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Studies on the Relationships between Leukocytosis and Haematocrit

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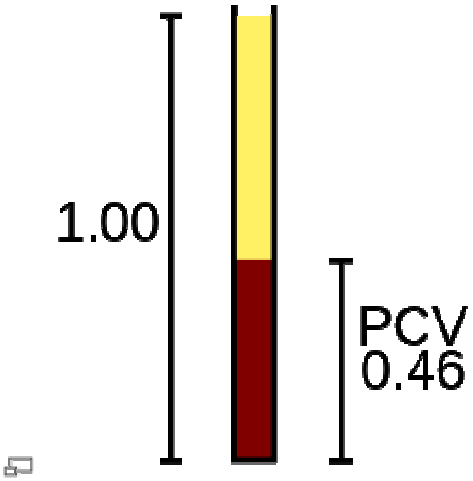
Abstract
In this study we measured white blood cells count and haematoccrits of 300 subjects. The study was divided into two groups. Group A constituted the controls of 100 subjects with normal leukocyte counts. The group B constituted the study group with a sample size of 200 subjects. The study group showed an elevated white blood cells count (leukocytosis). The average mean age of group A and B were 39±19 and 41±20 respectively. The haematocrit was measured using the microhaematocrit method, whereas the white cell count was estimated using the manual Neubauer method. The group A had a mean haematocrit and white cell count value of 35±8 and 7.1±1.6 respectively. Whereas the group B had a mean haematocrit and white cell of 29±10 and 22.2±15.8 respectively. The results showed a significant decrease ($p<0.05$) in haematocrit of the study group (group B) as compared against the control group (group A) using student t test. This study had satisfied that a relationship do exist between haematocrit and leukocytosis. Hence, patients diagnosed of leucocytosis be placed on blood boosting therapy and diet to avoid anaemia.
Keywords: Leukocytosis, haematocrit, anaemia, superoxide

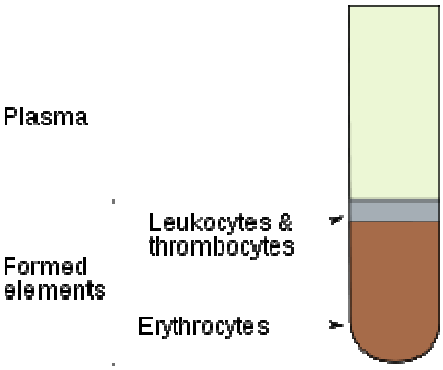
Introduction

The term *hematocrit* comes from the Greek words hema (Greek αιμα, meaning "blood") and criterion (Greek κριτηριον). It was coined by Magnus Blix at Uppsala in 1891 as *haematokrit*. (Hedin, 1981). The haematocrit also known as packed cell volume (PCV) or erythrocyte volume fraction (EVF), is the volume percentage (%) of red blood cells in blood. It is normally about 45% for men and 40% for women (Purves, 2004). It is considered an integral part of a person's complete blood count results, along with hemoglobin concentration, white blood cell count, and platelet count. The packed cell volume (PCV) can be determined by centrifuging heparinized blood in a capillary tube (also known as a microhematocrit tube) at 10,000 RPM for five minutes or with modern automated analyzer. An elevated or reduced haematocrit or PCV is a signal to system dysfunction that needs an emergency intervention (Rogers, 2011). Elevated cases of PCV are found in dengue fever dengue shock syndrome, Polycythemia vera (PV), Chronic obstructive pulmonary disease (COPD), Anabolic androgenic steroid (AAS), dehydrated and Capillary leak syndrome also leads to abnormally high hematocrit counts, because of the episodic leakage of plasma out of the circulatory system (Mitchell *et al.,* 2007). Sleep Apnea has been known to cause elevated hematocrit levels. Lowered PCV is mostly associated with anaemia, but does not indicate the type of anaemia. The mean corpuscular volume (MCV) and the red cell distribution width (RDW) can be quite helpful in evaluating a lower-than-normal hematocrit, because it can help the clinician determine whether blood loss is chronic or acute, although acute blood loss typically does not manifest as a change in hematocrit, since hematocrit is simply a measure of how much of the blood volume is made up of red blood cells. The MCV is the size of the red cells and the RDW is a relative measure of the variation in size of the red cell population. A low hematocrit with a low MCV with a high RDW suggests a chronic iron-deficient anemia resulting in abnormal hemoglobin synthesis during erythropoiesis. Groups of individuals at risk for developing anemia include:

