Severe Anemia in Non Suicide Self Injury as a Complication of Major Depression Disorder

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ABSTRACT

Non suicide self injury (NSSI) is a rare case in adults. Non suicide self injury is an act of hurting himself such as cutting, burning, punching without intending to commit suicide. NSSI itself is a complication of major depression that is not treated properly from the onset of symptoms. Severe depression that lasts for a long time, can aggravate illnesses such as the appearance of symptoms of psychosis and have an impact on various complications such as NSSI and somatic complications that can reduce the patient's health condition. Reported a case of a 22 year old woman with severe anemia due to chronic bleeding. It is known that chronic bleeding in the patient is the result of habitual cutting, in which the patient slashes her left forearm. Cutting habitualis is part of the action of NSSI where the management must be holistic and sustainable, the management of patients consists of psychotherapy as starting from dialectical behavior therapy is a form of cognitive therapy that can help a person adapt to activities that can pass through distress. Psychodynamic therapy is to help someone form new habits that previously could cause pleasure to the patient. Psychotherapy accompanied by psychopharmaceuticals can accelerate improvement in patient.

1. Introduction

Definition

Depressive disorder without psychotic symptoms is a subset of psychosomatic disorders. People with depression often come to a primary care doctor for somatic complaints that stem from depression, and it is very rare to see a psychosomatic medicine specialist. Some patients come because of somatic complications due to their severe depression.¹,⁹

Depression is a mood disorder that causes constant feelings of sadness and loss of interest. Also called major depressive disorder or clinical depression, it affects feelings, thoughts, and behavior and can cause a variety of emotional and physical problems. The patient may have difficulty carrying out normal daily activities.⁹

Epidemiology

Depressive disorders rank third as the cause of the world's disease burden in 2008, WHO projects that this disease will rank first in 2030.¹¹

Major depressive disorder is a very common psychiatric disorder. The depressive disorder has a lifetime prevalence of about 5 to 17 percent, with a mean of 12 percent. The prevalence rate in women is almost twice that of men.¹⁰

Depressive disorder is more common in people without close interpersonal relationships, people who are divorced or separated, or are widows. No differences in the prevalence of depressive disorders were found between race and socioeconomic status. People with depressive disorders often experience comorbid
disorders such as substance use disorders, panic disorders, social anxiety disorders, and obsessive-compulsive disorder. 

**Symptoms**

Symptoms of depressive disorders are generally recognized through triadic symptoms, namely, first, not being able to enjoy life, second, not paying attention to the environment, third, being tired all day long. Another component found in depression is the impaired cognitive triad, namely: Assessing himself as useless (I'm worthless). Feelings of hostility to the environment (the environment is hostile) and a gloomy future (nothing good can happen).

In some patients the symptoms of depressive disorder are severe enough to cause real problems in daily activities, such as work, school, social activities, or interpersonal relationships. In adolescents, symptoms include sadness, irritability, feeling negative and worthless, anger, poor performance or poor attendance at school, feelings of being misunderstood and very sensitive, using drugs or alcohol, eating or sleeping too much, selfharm, loss of interest in normal activities, and avoiding social interactions.

**Etiology and risk factors**

The causes of major depressive disorder are multifactorial, including biological, genetic, environmental, and psychosocial factors. Depressive disorders were previously thought to be caused by abnormalities in neurotransmitters, particularly serotonin, norepinephrine, and dopamine. This has been demonstrated by the use of antidepressants such as selective serotine receptor inhibitors, serotonine nor epinephrine receptor inhibitors, dopamine nor epinephrine receptor inhibitors in the treatment of depression. Patients with suicidal thoughts are known to have low levels of the metabolite serotonin. However, recent theories suggest that the condition is linked to a more complex neuroregulatory system and neural circuits that cause secondary disruption of the neurotransmitter system.

Risk factors that can trigger depression disorders include certain personality types, such as low self-esteem, too much dependence on others, self-criticism or pessimism. Traumatic events, such as physical or sexual abuse, death or loss of a loved one, or financial problems. Blood relatives with a history of depression, bipolar disorder, alcoholism or suicide. Sexual deficiencies such as lesbian, gay, bisexual or transgender. Alcohol or drug abuse is also a risk factor for depressive disorders.

