

Duration Of Untreated Psychosis In Early Schizophrenia: About A Study

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Abstract:

Background: Among the prognostic factors identified in recent decades in early schizophrenia is the duration of untreated psychosis (DUP). DUP is defined as the time between the onset of psychotic symptoms and the initiation of treatment. Indeed, studies in the literature have shown the detrimental effect of DUP, with more psychotic relapses and hospitalizations, poorer response to antipsychotics, more severe clinical symptoms, poorer functioning and impaired quality of life. It is against this backdrop that we conducted this research study, the aim of which is to assess the duration of untreated psychosis in patients with early-onset schizophrenia and its possible correlations with sociodemographic, clinical and therapeutic characteristics over a two-year follow-up.

Materials and methods: This was a prospective, descriptive study, including ninety-two patients with early-onset schizophrenia evolving for five years, over a 24-month period, from September 2021 to September 2023. Patients were recruited from the consultation or inpatient department of the specialized psychiatric hospital in Algiers. Cases were validated using DSM-5 diagnostic criteria. Two assessments were carried out: clinical (PANSS) and global patient functioning (GAF). Observation parameters: relapse, length of stay, therapeutic response and overall functioning.

Results: The overall sample comprised ninety-two patients, sixty-five men and twenty-seven women. The mean age was 27.4±6 years. The majority were single and lived with their families. Most had a level of education ranging from middle school to high school. Clinically, the majority of patients had a disease course of five years, with an insidious onset in 60.9%. The productive form of the disease was dominant (70.7%). 22.3% had made at least one suicide attempt before the first five years of the disease. 45.7% of patients had at least one relapse and 35.9% had 2 to 3 relapses and only 18.4% had no relapse. The average hospital stay was 52 days. Patients were judged to have moderate to severe impairment with mean PANSS of 70.6/210 at inclusion and mean GAF of 51.9±38, judged to have moderate to severe impairment of function. The mean DUP was 27±18 months, i.e. 2 years and 3 months. 59.8% of patients had a long DUP. We found a significant relationship between long DUP and certain sociodemographic and clinical variables, namely, male gender ($p=0.049$), celibacy ($p=0.018$), substance abuse, insidious mode of onset ($p=0.000$), predominantly positive symptomatology ($p=0.045$), poor insight ($p=0.000$) and therapeutic resistance ($p=0.049$). Long DUP was also correlated with symptom severity on PANSS and poor global functioning on GAF.

Conclusions: Our study confirms the correlations of long untreated psychosis duration with certain sociodemographic, clinical and therapeutic variables, joining those described in the literature. For this reason, efforts must be made in the early detection and management of schizophrenic disorders to shorten the UP in order to improve the prognosis of the illness and the overall functioning of the subject.

Key Word: Early-onset schizophrenia - duration of untreated psychosis - global functioning.

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I. Introduction

Schizophrenia is a chronic, disabling disease affecting 1% of the general young population ¹, whose prognosis has changed little in recent decades, despite recent advances in antipsychotic drugs and systematized psychotherapy. Indeed, a recent meta-analysis showed that only 13.5% of schizophrenic patients experience clinical remission and return to their pre-illness level of functioning ². This is why, in recent years, attention has been focused on the problem of the duration of untreated psychosis (DUP), which represents a decisive clinical marker in the evolution of schizophrenic disorders ³. Indeed, DUP is one of the most widely studied variables in early schizophrenia, with the aim of determining the effect of early intervention on the prognosis of schizophrenia ⁴. It corresponds to the time interval between the appearance of the first frank psychotic symptoms and the initiation of treatment ⁵.

This period is variable, but often long, lasting from a few weeks to several years, on average two years depending on a number of factors ⁶. Among the causes of long DUP are lack of insight, negative symptoms and

insidious onset of the disease, which hinder access to care and generate prolonged DUP⁷⁻⁸. This is why research has focused on the study of early-onset schizophrenia and the identification of potentially modifiable risk factors that can influence the prognosis of the disease, as well as determining the effect of early intervention in schizophrenia.

Indeed, the aim of this detection is to reduce DUP, which remains one of the most studied important variables conditioning the prognosis of this disease⁴. It is within this framework that we have conducted this research study, the aim of which is to evaluate the duration of untreated psychosis in patients with early-onset schizophrenia and its possible correlations with sociodemographic, clinical and therapeutic characteristics over a two-year follow-up.

II. Material And Methods

Type of study:

This is a prospective, descriptive study.

Study population:

We included in our research study, ninety-two patients with schizophrenia evolving for five years, of both sexes, aged between 16 and over 30, during a 24-month period, from September 2021 to September 2023. Patients were recruited from the inpatient or outpatient departments of the DRID Hocine psychiatric hospital, Kouba, Algiers-Algeria.

Exclusion criteria: all patients with schizophrenia for more than five years, delusional disorders and bipolar disorders with psychotic features.

Assessment tools:

Case validation was carried out with reference to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, 5^{ème} edition (DSM-5)⁹;

For this work, we chose to combine two evaluation scales:

A scale to assess the severity of clinical symptoms, **PANSS** (*positive and negative syndrome scale*) by Kay et al. It comprises 30 items, each with a specific definition, divided into three sub-scales: positive, negative and general psychopathology. The total score can range from 30 to 210: the higher the score, the more symptomatic the disease.

