RELAPSE AND RECURRENCE OF DEPRESSED PATIENTS: A RETROSPECTIVE STUDY

Gerardo Heinze*, Valerio Villamil*, José Cortés*

SUMMARY

Ten per cent of the world's overall population is affected by major depression. It is more common among 20-40 year old women, young people living in cities, bachelors, and people having a family background of alcoholism and suicide. According to its presentation, depression is divided in single and recidivant episodes, in remission, in recovery, in relapsing and in recurrence. While 50% of the depressed people recover after a one-year period, only 18% recover after four-years. Likewise, 70% of the subjects have subsequent depressive episodes, mainly related to stressing psycho-social events.

The goal of this paper was to identify the accumulated probability of recurrence after the first and second major depressive episodes.

During the first stage, 385 records belonging to major depression subjects were reviewed. Through these records, the number of depressive symptoms each patient had through his/her lifetime; onset date; remission; whether patients received any specialized attention, and any periods of time where patients showed no symptoms were researched. Only those patients who were first attended at this institute were included in the second stage. Two hundred and twenty-eight of them fell into these criteria. For statistical analysis, X^2 test, Kaplan-Meyer's test, and Log Rank test were used.

Results showed the following average ages: 42 years for single episodes, 50 years for relapses, and 48 years for recurrences. While anxiety disorders were more commonly related to single episodes, cluster C appeared more frequently in the three groups; psycho-social stress was more closely related to relapses; the accumulated probability of depression showed that the older the patient was, the higher the probability of having a depression relapse (r = 0.504; p = 0.0003). Tryciclics were the most commonly prescribed drugs in both stages. While dropping-out the treatment after a single major depressive episode significantly predicted recurrence (p= 0.002), it was not the case after a second depressive episode (p= 0.44).

Although our results resemble those reported in the international bibliography, it would be advisable to expand our sample in the future.

Key words: Depression, relapses, recurrences, accumulated probability.

RESUMEN

La depresión mayor afecta a 10% de la población mundial, y es más frecuente en las mujeres de 20 a 40 años, en los solteros jóvenes, en los que viven en la ciudad y en los que tienen antecedentes familiares de alcoholismo y suicidio. Según su presentación, la depresión se divide en episodio único y recidivante, en remisión, en recuperación, en recaída o en recurrencia. El 50% de los sujetos deprimidos se recuperan al año, mientras que cuatro años después sólo se recupera el 18%. El 70% de los sujetos vuelve a tener episodios depresivos subsecuentes relacionados, principalmente, con experiencias psicosociales estresantes .

El objetivo del presente trabajo fue el de identificar la probabilidad acumulada de recurrencia después del primero y del segundo episodios de depresión mayor.

En la primera fase se revisaron 385 expedientes de sujetos con depresión mayor, en quienes se investigó el número de cuadros depresivos que había tenido el paciente a lo largo de su vida, la fecha de inicio, su remisión, si recibió o no atención especializada y el periodo que permaneció asintomático. En la segunda fase sólo se incluyó a los sujetos que fueron atendidos desde el principio en este instituto; 228 pacientes cumplieron con este criterio. Para el análisis estadístico se utilizó la X^2, la prueba de Kaplan-Meyer y la prueba Log Rank.

Los resultados mostraron que el episodio único se presentaba, en promedio, a los 42 años; las recaídas a los 50 años y las recurrencias a los 48 años. Los trastornos de ansiedad se relacionaron más frecuentemente con el episodio único, mientras que el cluster C se presentó con más frecuencia en los 3 grupos. El estrés psicosocial estuvo más relacionado con las recaídas, y la probabilidad acumulada de desarrollar depresión mostró que a mayor edad más probabilidades tenía el paciente de recaer en depresión (r= 0.504; p= 0.0003). Los medicamentos que más se prescribieron en ambas fases fueron los tricíclicos. El abandono del tratamiento predijo, significativamente, la recurrencia después del primer episodio depresivo mayor (p= 0.002), pero no después del segundo episodio depresivo (p=0.44).

