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Early *versus* late-onset major depression in the elderly: a comparative study

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ABSTRACT

Aims: This study aims to investigate the distinctive characteristics between elderly with early-onset and late-onset major depression with respect to sociodemographic factors, self-perceived health, cardiovascular risk factors, MMSE scores, family history of depression, depressive symptoms, melancholic features, suicide risk and alcohol abuse/dependence.

Methods: Cross-sectional, descriptive and analytic study, with prospective data collection, in an random sample of 348 elderly people (≥60 years old) of the Family Heath Strategy, of which were identified 90 cases of DSM-IV unipolar major depression; subjects were divided according to early or late (≥60) age at onset of depression.

Results: The prevalence of major depression in the whole sample was 25.86%. The elderly subjects with depression were mainly of early-onset (69.14%) and female (74.4%); the mean age in years was higher in the late-onset major depression group ($p=0.028$); the groups did not differ with respect to the other factors; after multivariate analysis there was a trend toward a negative association between suicide risk and late-onset depression.

Conclusion: The early or late age at onset of depressive symptoms was not associated with different profiles. The results of this paper give support to the hypothesis that early- and late-onset major depressive disorders are clinically undistinguishable and do not represent distinct pathologies or subtypes.

INTRODUCTION

Depression is one of the most relevant mental disorders in the elderly, causing great distress for both patients and caregivers. It is linked to increased disability associated with physical diseases and cognitive disorders, greater health care costs and higher mortality[1]. Within the primary care setting, some 6.5% to 22.4% of the elderly have a diagnosis of major depression[2].

An important point of discussion when considering depression in the elderly is the distinction between those who experience their first major depressive episode in the first decades of life (early-onset depression), and those whose first symptoms occur in later life (late-onset depression)[3]. This distinction brings with it differences in etiology, clinical features and comorbidities[3,4,5].

While there is no consensus in the literature regarding the age at which onset of depression can be considered late, a cut-off point of 60 years has been adopted in the majority of studies conducted since the 1980s[6], through the 1990s[7], and on till the present day[8,9]. It is possible, therefore, to define early-onset major depression (EOD) as that which begins at or before the age of 59 years, and late-onset major depression (LOD) as that which begins from 60 years onwards.

One of the most recurrent findings in comparative studies is the association between EOD and the presence of a positive family history of depression, a fact that suggests a genetic etiology[7,10,11,12]. Some authors, however, have found no such association[8,13,14,15,16].

No identifiable consensus could be found in the literature regarding the existence of significant differences for other clinical characteristics. When looking at LOD, for example, Krishnan et al.[17] described increased loss of interest and fewer ideas of guilt, Heun et al.[18] observed less ideas of guilt, Rapp et al.[19] identified increased anhedonia and cognitive impairment, Brodaty et al.[20] reported more hypochondriasis and intense thoughts of guilt, Corruble et al.[21] noted more lassitude and apparent sadness and, finally, Gallagher et al.[22] found greater cognitive impairment and less feelings of guilt or thoughts of worthlessness. However, many studies have reported no significant differences regarding these and other symptoms[10,13,15].

In relation to depressive symptoms presenting as melancholia, Devanand et al.[12] found a positive association with EOD, although the majority of researchers have observed no significant differences between EOD or LOD and melancholia[10,14,20,23,24]. On the subject of suicide risk, many studies have been unable to detect differences between EOD and LOD[13,18,21,22,25]. Lyness et al.[26] however, found a positive association between LOD and a history of attempted suicide in a hospital sample of the elderly. Conversely, Reynolds et al.[27] found an association between EOD and history of attempted suicide in a sample of elderly outpatients, whilst Janssen et al.[15] found a higher frequency of suicide ideation among a community sample of the elderly with EOD.

Many authors argue that there is a division in the etiology of depressive disorders in the elderly, with early-onset cases being associated with genetic and psychosocial factors, and late-onset cases being associated with cardiovascular disease[10]. However, some researchers have found no relationship between age at first onset of depression and cardiovascular factors[8,12,13,15,17,22,28].

Several studies have found differences in relation to cognition, but the results are conflicting. For example, some authors found lower scores in the Mini Mental State Examination (MMSE) for LOD[6,22,29], while other studies have found no such differences[7,11,13,15,18,25].

