Comorbid Disorders in Outpatients with Major Depressive Disorder and Their Sociodemographical Aspects

Şadiye Visal Buturak[1], Ayşe Devrim Başterzi[1], Aylin Yazıcı[2], Kemal Yazıcı[2], Şenel Tot Acar[2]

ÖZET:

Majör depresyon hastalarında psikiyatrik ekhastalık

Son yıllarda, major depresif bozukluk (MDB) kronikleşmeye eğilimi, tedaviye direnci, etkilediği kişi üzerindeki tüketici semptomatolojisi ve bunlara bağlı yüksek sağlık harcamalarına yol açması nedeniyle, sağlık sistemi üzerinde giderek artan bir yük olmaya başlamıştır. Major depresyon ile birlikteliği bildirilen, diğer ekhastalıkların da bu yüke katkıda bulunduğu düşünülmektedir. Bu çalışmanın amacı major depresyon ile ilgili veri havuzuna, sonraki muhtemel MDB etyolojisine yönelik çalışmalara katkıda bulunmak ve MDB'e ait sağlık harcamaları için bir zemin hazırlamaktır. Bu makale ile Türkiye'de yer alan bir kıyı kenti olan Mersin yöresinde bulunan MDB hastalarının sosyodemografik özellikleri ve bu hastalarda izlenen ekhastalıklara ait verilerimizin değerlendirilmesini sunmaktayız. Bu çalışmada, Mersin Üniversitesi Tıp Fakültesi Ruh Sağlığı ve Hastalıkları Anabilim Dalının arşivleri detaylı bir şekilde taranmış ve MDB tanısı alan hastaların kayıtlarından yaş, cinsiyet, medeni durum, eğitim durumu, meslek, HAM-A (Hamilton Anksiyete Ölçeği) ve HAM-D (Hamilton Depresyon Derecelendirme Ölçeği) değerleri ve ekhastalık verileri elde edilmiştir. 64 (%20) erkek, 247 (%80) kadın olmak üzere toplam 311 hasta kaydı çalışmaya dahil edilmiştir. Sonuçlarımız hastaların %80.7 (251)'inde sadece major depresif bozukluk olduğunu, kalan %19.3 (60)'ında da bir ekhastalık olduğunu açığa çıkarmıştır. Ayrıca eğitim seviyesinde düşüşle beraber konulan MDB tanısın oransal olarak azaldığı ve MDB'a en sık görülen ekhastalığın panik bozukluk olduğu saptanmıştır. Depresif bozukluktaki ekhastalık depresif hecmenin süresini, genel işlevselliği ve tedaviye yanıtı etkiler. Bu nedenle major depresif bozukluk ve ekhastalıkları tanımak önemlidir.

Anahtar sözcükler: Major depresif bozukluk, ekhastalık, epidemiyoloji, sosyo-demografik veri

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ABSTRACT:

Comorbid disorders in outpatients with major depressive disorder and their sociodemographical aspects

In recent years, major depressive disorder (MDD) has began to become a very heavy burden for the public health system due to its various aspects like chronicity, resistant and debilitating symptomatology and apart from that, the eventual health care expenses. Reported comorbid psychiatric diseases are also suspected to be responsible for this burden. The objective of this study is to contribute the epidemiological data pool of MDD and subsequent researches to identify etiological factors of MDD and provide basis for resource managment studies for MDD. In this paper, we present the results of our study concerning the psychiatric comorbidity and sociodemographic aspects of MDD patients in Mersin region of Turkey, a seaside town on Mediterranean peninsula. The archives of our psychiatry department were searched thoroughly for the records of outpatients with established MDD diagnoses for the data about age, sex, marital status, education level, occupation, their HAM-A (Hamilton Anxiety Scale) and HAM-D (Hamilton Depression Rating Scale) scores and comorbidity. A total of 311 patient records 64 male (20%), 247 female (80%) were included in the study. Our results revealed that 80.7% of the subjects (251) were diagnosed as being affected from pure major depressive disorder, while the remaining 19.3% (60) were presented a comorbid psychiatric disorder along with the MDD. Results of this study point out that a decline in MDD diagnoses accompanies the decrease of education levels and MDD's most frequent comorbid psychiatric disorder is panic disorder. Comorbidity in depressive disorder affects the duration of depressive episode, functionality in general, and response to treatment. Hence, it is very important to notify major depressive disorder and its comorbid disorders.