Nuestros resultados son similares a los reportados en la bibliografía internacional, aunque sería conveniente ampliar nuestra muestra en el futuro.

Palabras clave: Depresión, recaídas, recurrencias, probabilidad acumulada.

INTRODUCTION

Major Depressive Disorder (MDD), also called Unipolar Depression in the DSM-IV, affects at least 12% women and 8% men according to the epidemiological studies of the United States. One of its main complications is suicide in 15% of the depressed patients, more in men than in women (1). Age of onset varies depending on sex. It is more frequent in women between 18 and 29 years, and between 30 and 44 years; and in men, between 30 and 44 years. Average age in both groups is from 20 to 40 years. On the other hand, epidemiological studies reported that depression is more frequent among young adults of medium age, single or divorced, living in cities (in twice as many when they live alone). Family history of suicide or alcoholism should also be considered, as it is more common among depressed patients than in controls (1, 8, 10, 16).

According to its presentation, MDD is classified as "a single episode" when it is the first time the patient experiences a major depression episode (MD) in his/her life, and as relapse or recurrent episode when he/she presents once and again the same symptoms after their total remission between episodes. The new episodes are classified as relapses and recurrences. Relapse refers to the depressive symptoms presented during the first six months after having remitted the last depressive symptom; and recurrence refers to the presence of depressive symptoms after six months of having remitted from the last depressive symptom; in both cases, the *sine qua non* condition is the total remission of symptoms during an interepisodic period of at least two months (1, 8). Frank et al. (1991) revised the concepts: **episode, remission, recovery, relapse** and **recurrence** in depression, and mentioned that an **episode** is the period during which the patient presents enough depressive disorder symptoms to be considered as such. **Partial remission** is the period during which an improvement of some magnitude is observed, therefore the episode does not comply entirely with the depressive disorder criteria, though the remaining symptoms are not light. **Total remission** is an improvement of such a magnitude that the patient seems asymptomatic, that is, his/her symptoms do not meet the criteria of a disorder. **Recovery** is the remission of symptoms during a determined period (days, months, years or indefinitely). This term designs the recovery occurring after the end of the episode but it is not the end of the illness *per se*, that is, the subject improved, but he/she is not healthy. **Relapse** is the return of symptoms meeting all criteria for an episode during the remission period, but before recovery. **Recurrence** is the presentation of a new MD episode that may only occur during recovery. These definitions do not include the duration of each one of them, for they are mainly clinic (6, 14).

Keller reported in one of his works that 50% of the patients presenting their first depressive episode recovered during the first year; 28% during the second year; 22% during the third year, and only 18% during the fourth year; 3% had a complete interepisodic recovery from recurrent episodes, and 25% did not have a complete interepisodic recovery from recurrent episodes (9, 4). Bibliography reports that 70% of the patients having a first MD episode suffer subsequent depressive episodes, generally related to psycho-social stressors. Other authors mention that there is a high prevalence of recurrent depression among women, young adults and uneducated people, besides a high association between psycho-social stress and the first MD episode, and probable vulnerability due to transcription factors in the proto-oncogen c-fos (1, 2, 4, 5, 9, 13).

The purpose of this work is to identify the accumulated probability of recurrence after the first and second MD episodes.

METHOD

Four hundred and fifty patients of the National Institute of Psychiatry Ramón de la Fuente, who had attended regularly the out-patient service between 1987 and 1999 (at least five times during two years), meeting the MD diagnostic criteria according to the DSM, were selected from the records.

From these records, the number of MD episodes presented by the patient during his/her lifetime were investigated, considering as "zero point" the date in which the patient identified his/her symptoms for the first time. The date of each episode was determined, as well as that of its remission, whether he/she received psychiatric, medical or psychological attention, and the time he/she remained asymptomatic. Sixty-five patients with incomplete, unprecise or confusing records were excluded from the study, therefore only 385 patients (319 women and 66 men) remained.

