“A CLINICO HAEMATOLOGICAL STUDY OF PANCYTOPENIA”

BY

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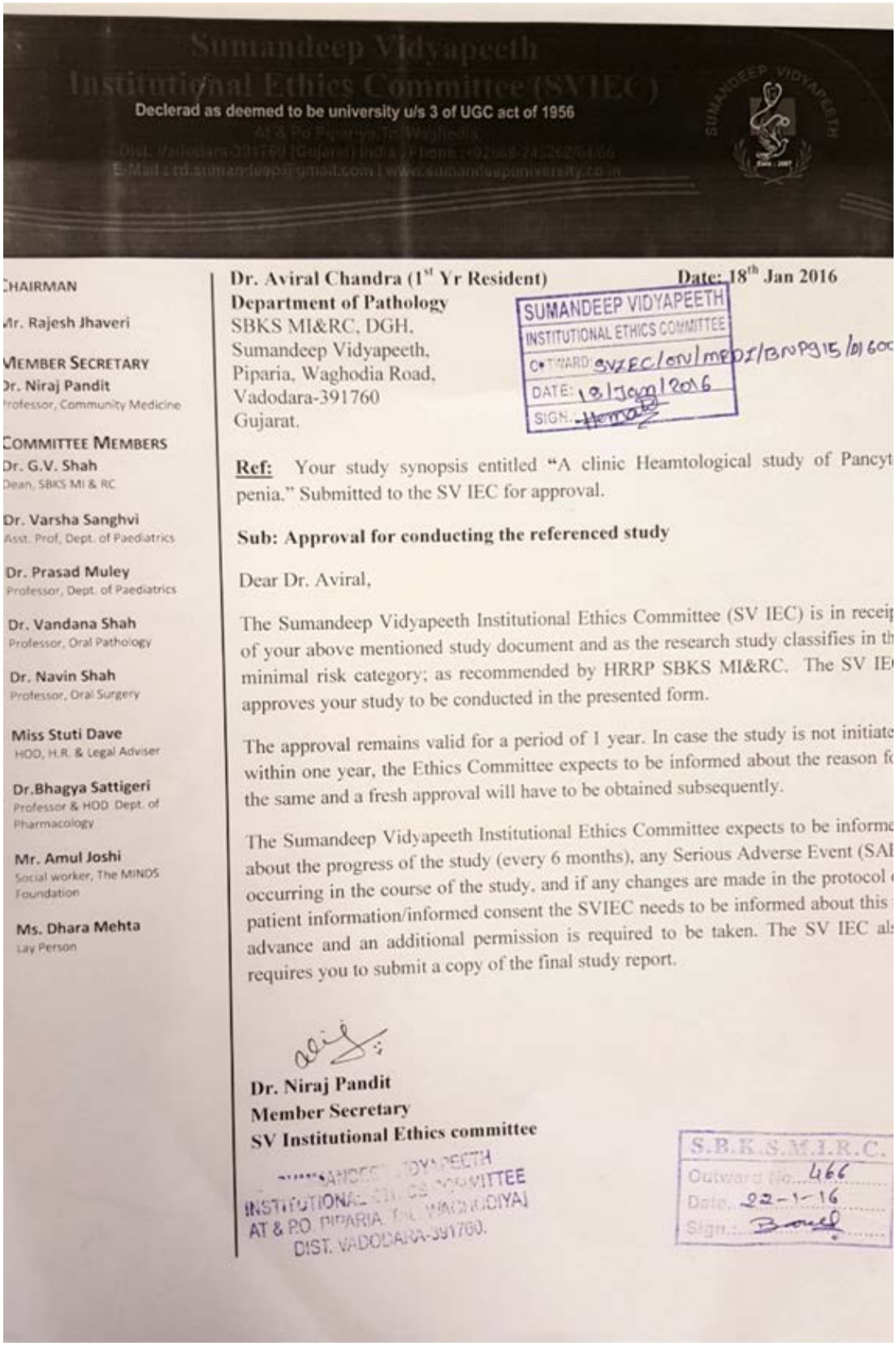

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ABSTRACT

Background: Pancytopenia is a common haematological entity characterized by anemia, leucopenia and thrombocytopenia. Various serious and life threatening illnesses ranging from simple drug induced bone marrow hypoplasia, megaloblastic marrow to fatal bone marrow aplasia and leukemias have pancytopenia common in them. The severity of pancytopenia and the underlying pathology determines the management and prognosis. Thus, identification of the correct cause will help in implementing appropriate therapy. Present study was conducted to assess the etiology, clinical profile and bone marrow morphology of pancytopenia.

Objective:

- To study the incidence and evaluate the etiological causes of pancytopenia in patient from age group 2 to 70 years.
- To study their clinico-haematological profile

Methods: The study was conducted at our Department of Pathology at Dhiraj Hospital, Sumandeep Vidyapeeth, Vadodara, from January 2016 to September 2017. Total 114 pancytopenia patients were studied to determine their clinical features, peripheral smear study and bone marrow morphology. The etiological pattern was assessed through relevant investigations in the respective patients.

Results: Out of 114 cases, megaloblastic anemia was the most common cause of pancytopenia (65.8%). The commonest age group was 11-20 years and more common in males. Pallor was the most common symptom and

generalized weakness as the most common sign.

Conclusion: If a patient presents with unexplained anemia, bleeding tendencies and prolonged fever then pancytopenia may be suspected. Detailed history and thorough examination with hematological examination along with bone marrow should be done. This will help in early and proper diagnosis of case followed by proper treatment.

Key words: Pancytopenia; Megaloblastic anemia; aplastic anemia.

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INTRODUCTION

Pancytopenia is a disorder in which red blood cells, white blood cells and platelets are all decreased than normal[1].

Pancytopenia is not a disease itself but a triad of findings that may result from a number of disease processes–primarily or secondarily involving the bone marrow. The presenting symptoms usually attributable to anemia, leucopenia or thrombocytopenia [2].

Pancytopenia has been found to be a common feature in many serious and life threatening illnesses which range can from simple drug induced bone marrow hypoplasia, megaloblastic marrow to fatal bone marrow aplasia and leukemia [3].

First step in the diagnosis of a disease is assessing the blood elements [3]. Physical examination findings and peripheral blood picture provide important information in the work up of pancytopenic patients and help in planning investigations on bone marrow samples [4].

Bone marrow evaluation is an invaluable diagnostic procedure in practice of medicine which may confirm the diagnosis of suspected cytopenia, from the clinical features and peripheral blood examination or occasionally give a previously unsuspected diagnosis [5].

The severity of pancytopenia and the underlying pathology determine the management and prognosis of these patients[4].

India is a large and diverse country. People have different age patterns, customs and dietary habits. The incidence of causes for pancytopenia is difficult and few studies

have discussed about it in the Indian scenario. However the studies available have shown megaloblastic anaemia as being the major cause of pancytopenia [4][6].

The present study has been undertaken to evaluate the various causes of pancytopenia and to evaluate clinical signs and symptoms and hematological parameters along with bone marrow aspirate. Thus it would help in planning the diagnostic and therapeutic approach in patients with pancytopenia.

AIM

The aim of this study is to study the incidence of the underlying causes of pancytopenia presenting at our institution with a clinical and pathological correlation.

OBJECTIVES OF THE STUDY

- To study the incidence and evaluate the etiological causes of pancytopenia in patient from age group 2 to 70 years.
- To study their clinico-haematological profile

REVIEW OF LITERATURE

Until 19th century, humans thought that blood cells were formed in lymph nodes or the liver and spleen [7].

Neuman and Bizzozero in 1868 found nRBCs in material which was taken out or 'squeezed' from the rib of human cadaver. They concluded that bone marrow was the source of blood cells [7].

Red cells, leucocytes and platelets constitute the essential cellular components of the blood. Formation of blood cells occurs at different anatomical sites during the course of the development from embryonic to adult life (Metcalf & Moore 1971) [8].

Production of blood cells begins in the yolk sac in the embryo. Then it shifts to liver and spleen in utero life and then superseded by the bone marrow which serves as the only important site of blood cell production after birth [8].

In an adult, the bone marrow daily produces approximately 2.5 billion RBC's, 2.5 million platelets and 1.1 billion granulocytes per kg of body weight. The rate of production varies and adjusts to the actual need required [7].

Anemia is said to be present when the hemoglobin level in the blood is below the lower extreme of the normal range for the age and sex of the individual [8].

Thrombocytopenia is defined as a reduction in the peripheral platelet count below the lower limit of $150X10^9/L$ [8].

Various studies have been carried out in past decades to know the causes, clinical manifestations and thus to know the treatment modality for pancytopenia,

although very few studies have been published in the literature.

In 1987 at Israel and Europe, International agranulocytosis and Aplastic anemia study was carried out to know the incidence and causes of pancytopenia, and found aplastic anemia as the commonest cause followed by myelodysplastic syndrome.

Same study was carried out in 1990 at same place by Keisu M, who revealed neoplastic diseases, radiation as common cause for pancytopenia followed by aplastic anemia [9].

Hence, there are various causes and different clinical presentation of pancytopenia.

Various causes of pancytopenia are [9].

1. Ineffective hematopoiesis with cell death in the marrow.
2. Formation of defective cells which are rapidly removed from circulation.
3. Sequestration and /or destruction of cells by the action of antibodies or
4. Trapping of normal cells in a hypertrophied and over-reactive reticulo-endothelial system.

Various causes of Pancytopenia are as follows [10].

I) Hypocellular bone marrow

1. Acquired aplastic anemia
2. Inherited bone marrow failure syndrome (e.g., Fanconi anemia, dyskeratosis congenita, megakaryocytic thrombocytopenia, and Shwachman-Diamond syndrome)
3. Hypoplastic myelodysplastic syndrome
4. Virus-associated aplastic anemia

II) Cellular bone marrow

1. Primary bone marrow disease

   Malignant/clonal

   Myelodysplasia

   Myelofibrosis

   PNH

   Acute myelogenous leukemia

   Acute lymphoblastic leukemia

   Hemophagocytic lymphohistiocytosis

   Osteopetrosis

2. Secondary to systemic disease

   Metastatic solid tumors

   Autoimmune

- Systemic lupus erythematosus
- Sjögren syndrome

Nutritional/toxic

- Vitamin B 12 deficiency
- Folate deficiency
- Alcoholism

Infections

- Overwhelming infection/sepsis
- Virus
- Brucellosis
- Ehrlichiosis
- Mycobacteria

Storage disease

- Gaucher
- Niemann-Pick

Sarcoidosis

Anatomic

Hypersplenism

APLASTIC ANAEMIA (AA):

In 1888, it was Ehlrlich who first described a case of Aplastic anemia in a young female patient who presented with anemia, fever and bleeding [10]. The term aplastic anaemia was given by Vaquez and Aubertin in discussions of the society of the hospital of Paris 1904 [10].

Scott in 1959, studied 39 cases and suggested that the term aplastic anaemia to be used only for cases in which pancytopenia existed. The production of all the elements of the blood formed in the marrow is decreased, severe hypoplasia or aplasia of the marrow is present, and no primary disease infiltrating, replacing or suppressing active haemopoietic tissue is evident [10].

The word aplastic in Greek word means “a” and plasso means “without form”[10].

Aplastic anaemia is defined as the presence of pancytopenia in the peripheral blood and a hypocellular marrow in which normal haemopoietic marrow is replaced by fat cells [10].

Aplastic anemia can be classified as [12].

1. Idiopathic

2. Secondary to other disorders (acquired aplastic anemia).

3. Constitutional when associated with inherited defects in DNA repair.

Two from the following is required for diagnosis of aplastic anemia along with hypocellular marrow.

i. Haemoglobin < 10 g/dl

ii. Platelet count < 100 x 10^9/L

iii. Neutrophil count < 1.5 x 109 / L

The pathogenesis is still unclear but it is suggested that an unidentified underlying genetic predisposition may be present. Some association of HLA DR2, specially the DR15 split, with acquired aplastic anaemia may be present [11].

There is evidence of both quantitative and qualitative stem cell defect in aplastic anaemia and increased apoptosis of remaining early haemopoietic progenitor cells. [11].

INHERITED BONE MARROW FAILURE SYNDROME

About 25% of pediatric patients and 10% of young adults who present with aplastic anemia, they may have an inherited etiology [13].

Pancytopenia is common in Fanconi Anemia, dyskeratosis congenita, Diamond blackfan syndrome and Severe Congenital Neutropenia / Shwachman Diamond Syndrome [13].

In 1927, Fanconi studied three brothers who had pancytopenia along with physical abnormalities. He called their anaemia as “perniziosiforme” [14].

In 1931 Naegeli suggested that the Fanconi anaemia be used for familial aplastic anaemia and congenital physical anomalies [14].

Fanconi Anemia is a rare recessive disorder which is characterized by diverse developmental abnormalities, progressive BM failure and predisposition to both

hematological malignancies and solid tumors (Okuyama and Mishina 1987) [15, 16].

Michel et al found that Reverse Transcriptase-Polymerase Chain Reaction, a simple direct semi-quantitative procedure, can be used to characterize specific gene expression stem and progenitors cell fractions in diagnosis of FA [16].

Dyskeratosis congenita is characterized by lacey reticulated pigmentation, dysplastic nails and oral leukoplakia. However many patients reach adulthood prior to the diagnosis [13].

MYELODYSPLASTIC SYNDROME (MDS)

These are a group of clonal hematopoietic stem cell diseases. They are characterized by cytopenia (s), dysplasia in one or more of major myeloid cell lines, ineffective hematopoiesis, and increase risk of development of AML [17].

A detailed history and physical examination, complete blood count with leukocyte differential, reticulocyte count, BM aspiration and biopsy with iron stain and cytogenetic studies, erythropoietin levels and iron studies is required for diagnosis of MDS [18].

Thanapoulou along with his colleagues together isolated bone marrow cells from 11 different MDS patients and showed that in most cases the cells could at least transiently repopulate the marrow of NOD/SCID B2 microglobin null mice [19].

Bone marrow fibrosis is rare in MDS. In a study by G.L. Deliliers and his colleagues which included 17 cases of MDS associated with myelofibrosis, reticulin fibre was evaluated on the basis of the system proposed by Manoharan et al (1979). All the patients had pancytopenia along with mild absent hepatosplenomegaly. Bone marrow

biopsy showed significant fibrosis and signs of trilineage dysplasia [20].

TABLE 1: BONE MARROW GRADING FOR FIBROSIS [20].

Grade	Bone marrow findings
1+	Represents a fine fiber network with occasional coarse fibers.
2+	a diffuse fiber network with increase in scattered coarse fibers.
3+	a diffuse coarse fiber network with no collagenization (negative trichome stain)
4+	a diffuse network with collagenization (positive trichrome stain)

MYELOFIBROSIS (MF)

Bone marrow fibrosis or Myelofibrosis refers to the abnormal deposition of reticulin network by bone marrow fibroblasts [20.21].

In 1879, Hueck first described myelofibrosis in two patients with myelogenous leukemia [21].

In 1963, Lewis and Szur described a syndrome of acute myelofibrosis with a fatal course [21].

Risk factors for myelofibrosis are exposures to toxins, ionizing radiation, chemotherapy, viruses or as a reaction to neoplastic invasion of the bone marrow [21].

Myelofibrosis may be reaction due to myeloproliferative disorder or to another neoplastic disorder. Bone marrow fibroblasts are of mesenchymal origin and not derived from bone marrow stem cells. In primary myelofibrosis, all red blood cells, granulocytes and platelets contain the same G-6-PD isoenzyme. This suggests a clonal

origin of this disorder. In contrast bone marrow fibroblast contain two different G-6-PD isoenzymes indicating separate origin of fibroblast [22].

Connective tissue framework of normal bone marrow is synthesized by fibroblasts and consists of a network of reticulin fibers that is continuous with the reticulin of blood vessel wall, sinusoids and endosteum [23].

Two patterns of fibrosis are seen. Normal pattern is exaggerated leading to reticulin fibrosis and secondarily by bone marrow obliteration by collagen deposition known as collagen fibrosis. Both fibrosis contain type I, III, IV and V with predominance of type III and its precursor [21].