Key words: Major depressive disorder, comorbidity, epidemiology, sociodemographic data

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[1]MD, Department of Psychiatry, Mersin Tarsus State Hospital, Mersin-Turkey
[2]MD, Department of Psychiatry, Mersin University Faculty of Medicine, Mersin-Turkey

Yazışma Adresi / Address reprint requests to: Şadiye Visal Buturak MD, Department of Psychiatry, Mersin Tarsus State Hospital, Mersin-Turkey

Telefon / Phone: +90-324-613-1250

Elektronik posta adresi / E-mail address: visalbuturak@hotmail.com

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INTRODUCTION

Depression is defined as a syndrome including symptoms like slowing down of physiologic functions, slowing of thoughts, speech and motion within a sad mood, and feelings and thoughts of dullness, worthlessness, unwillingness and pessimism (1). The term "major depressive disorder" was favored by the American Psychiatric Association to define this symptom cluster as a mood disorder in the 1980 version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III), and has become widely used since (2). Major depression is a disabling condition which adversely affects a person's family, work or school life, sleeping and

eating habits, and general health.

As stated above, in a major depressive state, the affected person tend to avoid and/or neglect everyday activites. MDD patients also present various behavioral patterns such as overeating, or loss of appetite, lack of interest in once pleasurable experiences, difficulty in concentration, remembering and in making decisions. Insomnia, oversleeping, constant fatigue, aches or pains are also common features of a depressive person (3). All this unpleasant and uncomfortable experiences put the patients under a constant strain which may lead to serious consequences like suicide.

Major depressive disorder (MDD) with a lifetime prevalence of 13%, is a widespread illness (4) affecting 340 million people in the world (5). With its very serious consequences, as stated above and high prevalance (3) MDD has the well-earned fourth place at World Health Organization's list of worldwide emergent health problems (4) and is also reported by WHO to become the most common reason of morbidity in the next century (5).

High risk of recurrence and suicide underlines the importance of early diagnosis and preventive measures for depression (8-10).

Comorbidity studies indicate the presence of at least one psychiatric disorder at a rate of 40-90% and two or more disorders at a rate of 20-50% occurring with major depressive disorder (11-14). Aragonès et al has reported that 45.7% of MDD patients had one another concomitant mental disorder, and 19.9% and 8.3% were affected from two and three more mental disorders, respectively. Also in the same study, generalised anxiety disorder was present in 55.2% of depressed patients, panic disorder in 33.8%, dysthymia in 15.7% and somatisation disorder in 6.6% (15).

The comorbid disorders affects the semptomatology, the risk of recurrence, the duration and the severity of the episode, the general functionality, prognosis and the response to treatment of MDD patients. Quarantini et al have reported that OCD (obsessive-compulsive disorder) patients with comorbid MDD had higher severity scores of OCD symptoms (16). Aragonès et al have noted that in the groups of patients with comorbidity, the depression was more severe and had a greater functional impact (15) pointing out the importance of diagnosing major depressive disorder and comorbid disorders (17). These which also served as basis during designation of our study. Our study is designed to determine the prevalence of other common mental disorders in patients with major depression and to analyse their relation with sociodemographic features.

MATERIALS AND METHODS

Subjects

We analysed the medical notes of 311 patients who attended the outpatient clinic of the psychiatry department of Mersin University Medical Faculty Hospital between 01.03.2003 and 01.09.2003 and with an established single episode major depressive disorder or recurrent major depressive disorder diagnosis. All the diagnosis were established after the application of structured clinical interview for DSM-IV (18) (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) axis I disorders (SCID) (19)– mood disorders section due to DSM-IV criteria at the first assay. All these diagnosis has been established by the psychiatrists who were working in the Psychiatry Department of Mersin University Medical Faculty Hospital. A major depressive episode was diagnosed when at least 2 weeks of persistent depressed mood or anhedonia were present, accompanied by a total of at least 5 or more of the 9 DSM-IV symptoms of major depression during the episode. The patients whose diagnosis were bipolar disorder depressive episode, organic mood disorders and other organic psychiatric disorders were not included to the study.