GAF: Global Assessment of Functioning - APA, 1994. The GAF assesses the functional impact of an individual's psychological functioning on the social and professional (school) spheres. The GAF score ranges are as follows:

GAF (70-61): normal

GAF (60- 51): average weathering

GAF (50-41): severe deterioration

GAF (score < 41): very impaired

Data collection method :

All patients fulfilling the DSM-5 diagnostic criteria were evaluated after being informed of the study's objectives, the medium to be used and the procedure to be followed. Patients were recruited for the study only after obtaining their informed consent. Data collection was carried out with respect for anonymity and confidentiality. The data collection procedure involved the completion of a questionnaire assessing :

Socio-demographic characteristics and addictions;

Clinical characteristics (dominant symptomatology, DUP (short and long), disease progression (duration of progression, number of relapses, causes of relapses, number of hospitalizations and duration of hospitalization) and treatment (therapeutic response and notion of treatment resistance).

Each patient took the same test. Case validation using specific scales: At the end of the interview, an average of 45 minutes to 1 hour was needed for each patient to confirm the diagnosis according to DSM-5 criteria, and for clinical assessment using the PANSS scale and the GAF.

The observation parameters at the end of the study were :

Clinical: relapse, length of hospital stay

Therapeutics: response to treatment

Overall patient functioning.

Statistical analysis:

All data collected on the pre-established questionnaire were entered into SPSS version 26. Qualitative variables were expressed by their percentages or effectives. Quantitative variables were expressed as means,

standard deviations and extremes. Qualitative variables were compared using Pearson's chi-square test. Comparisons between qualitative and quantitative variables were made using Student's T-test. The significance level was set at 5% ($p \leq 0.05$).

III. Results

Univariate analysis

Socio-demographic characteristics and addictive behavior (Tab. 1):

Our series comprised 92 patients. Sixty-five (71%) were men and twenty-seven (29%) women, with a sex ratio of 2.4. The mean age was 27.4 ± 6 years, with a predominant age range between 20 and 29 years. The study showed that schizophrenia mainly affected single people, with a rate of 77.20 %.

In terms of education, the majority (76%) of patients were in the middle and high school levels, 22.8% had a university degree and 6.5% a primary school education. In terms of employment, 58.7% were unemployed. In terms of addictive behavior, forty-two (46%) patients were involved in substance abuse, particularly cannabis.

Table. 1: Sociodemographic characteristics and addictive background of the sample

Variables	n=92 average / percentage
Averageage	26,3±4
Age class	
16 -19 years	18,5% (n=17)
20- 30 years	53,3% (n=49)
≥ 30 years	28,3% (n=26)
Gender	
Male	71% (n=65)
Female	29% (n=27)
Family situation	
Single	87,0% (n=80)
married	10,9% (n=10)
Divorced	02,1% (n=02)
Level of education	
Primary	32,6% (n=30)
Average	06,5% (n=6)
Secondary	26,1 % (n=24)
Academic	34,8% (n= 32)
Socio-professional category	
Civil servant	17,4% (n=16)
Middle management	06,5% (n=06)
Senior manager	00,0% (n=00)
Student	23,9% (n=22)
Liberal profession	04,3% (n=04)
On disability	02,2% (n=02)
Unemployed	45,7% (n=42)
Substance abuse	
- Oui	46%(n= 42)
- Non	54% (n= 50)

Clinical and developmental characteristics (Tab. 2)

Fifty-six (60.9%) patients had an insidious mode of onset. 70.7% had a productive subtype of schizophrenia and 28.3% were disorganized. Forty (21.7%) patients had a pre-morbid schizoid personality. Twenty-one (22.83%) had made at least one suicide attempt before the first five years of illness. Almost half (45.7%) of our patients had a single relapse, 35.9% had between 2 and 3 relapses and 18.4% had no relapses. The average length of hospitalization at inclusion for the entire sample was around 53 days. The majority of patients (89.1%) had an evolution of less than or equal to 5 years, and 10.9% had an evolution of less than one year. More than half the patients were taking 2^e generation antipsychotics as monotherapy.

The mean duration of untreated psychosis (DUP) was 27 ± 18 months, or two years and 3 months, with extremes ranging from six months to sixty months. Thirty-six (39.1%) patients had a DUP of between two and five years, thirty-two (34.8%) between one and two years, and twenty-four (26.1%) less than one year (Fig. 1). More than two-thirds of patients had a long DUP (more than one year). The short DUP was 40.2% (n=37) and the long DUP was 59.8% (n=55) (Tab.2).

