IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

Hematopathology of Mental Depression

A Review on Blood Counts

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Abstract : Depressive disorders, including Major Depressive Disorder (MDD), are a significant global health issue. Depression is more than a psychological condition; it's a physiological disorder involving brain neurochemistry and the interaction of brain areas. External stress releases cortisol, influencing the immune system via the HPA-axis. Patients with depression often have elevated cortisol levels and increased inflammation. Hematological profiling helps understand the immune system and metabolism functionality. Depression is linked with changes in white blood cell counts, indicating a complex interplay between the immune system and mental health. However, the relationship between depression, complete blood count (CBC), the immune system, and white blood cell count needs further research.
IndexTerms **-Depression, RBC, WBC, Platelets.**

I. INTRODUCTION

Mental depression or Major affective disorder is a leading cause of dysfunction and disability in the modern world. An estimated one in fifteen adults (6.7%) suffer from depression on any given year. Furthermore, 16.6% of people, or one in six, will at some point in their lives experience depression. While depression can strike at any age, it typically first manifests in late adolescence or early adulthood. Depression is more common in women than in males. According to certain research, one-third of women will go through a significant depressive episode at some point in their lives. An estimated 40% of first-degree relatives—parents, siblings, or children—have a high heritability of depression. Major depressive disorder, or depression, is a common yet dangerous medical condition that has an adverse effect on one's feelings, thoughts, and behaviour. Sadness and/or a loss of interest in once-enjoyed activities are symptoms of depression. There are evidences that people with depression have risks for high morbidity and mortality (Elliot & Eisdorfer, 1982). Clinical depression was associated with several large alterations in cellular immunity, a meta-analysis by Herbert & Cohen, 1993 indicated as such. There is a complicated and variable relationship between immunological tests and depression. Meta-analyses, however, have shown that depressed people are likely to exhibit altered responses in multiple immunological assays. Major immune cell classes are expected to alter in depressed patients, with overall white blood cell counts rising and neutrophil numbers relatively rising. On the other hand, depressed patients probably have fewer lymphocytes (Erwin, 1999). Additionally, it seems that depression is linked to increases in at least one immune activation measure.

Haematological profiling helps in developing a preliminary idea about the functionality of the immune system and metabolism in an individual. The areas of mental depression in brain overlap with that of the immune system (Palazidou, 2012). Mental depression is more than just a psychological state, it is a physiological disorder involving brain neurochemistry and interaction of brain areas like amygdala, hippocampus, locus ceruleus, among themselves and the endocrine system.

Any external stress releases cortisol in human and corticosterone in rhodents (CORT) which in turn influences the immune system via HPA- axis (Dziurkowska & Wesolowski, 2021). The class of steroid hormones known as glucocorticoids, which includes cortisol, is crucial for coordinating the body's reaction to stress. Depression patients have often been shown to have elevated cortisol levels and increased inflammation.

Even after the stressor is removed CORT levels remain high, however the immune function resumes normalcy. In people predisposed with mental depression, these stressors may act as trigger and induce the immune system to dysfunction.

II. NEED OF THE STUDY

The thin line between mental depression and physical ailments is getting thinner with new psychosomatic studies. What was a hypothesis has become a full-fledged research topic with psychiatry and psychology joining hands. With AI tools it will be easier to find biomarkers of behavioral disorders, and chalk out a treatment plan accordingly. Depression is a burning issue, especially

post pandemic. So, it is very important to get a comprehensive know how about changes, if any, in basic hematological profile in mental depression patients.

III. REVIEW METHOD

Data base and research articles about mental depression and haematology were reviewed.
The following Parameters were considered.
A) CBC:
A complete blood count (CBC) test measures the following:
The number of white blood cells (WBC count)
The number of red blood cells (RBC count)
The number of platelets
The total amount of hemoglobin in the blood
The fraction of the blood composed of red blood cells (hematocrit)

B) DC of WBC
The amount of each type of white blood cell in the blood is determined by the white blood cell differential count. It can be given as an absolute value (% x total WBC) or as a percentage (numbers of each type of WBC relative to the total WBC).

IV. OBSERVATIONS

Depression is widely recognized as a psychiatric disorder, but its underlying biological effects are still being explored. Recent research has highlighted the significant role of the immune system in the etiology of depression. A study conducted by researchers across four healthcare systems, including Vanderbilt University Medical Center, found a strong connection between depression polygenic scores and white blood cell count. This suggests that the immune system plays a crucial role in the development and severity of depression. The research team studied two groups of people: those who had depression and those who did not, but were at a high genetic risk for developing depression. They found that even having a high genetic risk for depression was enough to contribute to an elevated level of white blood cells. This study supports a "feedback model" where inflammation increases the risk for depression, and depression also increases or maintains inflammation. The results show a feedback loop in which people who are at a higher genetic risk for depression also have a higher baseline level of inflammation. If a person develops depression, that further increases the biomarkers related to inflammation.