Procedures

Moreover, test scores that have been obtained from HAM-A and HAM-D tests applied to those patients diagnosed as major depressive disorder by the psychitrists at the first assay and psychiatric comorbidity have been recorded. So that this is a retrospective descriptive study, we have some limitations in this study because of the inadequate datas.

Statistical Analyses

Data were analyzed using the SPSS 11.5 statistical package. Descriptive analysis of all data was made. To evaluate the severity of depression and anxiety between

patients who had just major depressive disorder and who had comorbid disorders, Chi-square method was used for the statistical analysis.

To investigate whether there are any significant differences at HAM-D and HAM-A scores between males and females, between the patients who had just major depressive disorder and who had comorbid disorders, Student T test was conducted. To evaluate the differences at HAM-D and HAM-A scores between the patient groups that had a different educational level, Oneway-Anova test was used and then Tukey test, which is one of the Post-Hoc tests, was conducted.

RESULTS

Analysis of the psychiatric records of the 311 MDD outpatients formed the basis of our study. The median age of the participant individuals was 36.09 (15–80). 251 patients (80.7%) had been diagnosed with solely major depressive disorder, 60 patients (19.3%) with major depressive disorder and comorbid psychiatric disorder (Table 1). 20% of the participants (64) were male and the remaining 80% (247) were female (Table 2). The male/female ratio in the two groups (only MDD, MDD with comorbidity) did not differ significantly. In the "only MDD group", 19.1% (48) of the patients were male, and 80.9% (203) were female (M/F = 19.1/80.9), in the "MDD with comorbidity group" 26.7% (16) of the patients were male, 73.3% (44) were female (M/F = 26.7/73.3).

Table 1: Distribution of the MDD and MDD with comorbidity patients

Psychiatric Disorder	Number and percentage of the participants
Only MDD group	251 (80.7%)
MDD with comorbidity	60 (19.3%)
Total	331 (100.0%)

Abbreviations: MDD, Major Depressive Disorder.

Table 2: Percentages according to sex

Sex	Only MDD	MDD with comorbidity
Male	48 (19.1%)	16 (26.7%)
Female	203 (80.9%)	44 (73.3%)

The number and the ratio of the patients with major depressive disorder and comorbid psychiatric disorders are shown in table 3.

Table 3: The number and the ratio of major depressive disorder and comorbid psychiatric disorders in the patient group

	Frequency	Percentage
Only Major Depressive Disorder	251.00	80.7
Comorbid OCD	17.00	5.50
Comorbid GAD	15.00	4.80
Comorbid Panic Disorder	9.00	2.90
Comorbid Somatization Disorder	4.00	1.30
Comorbid Delusional Disorder	2.00	0.60
Comorbid Social Fobia	1.00	0.30
Comorbid Conversion Disorder	6.00	1.90
Comorbid Anxiety Disorder NOS	1.00	0.30
Comorbid Alcohol Dependency	2.00	0.60
Comorbid Alcohol Abuse	1.00	0.30
Comorbid Anorexia Nervosa	1.00	0.30
Comorbid Brief Psychotic Disorder	1.00	0.30
Total	311.00	100.00

Abbreviations: OCD, obsessive-compulsive disorder; GAD, generalized anxiety disorder; NOS, not otherwise specified.

Analysis of participant's marital status and educational level revealed the following outcome; 80 of the participants were single, 199 were married, 6 were divorced, and 26 were widow or widowers. Among the participants, 9 had not any kind of formal education, 98 were primary school graduates, 113 were high school graduates, 88 were university graduates and, 3 were literate.

When considering marital status; in the "only MDD" group 25.1% of the patients were single, 65.3% married, 1.2% divorced, 8.4% widow or widowers. Marital status of the "MDD with comorbidity" group was; 28.3% single, 58.3% married, 5.0% divorced, 8.3% widow or widowers.