Early, severe stress can cause drastic changes in neuroendocrine response and behavior, which can lead to structural changes in the cerebral cortex, leading to major depression later in life. Structural and functional brain imaging in depressed individuals has shown increased hyperintensity in the subcortical area, and decreased anterior cerebral metabolism on the left side, respectively. Family, adoption, and twin studies have indicated a genetic role in depression susceptibility. According to cognitive theory, depression occurs as a result of cognitive distortions in people who are prone to depression.

Gamma aminobutyric acid (GABA), a neurotransmitter inhibitor that blocks glutamate and glycine, both of which are major neurotransmitters that have been found to play a role in the etiology of depression. Depressed patients were found to have lower brain GABA plasma levels. GABA is thought to exert its antidepressant effect by inhibiting monoamine pathways, including the mesocortical and mesolimbic systems.

**Diagnosis**

The diagnosis of depression begins with anamnesis, where the symptoms of depressive disorders are mainly obtained from a complete history taking. Depressive disorder can be diagnosed when a person has persistently low or depressed moods, anhedonia or decreased interest in pleasurable activities, feelings of guilt or worthlessness, lack of energy, poor concentration, changes in appetite, retardation or psychomotor agitation, disorders sleep, or thoughts of suicide.

According to the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5), a person must have five of the aforementioned symptoms, in
which a person has feelings of depression or anhedonia that cause social or work disorders, to be diagnosed with major depressive disorder. A history of manic or hypomanic episodes should be excluded to diagnose a depressive disorder. A complete physical examination, including a neurological examination, is still performed to rule out any medical or organic causes underlying the depressive disorder. A complete medical history, together with a family medical and psychiatric history, should be assessed.

Instruments used to diagnose depressive disorders in primary care, such as the Patient Health Questionnaire-9 (PHQ-9), is a standard depression rating scale usually used for screening, diagnosis, and monitoring of treatment response for depressive disorders. Based on DSM 5 scores more than 10, indicating a possible depressive disorder. Most hospital environments use the Hamilton Rating Scale for Depression (HAM-D) instrument. HAM-D used 21 items on depressive symptoms, but the assessment was based on only the first 17 items. Patients are said to be normal if the score is <7. If the score ≥20, it can be said that depression is moderate.

Another depression assessment instrument using the Beck Depression Inventory (BDI) was compiled by Aaron T. Beck (1996). The BDI consists of 21 self-report items that measure depressive symptoms and their severity. Interpretation of the sum of the BDI scores. Score <10: no depression, score 10-18: mild depression to moderate depression, score 19-29: moderate depression towards major depression. Score 30-36: Depression is severe (severe). Score > 40: On top of major depression, it is thought that there is a possibility of exaggerating depression, possibly having characteristics of histrionic or borderline personality disorder.

Non suicide self injury disorder (NSSI)

NSSI definition

The clinical trend in behavior where patients intentionally injure themselves, this disorder has been known since the 1930s and by the psychoanalyst Karl Menninger in 1952. Menninger uses the term self mutilation, and considers the act as a form of attenuated suicide.

Actions of self-harm such as cutting, burning, punching or various acts of hurting oneself without intending to commit suicide are called non-suicidal self-injury (NSSI). Cutting is the most common form of self-harm. Someone cutting is a form of coping mechanism against stress. By hurting oneself, a person can be distracted from the depression and anxiety he is experiencing. People who hurt themselves can also be a symbol of hurt emotions. Self-harm is also associated with childhood trauma such as physical abuse, sexual abuse and neglect.

NSSI cases are classified as rare, the Journal of the American board family medicine estimates that 1-4% of adults, approximately 15% of adolescents in America self-injure. Students are the group that has the greatest risk of committing self harm, namely 17-35%. Cutting can stop for several years but can relapse again and can become addictive.

Diagnosis of NSSI

According to Favazza’s definition and the DSM-5 diagnostic criteria, such behavior must be conscious and deliberate. The diagnostic criteria for NSSI are defined as a time limit for diagnosis, namely the patient commits self-harm such as injuring, burning, cutting, hitting etc. that occurred for 5 or more days during the past year.