We considered only those patients who received their first care at this Institute. Only 228 patients (193 women and 35 men) met these criteria. The onset of the disorder, its duration, recurrences during treatment at this institution, the time they lasted and the patient's therapeutic adherence were clearly stated.

In the 228 records, the following variables were considered: gender, age of patients classified in two groups (less than 40 years and more than 40 years), comorbidity with Axis I and II, psycho-social stress

and therapeutic adherence (good therapeutic adherence referred to those patients who accepted treatment and took their medicines as prescribed; and poor therapeutic adherence referred to those patients who did not take their medicines as prescribed, and dropped-out from the treatment).

STATISTICAL ANALYSIS

The X^2 test was used for categorical variables. The probability of recurrence was established with Kaplan-Meyer's test, and for estimating differences between overlife curves in categorical variables, the Log Rank test was used.

RESULTS

First stage

The results obtained show that from the 385 patients studied in the first stage, 51.2% had experienced a single MD episode, 36.4% recurrences, 5.5% relapses and in 6% of the patients the depressive episodes presented during their lifetime were not identified (graphic 1).

GRAPHIC 1
Distribution of subjects according to the type of episode presented at their first consultation (385 subjects)
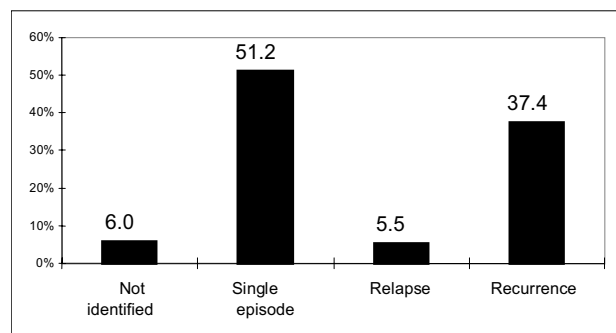

Patients with a single MD episode were 41.84 years in average, with 49.97-year relapses and with 47.69-year recurrences (graphic 2). The most frequent axis I comorbidity in those patients with a single episode were anxiety disorders in 43%; for relapses with psychotic and dysthymic disorders in 30%, and for recurrences with anxiety disorders in 33%, and with dysthymic disorders in 35% (graphic 3). According to axis II, the three groups were mostly related with cluster C personality disorders (single episode = 16%; relapse = 4%; recurrence = 23%) (graphic 4). Psycho-social stress conditioned the
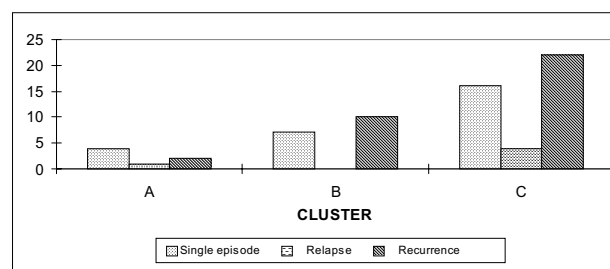
GRAPHIC 2
Patients average age according to the type of episode presented (385 subjects)
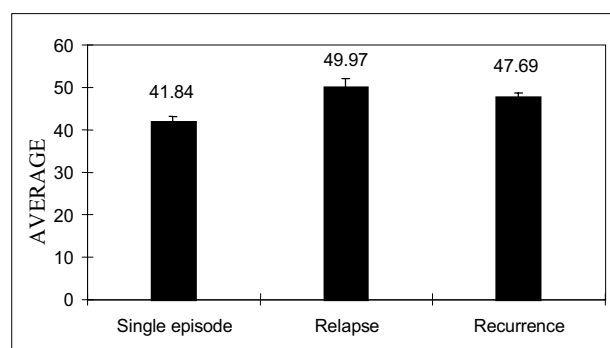
GRAPHIC 3
Distribution of Axis I comorbidity according to the type of episode (385 subjects)
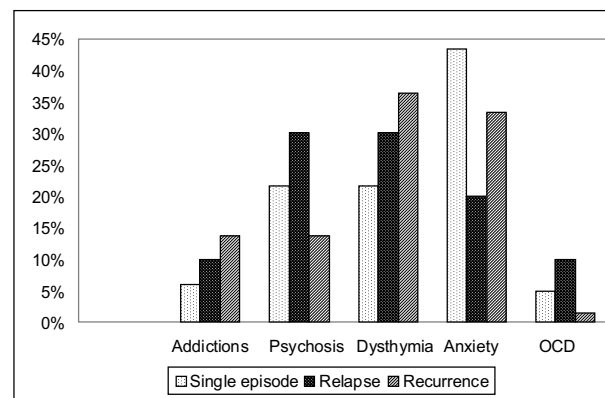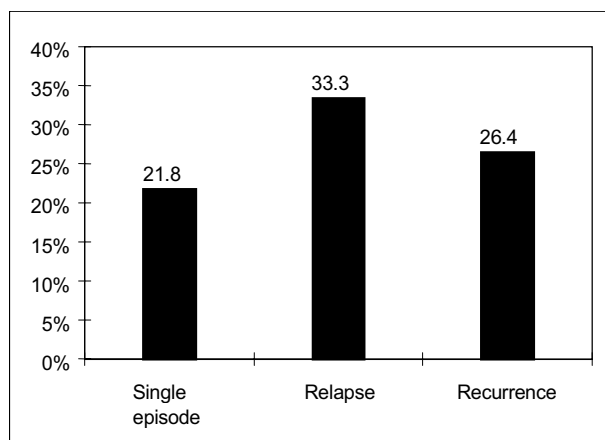