Patient groups regarding their occupations were as follows; in the "only MDD" group 4.8% of the patients were unemployed, 41,8% were housewives, 21.9 % civil servant, 12.0% retired 14.7% students, 1.6% employees, 0.4% military personnel, 0.4% teachers, 2.4% self-employed. In the "MDD with comorbidity" group; 6.7% of the patients were unemployed, 41.7% housewives, 13.3% civil servant, 10.0% retired, 13.3% students, 6.7%

Table 4: Occupational classification of the participants

Occupation	"only MDD"	MDD with comorbidity
Unemployed	4.8%	6.7%
Housewives	41.8%	41.7%
Civil Servant	21.9%	13.3%
Students	14.7%	13.3%
Retired	12.0%	10.0%
Military Personel	0.4%	-
Teachers	0.4%	1.7%
Employees	1.6%	6.7%
Self-employed	2.4%	6.7%

employee, 1.7% teachers, 6.7% were self-employed. (Table 4). Excess number (130) and the high ratios of the housewives in both groups was noteworthy.

The distibution of the participants according to their educational level was as follows; in the "only MDD" group 1.6% of the individuals were found out to have not any kind of formal education. The remaining participants were grouped as follows; 0.8% literate, 29.9% pıimary school graduates, 38.8% high school gratuates, 29.5% university graduates. The groups according to education levels were as follows in the "MDD with comorbidity group"; 8.3% no formal education education, 1.7% literate, 38.3% primary school graduates, 28,3% high school graduates, 23.3% were university graduates.

20.3% (13) of the male patients were primary school graduates, 42.2% (27) were high school graduates, 37.5% (24) were university graduates. Among the male patients there were not one individual in the "no formal education" group. 3.6% (9) of the female patients were in the "no formal education" group, 1.2% (3) were literate, 34.4% (85) were primary school graduates, 34.8% (86) were high school graduates, 25.9% (64) were university graduated.

Table 5: Comparison of the "only MDD" group and "MDD with comorbidity" group according to the educational level of participants

Education Level	Only MDD	MDD with Comorbidity
No Formal Education	(1.6%)	(8.3%)
Literate	(0.8%)	(1.7%)
Primary School Graduates	(29.9%)	(38.3%)
High School Graduates	(38.2%)	(28.3%)
University Graduates	(29.5%)	(23.3%)

Table 6: HAM-D and HAM-A points on different education levels

	Mean	Standard deviation
HAM-D Points		
no formal education	19.11	3.29
primary school graduates	20.21	4.88
high school gratuates	19.40	4.93
University gratuates	17.97	4.23
Literate	23.33	1.52
Total	19.28	4.74
HAM-A Points		
no education	23.00	4.35
primary school graduates	23.25	5.49
high school gratuates	20.83	5.46
university graduates	20.52	6.01
Literate	27.33	0.57
Total	21.63	5.71

While 120 patients (47.8%) with only major depressive disorder presented mild anxiety symptoms, 52 (20.7%) and 12 (4.8%) presented medium and severe anxiety symptoms, respectively. Intensity of anxiety symptoms observed in patients with a comorbid disorder accompanying major depression were as follows; mild anxiety symptoms were presented in 23 patients (38.3%), medium symptoms were presented in 25 patients (41.7%) and, severe sypmtoms in 5 patients (8.3%).

Severity of depression symptoms of patients presented with only major depressive disorder were as follows; mild symptoms in 234 (93.2%), and medium symptoms in 17 (6.8%). 57 patients (95.0%) with an accompanying psychiatric disorder presented with mild depression symptoms and, 3 of them (5.0%) presented with symptoms of medium intensity. Patients with only major depressive disorder had a mean score of 19.4±4.8 in HAM-D points, while the mean HAM-D score of patients with a comorbid disorder was 18.8±4.5, showing no statistically significant difference between two groups($p=0.395$). HAM-A mean scores were 21.1±5.7 and 23.9±5.2 in the only MDD and MDD with a comorbid disorder groups, respectively, revealing a statistically significant difference ($p<0.001$).

Table 6 shows HAM-D and HAM-A points on different education levels.