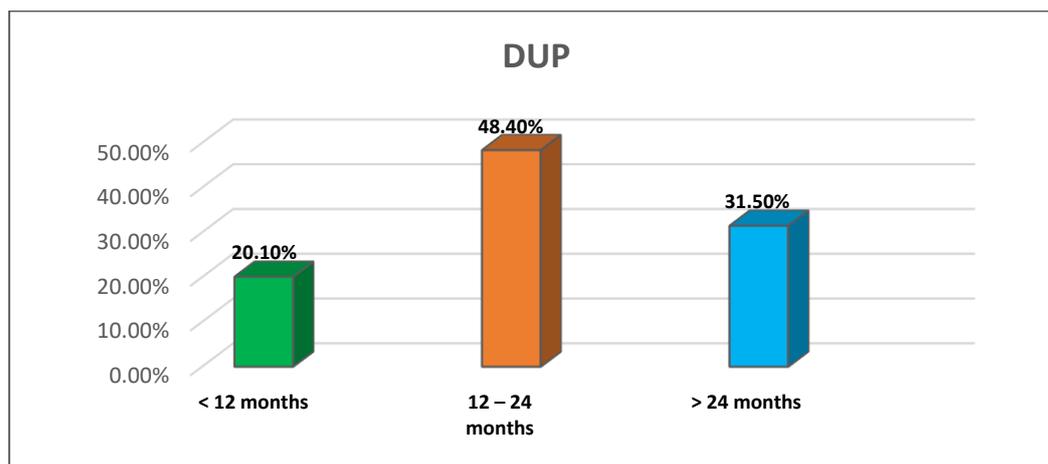


Figure 1: Distribution of patients by DUP intervals

In terms of assessment tests, the mean PANSS total score for our patients was 70.6/210 at inclusion. Patients were judged to have moderate to severe global impairment. Patient global function was poor, with a mean to severe GAF of 51.9±38. Twenty-four patients had a mean GAF impairment (60- 51). Thirty-eight patients had severe impairment (score 50-41) and ten patients had severely impaired GAF (score < 41). Twenty patients had normal GAF (70-61). Fifty patients (54.4%) had progressed well on antipsychotic treatment (disappearance of symptoms). 30.4% (n=28) had a partial response (persistence of negative symptoms) and 15.2% (n=14) had a poor therapeutic response (persistence of negative positive, negative and cognitive symptoms) (Tab.2).

Table 2: Clinical characteristics, evolution and evaluation scores of the sample

Variables	n=92 average / percentage
Premorbid personality	
Schizoid	21,7% (n=40)
Suicide attempt (SA)	
SA (+)	22,83% (n=21)
SA (-)	77,17% (n=71)
Mode of onset of disease	
Insidious	60,9% (n=56)
Acute	36,1% (n= 36)
Clinical forms	
Negative symptoms	35,8 (n=33)
Positive symptoms	45,7 (n=42)
Disorganized symptoms	18,5 (n=17)
Duration of course of the disease	
6 months – 1 year	10,9% (n=20)
1 - 5 years	89,1% (n=62)
Number of hospitalization	Mean = 3,4±6
Duration of hospitalization	Mean =53 days
PANSS Total Score	Mean= 70.6 /210
< 40	13
40 – 60	31
60 – 80	41
>80	7
EGF scores	Mean= 51,9±38
70-61	20
60-51	24
50-41	38
< 41	10
duration of untreated psychosis (DUP)	Mean= 27±18 months
< 12 months	20,1% (n=19)
12 – 24 months	48,4% (n= 44)
> 24 months (not exceeding 60 months)	31,5% (n=29)
Short DUP: ≤ 12 months	40,2% (n=37)
Long DUP: > 12 months up to 5 years	59,8% (n=55)
Treatment response	
good	54,4% (n=50)
partial	30,4% (n=28)
bad	15,2% (n=14)

Bivariate analysis

Analysis of DUP data according to sociodemographic, clinical and therapeutic variables had revealed the following results:

Socio-demographic variables and addiction to psychoactive substances:

Age: DUP according to age class in our series of patients, was not significant ($p=0.521$) (Fig.2).

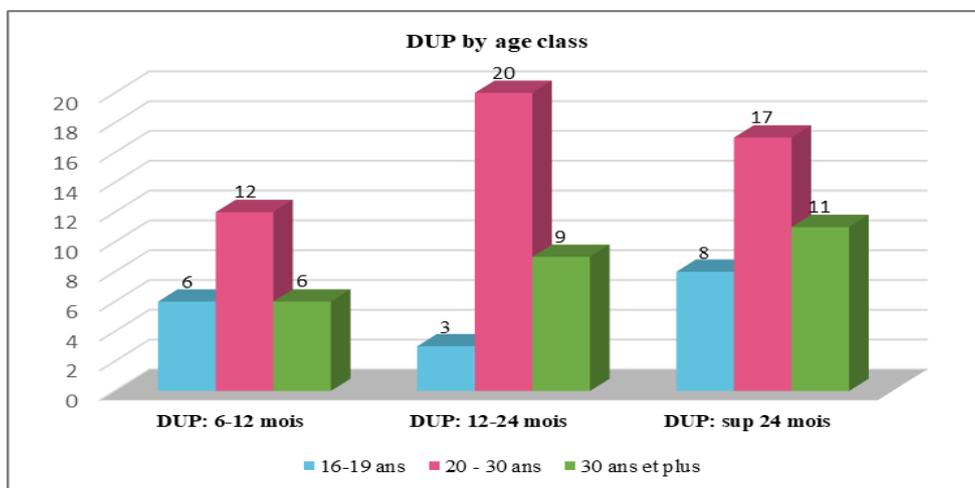


Figure 2: Distribution of DUP intervals by age group

Genre :

This result was statistically significant ($p=0.048$) (Fig.3). It was also noted that male subjects had longer DUPs of two to five years.