- infants without adequate iron intake
- children going through a rapid growth spurt, during which the iron available cannot keep up with the demands for a growing red cell mass
- women in childbearing years with a greater need for iron because of blood loss during menstruation
- pregnant women, in whom the growing fetus creates a high demand for iron patients with chronic kidney disease whose kidneys no longer secrete sufficient levels of the hormone erythropoietin that promotes RBC proliferation. Erythropoietin prevents the death of cells in the erythrocyte cell line in the bone marrow. Therefore, erythropoietin allows those cells to continue to mature, exit the bone marrow and become RBCs (Jelkmann, 2004)



Packed cell volume diagram



White blood cells (leukocytes) : White blood cells (leukocytes), unlike red cells, are nucleated and independently motile. Highly differentiated for their specialized functions, they do not undergo cell division (mitosis) in the bloodstream, but some retain the capability of mitosis. As a group they are involved in the body's defense mechanisms and reparative activity. The number of white cells in normal blood ranges between 4,500 and 11,000 per cubic millimetre. Fluctuations occur during the day; lower values are obtained during rest and higher values during exercise. Intense physical exertion may cause the count to exceed 20,000 per cubic millimetre. Most of the white cells are outside the circulation, and the few in the bloodstream are in transit from one site to another. As living cells, their survival depends on their continuous production of energy (Stanley, 1981). The chemical pathways utilized are more complex than those of the red cells and are similar to those of other tissue cells. White cells, containing a nucleus and able to produce ribonucleic acid (RNA), can synthesize protein. They comprise three classes of cells, each unique as to structure and function, that are designated granulocytes, monocytes, and lymphocytes.

Granulocytes: Granulocytes, the most numerous of the white cells, are larger than red cells (approximately 12–15 micrometres). They have a multilobed nucleus and contain large numbers of cytoplasmic granules (i.e., granules in the cell substance outside the nucleus). Granulocytes are important mediators of the inflammatory response (Isao *et al.,* 2013).. There are three types of granulocytes: neutrophils, eosinophils, and basophils. Each type of granulocyte is identified by the colour of the granules when the cells are stained with a compound dye. The granules of the neutrophil are pink, those of the eosinophil are red, and those of the basophil are blue-black. About 50 to 80 percent of the white cells are neutrophils, while the eosinophils and basophils together constitute no more than 3 percent.

Neutrophils: The neutrophils are fairly uniform in size with a diameter between 12 and 15 micrometres. The nucleus consists of two to five lobes joined together by hairlike filaments. Neutrophils move with amoeboid motion. They extend long projections called pseudopodium into which their granules flow; this action is followed by contraction of filaments based in the cytoplasm, which draws the nucleus and rear of the cell forward. In this way neutrophils rapidly advance along a surface. The bone marrow of a normal adult produces about 100 billion neutrophils daily. It takes about one week to form a mature neutrophil from a precursor cell in the marrow; yet, once in the blood, the mature cells live only a few hours or perhaps a little longer after migrating to the tissues. To guard against rapid depletion of the short-lived neutrophil (for example, during infection), the bone marrow holds a large number of them in reserve to be mobilized in response to inflammation

or infection. Within the body the neutrophils migrate to areas of infection or tissue injury. The force of attraction that determines the direction in which neutrophils will move is known as chemotaxis and is attributed to substances liberated at sites of tissue damage. Of the 100 billion neutrophils circulating outside the bone marrow, half are in the tissues and half are in the blood vessels; of those in the blood vessels, half are within the mainstream of rapidly circulating blood and the other half move slowly along the inner walls of the blood vessels (marginal pool), ready to enter tissues on receiving a chemotactic signal from them (Isao *et al.,* 2013).

Neutrophils are actively phagocytic; they engulf bacteria and other microorganisms and microscopic particles. The granules of the neutrophil are microscopic packets of potent enzymes capable of digesting many types of cellular materials. When a bacterium is engulfed by a neutrophil, it is encased in a vacuole lined by the invaginated membrane. The granules discharge their contents into the vacuole containing the organism. As this occurs, the granules of the neutrophil are depleted (degranulation). A metabolic process within the granules produces hydrogen peroxide and a highly active form of oxygen (superoxide), which destroy the ingested bacteria. Final digestion of the invading organism is accomplished by enzymes.