DISCUSSION

Depression is a common condition in the United States, with 12-month and lifetime prevalence rates of approximately 5 and 13 percent, respectively (20).

A good grasp of MDD epidemiology is of utmost importance for drawing public attention to MDD and further public awareness of MDD, an effective resource managment and also obtaining clues for the etiopathogenic process. Epidemiologic studies must be conducted with meticulous attention, for the obtained information from these studies will probably be constituting the basis of hypotesis of subsequent etiologic studies. Studies to illuminate the etiologic process of MDD became very popular in the last decade and many research groups try to find out biological (21,22), and enviromental factors (23,24) contributing to the pathogenesis of MDD with and without other disorders.

Sex is a prominent risk factor for major depressive disorder. Results of various researches point out the

susceptility of females (25,26). Also consistent with our results, in many societies women have been found to be affected more than men (27). Also specific events affecting only women, like pregancy, childbirth, premenstrual phase etc. are known to facilitate depression (28). High prevalance ratio of depression in women has been tried to clarify by different research groups. According to these groups; men are prone to show different behavior pattern than women in a depression inducing situation; men turn to substance (alcohol)-abuse or show more action-oriented behavioral patterns. Lacking these options, women tend to show more intense pyschological symptoms (29,30).

Low socioeconomic status, low education level and relative young age (18-44) are oher risk factors for depression (31). Mean age of our study group was 36.1±12.9.

It's also stated that marriage is another predisposing factor for women depression. Also stress of a probable divorce or seperation may enhance the susceptibility to depression (32). Our study group also included a great number of married women.

As stated above, low education level increases the risk for depression. Also, these patients are more resistant and have a low chance of positive response to depression therapies. Patients with low socioeconomic status and low education level have a longer interval between the beginnings of symptoms and the start of the therapy. This delay is probably the result of the lack of knowledge of depression and the lack of the knowledge of the access ways to reach depression related facilities (32). Our study revealed statistically significant difference between the Hamilton Anxiety Scale and Hamilton Depression Scale score in patient groups with different education levels. Mean value of the study-group scores was found to be higher in the "low-education level" group. The reason for this result may be that most of the patients who refered to our clinic had low socio-economic levels.

Psychiatric comorbidity of depression is common in primary care. Most depressed patients suffer from other disorders, often anxiety. Psychiatric comorbidity affects the impact, the prognosis and the management of depression (15).

Clinical (33) and epidemiological (34,35) studies find that anxiety and depressive disorders rarely ocur in pure forms. Comorbidity studies revealed that 40-90% of major depressive patients have at least one another concomitant pyschiatric disorder, 20-50% having more than one (11-14). Most frequently reported comorbidities are dysthymia, and anxiety disorders (30-80%) (12,13,36). Results of a 7-year follow-up study conducted by Munich group provided us the means to compare the psychiatric inpatients and the general population, consisting 218 and 1366 adults respectively. Comorbidity of major depression and anxiety disorder was found to affect 67.8% of pyschiatric patient population and 44.4% of general population (37). But this ratio differed greatly between the other studies (79% in Murphy's research (38), 41.6% in Sanderson's (39), 10% in Levitt et al.'s (40) and, 50.6% in Fava et al.'s (41) research). Our study results show the ratio of pyschiatric disorders concomittant to major depressive disorder as 19.3%. The underlying reason of this low ratio can be attributed to the first evaluation datas used in the study. All the patients enrolled to the study were selected according to their first psychiatric examination notes and some obscure or unpronounced symptoms of comorbid diseases might be overlooked and/or not recorded. Patients with anxiety disorder accompanying major depressive disorder corresponds 13.8% of the all the patients in the study group, that indicates anxiety disorder constitutes 72% of the comorbid pyschiatric disorders in major depressive patients and this result is consitent with the previous study results.