4.1. Influence of Depression on CBC

Red blood cells, white blood cells, and platelets are examined by CBC testing. The most prevalent type of blood cell is red blood cell, which is made up of hemoglobin, a crucial protein for oxygen delivery throughout the body. White blood cells are blood cells that combat bacteria, viruses, and parasites. The small cell fragments known as platelets are what allow blood to clot normally and circulate throughout the body. Hematocrit and hemoglobin are examined as part of the red blood cell count.

4.1.1. RBC

Anemia is indicated by low red blood cell, hemoglobin, or hematocrit counts. A study found that iron deficiency anemia, which results in low hemoglobin levels, can increase a person's risk of depression. This is because iron deficiency can cause low levels of serotonin, an important neurotransmitter and mood stabilizer (Hosseini, et. al.,2018). However, the association between anemia/hemoglobin and depression was not found to be significant in another study (Wang et al., 2023). Higher than normal values may suggest the presence of a medical illness such polycythemia vera or cardiac disease. An infection or inflammation may be the cause of a high white blood cell count. It may, however, also be a sign of immune system or bone marrow issues, or it could be a reaction to a drug. On the other hand, a low white blood cell count could be a sign of cancer, an inflammatory disease that kills white blood cells, or problems with white blood cell synthesis. An unusually high or low platelet count frequently points to a health issue. Medication side effects may also be to blame. Hemoglobin is a protein that carries oxygen around the body. Its normal range is 13.5 to 17.5 g/dL for men, 12 to 15.5 g/dL for women. Hematocrit indicates the proportion of the count of red RBCs. A normal range is a 0.33 to 0.42 ratio. MCV is mean cell volume, and should be 74 to 87 fL. MCH is the amount of hemoglobin per blood cell, and a normal range is 24 to 29 pg. WBC stands for white blood cells, and indicates the total number of white blood cells in the blood. A White blood cell normal range is 4.5 to 12 x 109/L.
Red blood cell (RBC) and mean corpuscular hemoglobin (MCH) levels were negatively correlated with anxiety and depressive symptoms (Mojtaba et al, 2017). Increased erythrocyte deformability in individuals was found who had mental depression. One-third of depressed patients have relatively low RBC folate levels (Kobrosly and van Wijngaarden, 2010). Research suggests that the miR191-Riok3-Mxi1 pathway plays important role in regulating emotions and red blood cell levels also nuclear removal in the mature red blood cells of mice depends on miR191. Mental depression downregulates this gene hence mature RBC are less (Zhang, 2024). It was found that people with depressive symptoms may have a higher prevalence of anemia than people without depression in another study by Hosseini et. al., 2018.

4.1.2. WBC

The proinflammatory cytokines, phagocytosis, Natural Killer cell activities change in mentally depressed individuals, so naturally there are relevant changes in WBC. Anxiety and depression are two prevalent mood disorders that are connected to inflammation in the system. In a wide range of pathological diseases, elevated red cell distribution width (RDW) and white blood cell (WBC) count are linked to worse clinical outcomes. RDW has a substantial correlation with other inflammatory markers, and WBC is a non-specific inflammatory measure. Thus, we hypothesized that these hematological inflammatory indicators and experiences of anxiety and sadness would be related (Mojtaba et al, 2017). Percentage (%) composition of lymphocytes (PL) or neutrophils (PN)

and total white blood cell count (TWBCC), both are linked to mid- and late-life depression (Beydoun, 2016). A number of studies that were part of this meta-analyses discovered a correlation between elevated depression symptoms and inflammatory markers related to white blood cells, such as elevated absolute leukocyte levels (total white blood cell count, or TWBCC) (Stein et. al., 1991; Herbert & Cohen, 1993; Zorrilla et.al., 2001). A significant correlation between white blood cell count, and depression polygenic scores. Elevated white blood cell counts could be caused by a high hereditary predisposition for depression alone. This was noted in a study by Sealock et.al., 2021.

4.1.3. PLATELETS

Mental depression can have an impact on platelet count. Several studies have investigated the relationship between depression and platelet parameters, such as mean platelet volume (MPV) and platelet count. A study observed a positive association between MPV and Major Depressive Disorder (MDD) in a Turkish population, which was significant in females, but not in males1. This association was later replicated in other studies. Regarding platelet count, contrasting evidence of association with MDD status has been reported1. A positive association with plateletcrit – i.e., the product of MPV and platelet count – was also found. In a small study comparing patients with lifelong recurrent depression treated with selective serotonin reuptake inhibitors and matched healthy controls, significantly greater MPV, platelet distribution width (PDW) and platelet-to-larger cell ratio were reported for depressed participants. More recently, a significant positive association between depressive symptoms and PDW was identified, suggesting partly shared genetic bases between depression risk and platelet traits. Hematocrit is the volume percentage of red blood cells in blood. A study by Amiri et al., found that there was a decrease in the level of hematocrit in women with severe depression.