The criteria for diagnosis of NSSI according to the DSM V consist of criteria A, B, C, D, E, and F. These six groups of criteria describe what personality disorders are dominant in the patient as described in Table 1.

Self-mutilation is part of the complications of major depressive disorders, therefore depressive disorders need to be an important concern to prevent the occurrence of NSSI disorders such as cutting habit.

Management

Depressive disorders can be treated with a variety of treatment modalities, including pharmacological modification, psychotherapy, intervention, and lifestyle. The initial treatment for depressive disorders
consists of medication and / or psychotherapy. Combined treatment, including medication and psychotherapy, has been shown to be more effective than this treatment alone.\textsuperscript{13}

The food and drugs administration (FDA) publishes medications for the management of depressive disorders including: Selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine, sertraline, citalopram, escitalopram, paroxetine, and fluvoxamine. SSRIs are first-line therapy. Serotonin-norepinephrine reuptake inhibitors (SNRIs) such as venlafaxine, duloxetine, desvenlafaxine, levomilnacipran, and milnacipran. Usually depressed patients are comorbid. Serotonin modulators such as trazodone, vilazodone, and vortioxetine. Atypical antidepressants such as bupropion and mirtazapine. Tricyclic antidepressants (TCAs) such as amitriptyline, imipramine, clomipramine, doxepin, nortriptyline, and desipramine. Other psychopharmaceutical therapies such as mood-stabilizers, antipsychotics can be added to increase the effect of the antidepressant drug.\textsuperscript{10}

Management that also plays an important role is psychotherapy such as cognitive-behavioral therapy and interpersonal therapy. The role of the family in the form of understanding the conditions of depression accompanied by positive support will greatly help the success of treatment.\textsuperscript{9}

In addition, in its implementation, there needs to be a good collaboration between doctors ahli psychosomatic, psychologists, and psychiatrists as well as nurses or caregivers so that patients get holistic and optimal therapy.\textsuperscript{9}

**Complications**

Depression often gets worse if not treated properly, can lead to emotional, behavioral, and health problems that reduce the quality of life. Examples of complications associated with depression include: Being overweight or obese, which can lead to heart disease and diabetes. Functional dyspepsia syndrome. Alcohol or drug abuse. Anxiety, panic disorder or social phobia. Family conflicts, relationship difficulties, and work or school problems. Suicidal feelings, attempted suicide or suicide. Self-mutilation, such as cutting habituals. Until premature death due to medical conditions.\textsuperscript{9}

**Clinical findings**

A female patient 22-year-old came to the UNAND Hospital Emergency Room on January 10, 2021. The patient’s main complaint was weakness and fatigue since 7 days ago and since the last 2 days the patient complained of not being able to do light daily activities due to lack of energy. The patient also complained of shortness of breath, was not accompanied by fever and cough. The heart often feels palpitations that come and go. Uluihati pain accompanied by nausea complained by the patient since 2 weeks before admission to the hospital.

Patients often hurt themselves by cutting their left forearm using a razor blade. Patients have started to do this cutting since 2018 until the time when the patient was hospitalized. Patients cut almost every day, usually the trigger is when the patient feels sad and depressed. In addition, patients often hit their own heads with their hands.

In our patient, we took a psychosomatic history and found complaints due to vegetative imbalance in the form of headaches, shortness of breath that appeared occasionally, chest palpitations, and nausea. From the psychological status, behavior, and habits of the patients, it was found that the concentration was reduced, they were easily tired, they often woke up during the night. There is an unusual addiction in the patient, namely cutting habituals. The patient’s mood tends to be sad accompanied by feelings of anxiety and fear. The patient’s character is introverted.

The patient is the 3rd child of 4 siblings. The patient is not married, the patient’s daily activity at this time is helping parents in the shop. The patient has hobbies of painting and drawing. At the age of 8, the patient experienced a traumatic incident, namely sexual harassment by the patient’s cousin. And a similar incident occurred again when the patient was 13 years old who was carried out by a friend of the patient’s brother. When a child, the patient is classified as a cheerful child and has many friends, but since this incident the patient often feels anxious when hanging
out, especially if he meets the abuser.