Our results reveal that comorbid anxiety disorders observed in major depression, in decreasing order, are as follows; obsessive-compulsive disorder (OCD), generalized anxiety disorder (GAD), panic disorder, social phobia, Anxiety Disorder NOS, but Lydiar and Marshall reported a contradictory ranking for the frequency of comorbid disorders with anxiety disorder being in the first place (42,43). Fava et al reported even more different results. According to Fava et al. Social phobia was the leading comorbidity with a ratio of 27% (41). The following comorbid disorders were as follows; simple phobia 16.9%, panic disorder 14.5%, GAD 10.6%, OCD 6.5% and agoraphobia 5.5% (41). The contradiction between these outcomes may result from the everchanging definitions of the investigated comorbid disorders and/or the routine change of the physicians in the outpatient clinic. Also inclusion of the diagnoses established after the first assay may contribute this difference. Symptoms of the major depressive disorder might have concealed symptoms of

the other comorbid psychiatric disorders at the first examination. Another limitation of our study is that we did not asses the last evaluations of the patients at their last psychiatric examination.

"Hamilton Anxiety Scale" points differs significantly between depression and depression and comorbid psychiatric disorder group. The latter group had higher points in the "Hamilton Anxiety Scale". Considering that anxiety constitutes 72% of the depression accompanying disorders, this result comes as no surprise.

Anxiety disorder and major depression comorbidity may enhance the symptom frequency and intensity. Also these patients have a higher ratio for consulting for psychiatric and general medical services, have more frequent suicide attempts and tend to become chronic and to be less responsive to medical treatment (37). Our results revealed no statistically significant difference for "Hamilton Depression Scale" points between major depressive group and major depression and comorbid disorder group. This can be related to the following causes; resemblance of the symptomatologies of major depressive disorder and anxiety disorder may cause difficulties in differential diagnosis, also patients participating in our study were all outpatients with a lower depression level and "Hamilton Anxiety Scale" contains mainly questions to evaluate somatic complaints.

In our counrty, patients suffering from major depressive disorder frequently express somatic complaints (44), leading us to think that in Turkey, physicological stres is being experienced as somatic complaints.

CONCLUSION

Major depressive disorder is a very common disorder, especially in primary healthcare services. Its frequency and consequences (slow and decreasing mental faculities leading to shortages in laborforce and increase in healthcare costs) compose a big burden for the national economies (45,46). Decreasing mental faculties in patients suffering from major depressive disorder has been found to be five times higher than the general population (45).

Patients with comorbidity of anxiety and depressive disorders, tend to be less responsive to treatment, to have a higher extent of loss in mental faculities and to become chronic and tend to seek more for medical help. For example Quarantini et al reported that depressed OCD patients present more severe general psychopathology (16).

To uncover that if the anxiety and depressive disorders are different facets of one spectrum or seperate disorders with well-defined limits, more studies analysing the etiological, and predisposing factors, epidemiology for these disorders are needed.

References:

1. Öztürk O. Ruh Sağlığı ve Bozuklukları, 7. Baskı, Ankara; Medikomat Basım Yayın. 1997; 223-261.
2. American Psychiatric Association (APA). Diagnostic and statistical manual of mental disorders 3rd ed.. Washington, DC: American Psychiatric Association. 1980.
3. Depression. National Institute of Mental Health. 2009-09-23. http://www.nimh.nih.gov/ health/publications /depression/ complete-index.shtml.
4. Pasic J, Wayne CL, Sullivan MD. Cytokines in Depression and Heart Failure. Psychosomatic Medicine. 2003; 65:181-193.
5. Escobar JI, Giomez J, Tuason VB. Depressive Phenomenology in North and South American Patient. Am. J. Psychiatry. 1983;140: 47-51.
6. Akiskal HS. Mood Disorders: Historical Introduction and Conceptual Overview. In: Sadock BM, Sadock VA, eds. Kaplan & Sadock's Comprehensive Textbook of Psychiatry, 7th ed. Philadelphia: Lippincott Williams and Wilkins. 2000: 1284-98.
7. Nemeroff C. Affective Disorders. Neuropsychopharmacology. In: Davis L.K, Charney D, Coyle J.T, Nemeroff C, eds. American Collage of Neuropsychopharmacology. Third ed. 2002: 1007-9.
8. Boyd JH, Weissman MM. Epidemiology. In: ES Paykel eds: Handbook of Affective Disorders. 1st ed. Edinburg-London, Churchill Livingstone. 1982;109-125.
9. Küey L, Güleç C. Depression in Turkey in 1980s: Epidemiological and Clinical Approaches. Clin Neuropharmacol. 1989;12 suppl. 2:1-12.
10. Küey L. Epidemiological Aspects of Depressive Disorders In Turkey: An Update Review Of Community Surveys. XIII. Dünya Sosyal Psikiyatri Kongresi'nde bildiri, Yeni Delhi, Hindistan, 1992.
11. Birmaher B, Ryan ND, Williamson D et al. Childhood Nnd Adolescent Depression. A review of the past ten years. Part I. J Am Acad Child Adolesc Psychiatry. 1996;35:1427-1439.
12. Goodyer IM, Herbert J, Secher S, Pearson. Short-Term Outcome of Major Depression, I: Comorbidity and Severity at Presentation As Predictors Of Persistent Disorders. J Am Acad Child Adolesc Psychiatry. 1997;36:179-187.