4.2. Influence of Depression on DC of WBC

Leukocyte differential count may be performed as part of a CBC test or as a follow-up to a CBC test that reveals if anyone has an abnormally high white blood cell count. The total WBC count increases with depression, but most of the time it is within normal ranges, however, differential count (DC) shows altered levels of different groups of Leukocyte or WBC. Normal ranges of DC WBC are as follows:
Neutrophils: 40% to 60%
Lymphocytes: 20% to 40%
Monocytes: 2% to 8%
Eosinophils: 1% to 4%
Basophils: 0.5% to 1%
Band (young neutrophil): 0% to 3%

Research has shown that mental depression, or major affective disorder, can have a significant impact on the immune system, including the differential count of white blood cells (WBCs) such as neutrophils.
A study published in the Journal of Neuroinflammation found that neutrophil counts were higher in patients with major depression (MD) compared to controls. The study also found that the improvement in depression symptoms correlated with changes in neutrophil counts. This suggests that neutrophils, a type of white blood cell, may play a role in the pathophysiology of depression. However, the study did not specifically mention band cells, which are immature neutrophils. More research is needed to understand the specific effects of depression on different types of white blood cells, including band cells. Depression can lead to changes in the immune system, and these changes may in turn contribute to the severity and progression of depression. It was found that the NLR or neutrophil to lymphocyte ratio could be a new biomarker for systemic inflammatory response. Patients with higher Hamilton Rating Scale for Depression (HAM-D) score had significantly higher NLR levels compared to patients with lower HAM-D score (Aydin Sunbul et.al., 2016). Research has shown that mental depression can also have a significant impact on lymphocyte counts. A study published in the Journal of Neuroinflammation found that baseline lymphocyte counts were elevated in patients with recurrent major depression (RMD) but not in those with first episode major depression (FEMD). Another study demonstrated that acute mental stress is associated with rapid peripheral blood lymphocyte changes, including the release of CD8+ and CD16+ cells into circulation2. During mental stress, the absolute number of lymphocytes, CD8+ cells, and CD16+ cells increased significantly. In addition, a study published in Frontiers in Psychiatry found that the Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), and Monocyte-to-Lymphocyte Ratio (MLR) were all elevated in patients with depression3.
Depression can have significant effects on various types of white blood cells (WBCs), including monocytes, eosinophils, and basophils.

Monocytes: Studies have shown that depression can lead to increased levels of monocytes12. One study found that the Monocyte to High-Density Lipoprotein ratio (MHR) and monocyte count values were higher in patients with Major Depressive Disorder (MDD) who had never received treatment compared to those who had.
Eosinophils: The count of eosinophils, a type of WBC that fights infection and plays a role in allergic reactions, has been found to be reduced in patients with depression1. However, one study found that eosinophil counts rose significantly in patients with first episode major depression (FEMD) after 6 weeks of treatment.
Basophils: Basophils, another type of WBC, have been found to decrease in patients with anxious depression3. This suggests that inflammation might be involved in the development of anxious depression.
Lymphocytes: Depression has been found to cause changes in lymphocyte counts. One study found that lymphocyte counts were elevated in patients with recurrent major depression (RMD) but not in those with first episode major depression (FEMD)4. Another study found that during mental stress, the absolute number of lymphocytes increased significantly

V. DISCUSSION

Depressive disorders, including major depressive disorder (MDD) and persistent depressive disorder (PDD; previously known as dysthymia), are among the leading causes of disability worldwide. The physiological manifestations of depression are largely

theoretical due to the current gaps in our understanding of the pathophysiology of these disorders. Research has indicated a link between depression and increased levels of inflammatory markers such as C-reactive protein (CRP), interleukin-6, and interleukin-1. The count of white blood cells and their subtypes can serve as indicators of chronic inflammation. Neutrophils and leukocytes, in particular, are integral to inflammatory processes. The neutrophil to lymphocyte ratio (NLR), derived from the white blood cell count, is a cost-effective and reproducible test that has been explored as a novel biomarker for systemic inflammatory response. It's noteworthy that acute psychological stress can lead to significant hemoconcentration, an increase in the concentration of cells and solids in the blood often due to loss of plasma fluid and sometimes associated with stress responses, which can influence hematocrit values. These observations highlight the intricate relationship between the immune system and mental health. In conclusion, these findings emphasize the need to consider the role of the immune system and inflammation in understanding the biological foundations of depression. However, further research is required to fully comprehend the complex relationship between depression, complete blood count (CBC), the immune system, and white blood cell count.

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