The patient aspires to continue studying architecture in China. In 2018 the patient took a Mandarin course in Surabaya. After being served for 2 years the patient stopped the course because of the covid 19 outbreak. While attending a course in Surabaya the patient mingled with several friends and often gathered, the patient and his friends had visited entertainment venues and had drunk alcohol.

From physical examination the vital signs were within normal limits. Blood pressure 106 / 65mmhg, pulse rate 105x / minute, breath rate 20x per minute. The conjunctiva of the eye appears anemic. On physical examination, pulmonary and heart were within normal limits. Physical examination of the abdomen revealed epigastric tenderness. There were quite a lot of sharp incisions on the lower left arm. Some of the incisions looked fresh.

Then we assessed the HADS scale and got an Anxiety score of 13 and a depression score of 16. From this score, it can be seen that the depression score is more dominant. Then proceed with the BDI score assessment obtained a score of 32 where this score falls into the category of major depression. Assessment with the Hamilton rating scale for depression (HAM-D) compressed a score of 21. Based on this score, it was seen that the patient was in a state of major depression.

The investigations that are carried out consist of routine blood tests. Obtained hemoglobin 5.8 g / dl, leukocytes 5.500 / mm$^3$, platelets 572.000 / mm$^3$, hematocrit 19.1%. The leukocyte count showed basophils 0%, eucinophils 1%, stem neutrophils 0%, segment neutrophils 59%, lymphocytes 35%, monocytes 5%. MCV value 70.2, MCH 21.3, MCHC 30.4. There is the impression of normocytic normochronic severe anemia.

The patient was diagnosed with primary occupational anemia with severe anemia ec chronic bleeding, a diagnosis of secondary occupational general anxiety disorder and major depressive disorder. The differential diagnosis in this patient was a neurotic disorder due to severe stress. The diagnosis and assessment of this patient are axis I anxiety disorder and severe depression, axis II introverted personality, axis III severe anemia and dyspepsia syndrome, axis IV victims of sexual harassment, desire.

**Failure to continue studying, axis V global value assessment of functioning, namely 60 - 51.**

The initial management of this patient was to treat somatic problems such as incision wound care, 4 units of Packed red cell (PRC) transfusion, other somatic complaints were given therapy according to symptoms such as dyspepsia syndrome, given 2x50mg intravenous injection of Ranitidine and 3x10cc suspension of sucralfate. Then given psychopharmaceutical therapy with merlopa 1x0.5mg. cetrail 1x50mg and alprazolam 2x0.5mg. Besides that we also do psychotherapy with adequate relaxation and ventilation. The psychopaatherapist approach is in the form of dialectical behavior therapy, which is a form of cognitive therapy that can help a person adapt to activities that can go through distress. Second, psychodynamic therapy is to help someone form new habits that previously could cause pleasure to the patient.

On January 11, 2021, complaints of fatigue decreased, heartburn and nausea decreased. The patient had been given PRC transfusions for 4 units and had routine blood tests again, obtained hemoglobin 11.4gr / dl, hematocrit 34%, leukocytes 5700mm$^3$, platelets 450.000 / mm$^3$. Feelings of anxiety, fear and restlessness are still there, sleep disturbances are still there. Symptoms of depressive disorders still exist, such as assessing yourself as useless, causing trouble for your family, sadness because you feel like you are a burden on your parents, assessing a gloomy future. Psychopharmaceutical therapy is continued.

In the follow-up on January 12, 2021, the patient shared that for several weeks, the patient really likes strange smells such as the smell of old clothes, the smell of bandages, and mosquito repellent. Often there is a sudden, very happy feeling when viewing videos on the internet. So that the heart becomes pounding violently, breathing is irregular, then suddenly without realizing it hits his own head, hits the cheeks or hits the table. After that he realized and confused himself.
Symptoms of hallucinations in patients are atypical. Then the patient was consulted by a psychiatric specialist and by a mental health specialist diagnosed with bipolar affective disorder episodes of now mixed psychotic indulgence. The patient was given a major tranquilizer mood stabilizer therapy, namely 2x1mg risperidone.