There are few studies, to date, regarding the association between age at first onset of depressive symptoms and alcoholism. A sample of 839 elderly British people[30] with a prior diagnosis of major depression and having died by suicide revealed that cases of LOD presented a lower frequency of past history of alcoholism.

This study involving a sample of elderly Brazilians living in an area covered by the Family Health Strategy (FHS), aimed to estimate the prevalence of EOD and LOD, and to examine their distinguishing sociodemographic and clinical features.

METHODS

This research forms part of the Multidimensional Study of the Elderly in the Family Health Strategy in Porto Alegre (EMI-SUS – *Estudo Multidimensional dos Idosos do Sistema Únicio de Saúde do Brasil)*, developed by the Institute of Geriatrics and Gerontology at the Pontifical Catholic University of Rio Grande do Sul (IGG/PUCRS) in association with the Municipal Secretariat of Health of Porto Alegre. The study is of a cross-sectional observational design, with prospective collection from a convenience sample taken from the elderly population covered by the FHS in Porto Alegre. A total of 348 individuals, all 60 years old or above, were selected from the catchment areas of 18 FHS teams.

Other than for the calculation of prevalence of major depression, the only people included in this

study were those with a diagnosis of a major depressive episode. The dependent variable chosen was major depression according to age at first onset (early or late), which includes subjects with a history of at least one previous or current episode of major depression. The independent variables adopted were: age, gender, race, marital status, widowhood, education attendance, living arrangements (whether alone or with spouse/family), retirement status, current paid employment, income, self-perceived health, diabetes mellitus, hypertension, smoker, cognitive deficit, Mini Mental State Examination (MMSE) score, family history of depression, loss of interest or pleasure, psychomotor agitation/retardation, feelings of worthlessness or excessive guilt, melancholic characteristics, suicide risk, and current or prior alcohol abuse/dependence.

Self-perceived health and sociodemographic and cardiovascular risk factors were collected by means of a global assessment questionnaire for the elderly, organized by researchers of EMI-SUS and applied by trained community health workers. The identification of major depressive episodes, depressive symptoms, melancholic features, alcohol abuse or dependence, and suicide risk was carried out by psychiatrists with experience in evaluating the elderly through the use of the diagnostic instrument, the Mini International Neuropsychiatric Interview 5.0.0 plus – Brazilian version (M.I.N.I. Plus), which is validated in the Portuguese language and produces diagnoses according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)[31]. Details of any family history of depression were also recorded at the same time. Global cognitive function was evaluated through application of the MMSE[32] by a board-certified neurologist with expertise in neurodegenerative disorders. The cut-off point used to define cognitive impairment was that proposed by Bertolucci et al.[33] who validated the MMSE for Brazil: 13 points for illiterate; 18 points for those with 1 to 7 years of education; and 26 points for people with 8 or more years of schooling.

Data was entered and analyzed using the IBM SPSS Statistics for Windows software, version 18. Categorical variables were described as frequencies and continuous variables as means and standard deviations. Differences were considered to be statistically significant when values corresponded to $p<0.05$. The chi-square test was used to compare the frequencies of categorical variables between the groups with EOD and LOD. Fisher's exact test was used for those analyses that presented an expected frequency of less than 5 in one or more cells.

Student's t-test (*two-tailed*) for independent samples was used in the comparison of the means of the continuous variables (age and MMSE score) between the groups with EOD and LOD (taking into consideration the equality of variance as determined by Levine's test). Binary logistic regression using the forced entry method was employed to determine the set of independent variables that best predicts late-onset major depression. *Cox and Snell's* and *Nagelkerke's* R^2 tests were used to calculate the pseudo R^2 as a goodness-of-fit measure.

The project was approved by the research and ethics committees of PUCRS and Municipal Secretariat of Health of Porto Alegre. All participants were clearly informed regarding the objectives and methods of the research and all signed a consent form.

RESULTS

A total of 90 cases of major depression (prevalence: 25.9%) were identified from the total sample of 348 subjects. Of these cases, 56 (16.1% of total sample) presented a history of at least one previous, but not current, major depressive episode, whilst 34 (9.8% of total sample) had a current major depressive episode, with or without a previous history. Of all the cases of depression, 74.4% were female. The record for age at first onset of depression was available in 81 cases and these formed the comparative analysis subgroups, with 56 (69.1%) being early-onset and 25 (30.9%) being late-onset for depression.

