or focal. It can include motor, sensory, vegetative and psychic signs [2]. The impact of epilepsy on the lives of patients makes this disorder a real public health problem. Indeed, the psychopathological, cognitive and social consequences of epilepsy are often significant and obvious, and their management is generally difficult [3].

Schizophrenia is a chronic multidimensional psychiatric pathology. It is present in all cultures, its prevalence is estimated at 1% of the world population. Several comorbid pathologies can be associated with schizophrenia and in particular neurological disorders, in particular epilepsy. According to several epidemiological studies, subjects with a neurological disorder present a higher comorbidity with psychiatric disorders [4]. These patients may present with cognitive and behavioral disorders which may be due to psychiatric disorders [5]. The onset of this psychiatric disorder may precede, be concomitant with or follow the onset of epilepsy.

Forsgren, in his study of the prevalence of epilepsy in the northern region of Sweden among 713 adult patients followed for epilepsy, found a prevalence of psychiatric disorder at 5.9% and schizophrenia at 0.8% [6]. Gudmundson and colleagues [7], studied this prevalence in patients diagnosed with epilepsy, and objectified the following results: 59% of patients presented with a psychiatric disorder at least once in their lifetime; including 7% of the latter have experienced at least one psychotic episode.

The comorbidity between epilepsy and psychiatric disorders, particularly psychosis, has long been known. A patient with epilepsy has a 2 to 12 times higher risk, compared to the general population, of developing a psychotic disorder. This same risk may tend to increase with temporal lobe epilepsy or with epilepsy resistant to treatment [8]. Indeed, psychosis develops in 2% to 7% of people with epilepsy. Other studies have reported a higher prevalence of epilepsy in patients with schizophrenia compared to the general population [9].

# The association of the two disorders can be seen in two cases:

- 1. Either epilepsy appears during the course of schizophrenia, in particular precocious schizophrenia.
- 2. Either schizophrenia develops on a pre-existing epilepsy [10].

Several methods of classification have been proposed, but the majority of authors currently agree to favor as the basis of the classification the temporal link of psychotic disorders vis-à-vis epileptic seizures, one distinguishes: ictal psychoses, post-acute psychoses. ictal, episodic or chronic interictal psychosis, in addition to iatrogenic disorders linked to antiepileptic treatments and epilepsy curative surgery [11].

The epilepsy-schizophrenia comorbidity raises problems of diagnosis, prognosis and therapeutic choice. Through our study, we want to shed more light on:

- 1. The socio-demographic and clinical characteristics of patients with schizophrenia and epilepsy, having been admitted to the Ar-Razi hospital in salé.
- 2. The main somatic and psychiatric comorbidities of patients
- 3. Evaluating the impact of epilepsy on the course and prognosis of schizophrenia.
- 4. Suicide risk assessment
- 5. The principles of care for these patients
- 6. The reasons for admission to the psychiatric service as well as the average length of stay
- 7. The comparison of the data collected with those of the literature.

# **Methods:-**

Our study is of a retrospective descriptive cross-section covering a period of 5 years, from January 01, 2017 to March 31, 2021.

The study looked at the medical records of patients with schizophrenia comorbid with epilepsy who were admitted to the Ar-Razi University Psychiatric Hospital in Salé.

The inclusion criteria are:

- 1. Patients hospitalized in the adult psychiatry department of the Ar-Razi university psychiatric hospital in Salé.
- 2. Diagnosed with schizophrenia (according to DSM 5 criteria) comorbid with epilepsy.
- 3. Age: no age limit
- 4. Respect for anonymity and data confidentiality.

Incomplete files and missing data were excluded.

The support used to gather information is a qualitative questionnaire selection of unique answers. We opted for this type of questionnaire for its simplicity and brevity, which allows us to collect the information necessary for our study within a period of time.

The questionnaire includes information about:

- 1. -Sociodemographic data: sex, age, profession, socio-economic level, level of education, social situation
- 2. History
- 3. -Personal: psychiatric, number of hospitalizations, addictive behavior, medical, surgical and legal history.
- 4. -Familial: psychosis, epilepsy, addictive behavior and mood disorders.
- 5. -Characteristics of epilepsy and schizophrenia
- 6. -Antipsychotic and antiepileptic treatments received
- 7. Reasons for admission to the psychiatric department and length of hospitalization.

Data analysis was performed using SPSS 20 software

#### **Results:-**

During the period of our study, which runs from January 01, 2017 to March 31, 2021, we collected 56 cases of patients with comorbid schizophrenia and epilepsy, who had been at the Arrazi University Psychiatric Hospital in Salé.

# **Sociodemographic characteristics:**

The socio-demographic characteristics are represented in Table N ° 1.

The average age of the patients is: 33.07 years +/- 9.83; the age group between 26 and 36 years was the most presentative with a rate of 34%.

Men were in the majority compared to women with a percentage of 55%, more than half of the patients in our sample were single (86%), while 7% were married and 7% were divorced.