Eosinophils: Eosinophils, like other granulocytes, are produced in the bone marrow until they are released into the circulation. Although about the same size as neutrophils, the eosinophil contains larger granules, and the chromatin is generally concentrated in only two nonsegmented lobes. Eosinophils leave the circulation within hours of release from the marrow and migrate into the tissues (usually those of the skin, lung, and respiratory tract) through the lymphatic channels. Like neutrophils, eosinophils respond to chemotactic signals released at the site of cell destruction. They are actively motile and phagocytic. Eosinophils are involved in defense against parasites, and they participate in hypersensitivity and inflammatory reactions, primarily by dampening their destructive effects.

Basophils: Basophils are the least numerous of the granulocytes, and their large granules almost completely obscure the underlying double-lobed nucleus. Within hours of their release from the bone marrow, basophils migrate from the circulation to the barrier tissues (e.g., the skin and mucosa), where they synthesize and store histamine, a natural modulator of the inflammatory response. When aggravated, basophils release, along with histamine and other substances, leukotrienes, which cause bronchoconstriction during anaphylaxis (a hypersensitivity reaction). Basophils incite immediate hypersensitivity reactions in association with platelets, macrophages, and neutrophils.

Monocytes: Monocytes are the largest cells of the blood (averaging 15–18 micrometres), and they make up about 7 percent of the leukocytes. The nucleus is relatively big and tends to be indented or folded rather than multilobed. The cytoplasm contains large numbers of fine granules, which often appear to be more numerous near the cell membrane. Monocytes are actively motile and phagocytic. They are capable of ingesting infectious agents as well as red cells and other large particles, but they cannot replace the function of the neutrophils in the removal and destruction of bacteria. Monocytes usually enter areas of inflamed tissue later than the granulocytes. Often they are found at sites of chronic infections.

In the bone marrow, granulocytes and monocytes arise from a common precursor under the influence of the granulocyte-macrophage colony-stimulating factor. Monocytes leave the bone marrow and circulate in the blood. After a period of hours, the monocytes enter the tissues, where they develop into macrophages, the tissue phagocytes that constitute the reticuloendothelial system (or macrophage system). Macrophages occur in almost all tissues of the body: those in the liver are called Kupffer cells, those in the skin Langerhans cells. Apart from their role as scavengers, it plays a key role in immunity by ingesting antigens and processing them so that they can be recognized as foreign substances by lymphocytes.

Leukocytosis is an increase of white blood cells in the circulatory system. Leukocytosis can be subcategorized by the type of white blood cell that is increased in number. Leukocytosis in which neutrophils are elevated is neutrophilia; leukocytosis in which lymphocyte count is elevated is lymphocytosis; leukocytosis in which monocyte count is elevated is monocytosis; and leukocytosis in which eosinophil count is elevated is eosinophilia (Mitchell et al,). Leukocytosis is very common in acutely ill patients. It occurs in response to a wide variety of conditions, including viral, bacterial, fungal, or parasitic infection, cancer, hemorrhage, and exposure to certain medications or chemicals including steroids. For lung diseases such as pneumonia and tuberculosis, WBC count is very important for the diagnosis of the disease, as leukocytosis is usually present. The mechanism that causes leukocytosis can be of several forms: an increased release of leukocytes from bone marrow storage pools, decreased margination of leukocytes onto vessel walls, decreased extravasation of leukocytes from the vessels into tissues, or an increase in number of precursor cells in the marrow. Certain medications, including corticosteroids, lithium and beta agonists, may cause leukocytosis (American Family Physician, 2000). A packed volume and haemoglobin relationship had been studied (Henrik and Leif, 1971).

PCV and white blood cell count are all components of full blood count. Assaying of PCV divides the heparinzed capillary blood into three sections. The packed red cells, the Buffy coat and the plasma. The buffy coat is the domain where white blood cells are located and at such is closely in touch with the packed cells. The pivotal reason for this research is the find out whether relationships do exist between high white blood cells and

pack cell volume. This work is solely designed to answer salient questions such as "does leukocytosis increase, decrease or of no effect to PCV?"

Methodology

Leukocyte count

A leucocytes count was counted using manual Neubauer method.

Well mixed whole blood in diluted 1 in 20 in an acid reagent which haemolyzes the red cells to be counted. Leucocytes are counted microscopically by the use of an improved Neubauer ruled counting chamber (haemocytometer) and the number of leucocytes per liter of blood calculated. The reagent used is called Tusk solution; leukocytes diluting fluid.