13. Kovacs M. Presentation and Course of Major Depressive Disorder During Childhood and Later Years Of The Lifespan. J Am Acad Child Adolesc Pyschiatry 1996;35:705-715.

14. Rohde P, Lewinsohn PM, Seeley JR. Comorbidty of Unipolar Depression II: Comorbidty with Mental Disorders in Adolescentes and Adults. J Abnorm Psychiatry. 1991;100:214-222.

15. Aragonès E, Piñol JL, Labad A. Comorbidity of major depression with other common mental disorders in primary care patients. Aten Primaria. 2009; 41:545-51.

16. Quarantini LC, Torres AR, Sampaio AS, Fossaluza V, Mathis MA, do Rosário MC et al. Comorbid major depression in obsessive-compulsive disorder patients. Comprehensive Psychiatry 2010; doi:10.1016/j.comppsych.2010.09.006.

17. Erdoğan İ, Tamar M. Çocuk Ve Ergenlerdeki Major Depresif Bozukluğa Eşlik Eden Tanıların Dağılım ve Sıklığının Araştırılması. Türkiye'de Psikiyatri. 2002; 2-3:100-10.

18. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), American Psychiatric Association, Washington DC, 1994.

19. First MB, Spitzer RL, Gibbon M, Williams JBW. Structured Clinical Interview for DSM-IV Axis I Disorders, Clinical Version American Psychiatric Press, Washington, 1997.

20. Hasin DS, Goodwin RD, Stinson FS, Grant BF. Epidemiology of major depressive disorder: results from the National Epidemiologic Survey on Alcoholism and Related Conditions. Arch Gen Psychiatry. 2005;62:1097-1106.

21. Nurnberger JI Jr, Foroud T, Flury L, Su J, Meyer ET, Hu K, Crowe R, EdenbergHJ, Goate A, Bierut LJ, Reich T, Schuckit MA, Reich W. Evidence for a locus on chromosome 1 that influences vulnerability to alcoholism and affective disorder. Am J Psychiatry. 2001;158:718-724.

22. Wang JC, Hinrichs AL, Stock H, Budde J, Allen R, Bertelsen S, Kwon KM, Wu W, Dick DM, Rice JP, Jones K, Nurnberger JI Jr, Tischfield JA, Porjesz B, Edenberg HJ, Hesselbrock V, Crowe R, Schuckit MA, Begleiter H, Reich T, Goate A, Bierut LJ. Evidence of common and specific genetic effects: association of the muscarinic acetylcholine receptor M2 (CHRM2) gene with alcohol dependence and major depressive syndrome. Hum Mol Genet. 2004;13:1903-1911.

23. Caspi A, Sugden K, Moffit TE, Taylor A, Craig IW, Harrington H, McClay J, Mill J, Martin J, Braithwaite A, Poulton R. Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. Science. 2003;301:386-389.

24. Grant KA, Bennett AJ. Advances in nonhuman primate alcohol abuse and alcoholism research. Pharmacol Ther. 2003;100:235-255.

25. Bruce ML, Hoff RA. Social and Health Risk Factors for First-Onset Major Depressive Disorder in a Community Sample. Soc Psychiatry Psychiatr Epidemol. 1994; 29:165-170.