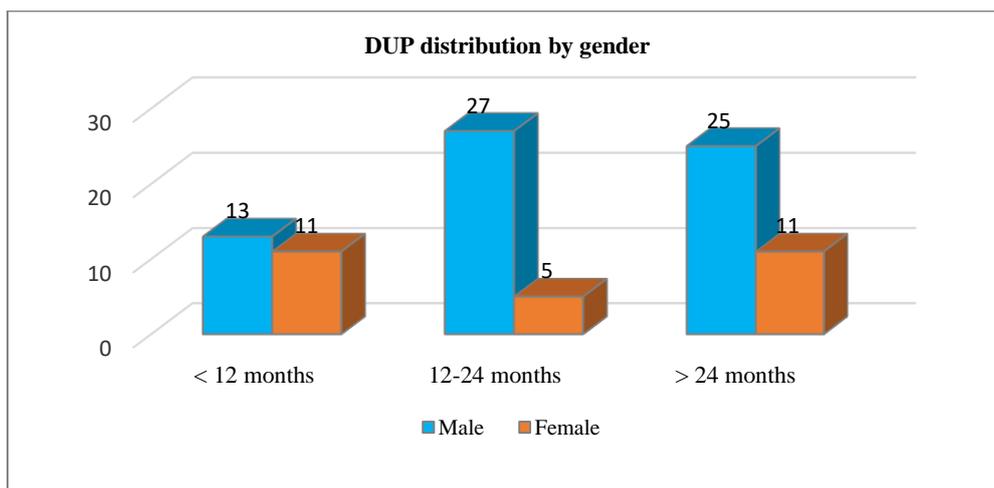


Figure 3: Distribution of DUP intervals by gender

Marital status, educational level and premorbid personality:

However, no association was found between DUP and marital status ($p=0.126$), level of education ($p=0.339$) or premorbid personality, particularly schizoid personality ($p=0.396$).

Substance abuse:

With regard to the use of psychoactive substances, our results showed a significant link with DUP, especially in the first two years of the disease ($p=0.018$) (Fig. 5).

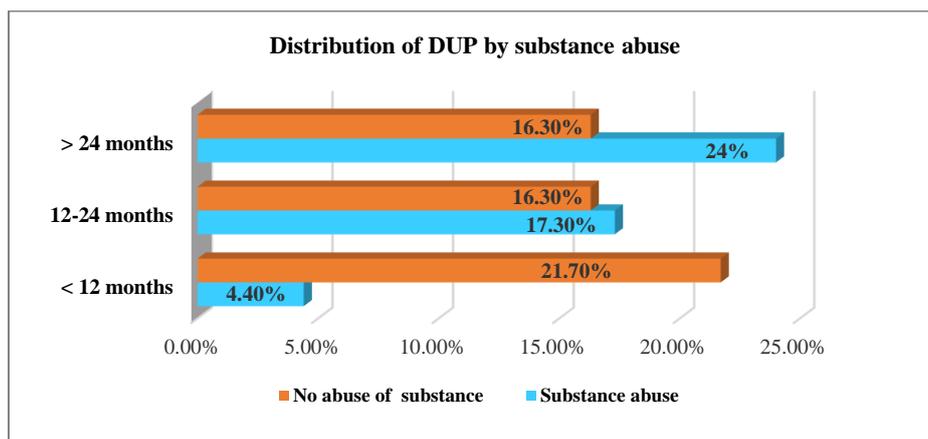


Figure 5: Distribution of DUP intervals according to substance abuse

Clinical and developmental characteristics (Tab. 2)

Suicide attempt:

Most (14.13%) of the patients who had attempted suicide (TS) had their DUP between 12 and 24 months. But there was no statistically significant correlation between DUP and attempted suicide ($p=0.327$). (Fig.4)

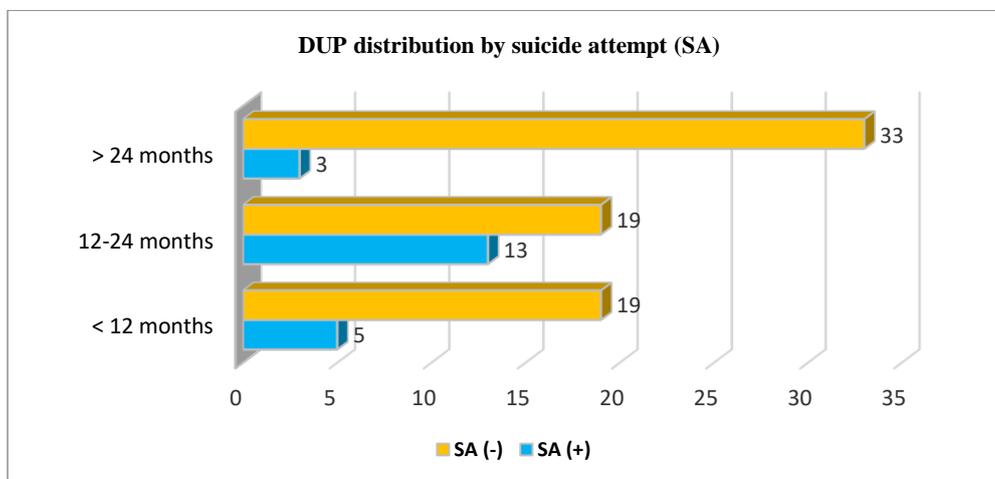


Figure 4: Distribution of DUP intervals according to TS history

Mode of onset of disorders:

Our study also revealed a significant link between the length of delay in treating psychotic disorders and the insidious onset of the disorder (0.000) (Fig. 6).