Myelofibrosis present in three stages [21].

1. Cellular phase with pancytosis.

2. Myelofibrosis without marked osteosclerosis

3. Osteosclerosis and hypocellularity with marrow failure.

Adverse prognostic indicators in myelofibrosis are hemoglobin < 10gm%, bone marrow hypocellularity, plasma volume >140% of expected and presence of constitutional symptoms. Myelofibrosis can occur as a secondary phenomenon with many myeloproliferative, malignant and non-malignant disorders and may regress after appropriate therapy directed towards the underlying process [21].

PARAOXYSMAL NOCTURNAL HEMOGLOBINURIA (PNH)

Paraoysmal nonturnal hemoglobinuria (PNH) also called as Marchiafava-Micheli syndrome is characterized by intravascular hemolysis, nocturnal hemoglobinuria , venous thrombosis and is associated with bone marrow failure [24,25].

It is an acquired disease due to non-malignant clonal expansion of one or several hematopoietic stem cells that have acquired, a somatic mutation of the phosphitidylinositol glycan complementation class A gene (PIG -A) [24].

Intravascular hemolysis is resulting from an intrinsic defect in the membrane of red cells which makes the red cells highly susceptible to complement [25].

The clinical syndrome can present in three types of symptoms including [25].

1. An acquired intracapsular hemolytic anemia due to abnormal susceptibility of the red cell membranes to the hemolytic activity of the complement.

2. Thrombosis in large vessel, such as hepatic, abdominal, cerebral and subdermal veins.

3. A defect hematopoiesis that may be mild/severe such as pancytopenia in aplastic anemia state.

In 1930, Ham and Dacie form UK, developed the acidified Ham's test. It became the diagnostic test for PNH [25]. If both acid hemolysis test and a sucrose hemolysis test are abnormal then diagnosis of PNH can be established [26].

Marcel E.C and James C. Barton studied 43 patients of pancytopenia with bone marrow biopsy specimen containing < 10% nucleated cells. They observed

among 43 patients with pancytopenia who had markedly hypoplastic bone marrow specimens, 11 had a positive sucrose test, and four of these had an abnormal quantitative sucrose hemolysis test. They concluded that it's difficult to differentiate PNH from idiopathic aplastic anemia, both presenting with pancytopenia and thus donor red blood cell survival studies, which differentiate intravascular from extra vascular hemolytic disorders, permits differentiation of both the disorders [26].

MALIGNACIES ASSOCIATED WITH PANCYTOPENIA

Massive marrow necrosis with bone marrow failure is apparently rare and has been noted in small number of patients with neoplasia, infection or sepsis and Acquired immune deficiency syndrome (AIDS). Hypoxic injury to the marrow, vascular obstruction and thrombosis as a consequence of disseminated intravascular coagulation (DIC) has been proposed to have a role in the development of this condition [27].

Charles Knupp and Phillip H. Pekala found two patients who had neoplasia with extensive bone marrow necrosis, without presence of sepsis or prior to any antineoplastic treatment, with subsequent fibrosis and tumor necrosis factor (TNF) activity. The observations suggested that excessive TNF production from mononuclear cells in response to cancer or infection could result in marrow necrosis in humans [27].

Patients with cancer may frequently have anaemia, with or without other cytopenias. Anemia related to cancer can be due to tumour invasion of the bone marrow, or indirectly due to tumour therapy or systemic symptomatology, or may be an incidental finding resulting from other pathology in the patient [28]. The cancer can have a major impact on bone marrow function [28].

Cytopenias as a direct result of the malignancy:

Malignant tumours especially haemopoietic malignancies can be the cause of primary one or more cytopenias. The anaemia is usually macrocytic and associated with a reticulocytopenia and clonal erythropoiesis. For confirmation evaluation of bone marrow aspirate smears and biopsy sections is done [28].

Other haemopoietic neoplasms can suppress the bone marrow and cause anemiane marrow. Acute leukemia directly suppresses the normal erythropoiesis and causes anaemia. Myelodysplasitic, anaemia caused by acute leukemia is often macrocytic and associated with a decreased reticulocyte count [28].

Cytopenias indirectly resulting from malignancy:

Many cancer patients who present with cytopenias can be due to a tumor. Autoimmune haemolytic anaemia has been described in association with a number of tumours, although it is more frequently noted in patients with CLL. Microangiopathy may be seen in patients with red cell destruction due to cancer. Gastric carcinoma, breast cancer and lung cancer can coexist with anemia.

One of the more common anaemia's noted in patients with cancer is characterized by a normal red cell size, a low reticulocyte count, and an apparent increase in bone marrow iron storage [28]. This process has been called the "anaemia of chronic disease" and is associated with the elaboration of inflammatory cytokines in the host [28]. In anaemia of chronic disease wide varieties of marrow histologies can be seen. The marrow is normocellular, with normal M:E ratio and an increase in histiocyte storage iron [28]. However, variable degree of myeloid hypoplasia may result in an overall marrow hypocellularity and a decrease in M:E ratio [28].

Occasionally erythroid hyperplasia may be present [28].

These abnormalities may be identified even in the absence of tumour invasion of the marrow and may reflect a systemic response to the presence of the malignancy [28].

Jordi Sans-sabrafen et al, established a hypothesis for association between MDS and malignant solid tumors in a cohort study of 155 patients with myelodyslasia,in which 21 patients had cancer [29].

Their hypothesis includes:

1. Patients suffering MDS have a higher incidence of malignant tumors than the general population.
2. MDS could be a paraneoplastic syndrome and could be present before, simultaneously with or after the diagnosis of the malignant tumor [29].

MULTIPLE MYELOMA:

Multiple Myeloma is a bone marrow based, multifocal plasma cell neoplasm characterized by a serum monoclonal protein and skeletal destruction with osteolytic lesions, pathological fractures, bone pain, hypercalcemia and anaemia [30].

The myeloma cells may be morphologically normal or may be moderately or severely dysplastic, common cytological features include marked pleomorphism, increased size of cells, a high N:C ratio, multinuclearity, nuclear lobulation, uniform cytoplasmic basophilia without a distinct golgi zone, presence of mitotic figures and cytoplasmic and nuclear inclusions [30].

The cytoplasm of myeloma cells contain abundant endocytoplasmic reticulum, condensed or crystallized cytoplasmic immunoglobulin producing a variety of morphologically distinctive findings, including, multiple pale bluish – white grape like accumulation (Mott cells, Morula cells), cherry red refractive round bodies (Russell bodies), vermilion staining glycogen rich IgA (Flame cells) and crystalline rods. Peripheral smear in majority of patients show anaemia, which is either normocytic, normochromic or, less often, macrocytic. Rouleaux formation with increased background basophilic staining may be present due to paraprotein. The blood film is occasionally leukoerythroblastic and it is often possible to find a small number of plasma cells or plasmacytoid lymphocytes [30].

On biopsy it is characterized by excess of marrow plasma cells, seen in large foci, nodules or sheets. In general when 30% of the marrow volume is comprised of plasma cells, a diagnosis of plasma cell myeloma is considered. In histological sections of marrow the myeloma mass may occasionally be associated with prominent osteoclastic activity [30].

Marrow destruction by tumour plasma cells results in anaemia, leucopenia and Thrombocytopenia [30].

LEUKEMIA

Leukemia is an unusual complication of aplastic anemia, estimated at less than 1% and less than 2% of patients with acute myeloid leukemia (AML) have history of aplastic anemia. 9% patients with aplastic anemia and 89% patients with MDS have risk of developing AML [31].

Beard et al, Needleman et al and Hona et al reported group of patients with

hypocellular or hypoplastic acute leukemia [32].

Hypocellular BM with increased blasts (HBMIB) is a rare condition with >30% blasts often showing myeloid differentiation. In general, patients are elderly men with nonspecific symptoms and lack physical findings, are leukopenic or pancytopenic and have rare to few blastic cells in peripheral blood smear [32].

Hypocellular bone marrow with increased blasts (HBMIB) and myelodysplastic syndromes (preleukemia) often present with similar clinical pictures. However, pathologic findings in these two entities are somewhat different. The bone marrow in myelodysplastic syndromes is normocellular or more commonly hypercellular with less than 30% blasts. As reported by Candece L, gladson and F.Naeim, the bone marrow in HBMIB is hypocellular with, in general, greater than 30% blasts [33].

HBMIB uncommonly progresses to a fulminant acute leukemia, BM failure could be induced by various complex events, such as absence of the proliferation and maturation of normal stem cells by humoral or cellular mechanisms, abnormal microenvironment, lack of hematopoietic growth factor, decrease in the number of normal stem cells, and presence of abnormal stem cells with either defect in proliferation or maturation [34].

Autoimmune hemolytic anemia, immune thrombocytopenia and pure red cell aplasia are well described complications associated with chronic lymphocytic

Leukemia [35]. Autoimmune hemolytic anemia and immune thrombocytopenia are antibody-mediated conditions, but the pathogenesis of pure red cell aplasia likely has to do with abnormal T-cell function in cases that are not related to parvovirus B19 infection. Jeffery A. Zonder quoted that despite the frequency of these immune

mediated cytopenias in CLL, to their knowledge, only two previous cases of pancytopenia with marrow hypoplasia have been reported [35].

SUBLEUKEMIC LEUKEMIA:

The total white cell count in acute leukemia ranges between subnormal to markedly elevated values. In about 25% of patients the total white cell count at the onset is reduced ranging between 1-4 x 109/L. In subleukemic patients blast cells may be present in very small numbers in peripheral blood. Buffy coat smear will help in detecting blasts under these circumstances [36].

Peripheral smear shows anaemia with moderate anisopoikilocytosis. Neutrophils show hypogranulation and Pelger – Huet like anomaly. Immature white and red cells are absent or present only in small numbers at onset, but appear in the course of the illness. Blast cells predominate in bone marrow examination [36].

HEMOPHAGOCYTIC SYNDROME (HPS):

HPS is a reactive disorder of the mononuclear phagocytic system characterised by benign, generalised histiocytic proliferation with marked hemophagocytosis in the bone marrow. HPS is diagnosed based on fever, splenomegaly, cytopenias affecting at least two of three lineages in the peripheral blood, hypertriglyceridemia and/or hypofibrinogenemia, hemophagocytosis (in bone marrow, spleen, or lymph nodes), low or absent NK-cell activity, hyperferritinemia, and high level of soluble interleukin 2 receptor. Total five of the eight above criterias must be fulfilled for the diagnosis [37].

The postulated mechanism of hemophagocytic syndrome has included the release of special lymphokines with the function to stimulate phagocytosis or

aberrant response of the host histiocytes to lymphokine release by the malignant lymphocytes.

An immunological etiology of pancytopenia is also suggested by extreme plasmocyte invasion of organs observed in fatal canine ehrlichosis [38].

MEGALOBLASTIC ANAEMIA

Megaloblastic anemia has been known as a clinical entity since last century. Pernicious anemia was first described as a cause megaloblastic anaemia by T Lomas Addison in 1849 [39]. Megaloblastic anaemia occurs due to abnormal maturation of haematopoietic cells due to fault in DNA synthesis. For DNA synthesis, Cobalamine (vit B_{12}) and folic acid are required. Deficiency of any of these vitamins results in asynchrony in the maturation of the nucleus and cytoplasm of rapidly regenerating cells. This causes abnormal nuclear maturation with normal cytoplasmic maturation, apoptosis, inefficient erythropoiesis, intramedullary hemolysis, pancytopenia and typical morphological abnormalities in the blood and bone marrow cells [40, 41].

Megaloblastic anaemia can cause increased morbidity if it is unrecognized or remains misdiagnosed. It has multiple causes which can be dietary deficiency, impaired absorption and transport or impaired utilization these vitamins in DNA synthesis [42]..

India has a diverse population. The dietary habits and customs vary throughout the country. However the incidence of Megaloblastic anaemia and its problems related to it have yet not been adequately demonstrated [42].

Laboratory evaluation of Megaloblastic anemia requires a complete blood cell count including all the red cell indices, examination of a well stained blood film and

assay of the vitamins are sufficient to make a definitive diagnosis of Pancytopenia [42].

Anemia is classified as macrocytic if MCV exceeds 95fl [43].

An elevated MCV may be the only indicator of conditions like vitamin B12 or folate deficiency, preleukemia or alcoholism [44].

In 1934 Wintrobe established the value of morphologic classification of anaemia. He characterized anaemia as macrocytic, normocytic, simple microcytic and lympochromic microcytic. In his study the most common cause of macrocytic anaemia was Megaloblastic anaemia produced by pernicious anaemia. Other causes in decreasing order were disorders of liver like cirrhosis, bone marrow disturbances like Leukemias, myelodysplasia and aplasia, the anaemia of acute blood loss and the anaemia of pregnancy [44].

1964 Haltersley et al, Davidson (1971), Mcphedran (1973), Davidson (1978) and Colon Otero et al (1992) studied various causes of macrocytic anaemia and observed Megaloblastic anaemia, cirrhosis, alcohol abuse as most common causes [44].

Megaloblastic anaemia remains the most important cause of macrocytic anaemia in the study carried out by Vineetha Unnikrishnan et al on 60 adult patients of macrocytic anemia [44].

It is generally believed in megaloblastic as severity of anemia increases; thrombocytopenia develops followed by neutropenia [45]. Thrombocytopenia is due to impaired DNA synthesis resulting in ineffective thrombocytosis and so the neutropenia, which in turn lead to impaired intracellular killing of ingested bacteria

by neutrophils and macrophages, thereby increasing susceptibility for infections [45].

IRON DEFFICIENCY CAUSING PANCYTOPENIA

Iron deficiency anemia is the one of the most common cause of nutritional deficiency in India. Iron deficiency anemia is usually associated with thrombocytosis but thrombocytopenia associated with Iron deficiency anemia is reported in few cases [46].

Iron deficiency anemia can be associated with pancytopenia, though thrombocytopenia has occasionally been reported in Iron deficiency anemia. Although iron deficiency is associated with a reactive thrombocytosis, increasing severity of iron deficiency leads to normalization and occasionally even decrease platelet counts.

The exact mechanism of this is not known but it may be due to the alteration in the activity of iron dependant enzymes in thrombopoiesis and leucopoiesis [47,48].

The mechanism of leucopenia in unclear. Animal experiments and invitro studies using human hematopoietic stem cells have demonstrated that addition of erythropoietin to the stem cells down regulates neutrophil production leading to neutropenia [47].

COPPER DEFICIENCY CAUSING PANCYTOPENIA

Copper deficiency is a recognized cause of anemia and neutropenia [49]. Copper deficiency anemia is described in patients receiving total parental or enteral nutrition lacking adequate amount of copper, after gastric resection, short bowel syndrome,children with malabsorption disease states, in infants with protein energy malnutrition, infants fed only on cow’s milk and in excessive zinc ingestion [49].

In 2002, Gregg et al described an adult patient with anaemia and neutropenia due to copper deficiency. The patient's bone marrow biopsy morphologically resembled Myelodysplastic syndrome with ringed sideroblasts [49].

Pathogenesis of anaemia in copper deficiency is complex. It may be due to various causes. Anemia, iron and copper deficiency have been associated since 1928 when Hart et al demonstrated that solution of copper sulphate and ferric chloride corrected the anemia in rat fed a diet with cow's milk [49].

Neutropenia associated with copper deficiency was first noted in pervnian malnourished children. Decrease in copper decreases survival of peripherally circulating mature granulocytes and arrested granulocytic maturation in the bone marrow [49].

ALCOHOL INDUCED PANCYTOPENIA

Alcohol associated pancytopenia with hypocellular bone marrow has only been described by Ballard. Thrombocytopenia is the most common abnormality in severe alcoholics and anaemia, leucopenia are often seen in association with heavy intake of alcohol. Pancytopenia with bone marrow hypoplasia as a direct result of excessive ingestion of alcohol is rare [50].

Invitro culture studies showed that the sensitivity of the patient's CFU-GM to ethanol was increased compared to normal individual. Nakao et al observed patient's clinical course and chemical findings with bone marrow hypoplasia resulted from excessive ingestion of alcohol [50].