26. Weissman MM, Klerman GL. Sex Differences and the Epidemiology of Depression. Arch Gen Psychiatry. 1977; 34:98-111.

27. Earls F. Sex Differences in Psychiatric Disorders: Origins and Developmental Influences. Psychiatr Developm. 1987; 1:1-23.

28. Swindle RW Jr, Cronkite RC, Moss RH. Risk Factors for Sustained Nonremission of Depressive Symptoms. J Nerv Ment Dis. 1998; 186:462-469.

29. Boyd JH, Weissman MM. Epidemiology. Paykel ES, eds. Handbook of Affective Disorders. Ediburg-London, Churchill Livingstone, 1982: 109-125.

30. Mazer M. People in Predicament: A Study in Psychiatric and Psychosocial Epidemiology. Soc Psychiatry. 1974; 9:85-90.

31. Antony JC, Petronis KR. Suspected Risk Factors for Depression among Adults 18-44 Years Old. Epidemiol. 1991; 2:123-132.

32. Yüksel N. Birinci Basamakta Depresyon: Tanı ve Tedavi, 1. Baskı. Ankara: Çizgi Tıp Yayınevi, 2000: 4-272.

33. Brown TA, Campbell LA, Lehman CL, Grisham JR, Mancill RB. Current and lifetime comorbidity of the DSM-IV anxiety and mood disorders in a large clinical sample. J Abnorm Psychol. 2001;110:585-599

34. Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication [published correction appears in Arch Gen Psychiatry. 2005;62(7):709]. Arch Gen Psychiatry. 2005;62:617-627.

35. Jacobi F, Wittchen H-U, Hölting C, Höfler M, Pfister H, Müller N, Lieb R. Prevalence, comorbidity and correlates of mental disorders in the general population:results from the German Health Interview and Examination Survey (GHS). Psychol Med. 2004;34:597-611.

36. Biderman J, Farrone S, Mick E, Lelon E. Psychiatric Comorbidity among Referred Juveniles with Major Depression: Fact or Artifact? J Am Acad Child Adolescent Psychiatry 1995; 34:579-590.

37. Gökalp GP. Depresif Bozukluklar ile Anksiyete Bozuklukları İlişkisi: Eştanılı Durumlar. 3P Dergisi 1998; 6:289-293.

38. Murphy JM, Maser JD, Cloninger CR. Diagnostic Comorbidty and Symptom Co-occurance: The Stirling County Study. Comorbidty and Mood and Anxiety Disorders 1990;152-176.

39. Sanderson WC, Beck AT, Beck J. Syndrome Comorbidity in Patients Major Depression or Disthymia: Prevalence and Temoral Relationships. Am J Psychiatry 1990; 147:1025-1028.

40. Levitt AJ, Joffe RT, Brecner D,MacDonald Cet. Anxiety disorders and anxiety symptoms in clinic sample of seasonal and nonseasonal depressives. J Affect Disord 1993; 28:51-56.

41. Fava M, Rankin MA, Wright EC, Alpert E, Nierenberg AA, Pava J, et al. Anxiety disorders in major depression. Compr Psychiatry 2000; 41: 97-102.

42. Lydiard RB. Coexisting Depression and Anxiety: Special Diagnostics and Treatment Issues. J Clin Psychiatry 1991; 52:48-53.

43. Marshall JR. Comorbidity and its Effects on Panic Disorder. Bull Menninger Clin 1996; 60:A39-A53.

44. Yıldız M, Göker MNK. Major Depresif Bozuklukta Bedenselleştirmenin Depresyon ve Bunaltıyla İlişkisi. 3P Dergisi 2000; 8:281-284.

45. Broadhead WE, Blazer DG, George LK, Tse CK. Depression, Disability Days, and Days Lost from Work in a Prospective Epidemiological Survey. JAMA 1990; 264:2524-2528.

46. Spitzer RL, Williams JBW, Kroenke K, Linzer M, deGruy Ill FV, Hahn SR et al. Utility of New Procedure for Diagnosing Mental Disorders in Primary Care. JAMA 1994; 272:1749-1756.