It can be seen from the variables of self-perceived health and sociodemographic and cardiovascular risk factors, that only the current age was significantly different between those cases with EOD and LOD, as shown in Table 1. The mean ($\pm$SD) age in years was higher for the group with LOD (69.3$\pm$6.8) than for the EOD group (66.1$\pm$5.5), using Student's t-test for independent samples ($P=0.028$).

Table 2 demonstrates that no statistically significant difference was found between the groups with EOD and LOD in relation to the MMSE scores, family history of depression, depressive symptoms, melancholic characteristics, suicide risk, and alcohol abuse/dependence.

A binary logistic regression was carried out to evaluate the impact of a group of predictors on the differentiation between cases of EOD and LOD, as can be seen in Table 3. The final model contained four independent variables (age, family history of depression, psychomotor agitation/retardation, suicide risk). The dependent variable (major depression according to age of first onset) was coded, taking EOD as the reference category. The complete model, containing all the predictors, was statistically significant ($P=0.008$),

indicating that it has been able to distinguish the cases of LOD from those of EOD; the pseudo R^2 was 0.156 (*Cox and Snell* R^2) and 0.22 (*Nagelkerke* R^2). The model correctly classified 92.9% of EOD cases and 44% of LOD cases, making a total of 77.8%. A positive association was verified between age in years and LOD ($p=0.026$, OR=1.105, CI 95%=1.012-1.205). A trend of negative association was also found between suicide risk and LOD but without statistical significance ($P=0.059$).

Table 1. Distribution of age, age at depression onset, sociodemographic variables and cardiovascular risk factors in an elderly population with a diagnosis of EOD or LOD.

Variable	Early-onset N (%) (n=56)	Late-onset N (%) (n=25)	*P*
Age in years (m±sd)	66.14±5.479	69.32±6.787	0.028
Age at depression onset in years (m±sd)	41.21±15.193	65.44±4.891	<0.0005
Gender			
Male	13 (23.2)	7 (28.0)	0.645
Female	43 (76.8)	18 (72.0)	
Race			
White	34 (61.8)	15 (60.0)	0.877
Non-white	21 (38.2)	10 (40.0)	
Married			
Yes	15 (27.3)	9 (36.0)	0.430
No	40 (72.7)	16 (64.0)	
Widowed			
Yes	24 (43.6)	10 (40.0)	0.760
No	31 (56.4)	15 (60.0)	
Attended school			
Yes	48 (85.7)	19 (76.0)	0.344*
No	8 (14.3)	6 (24.0)	
Living arrangements			
Alone	14 (25.0)	7 (28.0)	0.776
Spouse and/or family	42 (75.0)	18 (72.0)	
Retired			
Yes	38 (67.9)	17 (68.0)	0.990
No	18 (32.1)	8 (32.0)	
Currently in paid employment			
Yes	9 (16.1)	6 (24.0)	0.536*
No	47 (83.9)	19 (76.0)	
Income			
Up to 1 minimum salary**	40 (75.5)	16 (66.7)	0.422
More than 1 minimum salary	13 (24.5)	8 (33.3)	
Self-perceived health			
Excellent/good	14 (25.0)	6 (24.0)	0.478
Normal	32 (57.1)	17 (68.0)	
Poor/Very poor	10 (17.9)	2 (8.0)	
Hypertension			
Yes	38 (67.9)	17 (68.0)	0.990
No	18 (32.1)	8 (32.0)	
Diabetes mellitus			
Yes	13 (23.2)	6 (24.0)	0.939
No	43 (76.8)	19 (76.0)	
Smoker			
Yes	30 (53.6)	13 (52.0)	0.896
No	26 (46.4)	12 (48.0)	

* Fisher's exact test
** Minimum salary is the lowest legal monthly income for an employee in Brazil. The amount is set by the government.

Table 2. Distribution of MMSE scores, family history of depression, depressive symptoms, melancholic characteristics, suicide risk, and alcohol abuse/dependence in an elderly population with a diagnosis of EOD or LOD.

