

## **Risk Factors for Depression in General Medical Practice**

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It can be stated that in the early 21<sup>st</sup> century psychiatry has moved beyond psychiatric institutions and has been introduced in health care organizations hospitals, various medical centers, university hospitals. This trend of the development of psychiatry is the result of pathomorphism of both somatic and mental disorders, the development of diagnostic and therapeutic means of medical science, modern human "stressful" being, environmental changes, etc. In this regard, the mental health of the entire population formally considered as healthy, has attracted much attention [3,5,7-9,12,15,36].

Mental disorders are widespread in the population mainly due to the progressive growth of such non-psychotic mental disorders as depressive and dysthymic disorders, anxiety and phobic disorders, stress manifestations at different levels, personality decompensations, and many others [9]. That is the reason why mental health problems are the subject of special consideration of interstate and international organizations [18,26].

A special and focused examination of individual groups in primary health care and in general hospitals revealed a large number of individuals exhibiting "subclinical", "pre-manifest", "pre-diseased", "mortal", "masked" forms of mental pathology, primarily affective. It should be noted that normally they have no suspicion about their possible psychiatric pathology. Importantly, it must be noted that most of them are not even aware of having mental pathology. The existing manifestations are usually referred to somatic diseases or their consequences. In population there is an increase of functional mental disorders and somatic disorders, usually masking primary affective disorders, underlying them.

The reason for the growing interest in mental health issues both globally and on a particular country (especially, developing) scale is first of all the increasing economic-financial burden on the society. A brain analysis undertaken by the joint working group of the European Council and the European College of Neuropsychopharmacology detected that the annual overall cost of mental disorders is 300 billion Euros including 132 billion Euros for indirect costs. Direct costs are 110 billion Euros, and the cost of drug therapy is 4% of the total costs [11]. 10% of overall economic burden related to various diseases caused by mental disorders and their consequences [17,18].

These are the circumstances determining the need to study the affective and stress-related mental disorders, in particular, their prevalence, clinical forms, features as well as the targeted treatment strategies in medical institutions of Armenia.

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A huge number of studies are focused on the depressive issues. Moreover, special journals of "depressology" are published. Therefore, writing an overall review in this field seems to be not serious. However, we find it useful to present and analyze literature data about the most relevant, from our point of view, aspects, based on our goals of above-noted problems.

First of all, this problem is related to the susceptibility, the genesis and dynamics of depressive disorders caused by both external and internal conditions (factors). Even studies indirectly connected to the study of these factors are linked to those. These studies suggested that the number of factors associated with depressive disorders is quite high.

However, the question of validity of most of them needs to be addressed. The replacement in etiopathogenetic approaches and concepts of nosology with an operational approach in modern classification much more emphasizes the identification of crucial role of factors (conditions) that contribute to the formation of depression and related comorbid disorders. Moreover, there is a need to clarify the concept of "comorbidity". Was this concept created artificially in order to substitute the concept of "nozos", does it results from the nonclinical replacement trends in psychiatry substituting the clinical method for description of the genesis phenomenon, its mechanisms, forms, etc.? There are serious doubts concerning the correctness and validity of such categories as "somatization" (a supporter of this category was one of co-authors of this paper).

As a result, the detailed and comprehensive studies conducted both in Russia and in Europe, attempted to distinguish and define the range of the main factors associated with a high incidence of depression in the general somatic practice. Among them: female gender, elder age, occurrence of stressful situations, the loss of the family (divorce, widowhood) or work, low income, frequent visit to the hospital, hospitalization, the diagnosis of vegetovascular and/or neurocirculatory dystonia, chronic obstructive pulmonary disease, stomach ulcer, obesity as well as previous therapy based on plant preparations with sedative effect, tranquilizers, antidepressants, neuroleptics [2,13].

However, it should be noted that there are some contradictions in the descriptions of the correlation between depression and gender, age, social status, many other factors [14,16,22,35].