41% of our patients had a high school education, 32% primary, 9% university while 18% were illiterate.

88% of our patients did not have a professional activity while 12% had a regular profession.

46% of our samples were of average socio-economic level, 42% low and 12% of wealthy level.

**Table 1:-** socio-demographic characteristics of the sample.

Variables	Number of participants	Pourcentage (%)
Average age (years):	33.07 ans	(min = 16, max = 58)
Age range :		
Under 25 years	15	27 %
Between 26 et 36 years	19	34 %
Between 37 et 47 years	17	30 %
Over 48 years	5	9 %
Sex:		
Men	31	55 %
Women	25	45 %
Marital status :		
Single	48	86 %

Married	4	7 %
Divorced	4	7 %
Level of study:		
Unschooled	10	18 %
Primary	23	41 %
secondary	18	32 %
University	5	9 %
Profession		
Unemployed	49	88 %
Fixed employment	7	12 %
Socio-economic level		
better-off	11	12 %
Medium	26	46 %
Low	19	42 %
Living environment		
Urbain	50	89 %
Rural	6	11 %

#### Personal and family history:

- 1. Among our patients, 53.6% had a psychiatric follow-up for more than 5 years.
- 2. 50% had already made a suicide attempt
- 3. 25% had a history of a depressive episode, 16% of a manic episode.
- 41.1% had a substance use disorder, the substances used are: tobacco 41%, cannabis 30.4%, alcohol 17.9%, benzodiazepines 8.9%.
- 5. 14.3% had a criminal record.
- 6. 26.78% had a medical history other than epilepsy (15 patients), broken down as follows: neuroleptic malignant syndrome (5 patients), diabetes (3 patients), asthma (3 patients), arterial hypertension (2 patients)), idiopathic thrombocytopenic purpura (one patient) and cerebral angioma (one patient)

For the family history of our patients: 26.8% had a family history of psychosis, 7.1% of mood disorder and 16.1% had a family history of epilepsy.

#### Schizophrenia:

- 1. In our sample, the average age of onset of schizophrenia is 23.3 years +/- 5.62. The mean duration of schizophrenia was 9.18 years +/- 7.68.
- 2. 85.7% of our patients developed schizophrenia from pre-existing epilepsy, the time to onset of schizophrenia compared to epilepsy was 11.08 years +/- 7.71.
- 3. 14.3% of our patients presented with epilepsy during the course of their schizophrenia, after an average time of onset of 9.29 years +/- 8.59.
- 4. 55.4% of our patients were on monotherapy and 66% had good treatment adherence. 8.9% of patients had resistant schizophrenia and were put on clozapine. (figure 1)

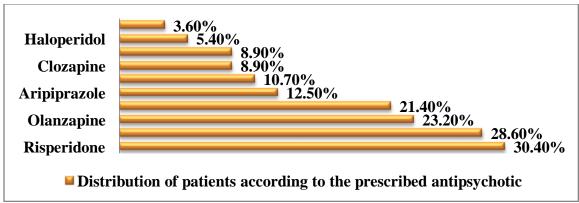


Figure 1:-Distribution of patients according to the antipsychotic drug administered

# **Epileptic disease:**

The average age of onset of epilepsy is 14.73 years. Most of our patients (84%) have generalized epilepsy, 14.3 developed epilepsy from pre-existing schizophrenia.

Monotherapy is prescribed in 55.4% of our patients, while dual therapy was prescribed in 35.76% and only 7.14% were on triple therapy for the persistence of seizures in monotherapy. (figure 2)

75% of our patients had stabilized epilepsy and 66.1% are regularly monitored in a neurology department for their epilepsy.

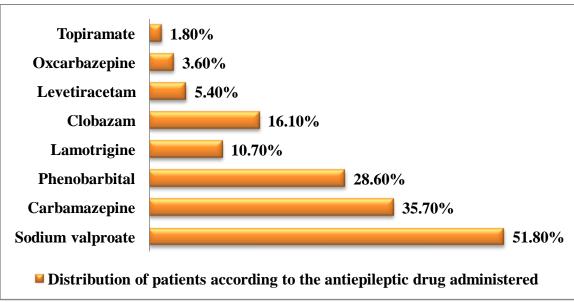
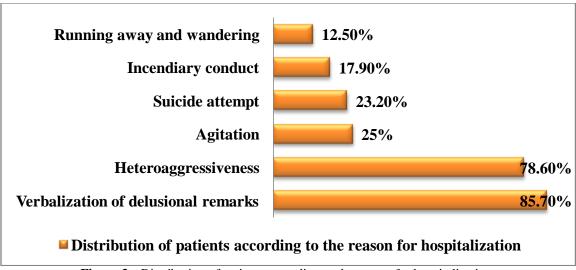


Figure 2:- Distribution of patients according to the antiepileptic drug administered

# Hospitalization in the psychiatric service:

The average length of stay in the psychiatric service is 42 days with a minimum of 5 days (discharge against medical advice) and a maximum of 180 days. The average frequency of hospitalizations in a psychiatric ward varied from one hospitalization to eight hospitalizations with an average of 2 hospitalizations for each patient. The reasons for admission to the psychiatric service are shown in figure 3.