Variable	Early-onset N (%) (n=56)	Late-onset N (%) (n=25)	*P*
MMSE (m±sd)	22.77±5.37	22.92±4.393	0.909
Family history of depression			
Yes	24 (42.9)	6 (24.0)	0.104
No	32 (57.1)	19 (76.0)	
Loss of interest or pleasure			
Yes	46 (82.1)	21 (84.0)	1.000*
No	10 (17.9)	4 (16.0)	
Psychomotor agitation/retardation			
Yes	44 (78.6)	23 (92.0)	0.206*
No	12 (21.4)	2 (8.0)	
Worthlessness/guilt			
Yes	34 (60.7)	17 (68.0)	0.531
No	22 (39.3)	8 (32.0)	
Melancholic characteristics			
Yes	13 (68.4)	8 (72.7)	1.000*
No	6 (31.6)	3 (27.3)	
Suicide risk			
Yes	23 (41.1)	6 (24.0)	0.139
No	33 (58.9)	19 (76.0)	
Alcohol: current abuse/dependence			
Yes	2 (3.6)	2 (8.0)	0.583*
No	54 (96.4)	23 (92.0)	
Alcohol: prior abuse/dependence			
Yes	10 (17.9)	2 (8.0)	0.325*
No	46 (82.1)	23 (92.0)	

* Fisher's exact test.

Table 3. Binary logistic regression showing the association of a model of four predictors (independent variables) with age at onset of depression (dependent variable) in an elderly population with a diagnosis of EOD or LOD. The EOD is the reference category. The odds ratio (OR) represents the likelihood of belonging to the LOD group related to the independent variable.

Variable	B	EP	Wald	df	*P*	OR	CI 95% for OR
Age in years	0.099	0.045	4.971	1	0.026	1.105	1.012-1.205
Family history of depression	-0.944	0.574	2.711	1	0.100	0.389	0.126-1.197
Psychomotor agitation/retardation	1.214	0.830	2.141	1	0.143	3.368	0.662-17.128
Suicide risk	-1.131	0.598	3.573	1	0.059	0.323	0.1-1.043

DISCUSSION

This study involving an elderly population with EOD and LOD in a representative sample from areas covered by the FHS in Brazil, investigated differences regarding the clinical condition and several associated factors, including sociodemographic, cognitive, cardiovascular risk and alcoholism factors. To our knowledge, it is the first such study on this topic in this country.

One of the most important results of the research was the high prevalence of major depression found (25.6%), which exceeded the level usually described in the literature for primary care environments[2]. This may be due to two reasons: firstly, the predominance of females in the sample as women are more likely to experience depression than men[34]; and secondly, the cases come from a socioeconomically disadvantaged population, a factor that has been associated with higher prevalence of depression[35]. In addition, the

data reflects not only the current prevalence, but also the prevalence of major depression over a lifetime. A study conducted in 2004 with 1,873 community-living, elderly French people (65 years of age or more) using the MINI psychiatric diagnostic instrument[36], found a prevalence of 26.5% for major depression over a lifetime, similar to that encountered in this present study.

The prevalence rates found for the age of early- or late-onset are similar to those described for outpatients by Kessing (18,192 elderly people)[23], by Corruble et al.[21] (6,850 elderly people) and by other authors[16,37], but not by all[12,25]. This finding, however, will need to be the subject of further research as few reports in this field systematically describe the prevalence rates according to age at first onset of symptoms[3].

The subjects with LOD had a significantly higher mean age. The positive association of late-onset of symptoms with the current age is one of the most frequently found characteristics in the literature. A possible explanation for this would be the association of early-onset depression with increased morbidity and mortality, as suggested by Van Ojen et al[38]. Increased time of exposure to a mood disorder may reduce the chances of survival into later life. Other possible explanations include recall bias in which older individuals may tend to more easily forget previous episodes of depression, especially if mild, and also the phenomenon known as the telescoping effect, whereby memories of a crisis that occurred many years before may be perceived as a more recent event[25]. As such, long-term longitudinal studies are required in order to avoid these potential confounding factors.

No significant difference was found between the subjects in terms of gender, race, marital status, widowhood, education, whether living alone or with spouse/family, retirement, current employment, income and self-perceived health. Similar results to these have been obtained by other authors[22,39]. It is possible, however, that a more in-depth evaluation of factors such as bereavement or social support network may arrive at different results. For example, Grace et al.[14] reported that individuals with early-onset depression told of more experiences of bereavement over their lifetime and had less support from a confidante than those individuals with late-onset depression. In relation to self-perceived health, Sneed et al.[40] identified that women with LOD were more likely to report poorer health, although this difference was not statistically significant.