Heamatocrit

The packed cell volume (PCV) was determined by centrifuging heparinized blood in a capillary tube (also known as a microhematocrit tube) at 10,000 RPM for five minutes. This separates the blood into layers. The tube used was measured by the haematocrit reader to get the PCV value after placing it at the tail of 0% to the head of 100%.

Results

Table 1.1: A comparison of mean±sd of the white blood cell count and haematocrit between control and leukocytomic subjects.

Parameters Measured	Reference Range	Control mean±sd Group A (n=100)	Leukocytomic subjects mean±sd Group B (n=200)	p-value	comment
Age (yr)		39±19	41±20	p>0.05	ns
White cell count (10^6)	08-15	7.1±1.6	22.2±15.8	p<0.05	s
Haematocrit %	2.5-5.6	35±8	29±10	p<0.05	s

Ns- non significant
S-significant

Table 1.1 shows a significant increase in leukocyte count of group B as against group A. Also, the table shows a decrease in haematocrit count of Group B as against group A.

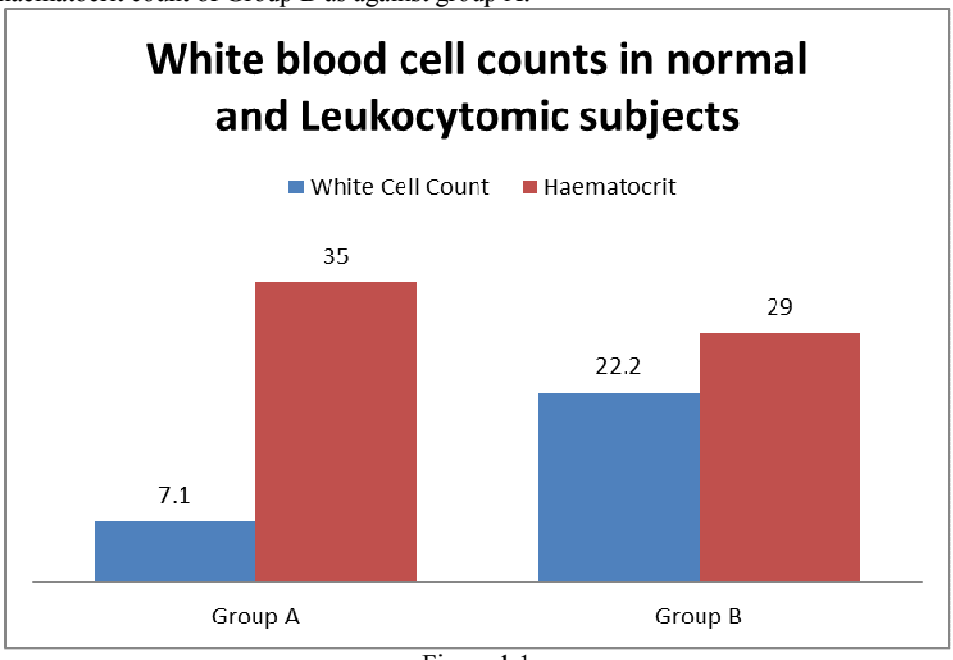


Figure 1.1

Discussion

We found a statistically significant correlation between leukocytosis and haematocrit. An inverse relationship

was established between leukocytosis and haematocrit. The increase white cell count tends to cause a decrease in haematocrit. White blood cells protect the body against infection. If an infection develops, white blood cells attack and destroy the causative agents. White blood cells are bigger than red blood cells but fewer in number. When a person has a bacterial infection, the number of white cells rises very quickly. The number of white blood cells is sometimes used to find an infection or to see how the body is dealing with cancer treatment. When a person has a bacterial infection, the number of *white cells* rises . If the RBC count is *low* (anemia), the body may not be getting the oxygen it needs. It is important to note, however, that the production of blood leukocytes and their numbers in circulation are regulated by complex interactions involving endogenous haematopoietic cytokines and interleukins (Quesenberry, 1995; Hock *et al.,* 1997). In contrast to study in the patients with severe abdominal pain, significant leukocytosis with neutrophilia along with increased levels of hematocrit were observed while levels of C-reactive protein (CRP) remained low (Isao et al., 2013). Also findings had also been shown in the interpretations of the influence of RBC hypertransfusion on hematopoiesis and in clinical and experimental studies of thrombopoiesis in polycythemic subjects (Jackson *et al.,* 1971).