The sudden onset of marrow hypoplasia may be due to cumulative effects of ethanol which are toxic enough to decrease hematopoietic stem cell growth. It has been suggested that sideroblasts and vacuolisation of pronormoblasts and promyelocytes are frequently seen in the bone marrow of alcoholic patients [50].

AUTOIMMUNE DISORDERS CAUSING PANCYTOPENIA

SYSTEMIC LUPUS ERYTHOMATOSIS (SLE)

Hematological complications constitute a common feature of SLE. Vongarellis et al studied 40 cases of SLE and observed that, anemia of chronic disease was most common cause of anemia in their patients [51]. Analysis of bone marrow biopsy findings and peripheral cytopenias was systemically analyzed in their study. Bone marrow specimens were characterized primarily by several distinct types of bone marrow necrosis, hypocellularity and stromal changes such as stromal edema and vascular changes .Second significant abnormality of bone marrow were dysplastic changes of all hematopoietic lineages and the presence of microarchitecture disorganization and presence of abnormal location of immature precursors [51].

Hematological abnormalities are due to presence of auto reactive lymphocytes, auto antibodies and the action of proinflammatory cytokines that act against the bone marrow progenitor cells and microenvironment as well as peripheral blood cells [51].

Hematological complications are found in approximately 85% of patients with SLE. During the disease course anemia is seen in 70% of SLE cases, 65% will have leucopenia and 25% will have thrombocytopenia [52].

SLE is an uncommon cause of bone marrow fibrosis with only few cases reported in literature [52]. Hassel bach et al demonstrated elevated levels of type I and III

procollagen in the serum of patients with myelofibrosis and SLE indicative of increased procollagen synthesis by the bone marrow fibroblast [52].

Feng et al evaluated 23 patients of SLE with pancytopenia and revealed frequent findings in bone marrow biopsies were dyserythropoiesis and hypoplasia. Similar results were obtained by Aziz et al and Paquette et al in their study [52].

SJOGRENS SYNDROME (SS)

Sjogrens Syndrome is characterized by the presence of mononuclear cells infiltrates in glandular and extraglandular sites [53].

The hematological complications include anemia, leucopenia, thrombocytopenia and lymphoproliferative disorders including lymphoma [53].

Thrombocytopenia is most common complication of primary Sjogrens Syndrome and is due to humoral autoimmune mechanism. It has been reported significant association between thrombocytopenia and anticardiolipin antibody and anti SS-A antibody [53].

Pancytopenia complicating primary SS is rare. The cause of pancytopenia is mediated through inhibition of mononuclear cells hematopoietic progenitors [53].

POLYARTERITIS NODOSA (PAN)

Polyarteitis nodusum is not commonly associated with hematological abnormalities. Leslie RH and Nancy Y repost first case of pancytopenia as presenting symptom of PAN [54].

It is a type of necrotizing vasculitis which affects medium and small sized

arteries. Idiopathic myelofibrosis, acute leukemia, CLL and hairy cell leukemia is seen associated with PAN, but pancytopenia is rare manifestation [54].

INFECTIONS CAUSING PANCYTOPENIA.

MALARIA:

It was the Italians in the 18th century who named the desire malaria meaning "foul air" [55].

Malaria is a parasitic infection caused by obligate intracellular protozoa of the genus plasmodium, four species causing human disease are P.falciparum, P.vivax, P.ovale and P.malarie [55].

Hemolytic anemia due to the destruction of erythrocytes by parasite can manifest as pallor, fatigue and hemodynamic derangement. Thrombocytopenia is a common manifestation and is immune related and in severe infection is due to disseminated intravascular coagulation [55].

Malaria due to P.falciparum infection has the distinction of being the most devastating of the malarial illness. Severe disease with multiorgan dysfunction is seen only in P.falciparum malaria and is due to the ability of the organism to achieve heavy parasite burden and the intravascular sequestration of parasitized erythrocytes leading to impaired oxygen delivery and subsequent end organ damage [55].

Plasmodium falciparum parasites usually are found in erythrocytes of normal size. In Plasmodium falciparum infection, ring forms predominate and finding numerous ring forms without mature stages is evidence for plasmodium falciparum infection, young rings being smaller. The presence of doubly infected cells and double

chromatin dots in ring trophozoites occur more commonly in plasmodium falciparum. Gametocytes of plasmodium falciparum are readily identified by their characteristic sausage shape [56].

An inadequate bone marrow response to anaemia is seen, with relative reticulocytopenia. Leucocyte number may be slightly increased or normal, but leucopenia as a result of splenomegaly and impaired marrow function is characteristic. Thrombocytopenia is seen in nearly 70% of infections [56].

The bone marrow reactions caused by plasmodium vivax are qualitatively similar to those caused by plasmodium falciparum not only in the red cell lineage but also in other cell lines, characterized by dyserythropoiesis and ineffective erythropoiesis [56].

BRUCELLOSIS:

Brucellosis is a zoonotic infection existing worldwide, with predominance in central Asia and some developing countries [57].

Brucellosis is caused by small, fastidious gram negative coccobacilli of the genus brucella. B.melitensis is the most invasive and causes the most severe disease [57].

Bone marrow and spleen are commonly involved. This may result in a hypoplastic pattern on the peripheral blood smear. Pancytopenia in Brucellosis may be seen due to hemophagocytosis, hyperspleenism, bone marrow granulomas, bone marrow hypoplasia and immune destruction [57].

Sari Ismail et al studied 202 cases of brucellosis out of which 30 patients had pancytopenia and concluded as histiocytic hemophagocytosis was a major cause of

pancytopenia in the patients with brucellosis [57].

EHRLICHIOSIS:

Ehrlichia belongs to family Rickettsiaceae. These are obligate intracellular bacteria that parasitized circulating mononuclear or neutrophils [38].

Most of the patients have nonspecific febrile illnesss with myalgia, headache, gastrointestinal symptoms, relative bradycardia and cytopenia. Bone marrow examination disclosed a variety of abnormalities including marrow hypoplasia mainly [38].

TUBERCULOSIS:

Tuberculosis produces a variety of hematologic effects. It is postulated that the release of TNF-alpha and other cytokines by TB – activated monocytes suppress the erythropoietin production that normally occurs in the setting of anemia of chronic disease [58].

The various postulated mechanism for pancytopenia include splenic sequestration and immune mediated bone marrow suppression. Decrease bone marrow reserve is also due to malnutrition [58].

Pancytopenia is a consequence of the combined effects of hypersplenism, excessive margination of neutrophils and or marrow granulopoietic failure mediated by the expansion of T-lymphocytes showing granulopoietic inhibitory activity [58].

HIV:

HIV produces various haematological abnormalities. It involves all the cell lines of blood. Viral replication and viral load influence the complications. Most common complication is anemia. Its incidence is strongly associated with the progression of the disease. In advanced stages of the diseases neutropenia becomes common. Thrombocytopenia is co-related with low CD4+ cell count and older age [59].

Mir et al did a cohort study of 60 HIV infected individuals and found anemia, thrombocytopenia, leukopenia and various combinations of these in majority of the individuals [59].

A known complication of HIV infection in the bone marrow is dyspoietic hematopoeisis termed as HIV myelopathy. HIV myelopathy, unlike a true myeloid dysplastic syndrome is not considered a true stem cell disorder but rather represents a spectrum of morphological changes secondary to direct HIV effect and HAART [60].

Until 1982 disseminated Mycobacterium avium-intracellulare infection was very rare. However later it began to appear in patients with HIV infection. Members of Mycobacterium avium-intracellulare are ubiquitous non-tuberculous mycobacteria in the environment and can cause disease in immunocompetent patients. The organisms commonly reside in soil and can be found in contaminated water, dairy products, eggs and dust [61].

Disseminated Mycobacterium avium-intracellulare is known to be associated with a high incidence of haematological abnormalities such as leukemoid reaction,

myelofibrotic changes, hemophagocytic syndrome, polycythemia and pancytopenia [61].

STORAGE DISEASES

In various inherited diseases the deficiency of an enzyme leads to accumulation of a metabolite in body cells, often in macrophages. The morphologically abnormal bone marrow macrophages containing an excess of the relevant metabolite are referred to as storage cells [62].

Both bone marrow aspirates and trephine biopsies are useful in the detection of storage diseases. Peripheral blood cells may show related abnormalities [62].

GAUCHER'S DISEASE:

It is an inherited condition in which glucocerebrosides accumulate in macrophages including those in the liver, spleen and bone marrow. There are usually no specific peripheral blood features, although very occasionally Gaucher's cells may be seen in the peripheral blood, particularly after splenectomy [62].

Pancytopenia develops slowly, as a consequence of hypersplenism. Gaucher cells are large, round or oval cells with a small, usually eccentric nucleus and voluminous weakly basophilic cytoplasm with a wrinkled or fibrillar or onion-skin pattern. They may be isolated or appear in clumps or sheets, sometimes replacing large areas of the marrow. There may be an increase in reticulin and collagen deposition [62].

NIEMANN-PICK DISEASE:

Inherited condition caused by reduced spingomyelinase activity characterized by the presence of foamy lipid containing macrophages in the bone marrow and other tissue. Anaemia and various cytopenias may occur as a consequence of hypersplenism. Foamy macrophages are large cells with multivacuolated cytoplasma and a nucleus in the center. They stain pale blue with Romanowsky stains [62].

HYPERSPLENISM:

Hypersplenism is a clinical syndrome; it does not imply a specific causal mechanism. It has the following characteristic features [63].

1. Enlargement of spleen.
2. Reduction in one or more of the cell lines in the peripheral blood.
3. Normal or hyperplastic cellularity of the bone marrow, often with orderly maturation of earlier stages but paucity of more mature cells.
4. Premature release of cells in the peripheral blood, resulting in reticulocytosis and/or large immature platelets.
5. Increased splenic red cell pool, decreased red cell survival and increased splenic pooling of platelets with shortening of their life span.

Hypersplenism can occur as a primary event due to an unknown pathogenic stimulus. Some of the important causes of secondary hypersplenism are haematological malignancies, storage disease, infections like malaria, typhoid, brucellosis, leishmaniasis, collagen vascular diseases, congestive

splenomegaly and splenic tumors [63].

CLINICAL FEATURES OF PANCYTOPENIA

The cardinal signs of moderate to severe pancytopenia are anemia, bleeding and infection, RBCs survive much longer than platelets and leucocytes, thus anemia develops slowly and the typical symptoms of tiredness, fatigue, puffiness of face, edema, lassitude and effort intolerance may not be striking in the initial phase [64].

Platelet count is first to be effected, muco-cutaneous bleeding is typical of thrombocytopenia with petechial hemorrhages in skin and mucous membranes.

Spontaneous bleeding with platelet <20000 cells/cu mm indicates severe bone marrow failure [64].

Infections usually occur with commensal organism of the skin and gastro-intestinal tract [64].

Unfortunately, patients with pancytopenia may develop overwhelming septicemia without any focal signs of infection, the only clinical features being malaise and fever [64].

Hence pancytopenia has striking feature of many serious and life threatening illnesses.

DIAGNOSIS OF PANCYTOPENIA

The causes of pancytopenia are diverse, and likely causes of pancytopenia differ in children and adults. Particular attention must be paid to patient and family

history. Of significance is any history of previous pancytopenia, aplastic anaemia, inherited bone marrow failure syndromes (IBMFS), early fetal loss, history of cancer, metabolic disorders, liver disease, or connective tissue disorders [1].

OUTLINE OF DETAILS IN THE INVESTIGATION OF A PATIENT WITH PANCYTOPENIA [8].

HISTORY

- Age, sex, occupation, diet.
- Exposure to chemicals, drugs or radiation.
- Bone pain
- Fever, night sweats, malaise, weight loss, pruritis.

PHYSICAL EXAMINATION

- Lymph node enlargement
- Hepatomegaly and splenomegaly.
- Bone tenderness, deformity or tumor, Gum hypertrophy.
- Signs of disorder causing hypersplenism, especially portal hypertension.
- Evidence of primary malignancies often associated with metastasis to bone, especially breast, prostate or lung

LABORATORY INVESTIGATIONS

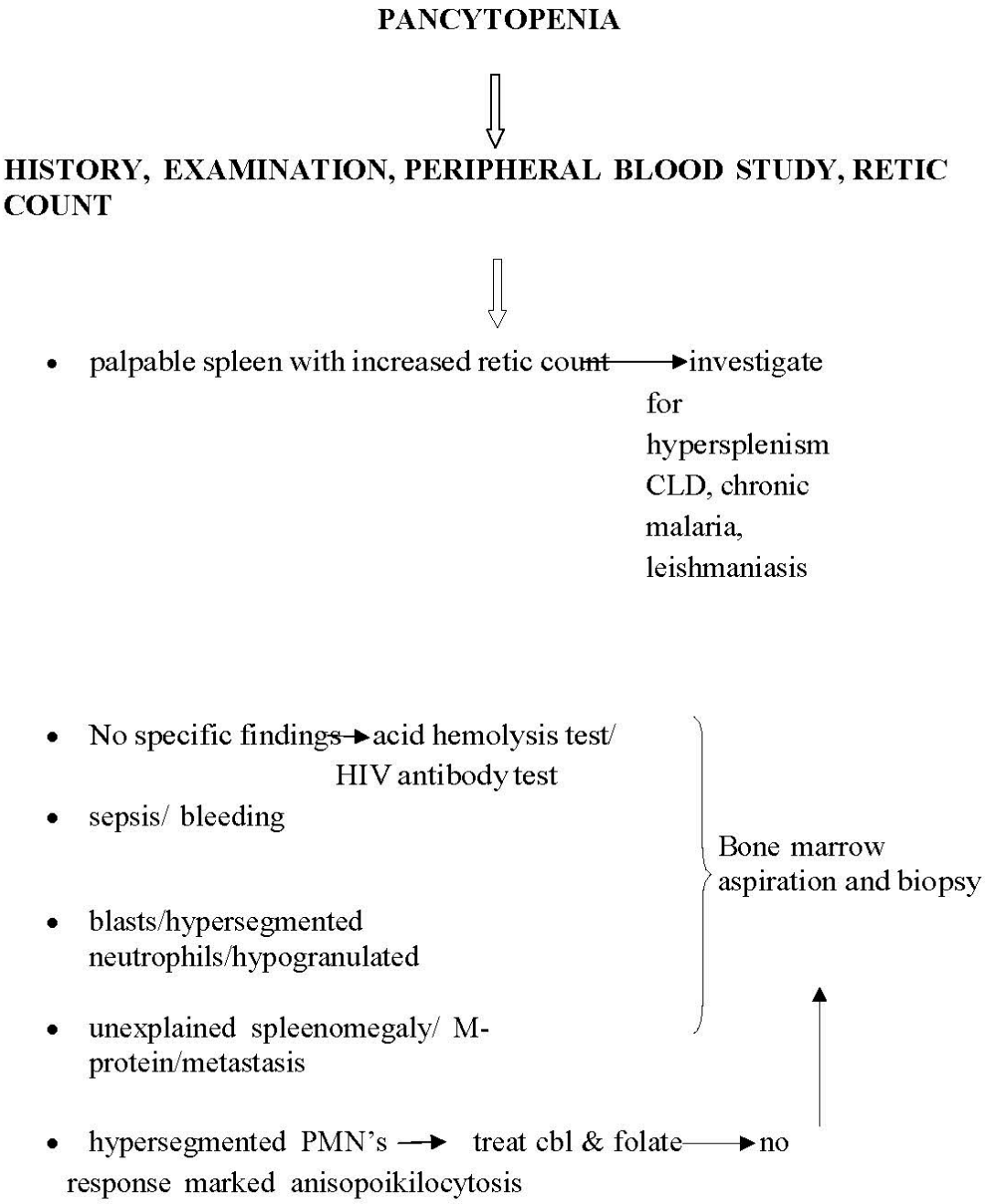
Essential investigations in all cases:

- Peripheral examination, especially note anisopoikilocytosis, nRBCS, immature white cells, granulations and segmentation of neutrophills, erythrocyte roulex formation.
- ESR
- Bone marrow study; aspiration and trephine biopsy.