The results of this present study in relation to global cognition support those obtained by other authors[15] who found no differences in the mean scores for the MMSE. However, a recent study carried out in Dublin[22] found a negative association between the MMSE score and late-onset depression. The higher level of education found in this sample of community-living elderly people may partly explain this discrepancy, and in addition, the Irish study did not define cases according to the major depression diagnostic criteria, as set out by the DSM-IV.

The groups did not differ in terms of the presence of cardiovascular risk factors (diabetes, hypertension and smoking). This contradicts the findings of an association between LOD and cardiovascular risk factors, originally reported by Baldwin et al.[7] in 1995, and subsequently replicated by others[16,19,27]. It is possible that differences in recruitment may have contributed to this disparity as the majority of the cited studies investigated populations from specialized reference centers. Furthermore, the results of this present research are supported by a large number of studies that also found no differences[12,15,22,28] and may signify that cardiovascular risk factors play an equally important role in the etiology of both EOD and LOD.

Contrary to expectation, no statistically significant difference was found between the two groups with regards to the presence of a family history of depression. This result is consistent with the report by Janssen et al.[15] and when considered together with the lack of difference in the distribution of cardiovascular factors, it may suggest that that the etiological separation between EOD and LOD proposed by certain authors and based on samples from specialist reference centers, does not find support in populations from other environments. In contrast, Gallagher et al.[22] recently found an association between a family history of depression and early-onset depression in a community sample, however, this discrepancy may be explained by the use of less stringent diagnostic criteria for mood disorders.

The groups were also similar with regard to depressive symptoms and melancholic presentation. This would appear to support a large number of studies that obtained similar results, and may mean that there is a continuity of depressive typology throughout life, including old age[10,13,15,23].

No differences were found between the groups for alcohol dependency or abuse and may mean that the etiological importance of this factor is the same for both early- and late-onset cases. However, the low prevalence of alcohol related problems in the sample makes it difficult to generalize the results and they should, therefore, be interpreted with caution. Given the higher association of early-onset cases with psychiatric comorbidities, as observed in the

literature[24], it would seem reasonable to expect that a positive association with EOD would occur with a larger number of elderly people. More studies are needed to clarify this issue.

A trend of negative association between suicide risk and LOD appeared following multivariate analyses, although this did not reach statistical significance. Some authors have reported an association between early age of onset and increased suicide risk, such as Reynolds et al.[27] in an outpatient sample, and Janssen et al.[15] in a community sample. More studies, however, will be needed to clarify the relationship between these variables.

This study has some strengths that should be highlighted. Firstly, the use of a validated diagnostic instrument for DSM-IV diagnoses enabling a more homogeneous sample to be found; the inclusion of only those subjects with unipolar major depression facilitates the interpretation and comparison of the findings. Secondly, the application of the MINI Plus instrument by trained psychiatrists with expertise in the evaluation of the elderly, which enabled cases to be diagnosed more reliably. And thirdly, the study of the elderly in an area covered by the FHS addresses the needs of a large population of socioeconomically disadvantaged people who are exposed to the consequences of the under diagnosis and treatment of mood disorders.

Some limitations of this study should be mentioned. Firstly, it is possible that the sample was too small to detect certain differences, and it is, therefore, not possible to exclude the Type II error. Secondly, recall bias may have affected the reported age of onset of depression, as already mentioned. Thirdly, knowledge passed on by the elderly about their family history of depression may be inaccurate due to the low educational level and possible cultural limitations of the research sample. Lastly, this sample is formed from elderly people living within the communities served by the FHS teams and, as such, it is probably not representative of the more severe cases as these are generally referred on to specialized services.

In summary, the early or late age at onset of depressive symptoms was not associated with distinct profiles, clinical condition or with risk factors, in this comparative study of elderly individuals with unipolar major depression living in communities belonging to areas covered by the FHS. The results of this research support the hypothesis that EOD and LOD are clinically indistinguishable and do not represent distinct pathologies or subtypes. These findings need to be replicated in future studies involving larger samples, and especially of a longitudinal design.

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