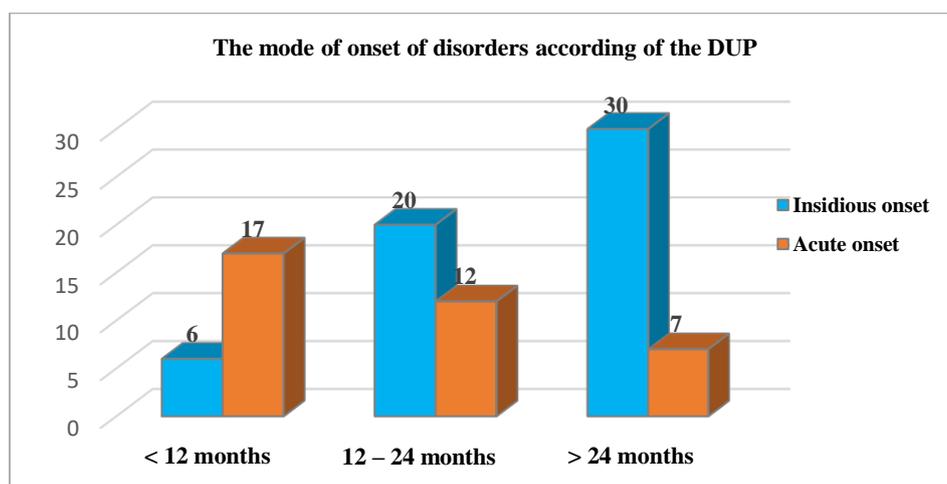


Figure 6: Distribution of DUP intervals by mode of onset of disorders

Predominant symptomatology:

The predominant symptoms as a function of DUP were significant for positive symptoms ($p=0.045$), which were distributed across the different DUP intervals and, in particular, at the very start of the disease (before 12 months) (Fig.7).

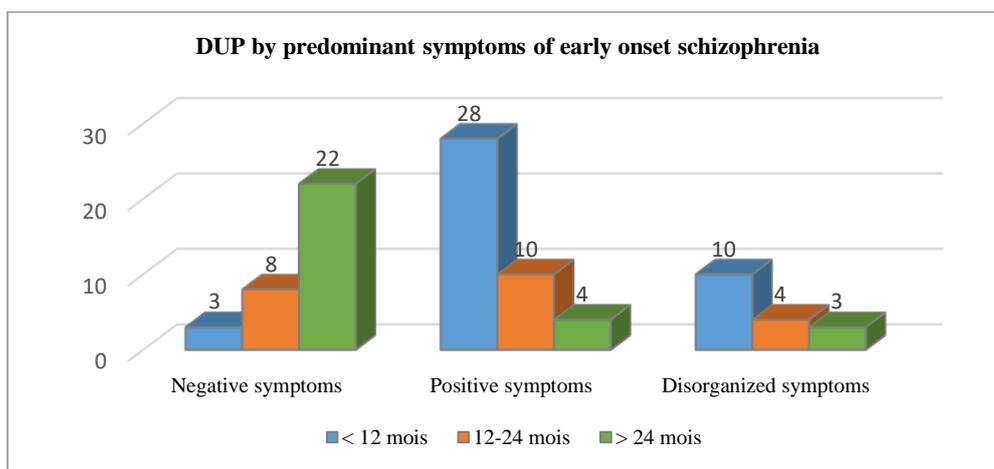


Figure 7: Distribution of DUP intervals according to predominant symptomatology

Rating scales (PANSS / GAF) :

There was also agreement between the long DUP and the severity of clinical symptoms on the total PANSS scores between the 60 and 80 range and above 80 (Tab. 3; Fig 8).

Table 3: Distribution of patients according to PANSS/GAF assessment scales

	Short DUP : < 12 months	Long DUP : > 12 months	Chi 2
PANSS scores			
< 40	9	4	0,045
40 – 60	14	17	
60 – 80	13	28	
>80	1	6	
GAF scores			
70-61	12	8	0,038
60-51	10	14	
50-41	12	26	
< 41	2	8	