FURTHER INVESTIGATIONS WHEN EVER REQUIRED.

- Bone X – ray {multiple myeloma, metastatic carcinoma, lymphomas}
- Chest X – ray {tuberculosis, carcinoma, lymphomas}
- Serum protein electrophorsis { MM , M acroglobulinemia }
- Serum alkaline and acid phosphatase level { metastatic carcinoma }
- DNA antibody , lupus erthryomatous cell test { SLE }
    - Urinary Bence – jones protein { MM}
    - Needle biopsy of liver { hyperspleenism, lymphomas , disseminated tuberculosis}

Figure 1 : Diagnostic approach to pancytopenia



ROLE OF BONE MARROW STUDY

First in vivo marrow be probably was done in 1876 by Mosler, who used a regular wood drill to obtain marrow particles from a patient with leukemia [7].

Fifty years later, studies done by Arinkin in 1929 established marrow aspiration as a safe, easy and useful technique [7].

Pancytopenia has either cellular or hypocellular bone marrow morphology. Hence bone marrow evaluation is an invaluable diagnostic procedure in pancytopenia cases [65].

ANATOMY:

Bone marrow provides unique microenvironment for the orderly proliferation, differentiation and release of blood cells [66].

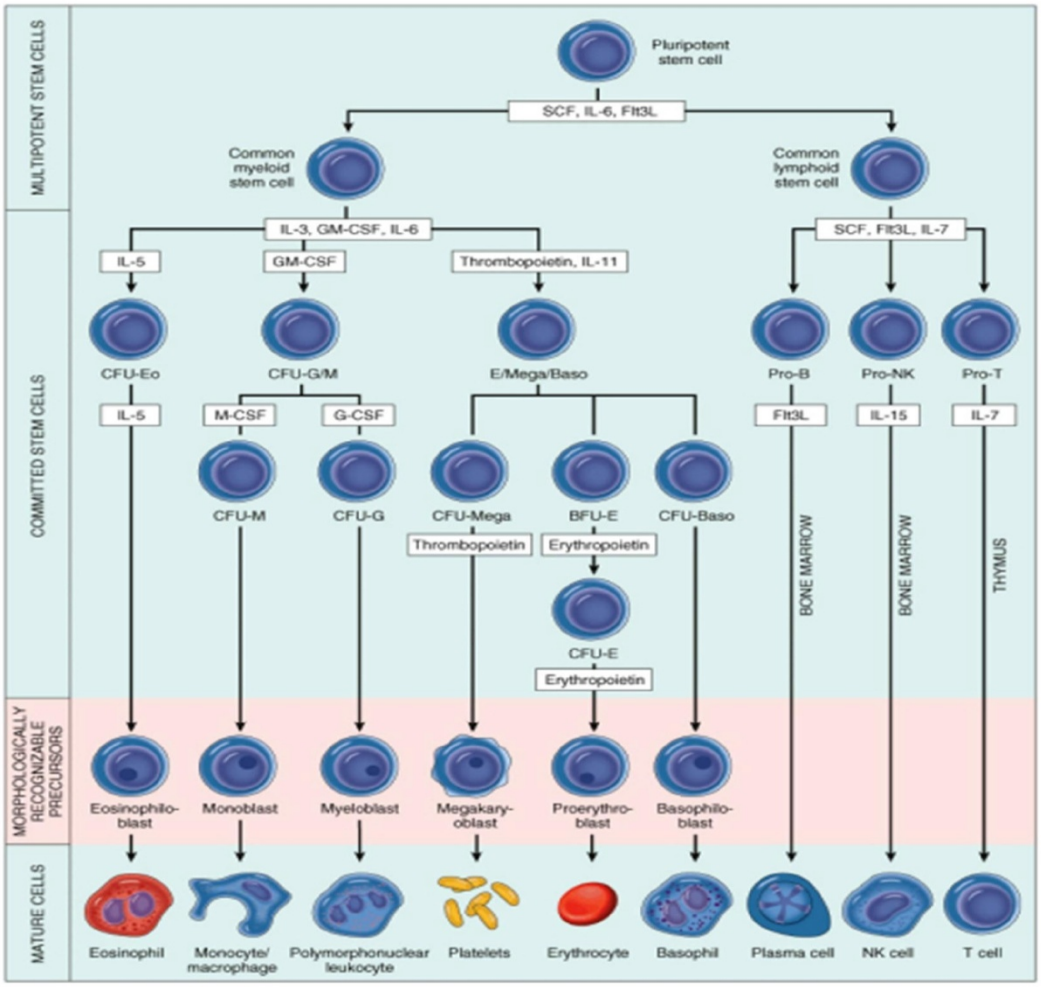
The formed elements of blood – red cells, granulocytes, monocytes, platelets and lymphocytes – have a common origin from pluripotent haemopoietic stem cells.

The pluripotent stem cell gives rise to two types of multipotent progenitors, the common lymphoid and the common myeloid stem cells. The common lymphoid stem cell in turn gives rise to precursors of T-cells (pro-T-cells), B-cells (pro-B-cells), and natural killer cells [66].

From the common myeloid stem cell arise at least three types of committed stem cells capable of differentiating along the erythroid / megakaryocytic, eosinophilic and granulocyte-macrophage pathways. From the various committed stem cells are derived intermediate stages and ultimately the morphologically recognizable precursors of the differentiated cells, such as proerytharoblsts,

myeloblasts, megakaryoblasts, monoblasts, and eosinophiloblasts, which in turn give rise to mature progeny [66].

Fig 2 [66]



Bone marrow evaluation confirms a diagnosis suspected from the clinical features and peripheral blood examination or occasionally gives a previously unsuspected diagnosis. Though bone marrow aspiration is able to provide the diagnosis in the majority of the cases, marrow trephine biopsy is mandatory in few conditions [67, 68]. Bone marrow aspirate are superior for morphological detail over biopsy, while biopsy specimens provide a more reliable index of cellularity and often reveal marrow infiltration, fibrosis or granulomas that are not detected on aspiration [67,68].

Examination of bone marrow iron is accepted for establishing the adequacy of body iron stores [69].

Special histochemical staining of bone marrow specimens is used for storage iron. The specimens commonly used are aspirate smears and aspirate particles. Core biopsies may reveal iron, however if absent staining is there it may represent a false negative result owing to bleaching of iron from specimen during decalcification. Iron which is identified by microscopy is generally considered to represent the insoluble iron storage compound and hemosiderin [69].

Adequate trephine biopsy should contain at least 5-6 intertrabecular spaces and after processing should be at least 2-3cms in length [70].

Low power examination is important for evaluation of the adequacy of the biopsy and for assessment of cellularity and in detection of focal lesions .Medium power examination is useful in location of cells of erythroid, granulocytic lineages and their relative proportions can be assessed, the nature of any focal lesions can be determined and blood vessels examination done .High power is important if fungal or protozoal infections are detected [70].

TABLE 2: HAEMATOLOGY REFERENCE VALUES IN NORMAL DULTS [71].

TEST	MEN	WOMEN
HEMOGLOBIN	14-17 g/dl	12.3-15.3 g/dl
HEMATOCRIT	41.5 – 50.4%	36 – 45%
RED CELL COUNT	4.5 – 5.9 x 106 / µl	4.5 – 5.1 x 106 /µl
WHITE CELL COUNT	4.4 – 11.3 x 103 /µl	4.4 – 11.3 x 103 /µl
MCV	80 – 96 fl	80 – 96 fl
MCH	27.5 – 33.2 pg	27.5 – 33.2 pg
MCHC	33.4 – 35.5 g/dl	33.4 – 35.5 g/dl
PLATELET COUNT	150 – 450 x 103 / µl	150 – 450 x 103 / µl
RETICULOCYTE COUNT	0.5 – 2.5%	0.5 – 2.5 %
ESR	0 – 15 mm / hr	0 – 20 mm / hr

TABLE 3 DIFFERENTIAL COUNTS OF BONE MARROW ASPIRATE

	OBSERVED RANGE(%)	**MEAN(%)**
• NEUTROPHILIC SERIES (TOTAL)	49.2 – 65	53.6
Myeloblasts	0.2-1.5	0.9
Promyelocyte	2.1-4.1	3.3
Myelocyte	8.2-15.7	12.7
Metamyelocyte	9.6-24.6	15.9
Band form	9.5-15.3	12.4
Segmented	6.0-12.0	7.4
• EOSINPHILIC SERIES (TOTAL)	1.2-5.3	3.1
Myelocyte	0.2-1.3	0.8
Metamyelocyte	0.4-2.2	1.2
Band form	0.2-2.4	0.9
Segmented	0-1.3	0.5
• BASOPHIL AND MAST CELLS	0-0.2	<0.1
• ERYTHROID SERIES (TOTAL)	18.4-33.8	25.6
Pronormoblast	0.2-1.3	0.6
Basophilic	0.5-2.4	1.4
Polychromatophilic	17.9-29.2	21.6
Orthochromatic	0.4-4.6	2.0
• LYMPHOCYTE	11.1-23.2	16.2
• PLASMA CELL	0.4-3.9	1.3
• MONOCYTE	0-0.8	0.3
• MEGAKARYOCYTE	0-0.4	<0.1
• RETICULIN CELLS	0-0.9	0.3
• MYELOID TO ERYTHROID RATIO	1.5-3.3	2.3

MATERIAL AND METHODS

The present study "A clinic hematological study of pancytopenia was carried out from January 2016 to September 2017, in the Department of Pathology, Dhiraj Hospital, Sumandeep Vidyapeeth.

The cases from Dhiraj Hospital formed the material of the study. The cases were selected on the basis of clinical features and laboratory results. Bone marrow aspiration was carried out after getting a written consent from the patient or the guardian.

Inclusion criteria:

Presence of all three of the following:

- Hemoglobin < 10gm/dl
- Total leukocyte count (TLC) < 4000/microL
- Platelet count < 1,50,000/ microL

Exclusion Criteria:

- Patients who have recently received blood transfusions.
- Patients on radiotherapy.
- Patients on cytotoxic drugs.

FOLLOWING INVESTIGATIONS WERE CARRIED OUT.

1. Hemoglobin
2. RBC count
3. WBC count
4. Platelet count
5. Reticulocyte count
6. Hematocrit
7. Red cell indices
8. Bleeding time and clotting time when required
9. Peripheral smear study
10. Bone marrow study

SAMPLE COLLECTION: Two ml of blood was collected by venepuncture under aseptic precaution in a dry bulb containing ethylene di-amine tetra acetic acid (EDTA) anticoagulant.

Samples were processed by an automated autoanalyser (SYSMEX Kx-21) or (BECKMAN COULTER) , and blood counts with other details were obtained.

SYSMEX (Kx-21)

Sysmex Kx- 21 is an automatic multi-parameter blood cell counter for in-vitro diagnostic use in clinical laboratories. The instrument analyzes the following parameters using detector blocks and 2 kinds of reagent.

Neutrophil% (neutrophil#), Lymphocyte% (lymphocyte#), Mixed % (mixed#), Red blood cell count ,Hb percentage, Hematocrit (Hct), MCV, MCH, MCHC, RDW. Platelet count, its mean volume.

The Kx – 21 is fast and we can get accurate analysis of 18 parameters. In this it uses three detector blocks and two types of reagents for blood analysis. White blood cell count is measured by the WBC detector block using the DC detection method. The red blood cells and platelet count are taken up by the RBC detector block, also using the DC detection method. The HB detector measures haemoglobin concentration using the non-cyanide method. In cases of very low counts or errors, manual methods were done.

BECKMAN COULTER LH 750

TheLH 750 Hematology analyzer is a quantitative, automated hematology analyzer and leukocyte differential counter for in Vitro Diagnostic Use in clinical laboratories. It automated reticulocyte analysis and enumeration of nucleated red blood cells (NRBCs) as well as an automated method for enumeration of RBCs and WBCs in body fluids.

Its purpose is toseparate the normal patient, with all normal system-generated parameters, from the patient who needs additional studies of any parameters. The studies include measurements of cell size and platelet distribution, manual WBC differential or any other definitive test.

It is based on Coulter principle method of automated cell counting and spectrophotometric hemoglobin determination. It counts and sizes cells by detecting and measuring changes in electrical resistance when a particle (such as a cell) in a conductive liquid goes through a small aperture. Each cell suspended in a conductive liquid (diluent) acts as an insulator. As each cell goes through the aperture, it momentarily increases the resistance of the electrical path between two submerged electrodes, one located on each side of the aperture. This causes an electrical pulse

that can be counted and sized. While the number of pulses indicates particle count, the size of the electrical pulse is proportional to the cell volume.

Differential and reticulocyte analysis is based on the Coulter volume, conductivity and light scatter technology (VCS). Differential analysis classification and reticulocyte analysis occur in the flow cell, where: Low-frequency current measures volume; High-frequency current senses cellular internal content through measuring changes in conductivity; Light from the laser scattered off the individual cells characterizes cellular surface, shape, and reflectivity. [73]

Following parameters can be achieved from this instrumernt:

WBC, RBC, Hgb, MCV,MCH, MCHC, RDW, Plt,MPV, LY%, MO%, NE%,EO%, BA%, LY#, MO#,NE#, EO#, BA#, NRBC%,NRBC#, RET%, RET#,IRF, & MRV.[73]

PERIPHERAL SMEAR STUDY:

Peripheral smears were prepared, the films were air dried, and stained with Field stain and Leishman's stain.

Smears were examined under microscope for following features,

- RBC morphology- type, morphological anemia, immature RBC's , any inclusions.
- WBC morphology – for differential count, morphology of each cell, immature cells.
- PLT count and its morphology.
- Any parasites.

RETICULOCYTE COUNT:

The procedure for reticulocyte count is by taking a small test tube and adding two drops of new methylene blue filtrate along with two drops of well-mixed blood specimen. Mix the sample well and leave it for 30-45 minutes in an incubator. Now prepare a thin smear, air dry it for few minutes and then examine it under microscope and identify the reticulocytes by their fine violet filaments which are arranged in a network and appear as fine dot like structure.

A small circular piece of black paper with a hole (5 mm diameter) was placed in the eye piece. Ehrlich's eye piece was also used sometimes. Ten consecutive fields or 150-200 red cells including reticulocytes were counted and the percentage was calculated using the formula

Reticulocyte count =

$$\frac{\text{Number of reticulocyte counted X 100}}{\text{Number of red cells counted (Normal value } 0.5 - 2.5\%)}$$

Based on these basic hematological investigations in suspected cases, clinical details like age, sex, symptoms such as bone pain, fever, night sweats, malaise, weight loss and pruritis were taken (Annexure I). Physical examination was also carried out to check any hepatomegaly, splenomegaly, lymphadenopathy or sternal tenderness. Bone marrow evaluation was done in all cases.

BONE MARROW ASPIRATION:

A written consent from the patient or the patents/guardians were obtained prior to the procedure.

Needle used: Salah needle

The aspiration site was posterior iliac crest or sternum.

- All aseptic precaution was taken and under local anesthesia (2% lignocaine) aspiration was done.
- The aspirate was then transferred to a set of slides. The marrow particles were crushed and the slides were prepared.
- After that the needle was taken out and the puncture site was sealed with tincture benzoin swab.

Repeat aspiration was done at a different site if there was an unsuccessful attempt.

Slides were fixed in methanol for 15 minutes, dried and later stained with Geimsa stain and marrow aspiration smears were examined for

i) Cellularity
ii) M:E ratio
iii) Erythropoiesis
iv) Myelopoiesis
v) Megakaryopoiesis
vi) Others – plasma cells, lymphocytes, mast cells
vii) Parasites
viii) Abnormal cells

Special stains like Prussian blue stain were done for all cases to assess iron stores, and grading was carried out.

TABLE 4: BONE MARROW IRON GRADING

Grade	Criteria	Iron content (µg/g)
0	No iron granules observed	42+/-23
1+	Small granules in reticulum cells(seen only in oil immersion)	130+/-50
2+	Few granules visible under high power field	123+/-75
3+	Numerous small granules in all marrow particles	406+/-131
4+	Large granules in small clumps	762+/-243
5+	Dense ,large clumps of granules	1618+/-464
6+	Very large deposits obscuring marrow detail	3681+/-1400

Other special stains were done wherever required.