**Figure 3:-** Distribution of patients according to the reason for hospitalization.

# **Discussion:-**

Our study aims to establish a socio-demographic and psychopathological profile of patients with schizophreniaepilepsy comorbidity as well as to assess the risk of suicide, the reasons for admission to a psychiatric facility, the average length of stay and the principles of therapeutic management.

Our sample included 56 patients. The average age of the patients included in our study is 33 years +/-9.83, this value is close to that found in the literature, in particular that of Kimiskidis KV et al (32, 2 years +/-10) and that of Souza EAP et al (32.43 years +/-6; 61) [12]. 55% of our patients are male, this agrees with the study by Kimiskidis KV et al [13].

41% of our patients had a secondary education level and 88% had no professional activities, however only 12% exercised a regular profession, this result is different from that found by Nubukpo P et al. (13.2%) [13].

In our sample, 50% of patients had already attempted suicide, which would explain the high mortality in this category of patients. Indeed, the mortality of people with epilepsy and schizophrenia is very high; more than one in four people with both disorders died between the ages of 25 and 50. The study conducted by the team of Andersen [14] in Denmark found a mortality rate of patients with schizophrenia and epilepsy was 4.4 for people with epilepsy, 6.6 for people with epilepsy. Schizophrenia and 12.8 for people with both disorders, compared to people without these disorders. This indicates that these patients require special clinical attention.

In our study, the prescription of monotherapy was adopted in 55.4% of our patients; these results are similar to those indicated by the study by Kimiskidis VK et al (50.2%) [15].

In our sample, the mean age of onset of schizophrenia is 23.3 years +/- 5.62 and 85.7% of our patients developed schizophrenia on pre-existing epilepsy, the time to onset of schizophrenia versus epilepsy was 11.08 years +/- 7.71.

Our results agree with those of the literature. Indeed, the time between the onset of epilepsy and the onset of psychotic disorder has been particularly studied in chronic epileptic psychoses of schizophrenic appearance (schizophrenia-like psychosis) based on the work of Slater et al [16]. The Anglo-Saxon authors had drawn attention to the age of onset of the psychotic disorder, which was on average 29.8 years. It took 14.1 years between the onset of epilepsy and the onset of schizophrenia. The analysis of the age of onset of the psychotic disorder was clarified in later work according to the syndromic diagnosis of epilepsy: it is all the later that the epilepsy is focal and refractory, that it subsides. accompanied by cognitive impairment and there is a family history; it is all the more precocious when the epilepsy is generalized and a genetic component is present, there is no family history and intelligence is normal [17].

A study carried out by (Vuilleumier and Jallon, 1998) showed that 4.7 to 9.7% of patients hospitalized in psychiatry are epileptic and that 1.9 to 9.7% of urgent psychiatric admissions concern epileptics with the following distribution: confusional or delusional states (22 to 26%), behavioral problems (17 to 21%), suicide attempts (18 to 19%). This is consistent with the results of our study, where the average number of hospitalizations was 2 with a maximum of 8 hospitalizations. The reasons for admission were as follows: Heteroaggression 78.6%, verbalization of delusional words 85.7% and suicide attempt 23.2%.

As for the care, it is based on drug treatment based on antipsychotics, psychotherapeutic and psycho-educational help as well as social support. Some antipsychotics are recommended according to the data in the literature: Aripiprazole, Risperidone or Amisulpride. In addition, the majority of our patients were treated with atypical antipsychotics: Risperidone 30.4%, Amisulpride 21.4% and Aripiprazole 12.5%. Long-acting treatment can be considered if necessary [15].

## **Limitations:-**

To our knowledge, our study is the first to assess the comorbidity of schizophrenia and epilepsy, however it has some limitations: retrospective design, small sample size and lack of patient follow-up to better assess the evolution and impact of the two disorders on their functioning, on the prognosis of the disease as well as on their quality of life.

Despite these limitations, this study made it possible to highlight the socio-demographic and clinical characteristics of these patients as well as the methods of their management.

#### **Conclusions:-**

The comorbidity between epilepsy and schizophrenia has long been described under several names and several hypotheses have been submitted to explain this comorbidity or to establish a causal link between these different disorders.

The lack of individualization of epileptic psychoses in international classifications complicates the management of these disorders located at the border between neurology and psychiatry, knowing that this comorbidity is little or poorly recognized by neurologists as well as by psychiatrists.

Therefore, knowledge and recognition in clinical practice are of paramount importance. Further studies are needed in order to establish a well-codified treatment for these disorders without forgetting that their management is based on a comprehensive neuropsychiatric approach.

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