GRAPHIC 4
Distribution of Axis II comorbidity according to the type of episode (385 subjects)
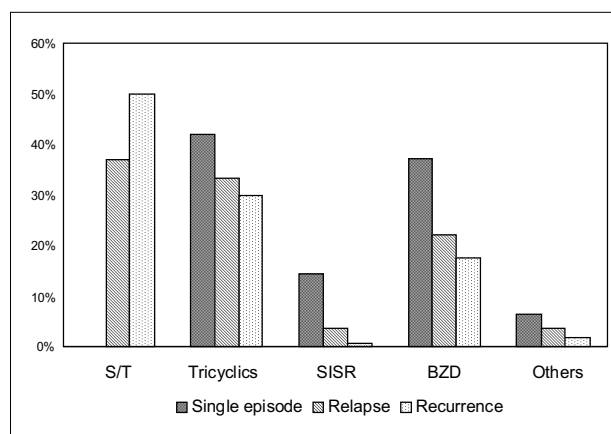

presence of relapse episodes in 33.3% of the patients; of recurrence in 26.4%, and of a single episode in 21.8% (graphic 5). From all patients who had suffered recurrences or relapses, from 37% to 50% had not received any previous treatment before attending this hospital. The most commonly prescribed drugs to the three groups were tricyclics (28-42%) and benzodiazepines (15-35%). Selective
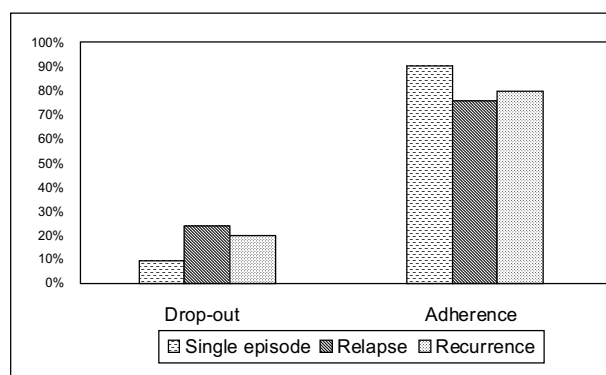
Distribution according to psycho-social stressor and type of episode

Distribution according to therapeutic adherence and type of episode

Distribution according to treatment received and type of episode

inhibitors of serotonin recapture were generally indicated in 12% of those with a single episode (graphic 6). Therapeutic adherence in all groups was from 80% to 90 %. Drop-outs were mainly related with relapses and recurrences in 18 to 22% of the patients (graphic 7).