BONE MARROW BIOPSY:

Needle: Jamshidi needle

Site: Posterior iliac crest

Procedure: Local anesthesia (2% lignocaine) was used at the site and biopsy was done under aseptic conditions. The needle, with stylet locked in place, is held with the palm and index finger and repositioned at insertion site. Once the needle touches the bone surface, the stylet is removed.

- Applying a firm pressure along with a rotatory motion, an adequate bone marrow specimen measuring approximately 1.5-3cm in length was removed.

- Biopsy tissue was then removed from needle and taken on a slide. Now the tissue imprint was taken on a different slide..

Processing of tissue:

Decalcification was done using 14% EDTA. Then the tissue was processed as routine histological processing. Routine hematoxyline and eosin stain done.

Special stain like Prussian blue stain, Reticulin stain and Masson's trichome stain were done.

Reporting: slides were examined and reported as follows

- Adequacy of biopsy.
- Cellularity and topography.
- Any abnormality

Compiling clinical details, hematological parameters and bone marrow study, the cases were studied (Annexure II). The cause for pancytopenia, age and sex distribution and other relevant details were noted and analyzed.

RESULTS

In our study total 114 patients presented with pancytopenia. They were studied during the period of January 2016 to September 2017 at Dhiraj Hospital. Following results were recorded and analysed.

TABLE 5: INCIDENCE OF PANCYTOPENIA IN DIFFERENT AGE GROUPS

Sl No	Age group	No of cases	(%)
1	02-10	5	(4.3)
2	11-20	30	(26.3)
3	21-30	26	(22.8)
4	31-40	14	(12.3)
5	41-50	15	(13.2)
6	51-60	12	(10.5)
7	61-70	10	(8.7)
8	71-80	2	(1.8)

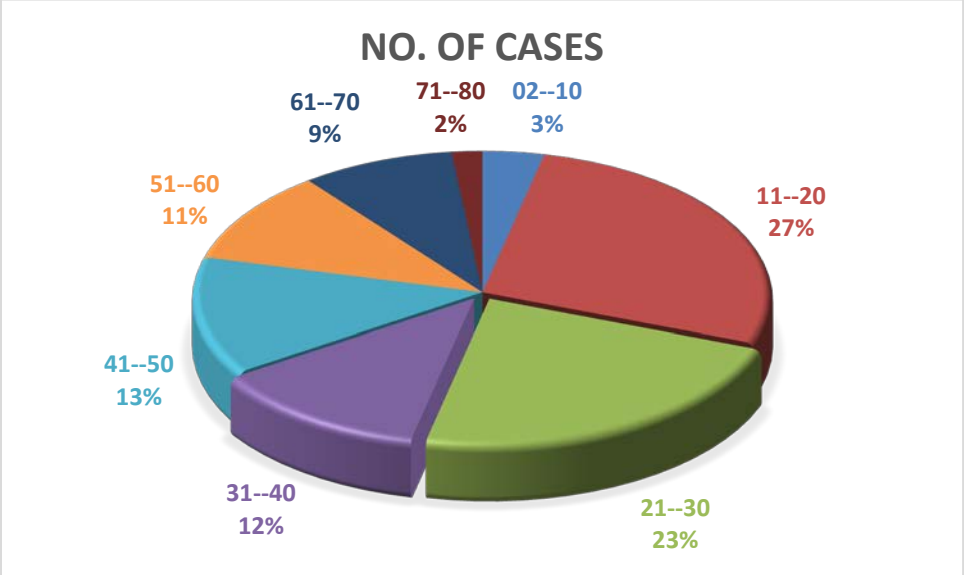


Chart 1 : INCIDENCE OF PANCYTOPENIA IN DIFFERENT AGE GROUPS

The commonest age group affected was 11-20 year age group (26.3%) and least age group affected was 71-80 years (1.8%).

TABLE 6: INCIDENCE OF PANCYTOPENIA IN DIFFERENT SEX GROUPS

Sno.	Sex	No. of cases	Percentage
1.	Male	65	57.1%
2.	Female	49	42.9%
	Total	114	

In this study males had more cases of pancytopenia with 57.1% than females with 42.9%.

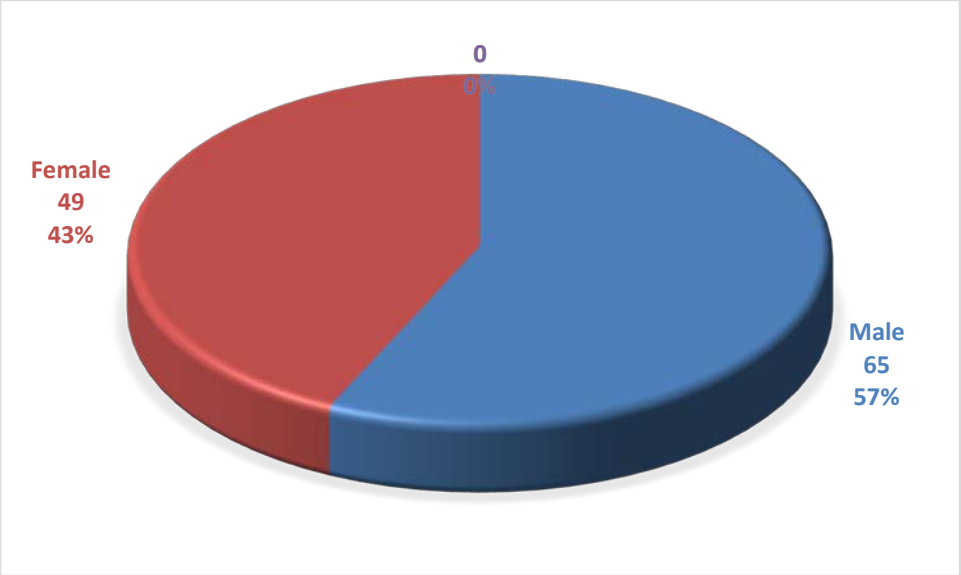


Chart 2 : INCIDENCE OF PANCYTOPENIA IN DIFFERENT SEX GROUPS

TABLE – 7 : PRESENTING COMPLAINTS AND PHYSICAL FINDINGS IN PANCYTOPENIA

Sno.	Presenting complains and physical findings	No. of cases	Percentage %
1.	Fever	65	57.0
2.	Generalised Weakness	113	99.1
3.	Breathlessness	2	1.8
4.	Bone Pain	2	1.8
5.	Weight Loss	1	0.9
6.	Dyspnoea	43	37.7
7.	Bleeding	6	5.3
8.	Pallor	114	100.0
9.	Hepatomegaly	29	25.4
10	Splenomegaly	21	18.4
11	Lymphadenopathy	22	19.3

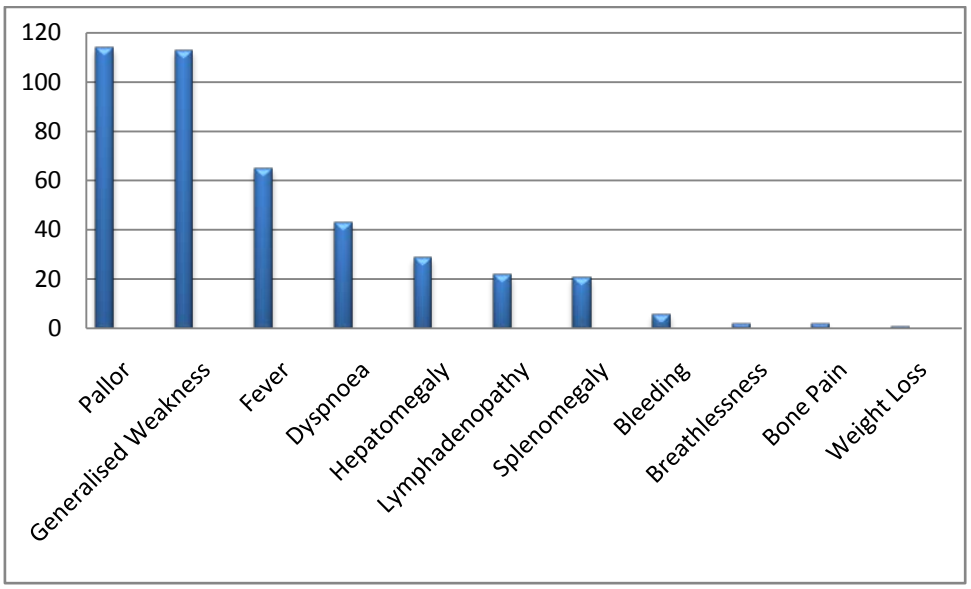


Chart 2 : PRESENTING COMPLAINTS AND PHYSICAL FINDINGS IN PANCYTOPENIA

Presenting complaints and physical findings:

The commonest, mode of presentation was generalised pallor, which was present in all patients constituting 100%. It was closely followed by generalised weakness with 99.1%.

The other main symptoms were fever (57.0%), dyspnoea (37.7%), hepatomegaly (25.4%), splenomegaly (18.4%), and lymphadenopathy (19.3%).

Bony tenderness (1.8%) was seen in multiple myeloma. Weight loss (0.9%) was seen in granulomatous infection.

TABLE: 8 VITAL HAEMATOLOGICAL PARAMETERS

Sno.	Parameters	Range	No of cases (%)
1	Haemoglobin (gm%)	1.8 -5	19 (16.7%)
		5 – 8	67 (58.8%)
		8.1-9.6	28 (24.6%)
2	Total leucocyte count (cells /cumm)	500-1000	4 (3.5%)
		1001-2500	31 (27.2%)
		2501-4000	79 (69.3%)
3	Platelet count(cells/cumm)	10000-50000	38 (33.3%)
		50001-100000	35 (30.7%)
		100001-150000	41 (36.0%)
4	RBC mass	0.8-2	47 (41.2%)
		2.1-3	58 (51.9%)
		3.1-4	9 (7.9%)
5	Reticulocyte count (%)	0-0.5	24 (22.64%)
		0.6-1	58 (54.71%)
		1.1-2	24 (22.64%)

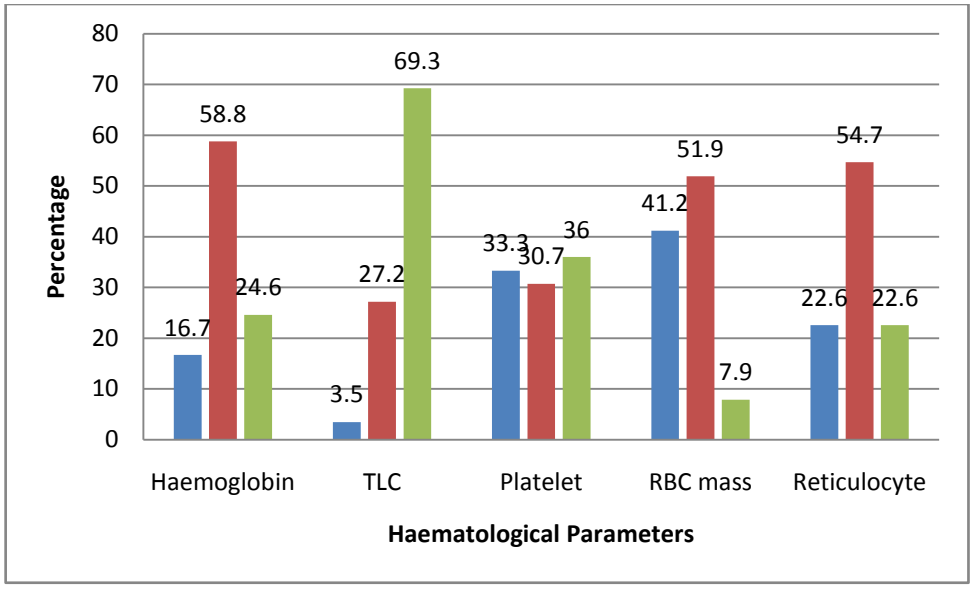


Chart: 4 : VITAL HAEMATOLOGICAL PARAMETERS

Haemoglobin:

Haemoglobin percentage varied from 1.8 – 9.6g%.

In most patients the haemoglobin ranged from 5- 8g%.

Lowest haemoglobin was 1.8g% found in a case of megaloblastic anaemia.

Total leucocyte count:

TLC ranged from 500 – 4000 cells/mm3.

Most of patients had white cell count in range of 2501 – 4000 cells/mm3. Lowest count of 900 cells/mm3 was seen in a case of megaloblastic anaemia.

Reticulocyte count:

Reticulocyte count ranged from 0.5 – 2%. Most of patients had reticulocyte count between 0.6 – 1%.

Platelet count:

Platelet count ranged from 10,000 – 1, 50,000 cells/mm3.

Most of patients had platelet count between 10,000 – 50,000 cells/mm3.

Lowest platelet count of 10000 cells/mm3 was seen in a case of megaloblastic anaemia.

TABLE: 9 PERIPHERAL BLOOD SMEARS IN PANCYTOPENIA

Sno.	Peripheral Blood Smear	Cases	Percentage (%)
1	Microcytic hypochromic	2	1.8
2	Macrocytic hypochromic	35	30.7
3	Dimorphic hypochromic	60	52.6
4	Normocytic hypochromic	17	14.9
	Total	114	

In present study dimorphic anemia was seen in majority of cases with 52.6%. Macrocytic anemia was seen in 30.7%, Normocytic anemia in 14.9% and microcytic anemia in 1.8%.

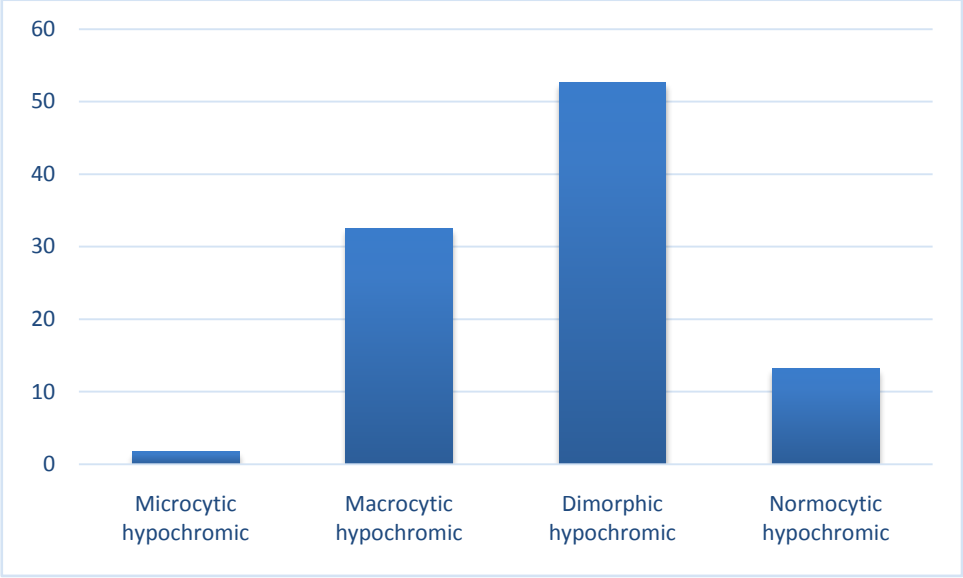


Chart : 5 PERIPHERAL BLOOD SMEARS IN PANCYTOPENIA (%)

TABLE 10: BONE MARROW CELLULARITY

Sno.	Bone Marrow Smear	Cases	Percentage (%)
1	Hypercellular	92	80.7
2	Hypocellular	19	16.7
3	Normocellular	3	2.6
	Total	114	

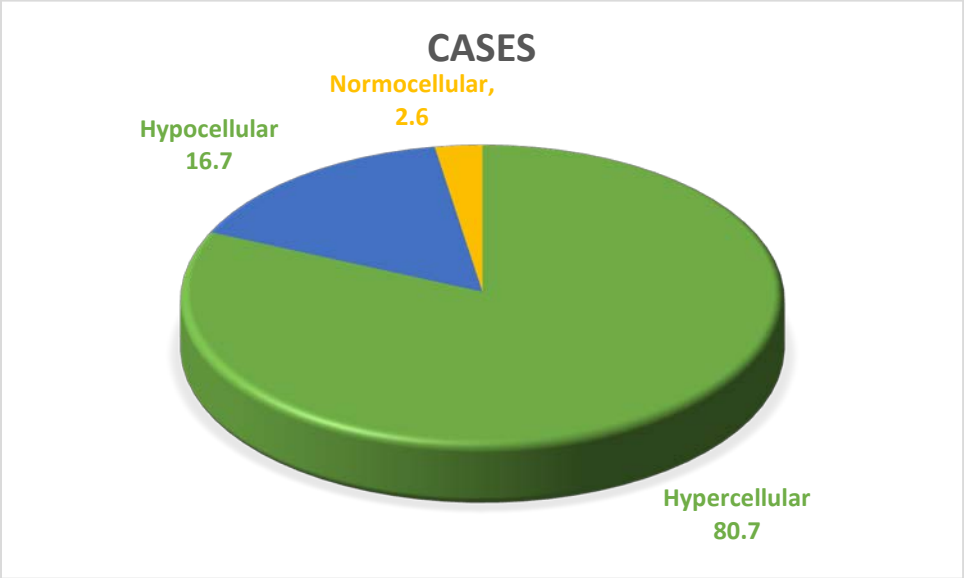


Chart: 6 BONE MARROW CELLULARITY

In this study there were 92 cases who had hypercellular bone marrow, 19 cases with hypocellular and 3 with normocellular bone marrow.