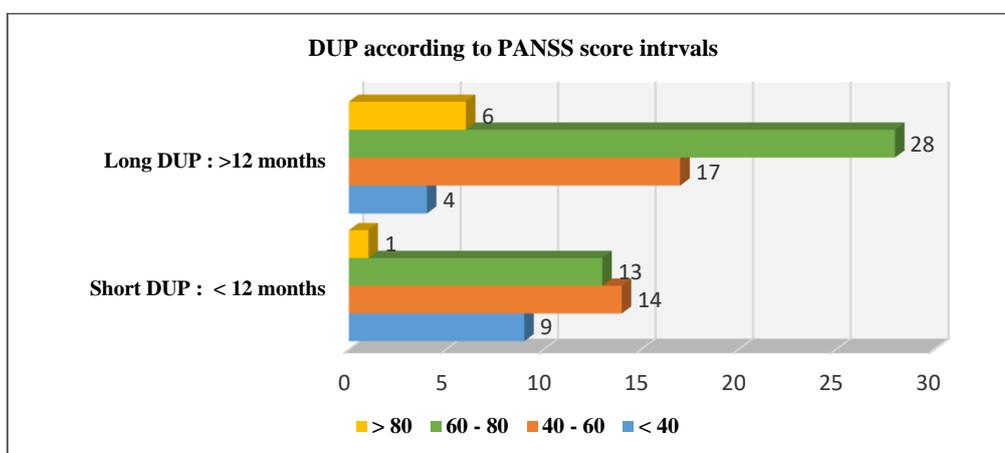


Figure 8: Distribution of DUP according to PANSS score intervals

There was also a significant link between long DUP and impaired global functioning in patients with Gaf between 50-41 (Tab. 3; Fig 9).

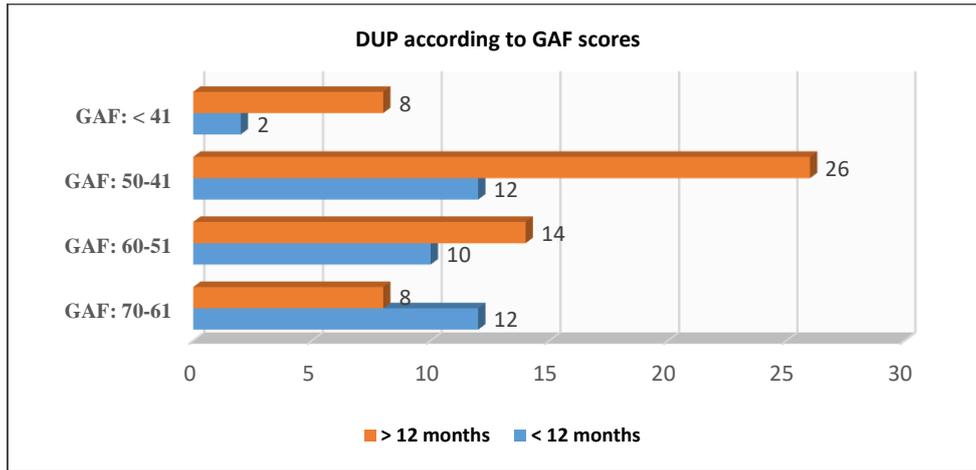


Figure 9: Distribution of DUP according to GAF score intervals

Psychotic relapses:

No relationship was observed between relapse and DUP. However, hospital stays were particularly long (> 60 days) in subjects with long DUP (2 to 5 years) (Fig. 10).

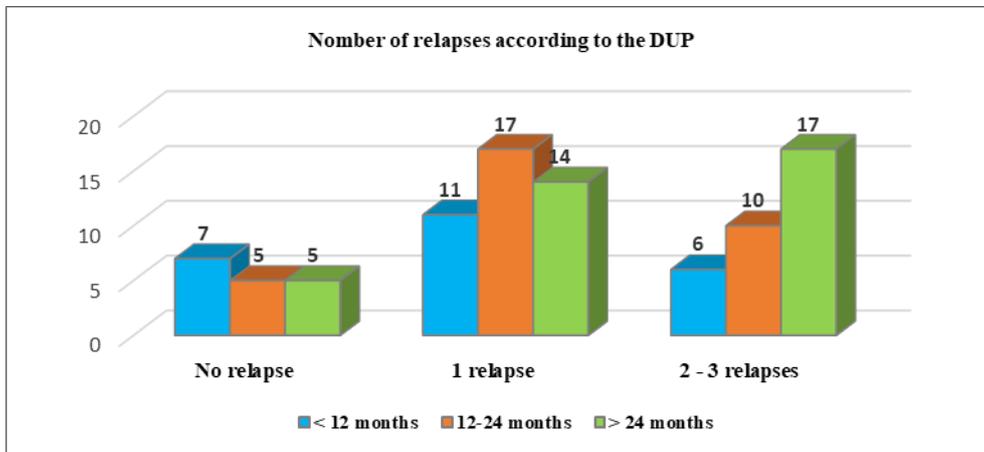


Figure 10: Distribution of DUP intervals by number of relapses

The causes of relapse were due to therapeutic non-compliance. Consequently, there were many factors contributing to non-adherence to antipsychotic treatment, but the problem of poor insight was the factor most significantly linked to the duration of untreated psychosis exceeding 12 months ($p= 0.000$) (Fig. 11).