Follow-up on January 14, 2021, the patient feels that his mind has calmed down somewhat. The desire for cutting is reduced. Unusual thoughts have rarely appeared. The patient is planned to continue the therapy from an outpatient clinic. Patients and families are given education about the importance of psychotherapy in the form of cognitive-behavioral therapy and interpersonal therapy. The role of the family in the form of understanding the condition of depression along with positive support will greatly assist the success of treatment.

Table 1. Summary of NSSI Diagnostic criteria (DSM V)

| A | Self-administered actions such as cutting, burning, or punching intended to cause moderate physical damage to the body (for example, bruising, bleeding, or pain) that occurred for 5 or more days during the past year. |
|---|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| B | Engaging in self-injurious behavior in the hope that at least one of the following consequences will occur soon after:  
1. Relief from negative feelings or thoughts.  
2. Interpersonal problem solving.  
3. Creation of a positive mood. |
| C | At least one of the following occurred immediately prior to intentional self-harm:  
1. Negative thoughts or feelings (eg, distress, depression, anger, anxiety, tension, or self-criticism).  
2. Preoccupation with planned self-defeating behavior that is difficult to control.  
3. Frequent thoughts of self-injurious behavior - even if no action is taken. |
| D | Socially sanctioned behavior such as tattoos or body piercing is excluded, such as self-inflicted damage imposed in a cultural or religious context. General and mild behaviors such as nail biting and scab removal were also excluded. |
| E | Engagement in nonsuicidal self-injury results in clinically significant distress or causes problems in social or occupational functioning or impairments in other important areas of life. The self-damaging behavior cannot be better explained by another mental disorder or medical diagnosis. It is also required that the self-injurious behavior not occur only during psychotic episodes, intoxication, periods of delirium, or be stereotyped and repetitive. |

2. Discussion

One reported case was a 22 year old woman, the patient was treated for severe anemia ec chronic bleeding. Chronic bleeding in this patient is the result of habitual cutting that is often done by the patient. Cutting performed by the patient is to cut the left forearm whenever the patient feels depressed, sad, and anxious. The first cutting of the patient was done in 2018 until the patient was treated in 2021.

Cutting habitualis is part of non suicide self injury (NSSI), Timothy J et al in 2017 stated that the incidence of NSSI in adults is classified as rare. The American board family medicine journal estimates 1-4% of adults, approximately 15% of adolescents in America self-harm. NSSI itself is a poorly managed complication of major depressive disorder.

Non suicide self injury is an act of hurting himself such as cutting, burning, punching or various acts of hurting himself without intending to commit suicide. Cutting is the most common form of self-harm as happened to this patient. Patient cutting is a form of coping mechanism against stress. Jill M Hooley el al in
Self harm is also related to childhood trauma such as physical abuse, sexual abuse and neglected, this statement is in accordance with what is experienced by patients.3

The patient was diagnosed with a major depressive disorder. The diagnosis of depressive disorders in patients is confirmed through a complete history by identifying predisposing factors, precipitation factors, and aggravation factors that cause major depressive disorders in patients. In this patient the predisposing factor for depressive disorders was a history of sexual abuse that the patient experienced when he was in grade 3 elementary school, a similar incident occurred again when the patient was in grade 1 junior high school. Research report: Psychiatry and psychology, 2016-2017. The Mayo Clinic mentions that one of the risk factors for major depressive disorders is sexual abuse and psychological abuse.22 Severe stress experienced by patients classified as early (the age of children) Navneet Bains and Sara Abdijadid in their journal 2021 Severe early stress can cause drastic changes in neuroendocrine response and behavior, which can lead to structural changes in the cerebral cortex, leading to major depression later in life.10

The precipitating factor for depression disorder in patients is that the patient’s dream to continue studying architecture in China is not fulfilled so that the patient is increasingly depressed as if there is no future. Aggravation factors that play a role in aggravating the patient’s depressive disorder are anxiety, feelings of worthlessness, guilt when seeing a difficult parent, and some somatic disorders that arise in patients such as functional dyspepsia syndrome, severe anemia due to cutting habitualis, where somatic disorders experienced by patients often causing the patient to be hospitalized.

The instrument used to assess depressive disorders in patients is by using the Hamilton Rating Scale for Depression (HAM-D) and the Beck Depression Inventory (BDI), the HAM-D score in this patient is 21 which is classified as major depression.22 While the BDI score is 32 according to major depression.