TABLE –11: DISTRIBUTION OF VARIOUS CAUSES OF PANCYTOPENIA

SNO.	Causes	No. of cases	Percentage
1.	Megaloblastic Anemia	75	65.8
2.	Dimorphic Anemia	13	11.4
3.	Aplastic Anemia	11	9.6
4.	Malaria	4	3.5
5.	Subleukemic leukemia	2	1.8
6.	Multiple Myeloma	2	1.8
7.	Infections	2	1.8
8.	MDS	2	1.8
9.	Metastasis	1	0.9
10.	SLE	1	0.9
11.	Myelofibrosis	1	0.9

In the present study megaloblastic anaemia was the commonest cause (65.8%), followed by dimorphic Anaemia (10.5%), aplastic anemia (9.6%), malaria (3.5%), subleukemic leukemia (1.8%), multiple myeloma (1.8%), infections (1.8%), metastasis (1.8%), MDS (1.8%), SLE (0.9%), myelofibrosis (0.9%) and sickle cell anemia (0.9%).

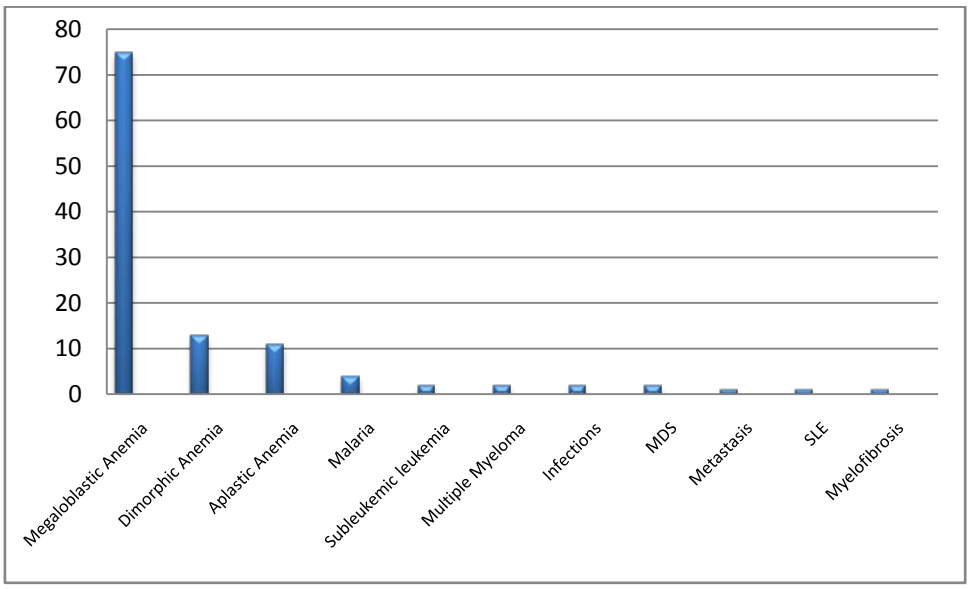


Chart : 7 DISTRIBUTION OF VARIOUS CAUSES OF PANCYTOPENIA

PANCYTOPENIA ASSOCIATED WITH MEGALOBLASTIC ANEMIA

Total 75 cases had megaloblastic anemia. It was more common in males with 61.3% as compared to females with 38.7%. Majority of cases had hemoglobin in the range of 5-8gm%, TLC: 2500-3900cumm and platelet count 50000-100,000cumm.

Bone marrow study showed hypercellularity with erythroid hyperplasia. The erythroid series showed megaloblasts.

PANCYTOPENIA ASSOCIATED WITH DIMORPHIC ANEMIA

Out of 114 cases 12 had dimorphic anemia. The peripheral smear showed macrocytes and microcytic red blood cells with occasional presence of hypersegmented neutrophils in some cases. The bone marrow showed micronormoblasts along with megaloblasts.

PANCYTOPENIA ASSOCIATED WITH APLASTIC ANEMIA

In the study there are 11 cases of aplastic anemia. The patients complained of fever and generalised weakness. On examination there was pallor and few cases had cervical lymphadenopathy. Haemoglobin percentage ranged from 6-8 gm%, total leucocyte count ranged from 1500-4000 and platelets from 20000-94000 cells/m^3.

Peripheral smear showed mild anisopoikilocytosis with microcytic or normocytic hypochromia. In 5 cases of bone marrow aspiration there was dry tap. Rest were hypocellular with increased fat cells. Bone marrow biopsy showed hypoplastic marrow.

PANCYTOPENIA DUE TO MALARIAL INFESTATION:

In present study, malarial infestation was seen in 4 cases. The patients presented with fever, chills and headache. Their clinical examination revealed pallor and hepatosplenomegaly.

The peripheral smear of all the cases showed macrocytic hypochromic anaemia with neutropenia and thrombocytopenia. 3 cases showed gametocytes of Plasmodium falciparum .

The bone marrow was hypercellular with megaloblastic changes, P.falciparum gametocytes were seen on bone marrow smears of all the cases.

PANCYTOPENIA ASSOCIATED WITH SUBLEUKEMIC LEUKEMIA:

The study had 2 cases of subleukemic leukemia.

They presented with complains of fever, generalised weakness and abdominal discomfort. On clinical examination they had pallor and hepatosplenomegaly. The peripheral smear showed normocytic anemia with neutropenia and thrombocytopenia along with myeloblasts.

The bone marrow was hypercellular with increased blasts.

PANCYTOPENIA ASSOCIATED WITH MULTIPLE MYELOMA:

The study had 2 cases of multiple myeloma. They presented with complains of generalised weakness and bone pain. The peripheral smear showed macrocytic anaemia with neutropenia and thrombocytopenia. The bone marrow biopsy was

hypercellular with abnormal proliferation of plasma cells. The erythropoiesis, leucopoiesis and megakaryopoiesis was suppressed.

PANCYTOPENIA ASSOCIATED WITH INFECTIONS:

The study showed 2 cases of pancytopenia with infections. One case was diagnosed as tuberculosis and the other diagnosed as hepatitis B infection.

The first case peripheral smear showed normocytic anemia. The bone marrow aspiration revealed necrosis. The biopsy showed hypocellularity with areas of necrosis surrounded by fibroblasts.

The second case showed normocytic anemia on peripheral blood smear and normocellular in bone marrow biopsy.

PANCYTOPENIA ASSOCIATED WITH METASTASIS:

The study had one case of pancytopenia associated with metastasis. The patient had normocytic anemia on peripheral blood smear. Bone marrow aspiration revealed dry tap. The biopsy found metstasis.

PANCYTOPENIA ASSOCIATED WITH MDS:

There were two cases with myelodysplastic syndrome who presented with fever, pallor and hepatosplenomegaly. Peripheral smear was normocytic normochromic anemia. Bone marrow was hypercellular and showed dysplastic changes.

PANCYTOPENIA ASSOCIATED WITH SLE:

SLE was seen in 1 case with pancytopenia. She presented with fever, weakness and skin rashes, and classical butterfly rash. On physical examination pallor and

lymphadenopathy was seen.

Peripheral smear was microcytic hypochromic picture.

Bone marrow aspirate had scanty material and reported as hypoplastic bone marrow.

PANCYTOPENIA ASSOCIATED WITH MELOFIBROSIS:

The study had one patient who had pancytopenia associated with myelofibrosis.

The patient presented with fever and weakness. On physical examination hepatosplenomegaly was seen. Peripheral smear showed microcytic hypochromic anemia.

Bone marrow aspirate showed scanty cellularity and bone marrow biopsy showed hypocellularity along with increased fibrosis.

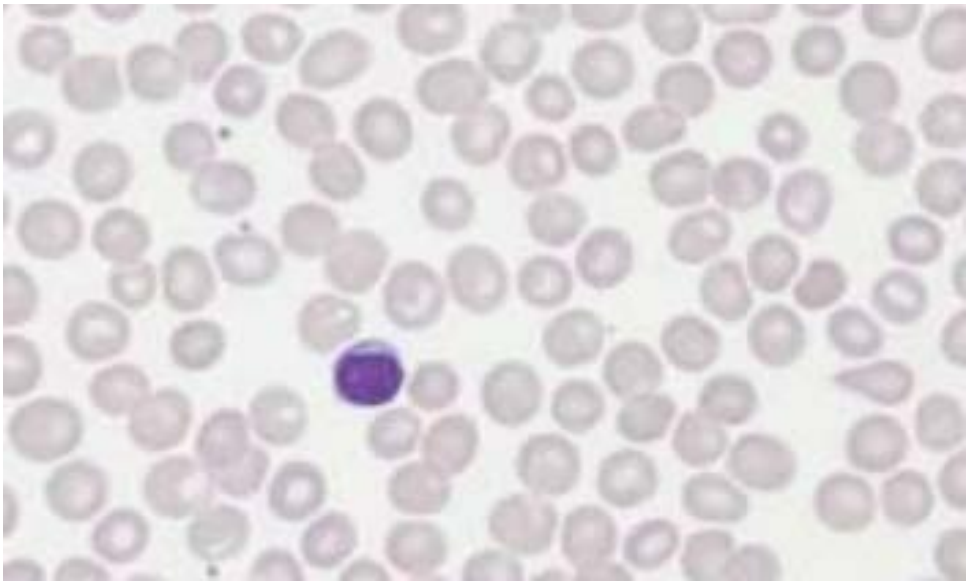


Fig: 3 Macroovalocytes in megaloblastic anemia (H&E)

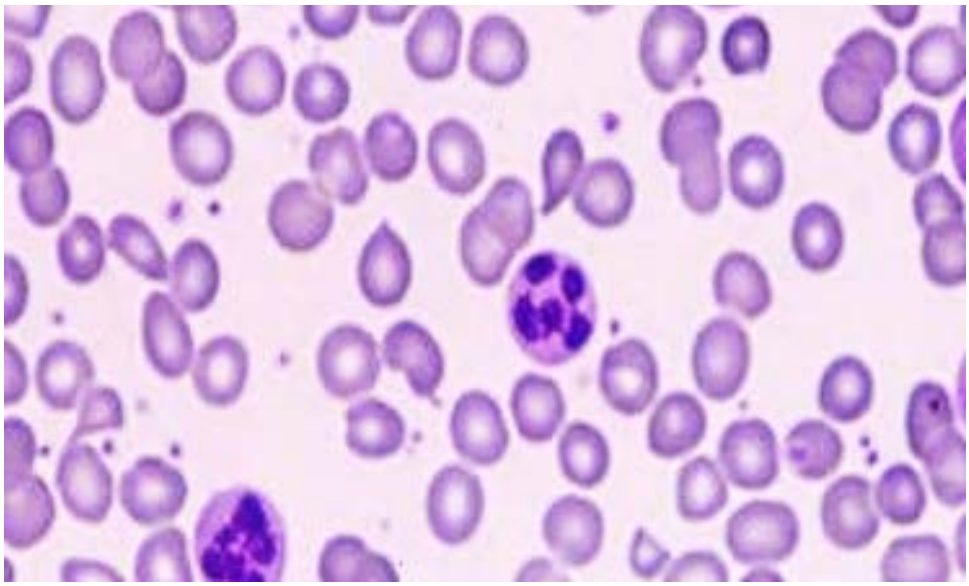


Fig: 4 Hypersemented neutrophils in Megaloblastic anemia (Leishman stain 1000x)

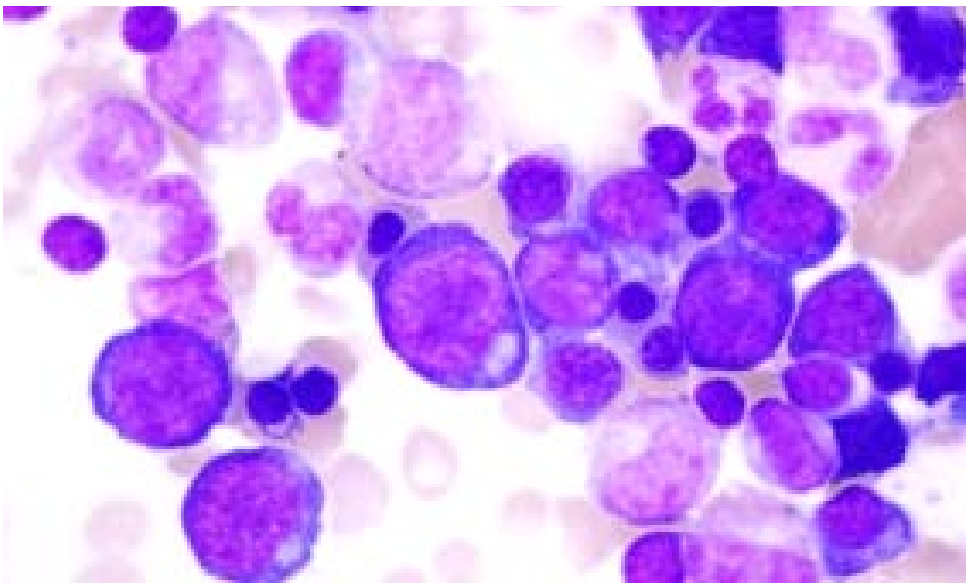


Fig: 5 Hypercellularity with maturation arrest of erythroid and myeloid series (megaloblastic changes) (Giemsa stain 1000x)

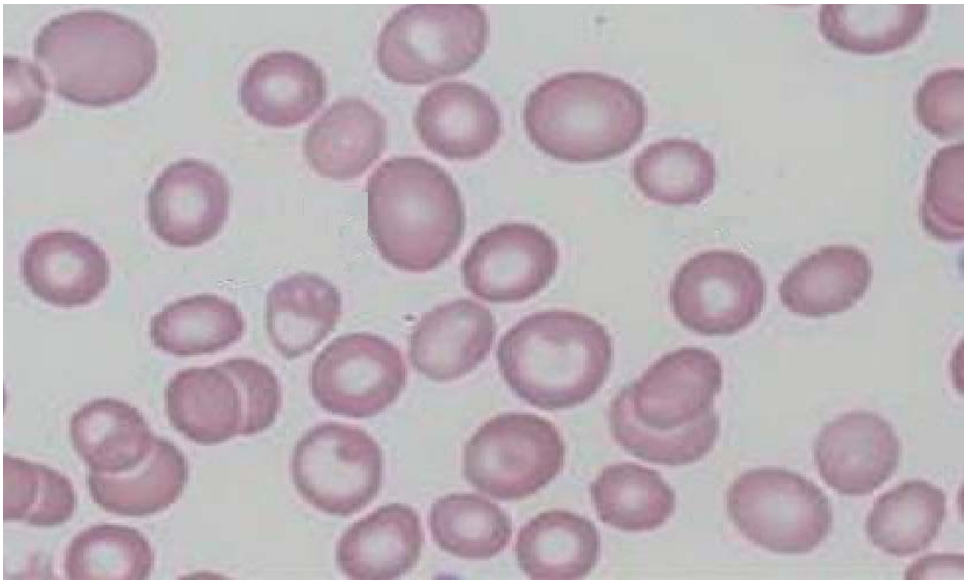


Fig: 6 Dimorphic anemia. (Leishman Stain, 1000x)