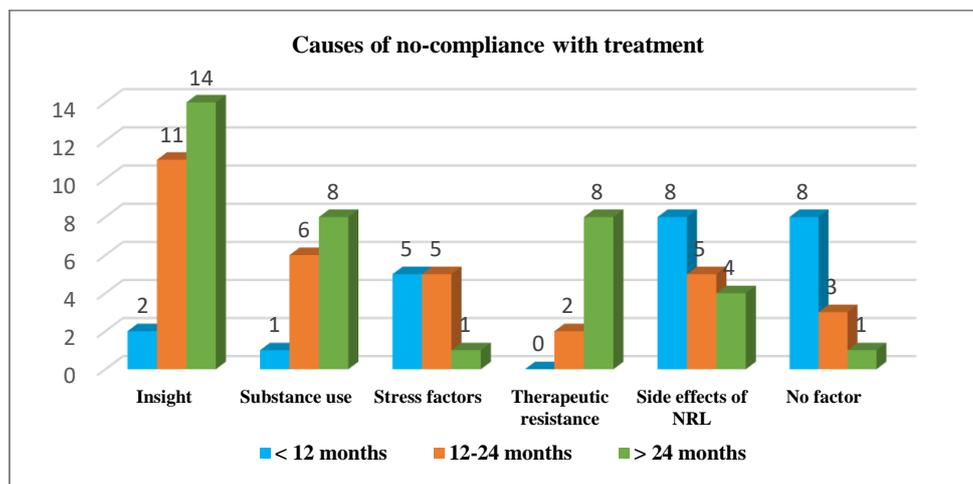


Figure 11: Distribution of DUP intervals by cause of relapse

Response to antipsychotic treatment:

Fifty-five (75%) of patients with a DUP between 1 and 2 years had a good response to antipsychotic treatment, compared with 13% with a partial response and 12% with a poor response within the same DUP. It should be noted that between two and five years of DUP, the therapeutic response weakens. Therapeutic resistance in 19.6% of our patients was significantly associated with a long DUP ($p=0.049$). (Fig.12)

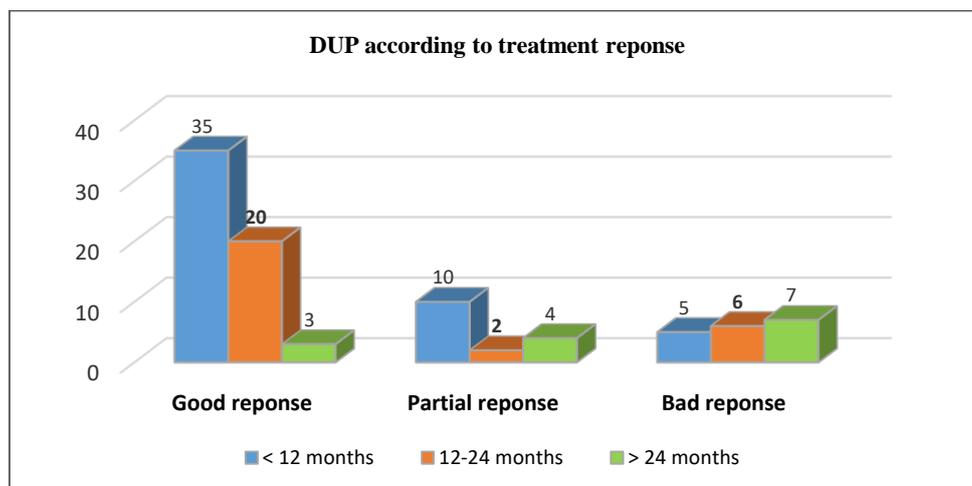


Figure 12: Distribution of DUP intervals according to therapeutic response

IV. Discussion

Profile of the overall results of our study:

The main aim of this study was to evaluate the duration of untreated psychosis in patients with early-onset schizophrenia and its possible correlations with sociodemographic, clinical and therapeutic characteristics over a two-year follow-up. The results were as follows: the mean DUP obtained was 27 months, or 2 years and 3 months, with almost 60% of patients having a long DUP.

Statistical analysis of ninety-two patients revealed a population of young, predominantly male patients with early-onset schizophrenia lasting no more than five years, who, despite new-generation antipsychotic therapy, presented an average of one to two relapses per year, with hospital stays of over fifty days. Nearly half were addicted to psychoactive substances, particularly cannabis. More than half the patients had started their illnesses insidiously. Almost a third of patients had made at least one suicide attempt during the first five years of their illness. The majority of patients had a predominantly positive symptomatology.

Half the patients were on atypical antipsychotics as monotherapy. A third of patients had a partial response to treatment, and 15% had no response at all. We also found correlations between long DUP and certain variables, notably male gender, substance abuse, insidious onset of illness, predominance of positive symptomatology, therapeutic resistance, poor insight, symptom severity on PANSS and poor overall GAF functioning.

Comparison of results with the literature:

In comparison with other studies in the literature, it can be said that the demographic, clinical and evolutionary profile of the patients was similar to that described in the various studies conducted with patients suffering from early-onset schizophrenic disorders¹⁰⁻¹².

The mean DUP value obtained was in perfect agreement with the value usually found in most studies in the literature, which is 1.5 years to 2 years¹³. However, the distribution of the DUP value has also been described as taking a bimodal form, with two frequency peaks, one at three months and the other at two years⁶. A long DUP can be due to a number of causes⁷. Firstly, patients' delay in seeking care may be due to a lack of insight¹⁴, which is the case with our patients. Secondly, early identification of the pathology by family and friends can be difficult, particularly if it is an insidious evolution with global impairment of functioning, as was the case with our patients. This mode of onset and behavioural dysfunction have been identified as potential factors in long delays in treatment⁶.