It is assumed that the presence of these factors significantly increases the risk of depression development. The majority of the mentioned factors by themselves, of course, can be considered as "having depressive genisis" for any person. The question is whether the severity and the incidence of depression is normal, in other words, how they can define the perception of their own health and determine human behavior.

Based on the study of 876 patients with depressive symptoms in the context of their relationship with health perception and health behavior Lynch D., *et al.* [25] showed that the presence of stress, indisposition (poor health conditions), alcohol use are the predictors of depressive symptoms in men and women. Also, smoking is an additional contributing factor in women. These predictors are considered by the authors as "the behavior of the disease".

Better general predictor is "the perception of disease". American researchers consider alcoholic dependence in family as anamnestic record of depressive disorders [29]. The study included 209 depression patients with burdened familial history of alcohol revealed that alcohol in family is significantly considered as a risk factor for increased suicidality and posttraumatic stress disorder. They also found that in such families the patients were more frequently subject to physical and sexual violence as well as attempted suicides more frequently. The role of the sex factor is already proved in a number of epidemiological studies, in particular, in the Russian study in the framework of "COMPASS" project [2]. Depressive spectrum disorders and depressive conditions are, respectively, 1.5 and 1.8-times more frequent in men than in women.

Data obtained by Simonds VM., *et al.* [30] indicated that depression and comorbid disorders, in particular anxiety, are observed more often in females. Lucht M., *et al.* [24] confirmed these data for unipolar depression. Moreover, the epidemiological study (general popula-

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tion from the North of Germany) showed that besides sex, the risk of unipolar disorder is higher in married women having children while the high level of education reduces the vulnerability of depression in women.

The risk in both sexes is dramatically increased in divorce, widowhood, in loneliness. Unemployment increases the risk for men while has no effect on women. However, the authors do not specify what determines a high risk of unemployment, is it determined biologically or by the social-psychological role of men. It is well known that women's high predisposition to depression has biological and psychosocial bases. Women's hormonal system provides an appropriate mental and physiological activity and functioning: greater susceptibility to stress, insecurity in social life, original regulation of behaviour, reproductive activity (menstruation, pregnancy, lactation).

The last one causes purely female manifestations of affective disorders such as premenstrual syndrome, depression during pregnancy, postnatal depression, climacteric depression. However, it has been suggested that the onset and clinical course of premenstrual disorders are associated with traumatic events [28]. These disorders by type, basic clinical structure, adherence to antidepressant therapy, a number of clinical and dynamic features definitely belong to the category of mood disorders. However, in ICD-10 [6] they are in a different category and are considered by many researchers as psychosomatic disorders [10].

The relationship between depression and psychogenic factors has been known for a long time, and Keilholz P [4] has even described psychogenic depression in his classification. Concerning the revision of psychogenic concept, the further development of the stress concept, nowadays the authors in the terms of affective and neurotic disorders often speak about "life events", some of which certainly play a definite psychogenic, in other words, stressful role. Pagano ME., *et al.* [27] discussed the role of especially stressful life events in the development of depression.

However, the authors refer to them in the context of personal characteristics, which is also known to play a pathogenetic role in the development and formation of psychopathology including the affective one. The authors found significantly more negative life events in individuals with borderline personality disorders than in other individuals and patients with major depression. Tyrer P., *et al.* [33] studying 17 predictors in psychiatric patients and general practitioners suffering from panic, anxiety disorders, and dysthymia, including mixed anxiety-depressive disorder (cothymia) with an interval of 12 years, concluded that patients with severe mood disorders and premorbid personality disorders showed less positive outcome despite some benefits in therapy.

The authors suggest that personality disorders and environmental factors are predictors of depression and determine the resistance to therapy. Personality characteristics mainly determine the individual perception of stressful life events that are also considered as predictors of depression. Family conflict, professional failure, unemployment, moving to another residence, loss of family, the presence of severe somatic disease can represent a personality significant event. Individual perception of stress depends on the personal characteristics of the individual, the individual strategy of overcoming stress, as well as the stability of the system of social support.