Management of these patients begins with the management of the patient’s somatic problems. Patients were given PRC transfusions for severe anemia, followed by therapy for functional dyspepsia syndrome, namely by administering lansoprazole, sucralfate suspense, paracetamol, and curcuma. During the treatment, the patient is given psychotherapy in the form of ventilation and relaxation. The approach in the form of dialectical behavior therapy is a form of cognitive therapy that can help a person adapt to activities that can pass through distress. Then psychodynamic therapy, which is helping someone form new habits that previously can cause pleasure in patients. Psychotherapy is followed by psychopharmaceuticals. Cuijpers P et al 2009 Combined treatment, including drugs and psychotherapy, has been shown to be more effective than psychotherapy alone.13 Patients are given first-line psychopharmaceutical drugs, namely Selective serotonin reuptake inhibitors (SSRIs) such as sertraline 1x50mg, patients are also given tranquilizers. minor to overcome the symptoms of anxiety, namely alprazolam 2x0.5mg.

On the 4th day of hospitalization, the patient showed psychotic symptoms in the form of fluctuating mood changes accompanied by symptoms of manic episodes in addition to depressive episodes. The patient tells of his mood suddenly rising when watching videos on the internet and then immediately the patient is upset and hits himself on the head. The patient was consulted to a psychiatric specialist and diagnosed with bipolar affective disorder episodes of current mixed psychotic symptoms. The patient was given major tranzulizer mood stabilizer therapy, namely 2x1mg risperidone.

The sixth day of hospitalization, the patient showed improvement in anxiety complaints, reduced sleep disturbances, decreased mood fluctuation. The patient feels calm, the desire to cut his own arm is still there but can still be controlled. The addition of mood stabilizer therapy in these patients accelerates the stabilization of anxiety disorders and depression in patients, as in the journal by Navneet Bains 2021 states that the addition of antipsychotic mood stabilizer drugs can increase the effect of antidepressants.10

An interdisciplinary approach An interdisciplinary
approach is essential for the effective and successful treatment of depressive disorders. Primary care physicians and psychiatrists, along with nurses, therapists, social workers, and case managers, are integral parts of this collaborative service. In most cases, a psychosomatic specialist is the first provider to receive somatic complaints by individuals with. Depression screening in primary care settings is essential for early intervention and thus improves the overall outcome of depressive disorders.

Psychoeducation plays an important role in improving patient medication adherence. Recent evidence also supports that lifestyle modifications, including moderate exercise, can help improve mild to moderate depression. Because patients with depressive disorders are at increased risk of suicide, close monitoring and follow-up by mental health workers is important to ensure safety and adherence to mental health care. Subsequent family involvement can contribute to better overall mental health care outcomes. Meta-analyses of randomized trials have shown that depression outcomes are superior when using collaborative care compared to usual care.23

3. Conclusion

Cutting habitualis is a rare part of non suicide self injury. This case is a complication of major depressive disorder that was not treated properly since the first symptoms appeared. Depressive disorders need to be detected early before the symptoms get worse and cause further complications. Patients come for treatment often because of their somatic complaints so that psychosomatic specialists are the first providers to receive patients' somatic complaints and then need interdisciplinary collaboration, namely primary care doctors, psychiatric specialists, nurses, therapists and social activists for early detection and treatment of depressive disorders.