We deduce that DUP is dependent on the presentation and clinical course of the episode. It should also be noted that there are always exceptions to the rule: some subjects, despite a brief DUP, develop "resistant" schizophrenia, while others, despite a very prolonged DUP, respond well to treatment¹⁵.

Furthermore, the study population was young, with an average age of 27 years, which correlates well with the results of the literature, which found an average age of 26.3 years¹⁶. Other studies, such as that by

Mouchabac S et al, consider that the age of onset of the disorder influences DUP and therefore the prognosis of the disease. Late onset is associated with shorter DUP. On the other hand, when the onset of the disorder occurs in adolescence, it is again difficult to distinguish between psychotic symptoms and the impulsive and oppositional behaviours seen at this time¹⁷. In contrast to this study, our results showed no statistically significant difference in DUP according to the age of onset of the disorder. It is worth recalling that, in the literature; the endpoint of DUP corresponded to the start of treatment, and could be precisely defined in different ways. Indeed, in the work Register-Brown et al, in 2014¹⁸ on methods of measuring DUP, the most frequently used definition is the first antipsychotic treatment and the first hospitalization would be better prognostic predictors. In our study, in order to have a precise final terminal date, representative of the management, and in line with the literature, we took into consideration the presence of the first prescription of an antipsychotic, in the absence of the presence of hospitalization.

We had a significant result concerning the predominance of the male sex, which is in line with the results of the literature^{3,16}. Indeed, it is described in the literature that male subjects had longer DUPs than female subjects did. Indeed, in 2005, Morgan et al conducted a prospective study involving 495 subjects and concluded that male sex increased DUP¹⁹. The study by Wunderink et al came to the same conclusion regarding the association of long DUP with male sex in a sample of 157 patients with a one-year follow-up²⁰. It should be noted that long DUP is not influenced by gender, which was earlier in men than in women in some studies of first-episode psychosis and, in particular, the results of the meta-analysis by Cascio M-T and al, in 2012 reviewing 22 studies, the age of men at first contact is lower than that of women². Unlike the study by Kirkbride J-M and his team in 2017, with 687 patients, there seems to be no difference in median age for the first psychotic episode³.

With regard to family situation, most studies have found a causal link between long DUP and marital status "celibacy"¹⁹⁻²⁰, which was not the case in our study, this being explained by the duration of the disease, which was less than five years, compared with the studies cited, which was more than five years.

Also, with regard to occupational status, DUP and occupational status were statistically non-significantly related. This non-significance can be explained by the fact that our sample concerns early-onset schizophrenia evolving from 6 months to five years. Indeed, the subjects were young, and most of them were still at school or had not yet embarked on a professional career. This finding has been reported in a number of studies^{2,21}.

In the general population, 9-13% of schizophrenic patients attempt suicide. Suicide attempts generally occur in the early years of the illness, in patients with risk factors such as male gender and insidious onset. These risk factors have been cited above as predictors of long DUP, and we therefore deduce that the longer the DUP, the greater the risk of suicide attempt²². In our study, we were unable to establish a statistically significant link between DUP and suicide attempts. This may be explained by the conservative lifestyle and culture of our country.

Regarding substance abuse, our study had found a correlation between long DUP and addictive behaviors. This result was in line with some studies in the literature with, in particular, the study by Souiaiby and colleagues in 2016, who had noted an association between cannabis use and a long DUP in patients suffering from schizophrenia².

Clinically, long DUP was influenced by multiple factors, including insidious onset, predominance of the productive type of schizophrenia, severity of symptomatology on the PANSS, low insight and moderate to severe impairment of the patient's global functioning on the GAF. Our results concur with most of the findings of meta-analyses⁷⁻⁸. Indeed, these factors delay access to care and generate prolonged DUP. It should be noted, however, that some of these studies have shown a correlation between a shorter DUP Malla et al in 2006²³ and a higher remission rate at 2 years, and a lower relapse rate. Our study found no correlation between DUP and the number of hospital admissions and length of stay, a finding in line with the literature²⁴.

The literature describes the influence of DUP on response to treatment. In fact, the longer the DUP, the poorer the therapeutic response. The disease becomes resistant to treatment, which complicates management and considerably impairs prognosis. Indeed, the 2005 study by Marshall and his team analysed 26 studies on this subject and concluded that there was an association between DUP and therapeutic response²⁵. In 2007, a study by P. Singh and colleagues clearly showed that DUP influenced therapeutic response²⁶. Our results confirm the statistically significant association between long DUP and therapeutic resistance.

Declaration of interest

The author declares that he has no conflicts of interest in relation to this article.

V. Conclusion

Our study confirms the correlations of long untreated psychosis duration with certain sociodemographic, clinical and therapeutic variables, joining those described in the literature. For this reason, efforts must be made in the early detection and management of schizophrenic disorders to shorten the UTP, with the aim of improving the prognosis of the illness and the overall functioning of the subject.

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