Women were more likely to present a new depressive episode, even though no differences were found when compared with men (log rank = 9.18; p = 0.972). No significative differences were found with axis I and axis II comorbidities, nor with age after a 24-month follow-up (table 1).

Second stage

Considering only those patients who were attended for the very first time at this institute (228 subjects), it was found that 84.7% were women and 15.3% men (log rank = 0.60; p = 0.44), and 67% were more than 40 years. The accumulated probability

TABLE 1
Accumulated probability of presenting the first recurrence after a major depressive episode

	3 months	6 months	12 months	24 months	p (log rank)
Global	89.9%	80.7%	68.0%	62.7%	
NIMH Study	95.0%	87.0%	75.0%	58.0%	
Gender					
Masculine	97.1%	88.6%	71.4%	60.0%	
Feminine	88.6%	79.3%	67.4%	63.2%	0.972
Axis I Comorbidity					
Yes	86.3%	75.8%	64.2%	60.0%	
No	92.48%	80.5%	68.4%	62.1%	0.359
Axis II Comorbidity					
Yes	87.0%	81.5%	66.7%	64.8%	
No	90.8%	80.5%	68.4%	62.1%	0.779
Drop-out					
Yes	83.6%	70.2%	53.7%	49.3%	
No	92.6%	85.1%	73.9%	68.3%	0.002
Age					
≤ 40 years	90.7%	84.0%	69.3%	62.7%	
> 40 years	89.5%	79.1%	67.3%	62.8%	0.855

TABLE 2
Accumulated probability of recurrence after recovering from a depressive episode. Comparison between NIP and NIMH (385 subjects)

	n	3 months	6 months	12 months	24 months
First					
NIP	228	10.10%	19.30%	32.00%	37.30%
NIMH	318	5.00%	13.00%	25.00%	42.00%
Second					
NIP	85	14.10%	24.70%	41.20%	56.50%
NIMH	172	9.00%	22.00%	41.00%	59.00%

GRAPHIC 8
Accumulated probability of recurrence after recovering from a major depressive episode (228 subjects)

GRAPHIC 9
Accumulated probability of recovery from the first major depressive episode. Therapeutic adherence (228 subjects)

Log Rank (1) = 9.18, p = 0.002

of recurrence after the first MD episode (228 subjects) was 10.1% after 3 months; 19.3% after 6 months; 32.0% after 12 months and 37.3% after 24 months. In the second MD episode (85 subjects), the accumulated probability of recurrence after the second depressive episode was 14.1% after 3 months, 27.7% after 6 months, 41.2% after 12 months and 56.5% after 24 months (table 2). When we analyzed the time between the first and the second recurrence after the 24-month follow-up, a statistically significative correlation was found (r = 0.504; p = 0.0003) (graphic 8).
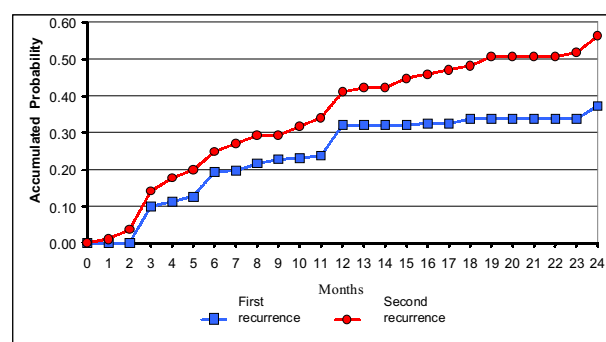
On the other hand, a poor therapeutic adherence proved to be an statistically significative predictor for a new depressive episode after recovery from the first depressive episode after the 24 follow-up months (p = 0.002) (graphic 9), but not for predicting the second depressive episode (p=0.44) (graphic 10).
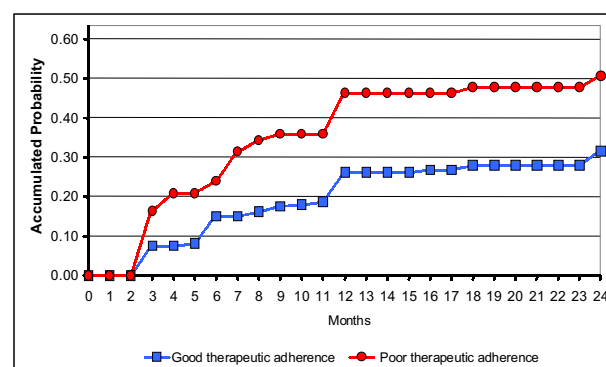
CONCLUSION