Personal and interpersonal factors, in interaction with stressful events in peoples' lives, predetermine a reduced psychosocial activity over time. It is known that stressful life events play a major role in the development of depressive disorders. The frequency of depressive disorders and psychotraumatic situations (such as retirement, divorce, or separation from a spouse, professional failures, financial problems, death or illness of a close person) are closely related to each other. Moreover, the so-called cumulative effect of stressful situations is very important.

In case of history with a psychotraumatic situation the depressive spectrum disorders, namely, less severe depressive disorders were detected in 40.8% of cases, while severe depression in 21.7%. In the presence of two stressful circumstances these disorders were observed, respectively, in 49.7% and 29.7% of cases, in case of three respectively, in 36.5 and to 59.8%, etc. (p < 0.001) [2].

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Farabaugh AH., *et al.* [20] associated the level of the previous stress with the severity of depressive disorders, such as melancholic depression, atypical depression, bipolar depression, and major depression with aggressive outbursts.

An important risk factor for depression is the presence of depressive episodes and other affective spectrum disorders in history. Information about the episodes of depression, periodic binges concerning the patient or his family confirm assumptions about the relationship of actual complaints with depression. The experience of patient's psychotropic therapy can be considered as a marker of previous affective disorders [2].

Dong C., *et al.* [19] showed that the probability of depression increases with body mass index and the number of chronic somatic diseases (p < 0.0001). Multivariate regional analysis indicated that mass index, race, marital status, chronic somatic illness and family history are predictors of depression in both genders. Hierarchical analysis revealed that body mass index increases the risk more than all other factors together.

The above-mentioned factors significantly increase the probability of the depression development. According to the "COMPASS" study [2], the average probability of detecting of depressive spectrum disorders in women was 1.71 (1.49 - 1.97) times higher than in men, in single people (divorced, widowed, etc.) in 1.55 (1.78 - 1.34) times higher than in married ones, in people of brainwork its average was 0.76 (0.63 - 0.92) times lower than in humans of physical labor, in patients hospitalized during the past year it was in average 1.25 (1.08 - 1.44) times higher than in non-hospitalized patients. The probability of detecting these disorders in patients survived from the traumatic events during the past year was in average 2.24 (1.97 - 2.56) times higher.

Among other factors important for identification of depressive spectrum disorders are the income per person in the family, the age of the patient together with his employment, the age of the patient together with his income, the therapy with psychotropic drugs in history. The frequency of depressive disorder detection is directly correlated with the severity of state health assessment and the evaluation of patient health by a physician.

One of the leading predictors associated with depression is the age factor. Some people believe that depression is often characterized by older age groups for which it represents a global medical and social problem. However, current studies do not support this point of view. It has been shown that not only adults but also children can have depression. It has traditionally been assumed that age with its own nuances contributes to the clinical manifestations of mental disorders, including depression. Luby JL., *et al.* [23] showed that clinical characteristics of depression in children are the same as those in adults and proved that melancholic depression can occur even in 3 years old children. A rather high level of depression in urban adolescents visiting general practitioners was detected [37]. In adolescents an association of the high level of depressive symptoms was associated with such demographic and constitutional factors as higher age, female gender, and psychiatric symptoms in parents. Also, the authors associate the depressive symptoms with the physical symptoms causing psychosocial disorders (cannabis use, drug dependence, frequent treatment in primary health care and mental health services).

In somatic hospital studying children and adolescents (from 3 to 16 years) with painful sensations, in all patients with various degrees of intensity of depressive disorders Antropov YF [1] found depression of neurotic level. He suggested that in children and adolescent allergic sensations not associated with the organic pathology of the corresponded organs and systems can be caused by neurotic level depression, characterized by the prevalence of asthenic and anxiety-asthenic symptoms in children.

However, depression and depressive spectrum disorders are, of course, more common in the elderly [2,32,34]. In order to clarify the diagnosis of depression Volkers AC., *et al.* [34] studied 237 elderly patients in primary health care. They revealed 55 patients with a diagnosis of major depression most of which (96.4%) one or more times visited their family physician within the past year.