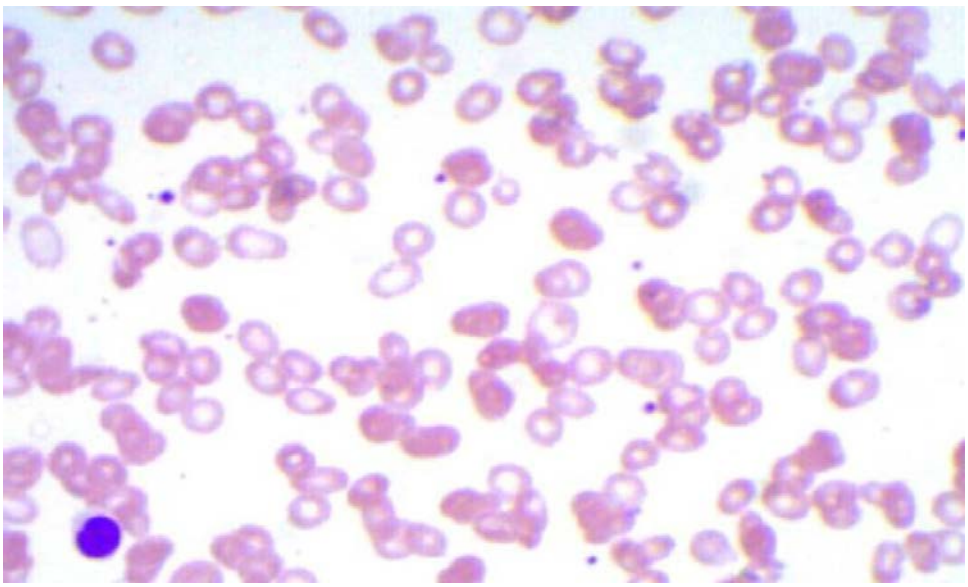


Fig : 7 Normocytic hypochromic anemia (Leishman Stain)

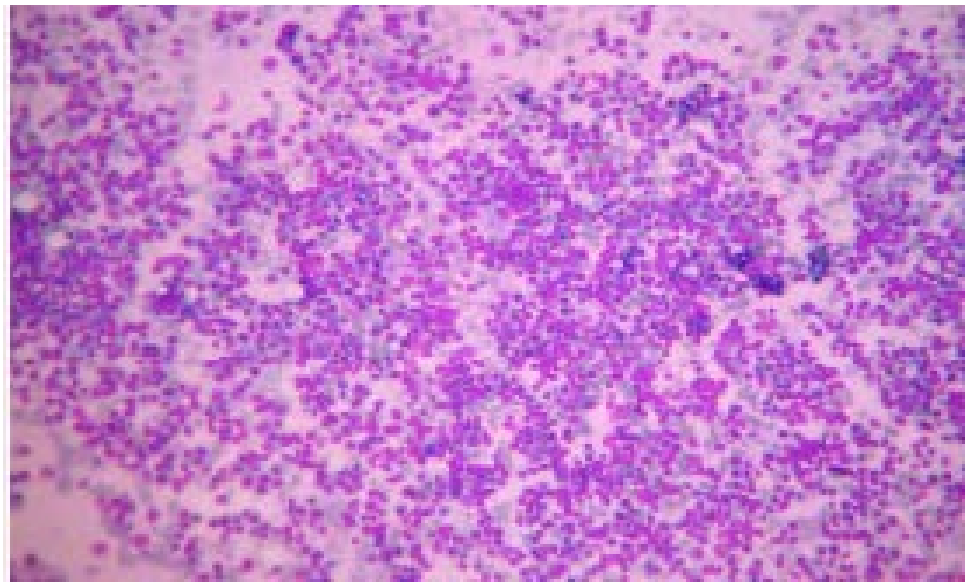


Fig : 8 Hypercellular Bone Marrow

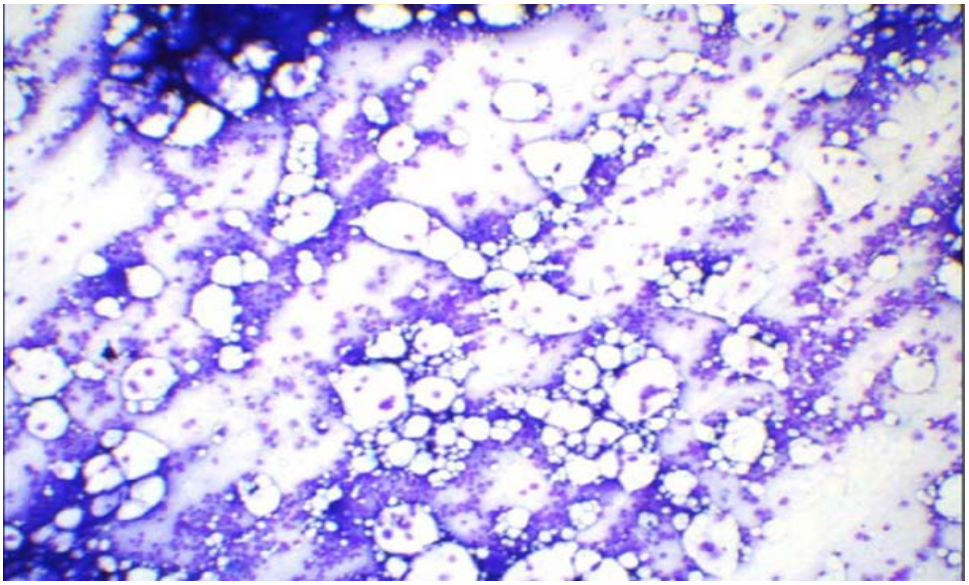


Fig : 9 Hypoplastic Marrow (Geimsa Stain)

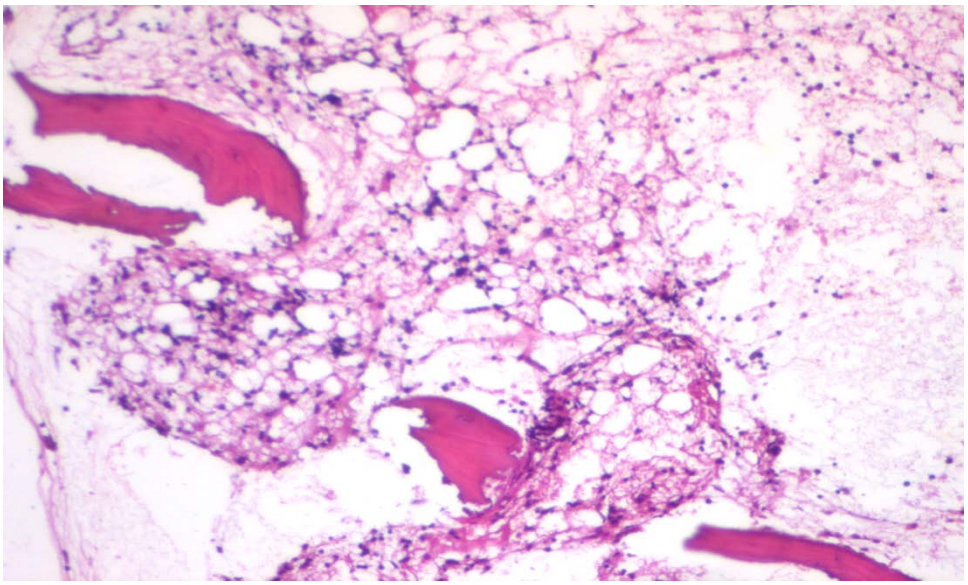


Fig : 10 Hypoplastic Bone Marrow (Aplastic anemia)

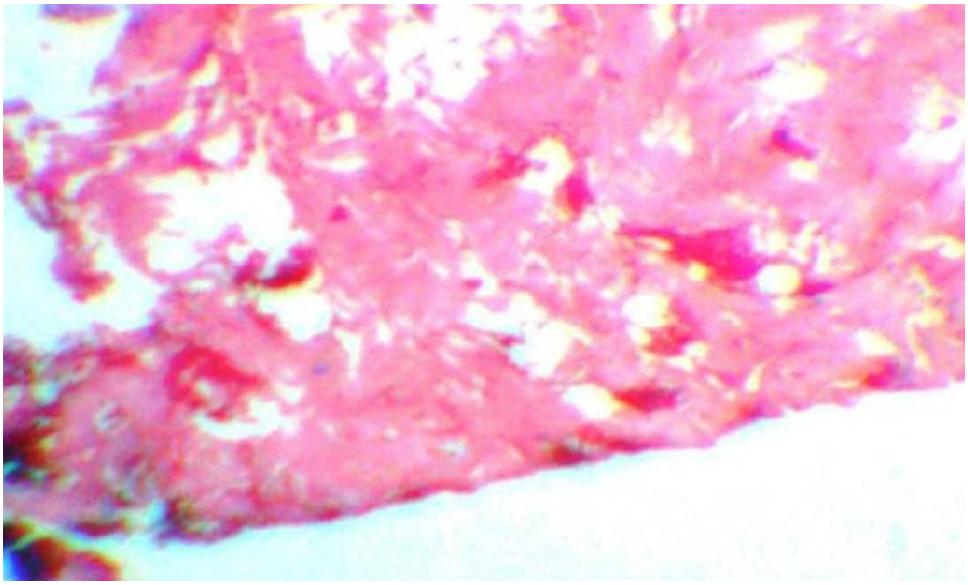


Fig : 11 Myelofibrosis Bone Marrow biopsy (H&E 400x)

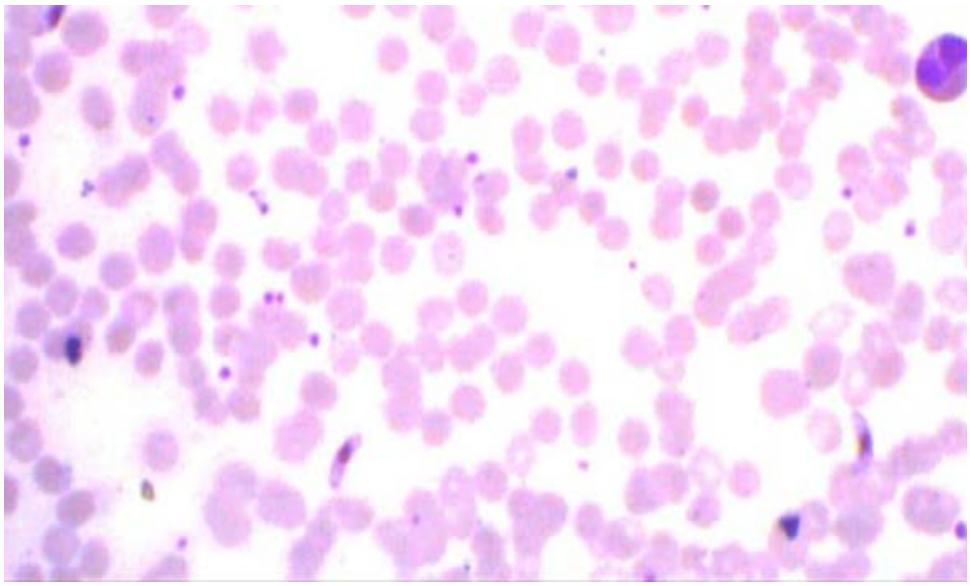


Fig 12. P Falciparum gametes in Bone Marrow (Leishman Stain, 400x)

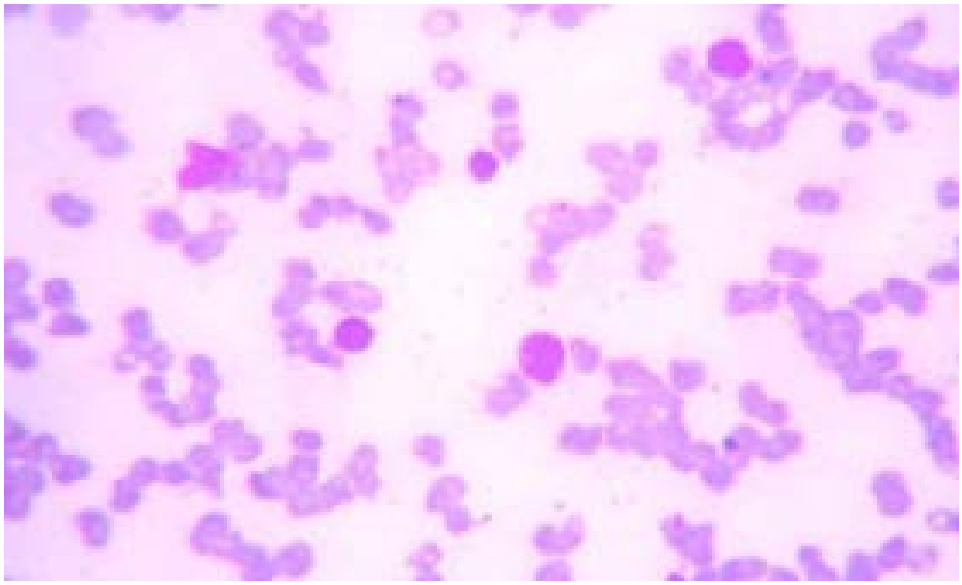


Fig : 13 Subleukemic Leukemia (Leishman 400x)

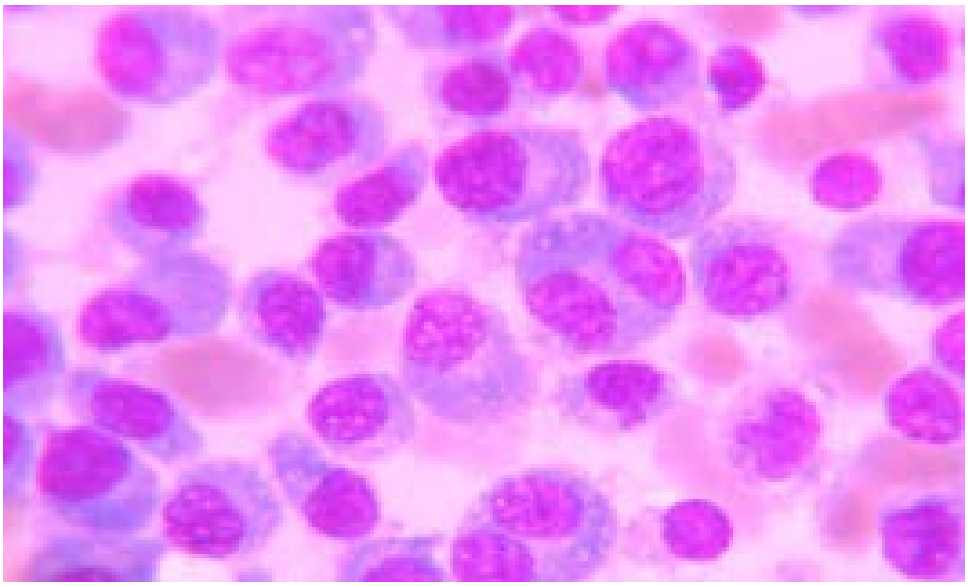


Fig : 14 Increased Plasma Cells (Multiple Myeloma) Leishman Stain 1000x

DISCUSSION

Pancytopenia is commonly seen in various clinical settings all over the world.

Total 114 cases of pancytopenia were studied from January 2016 to September 2017 at Dhiraj Hospital.

All the statistical data regarding age, sex, signs, symptoms, peripheral smear and bone marrow aspiration and biopsy smears were studied and compared with those published in previous literatures.