The continual functioning of the red blood cell in the circulatory system is anchored on the utilization of glucose for the generation of energy to drive its activities. The continual exercise of the function of red blood cell is based on an extraordinary number of enzyme systems and energy generation. The energy generated is important for the maintenance of an appropriate balance between potassium in the red cell and sodium in the extracellular fluid. This maintenance is to avoid the leak out of potassium from the red cells and inflow of sodium into the red cells is exercised by a pump which function is energy dependent. Energy is not necessary for oxygen and carbon dioxide transport, which depends principally on the properties of hemoglobin. Energy is also required to convert methemoglobin to oxyhemoglobin and to prevent the oxidation of other constituents of the red cell. Red cells have an average life span of 120 days. Because red cells cannot synthesize protein, reparative processes are not possible. As red cells age, wear and tear leads to loss of some of their protein, and the activity of some of their essential enzymes decreases. Chemical reactions necessary for the survival of the cell are consequently impaired. As a result, water passes into the aging red cell, transforming its usual discoid shape into a sphere. These spherocytes are inelastic, and, as they sluggishly move through the circulation, they are engulfed by phagocytes. Phagocytic cells form a part of the lining of blood vessels, particularly in the spleen, liver, and bone marrow. These cells, called macrophages, are constituents of the reticuloendothelial system and are found in the lymph nodes, in the intestinal tract, and as free-wandering and fixed cells. Within the reticuloendothelial cells, erythrocytes are rapidly destroyed.. Protein, including that of the hemoglobin, is broken down, and the component amino acids are transported through the plasma to be used in the synthesis of new proteins (Zorc, 2009). The iron removed from hemoglobin passes back into the plasma and is transported to the bone marrow, where it may be used in the synthesis of hemoglobin in newly forming red cells.

The lifespan of white blood cells is about 13 to 20 days. White blood cells manufactured by the bone marrow are called leukocytes while those by the lymph nodes in the lymphatic system are called lymphocytes. The force of attraction that determines the direction in which neutrophils will move is known as chemotaxis and is attributed to substances liberated at sites of tissue damage. Of the 100 billion neutrophils circulating outside the bone marrow, half are in the tissues and half are in the blood vessels; of those in the blood vessels, half are within the mainstream of rapidly circulating blood and the other half move slowly along the inner walls of the blood vessels (marginal pool), ready to enter tissues on receiving a chemotactic signal from them (Isao *et al.,* 2013). Neutrophils are actively phagocytic; they engulf bacteria and other microorganisms and microscopic particles. The granules of the neutrophil are microscopic packets of potent enzymes capable of digesting many types of cellular materials. When a bacterium is engulfed by a neutrophil, it is encased in a vacuole lined by the invaginated membrane. The granules discharge their contents into the vacuole containing the organism. As this occurs, the granules of the neutrophil are depleted (degranulation). A metabolic process within the granules produces hydrogen peroxide and a highly active form of oxygen (superoxide), which destroy the ingested bacteria. Final digestion of the invading organism is accomplished by enzymes (Porth, 2011).

The decreased in haematocrit in contrast to the elevation of white blood cell could be attributed to the destruction of foreign bodies. In course of the foreign bodies' destruction, red cells are also destroyed. This because, some organisms access the red cells and its destruction is accompanied by of red cell. Also, normal red cells are destroyed after 120 days, but in a pathological instance, the destruction is shorter, and the time frame for replenishment is somewhat longer than that of white cells that takes about 20 days. It should also be noted that, the attack on foreign bodies by white cells are made potent by the secretion of some chemicals such as hydrogen peroxide and superoxide. These chemicals are potent destroyers of red cells. Also, the membranes of the red cells are fragile and prone to destruction. The secretion of superoxides by the white cells interrupts the activities of the pump and makes its susceptible for phagocytosis. Also, the the superoxides and the hydrogen peroxides of the white blood cell could impede the activities of the haemoglobin in the carriage of oxygen, hence collapsing the already fragile structure of the reds. Also, these contributory factors can one way or the other cause a decreased haematocrit in a leukocytosis subjects.Monocytes are actively motile and phagocytic,

they are capable of ingesting infectious agents as well as red cells and other large particles. This another contributory factor of decrease in haematocrit in leukocytosis situation. Based on this discovery, patients with elevated white blood cells should be placed on anaemic replenishment therapy to combat anaemia.

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