4. References

1. Mudjaddid E. Understanding and managing psychosomatic anxiety disorders and depression: in the field of internal medicine. Internal Medicine Textbook in Internal Medicine Textbook Volume II Edition VI. Jakarta: Interna Publishing, 2015. Pages 2105-2108
2. Maslim R. Diagnosis of mental disorders, a brief reference from PPDGJ III and DSM V. Department of mental medicine, Faculty of Medicine, Atmajaya University, Jakarta 2013.
3. Jill M Hooley. Kathryn R Fox. Chelsea Boccagno. Nonsuicidal Self-Injury: Diagnostic Challenges And Current Perspectives. Department of Psychology, Harvard University, Cambridge, MA 02138, USA; Dove Press journal: Neuropsychiatric Disease and Treatment.2020
4. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Arlington, VA: American Psychiatric Publishing; 2013
5. Muehlenkamp JJ. Self-injurious behavior as a separate clinical syndrome. Am J Orthopsychiatry. 2005;75(2):324–333. doi:10.1037/0002-9432.75.2.324
6. Javenport, J. Diagnostic and Statistical Manual of Mental Disorders V. American Psychiatric Association. 2013
7. Audrey R. Tyrka, Lawrence H. Price, Marcelo F. Mello, Andrea F. Mello and Linda L. Carpenter. Psychotic Major Depression A Benefit-Risk Assessment of Treatment OptionsMood Disorders Research Program, and the Department of Psychiatry and Human Behavior, Brown Medical School, Butler Hospital, Providence, Rhode Island, USA. 2006.
8. Witrin Gamayanti, Ila Nurlaila Hidayat. Anger And The Quality Of Life Of People Who Experience Psychosomatic. Journal of Psychology Vol. 18 No. October 2, 2019, 177-186
9. Frank R. Giannelli, MS, PA-C. Major depressive disorder. PA program at Rutgers University in Piscataway, N.J. Journal of the American Academy of Pas. 2020
10. Navneet Bains; Sara Aldijadid. Major
Depressive Disorder. UCLA. NCBI booksheft. Copyright ©, StatPearls Publishing LLC 2021.

11. Malhi GS, Mann JJ. Depression. Lancet. 2018 Nov 24;392(10161):2299-2312. [PubMed]

12. Ratheesh A, Davey C, Hetrick S, Alvarez-Jimenez M, Voutier C, Bechdolf A, McGorry PD, Scott J, Berk M, Cotton SM. A systematic review and meta-analysis of prospective transition from major depression to bipolar disorder. Acta Psychiatr Scand. 2017 Apr;135(4):273-284. [PubMed]

13. Cuijpers P, Dekker J, Hollon SD, Andersson G. Adding psychotherapy to pharmacotherapy in the treatment of depressive disorders in adults: a meta-analysis. J Clin Psychiatry. 2009 Sep;70(9):1219-29. [PubMed]

14. Hamilton Depression Rating Scale (HDRS). Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960; 23:56–62

15. Maria Zetterqvist. The DSM-5 diagnosis of nonsuicidal self-injury disorder: a review of the empirical literature. Department of Clinical and Experimental Medicine, Linköping University, 581 85 Linköping, Sweden. Child Adolesc Psychiatry Ment Health (2015) 9:31

16. Muehlenkamp JJ, Claes L, Havertape L, Plener PL (2012) International prevalence of non-suicidal self-injury and deliberate self-harm. Child Adolesc Psychiatry Ment Health. doi:10.1186/1753-2000-6-10

17. Shaffer D, Jacobson C (2009) Proposal to the DSM-V childhood disorder and mood disorder work groups to include non-suicidal self-injury (NSSI) as a DSM-V disorder. American Psychiatric Association. http://www.dsm5.org/Pages/Default.aspx. Accessed 1 Dec 2009

18. Gratz KL, Dixon-Gordon KL, Chapman AL, Tull MT (2015) Diagnosis and characterization of DSM-5 nonsuicidal self-injury disorder using the clinician-administered nonsuicidal self-injury disorder index. Assessment. doi:10.1177/1073191114565878

19. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 5th edn. American Psychiatric Association, Washington DC. 2013

20. Aaron T. Beck, MD, Robert A. Steer, Gregory K. Brown. Beck Depression Inventory-II. Manual. 1996

21. Research report: Psychiatry and psychology, 2016-2017.MayoClinic.http://www.mayo.edu/research/departments-divisions/department-psychiatry-psychology/overview. Accessed Jan. 23, 2017.

22. M. Hamilton. A rating scale for depression. J Neurol Neurosurg Psychiatry. 1960 Feb;23(1):56-62. doi: 10.1136/jnnp.23.1.56.

23. Sighinolfi C, Nespec C, Menchetti M, Levantesi P, Belvederi Murri M, Berardi D. Collaborative care for depression in European countries: a systematic review and meta-analysis. J Psychosom Res. 2014 Oct;77(4):247-63. [PubMed]