From these results we may conclude that 51% of the patients presented their first MD episode at an average age of 42 years; relapses at 50 years and recurrences at 48 years. MD comorbidity was generally associated with anxiety, psychotic and dysthymic disorders, as well as with cluster C personality disorders. Psycho-social stress was present in all three types of episodes (in single episode, in relapses and in recurrences), however, it was more frequently associated with relapses. The common treatment received by patients with a single episode were tricyclics and benzodiazepines, and all three groups had a good adherence. In the graphics of the accumulated probability of depression, we observed that older patients were at a higher risk of relapsing; women were more susceptible than men, even though no statistical significance existed among groups. Finally, dropping-out from treatment predicted significant accumulated probability of recurrence after the first MD episode but not after the second depressive episode.

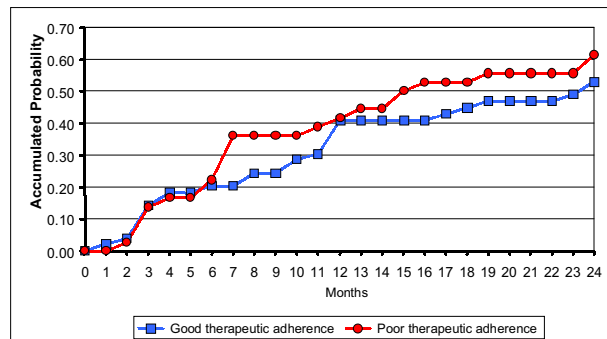Our results are in accordance with those reported by the international research, as many of the epidemiological studies show that the age of onset for the first depressive episode varies between 30 to 40 years. Our findings show an age of onset of 42 years, which is slightly higher than the one described in world bibliography. However, it must be mentioned that the National Institute of Psychiatry Ramón de la Fuente is mainly dedicated to the attention of adults of more than 18 years (1, 8).

On the other hand, studies on the comorbidity of depressive illness have been contradictory and frustrating, as there is no proof of an specific pattern of the association of depression with any other nosologic entity, however, some studies indicate that there is more association with anxious, psychotic and dysthymic spectrum disorders of axis I and with cluster C of axis II; these data were also found in our study (7, 12, 15).

Psycho-social stress is another very important varia-

Accumulated probability of relapse after recovering from the second major depressive episode. Therapeutic adherence (228 subjects)

Log Rank (1) = 0.60, p = 0.44

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ble in depressed patients, as their environment might cause a poor emotional adjustment which may result in new depressive episodes (depressive illness is described as the result of poor social and cultural environments). Our results confirm this association, which is closer in the case of relapses than in that of recurrences. Probably this finding is one of the most important causes for determining that MD is more frequent in women than in men, as women are more vulnerable to environmental factors (3, 11).

Poor therapeutic adherence showed an statistical significance for predicting the first MD recurrence. We might think that if a poor therapeutic adherence was related to the first recurrence, then the same relation should be expected with the subsequent recurrence. However, our study did not find such an association with the latter, but the small size of our sample, which decreased in 50% (from 228 to 85 subjects) could be a probable cause, as not all patients suffering from a first relapse, experienced a second one.

Finally, when correlating the first and the second depressive episodes, we found an statistical significance for predicting a new depressive episode (graphic 8). These results were similar to those found by the National Institute of Mental Health of the United States (Keller, 1997) (4). However, as our study only compared the first and the second recurrences during two years, confirmation by further research is required.

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