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The 20.8% of patients were diagnosed by family physician as depressive, and 32.1% as patients with psychological problems. Interestingly, it should be noted that the appropriate diagnosis was associated with older age. This leads to the issue of the correct differentiation of depression from psychological problems in the elderly by family physicians.

The "COMPASS" showed that the risk of depressive spectrum disorders and depression in each 10 years of life is increased 1.2 and 1.4 times, respectively. In patients older than 65 years depressive disorders in 59% of cases were detected. Interestingly, one third of depressed elderly patients was strongly manifested and required a mandatory antidepressant treatment [2].

Elder age, of course, leads to specific clinical manifestations. According to the data provided by Taylor WD., *et al.* [32] depressed elderly patients are significantly more likely to have atherosclerosis, hypertension, heart disease, peptic ulcer disease. The authors support the idea of accompanying of vascular disease with elder age depression. Patients with subcortical depression were of older age, were more likely to suffer from depression, more often had hypertony, and more likely were men. Many studies, including this paper confirm the role of the vascular pathology in the development of late depressions [32].

Not only somatic diseases complicate the course of depression, but also depressions themselves, usually complicate the course of somatic diseases in the elderly and lead to some exacerbations of chronic diseases in the elderly. Himelhoch S., *et al.* [21] examined the association of depression with an ambulance appealability and preventive health care in chronic elderly patients. A total of 8 patients with chronic diseases were enrolled.

It has been shown that depression affects white women and at older ages more than older people without depression (p < 0.001). Also, it was found that patients with depression in the presence of at least one somatic disease seek medical aid including an ambulance twice as often. In addition, depression was closely associated with disability and decreased cognitive functioning [31].

Internists are well aware that the elderly people represent a group of patients requiring special attention and time. Clinically, these states are usually dominated by the phenomenon of cognitive deficit (lack of attention, short-term memory). These symptoms of the described "dementia" are completely reversible in case of the appropriate treatment.

Depression does not represent a hardly diagnosed psychopathological condition. It is quite easy to diagnose even without revealing any syndrome structural differences and details. Nevertheless, the differentiation of the nature of depression is always difficult. It should be clarified whether it is the result of brain organic damage, i.e. the result of morphological changes of the brain substance, or it has a functional nature. However, today the concept of "functional" is changing due to the detection of subtle changes at the molecular level. Based on certain advances in the field of antidepressant psychopharmacology, it can be stated at least preliminarily that depression is always the result of some (even though non-specific) changes in the brain. Based on our current knowledge of the metabolism of neurotransmitters (serotonin, norepinephrine, dopamine) we can more correctly consider the problems of the diagnostic evaluation of different psychopathological manifestations in the structure of depressive disorders and the assessment of the role of various factors, potentially related to the development of depression. The questions of whether a particular psychopathological phenomenon is a specific sign of endogenous depression, organic depression or has a purely situational character are out of consideration. It is known that the history of modern psychiatry is full of these specific searches for certain symptoms of depression such as the vital anguish, loss of emotional resonance, the circadian rhythm, etc. However, it should be noted and taken into account that unlike schizophrenic, delirium and several other disorders, depression refers to the range of psychological category, i.e. it can be considered as a normal mental activity. Moreover, many psychiatric (mental) symptoms of depression (melancholy, fear, sadness, anxiety) can be detected in mentally healthy people, not being a sign of psychiatric disorder. This aspect emphasizes the problem of separating the "normal" and "pathological" depression, the problem of specification of its diagnostic criteria, the problem of the clinical reasoning in therapy and the selection of effective therapeutic method or

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means, and, of course, a problem of associated with it factors. Depression, like any other disease, is undergoing certain pathomorphological changes today. They primarily affect formal rather than the essential manifestations of depression that from our point of view leads to a search for a variety of factors somehow associated with depression and determining its development.

The presence of multiple factors leads to a variety of depressive symptoms. Depression in primary care, in somatic and psychiatric hospitals is manifested in different ways and degrees of severity, the structure of the disorder, dynamic (evolutionary) features, compatibility with somatic and other mental disorders, as well as depending on age.

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