TABLE –12 AGE COMPARISON TO OTHER STUDIES OF PANCYTOPENIA

Sl. No.	Authors	Age distribution	Number of cases
1	Tilak et al[4] (1999)	5-70 yrs	77
2	Kishore Khodke et al[9] (2001)	3-69 yrs	50
3	Khunger et al[6] (2002)	2-70 yrs	200
4.	Yadav A[72] (2017)	5m-70yrs	180
5.	Present study	2-70 yrs	114

The age of the patients in this study ranged from 2 years to 70 years with mean age of 34 years.

Most common age group affected in Tilak et al[4] was between 5-20 years, in Khodke et al[9] it was 12-30 years, in Khunger et al[6] it was in 3rd decade. In this study it was 11-20 years.

TABLE 13: COMPARISION OF SEX DISTRIBUTION WITH OTHER STUDIES

Sl. NO.	AUTHORS	M:F RATIO
1	Tilak et al[4] (1999)	1.138:1
2	Kishore Khodke et al[9] (2001)	1.3:1
3	Khunger et al[6] (2002)	1.2:1
4	Yadav A et al[72](2017)	1.76:1
5	Present Study (2017)	1.3:1

In this study pancytopenia was found more in male as compared to females (1.3:1). This was similar to studies done by Tilak et al[4] (1.138:1) and Khodke et al[9 (1.3:1). In Khunger et al[6] and Yadav A et al[72], pancytopenia was predominant in male with 1.2:1 and 1.76:1 respectively.

TABLE: 14 CLINICAL FEATURES COMPARED WITH OTHER STUDIES

Sno.	Signs and Symptoms	Tilak et al[4]	Khunger et al[6]	Khodke et al[9	Yadav A et al[72]	Present study
1.	Pallor	77	200	50	177	114
2.	Fever	-	-	20	126	65
3.	Generalised Weakness	-	-	30	176	113
4.	Breathlessness	-	-	-	135	2
5.	Bone Pain	2	14	-	-	2
6.	Weight Loss	-	-	-	-	1
7.	Dyspnoea	-	-	-	-	43
8.	Bleeding	-	-	10	76	6
9.	Hepatomegaly	34	65	19	33	29
10.	Splenomegaly	39	65	20	46	21
11.	Lymphadenopathy	9	8	-	23	22

In this study the most common symptom was pallor. This was similar to studies of Tilak et al[4], Khunger et al[6], Khodke et al[9 and Yadav A et al[72].

Generalised weakness was present in 99.1 % in this study which is similar to Yadav A et al[72] (97.8%) and Khodke et al[9 (60%). Fever is present in 57.1% cases in this study. It was 70% in Yadav A et al[72]. Other symptoms are breathlessness, dyspnoea and weight loss.

Hepatomegaly is 25.4% in this study while it was 28.9% in Yadav A et al[72]32.5% in Khunger et al[6].

It was higher in Khodke et al[9] with 38% and 44.1% in Tilak et al[4]. Splenomegaly is 18.4% as compared to 25.5% in Yadav A et al[72], 40% in Khodke et al[9], 32.5% in Khunger et al[6] and 50.6% in Tilak et al[4].

Other clinical features were bone pain, weight loss, dyspnoea, breathlessness and lymphadenopathy.

TABLE – 15 VARIOUS CAUSES OF PANCYTOPENIA COMPARED TO OTHER STUDIES

Sno.	Causes	Tilak et al[4] (1999)77	Khodke et al[9] (2001)50	Khunger et al[6] (2002)200	Yadav A et al[72] (2017)180	Present Study 114
1	Megaloblastic Anemia	53	22	144	45	75
2	Dimorphic Anemia	-	-	-	31	13
3	Aplastic Anemia	6	7	28	23	11
4	Malaria	3	-	2	-	4
5	Subleukemic leukemia /aleukemic leukemia	1	1	10	25	2
6	Multiple Myeloma	1	2	2	3	2
7	Infections	1	1	1	31	2
8	MDS	-	1	4		2
9	Metastasis	-	-	-	-	1
10	SLE	-	-	-		1
11	Myelofibrosis	1	-	2		1
12	Lymphoma	2	-	2	4	-
13	Storage Disorder Diseases	-	-	-	3	-
14	Hypersplenism	-	-	4	7	-
15	Waldenstrom’s macroglobulinemia	1	-	1	-	-

India is a large with country with geographical diversity. People have difference in genetics, customs and dietary habits.

The incidence of megaloblastic anaemia varies from 0.8% to 32.26% of all pancytopenia patients and the incidence of aplastic anaemia varies from 10% to 52.7% of all pancytopenic patients.

The present study shows megaloblastic anaemia as the most common cause of pancytopenia with 65.8% cases which coincides with studies done by Khunger et al[6] (72%) and Tilak et al[4] (68%).

The second most common cause of pancytopenia in our study is Dimorphic anemia. It was similar to study done by Yadav A et al[72] (17.2%).

Third cause was Aplastic anemia (9.6%). It was second most common cause in the studies done by Tilak et al[4] and Khunger et al[6]. Yadav A et al[72] reported aplastic anemia with 12.8% cases while Khodke et al[9] with 14 %.

In this study there were four cases of malaria. Khunger et al[6] and Tilak et al[4] reported 2 and 3 respectively.

There were 2 cases (1.8%) of subleukemic leukemia in this study. It was similar to Khodke et al [9] and Tilak et al[4] with one case each. However Yadav A et al[72] reported 25 (13.9%) cases and Khunger et al[6] with 10 (5%) cases.

We had one case of multiple myeloma, incidence being 1% compared to Khunger et al[6] JM et al who also reported 1% cases of multiple myeloma in his study.

The study included 2 cases of infections (TB and Hep B). This was similar to Khunger et al[6] Khodke et al[9] and Tilak et al[4] with 1 case each. However Yadav

A et al[72] study showed 31 cases.

Two cases of MDS were found in our study. Khodke et al[9] study had one case while Khunger et al[6] had 4 cases.

There was 1 case each of metastasis, SLE and myelofibrosis. Khunger et al[6] encountered 2 cases of myelofibrosis in his study and Tilak et al[4] encountered 1 case.

PERIPHERAL BLOOD FINDINGS

In our study we found that dimorphic anemia was most common and anisopoikilocytosis was predominant among all the cases. In some dimorphic anemia's the peripheral blood smear showed both macro-ovalocytes and microcytes.

Macro-ovalocytes along with hypersegmented neutrophils were commonly found in megaloblastic anemia. Few cases showed reticulocytes and mild lymphocytosis. Tilak et al[4] and Khunger et al[6]also found periphetral blood findings in megaloblastic anemia similar to above.

Yadav A et al[72]found microcytic anemia with 27.2% followed by normocytic anemia with 26.7%.

Khodke et al[9]found dimorphic anemia to be most common.

Thus peripheral blood smear is important in diagnosing a case of pancytopenia.

BONE MARROW FINDINGS

Bone marrow examination is very helpful in evaluating a case of pancytopenia.

In present study we found hypercellular marrow in 92 cases (80.7%), followed by hypocellular (16.7%) and normocellular marrow with 3 cases (2.6%). It was similar to Yadav A et al[72] study with 70 % hypercellular bone marrow. Most common cause for hypercellular bone marrow in our study was Megaloblastic anemia. They had megaloblast with sieved chromatin and asynchronic nucleus: cytoplasmic ratio in the marrow aspirates. Other causes for hypercellular marrow were MDS, multiple myeloma, subleukemic leukemia. This was similar to study by Khunger et al[6].

One case had increased plasma cells and plasmablasts in bone marrow biopsy and multiple myeloma was suggested along with further ancillary tests. Yadav A et al[72], Khunger et al[6], Khodke et al[9] and Tilak et al[4] all had cases of plasma cell dyscrasis with increased plasmablasts in the bone marrow.

Two cases of MDS with pancytopenia showed dysplastic changes in cells in the bone marrow. It was similar to cases of MDS in Khodke et al[9] and Khunger et al[6]. The hypercellularity of the bone marrow along with abnormal cells confirmed the diagnosis.

Hypocellular bone marrow was seen in aplastic anemia, myelofibrosis, SLE and Tuberculous infection.

CONCLUSION

Pancytopenia is a frequently encountered hematological problem in clinical practice. If a patient presents with unexplained anaemia, prolonged fever and tendency to bleed then pancytopenia should be suspected and laboratory evaluation must be carried out.

The physical findings, peripheral blood picture and bone marrow evaluation provides valuable information.

The peripheral blood film examination helps in evaluating the most probable cause of anaemia while bone marrow evaluation is diagnostic.

Bone marrow examination is accurate, reproducible, rapidly available information at an economical cost and with minimal discomfort to the patient. Bone marrow aspiration is sufficient to make a diagnosis in cases of nutritional anemias and initial diagnosis of leukemia.

Megaloblastic anaemia was the commonest cause which indicates the high prevalence of nutritional anaemia in our region. The other common causes were dimorphic anemia and aplastic anemia. However, uncommon and rare causes such as multiple myeloma, tuberculosis and malaria infection should be kept in mind while planning investigation for complete work up of cytopenic patients.

Present study concludes that detailed primary haematological investigations along with bone marrow aspiration in cytopenic patients is helpful for understanding of the disease process, to diagnose or to rule out the causes of cytopenia and helpful in planning further investigations and management of cytopenic patients.

SUMMARY

- The present study " A clinic haematological study of pancytopenia " was carried out from January 2016 to September 2017, in the department of pathology, Dhiraj Hospital, Sumandeep Vidyapeeth.
- Total 114 patients aged between 2 -70 years age group, presenting with pancytopenia were evaluated.
- A combined evaluation of physical findings, primary haematological investigations and bone marrow aspiration were done in all patients.
- Commonest age group affected is 11-20 yrs.
- Males accounted for 65 cases (57,1%) and female 49 cases (42.9%).
- Commonest presenting complaint was generalized weakness.
- Commonest physical finding was pallor.
- Other sign and symptoms were fever, breathlessness, bone pain, dyspnea, bleeding hepatomegaly, splenomegaly and lymphadenopathy.
- Megaloblastic anaemia (65.8%) was the commonest cause of cytopenia, followed by dimorphic anemia (11.4%).
- Lowest haemoglobin percentage was 1.8 gm/dl and noted in a case of megaloblastic anaemia.
- Lowest total leucocyte count was 1000 cells/mm3 and noted in a case of dimorphic anemia.

- Lowest platelet count of 10,000 cells/mm3 was noted in a case of megaloblastic anemia and dimorphic anemia.

- Hypercellular marrow was noted in 92 patients and the common cause was megaloblastic anaemia, followed by,dimorphic anemia.

- Hypocellular marrow was seen in 19 cases and normocellular in 3 cases.

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ANNEXURES

LIST OF ABBREVATIONS

AML:Acute myeloid leukemia.

AA: Aplastic anemia

AIDS: Aquired immuno deficiency syndrome

BM: Bone marrow

CFU-GM: Colony forming unit-granulocyte

CBC: Complete blood count

DNA: Deoxy nucleic acid

EDTA: Ethylene diamine tetra acetic acid

FA: Fanconi's anemia

G-6-PD: Glucose – 6 – phosphate

dehydrogenase HSC: Hematopoeitic stem cell

HV: Herpes virus

HIV: Human immune deficiency virus

HBMIB: Hypocellular bone marrow with increased blasts

HPS: Hemophagocytic syndrome.

IHBMFS:Inherited bone marrow failure syndrome .

MA:Megaloblastic anemia

MF:Myelofibrosis

MDS: Myelodysplastic syndrome

MCV: Mean corpuscular volume

NASIDS: Non steroidal anti-inflammatory drugs

n RBC : nucleated red blood cells

PNH : Paroxysmal nocturnal hemoglobinuria.

SLE: Systemic lupus erythromatosis

SS: Sjogren's syndrome

WBC : White cell count

PERFORMA/QUESTIONNAIRE

Name of the patient:

Age:

Sex:

Address:

Occupation:

Education:

Marital status:

Income:

Date of admission:

Date of examination:

IPD/OPD number:

Chief Complaints:

Clinical Findings:

Laboratory Findings: Complete Blood Count

Bone Marrow aspiration/biopsy (wherever needed)

Sumandeep Vidyapeeth University

Pipariya, Ta. Waghodia, Dist. Vadodara Pin 391760

PARTICIPANT INFORMATION SHEET

Title of the study**: "A CLINICO HAEMTOLOGICAL STUDY OF PANCYTOPENIA"**At Dhiraj Hospital, Pipariya**."**

Study No. _____

Date_____

Invitation to participant

Purpose & nature of the study: This study is carried out to study the incidence of causes of pancytopenia

and evaluating clinical and pathological parameters.

Nature of the participation: It is an absolutely voluntary participation in the study program.

Study methods:

It will be a prospective (observational) type of study,. This work will be carried out in the *Department of*

Pathology, S.B.K.S.MI&RC, Pipariya. The patients will be selected from indoor and outdoor at Dhiraj

general hospital Participants responsibilities:

After agreeing to participate in the study, the patients should extend full support. They should provide real facts when inquired into.

PARTICIPANT INFORMATION SHEET

Introduction

My name is AVIRAL CHANDRA. I am a doctor working here DHIRAJ GENERAL HOSPITAL and training to be a Pathologist (doctor who study disease and investigation). I am conducting a study as part of my training.

In this study the patient will be examined clinically and laboratory tests will be performed. Details like age, clinical signs and symptoms, various haematological parameters, and bone marrow aspiration (if the patient gives consent for bone marrow aspiration) will be recorded in the Performa.

If you agree to take part in this study, you will be required to sign a consent form or thumbprint it if you are not able to write. You are free to withdraw from the study if you so wish for any reason and the treatment of the child will not be affected in any way.

Please note that there will be no payments or gifts offered if you agree to take part in the study.

Information regarding patients health and other personal facts if any, will be kept confidential.

Obtaining additional information:

If need arises, the patient may be contacted to inquire about past, personal and family history. Also religious background, social customs, beliefs etc can be inquired into.

1. **What is the purpose of this study ?**
   This study would help in better planning the diagnostic and therapeutic approach in patients with pancytopenia.

2. **Why have I been chosen?**
   Your clinical and laboratory findings coincide with the study which can help us in better evaluation.

3. **Do I have to take part?**
   Participation is of voluntary nature.

4. **ow long will the study last?**
   Study will last in one year.

5. What will happen to me if I take part?

After the clinical examination and laboratory investigations no further active participation is required. If need arises, you will be informed.

6. What do I have to do?

You have to give complete medical history along with chief complaints to the clinician. Also blood sample to be given for laboratory investigation. If you give consent fo bone marrow biopsy, it can be performed for better results.

7. What is the drug being tested?

No drug will be tested in this study.

8. What are the benefits of the study?

This study has both individual and community benefits. It would help in better planning the diagnostic and therapeutic approach in patients with pancytopenia.

9. **What are the alternatives for treatment?**

Blood transfusion or bone marrow replacement from clinical aspect. No active intervention will be performed from my side.

10. What are the side effects of the treatment received during the study?

There is no side effect of any treatment during study with patient's full co-operation.

11. What if new information becomes available?

It will have a benefit in patient's outcome. But the study will target the issue concern with the topic only.

12. What happens when the study stops?

Error from any parts will be analyzed. Mistakes will be corrected and try to proceed the study. If at all the study stops inspite of these than data will be collected with whatever the study has been done. It will be analyzed using appropriate statistical test like mean, mode, standard deviation or chi- square test.

13. What if something goes wrong?

If any problem develops you can contact:

Dr. Aviral Chandra

Department of Pathology, S.B.K.S MI & RC, Pipariya. Tal. Waghodia. District Vadodara.

Ph. No.- 7573096316

14. Will my taking part be kept confidential?

Information regarding patient's health and other personal facts if any, will be kept confidential.

15. What else should I know?

If need arises, the patient may be contacted to inquire about past, personal and family history. Also religious background, social customs, beliefs etc can be inquired into.

16. Additional Precautions

As such in this study no experiment will be done on patient so there is no issue of adverse effect or risk and so no need of any additional precautions.

17. Who to call with questions?

Dr. Aviral Chandra

Department of Pathology, S.B.K.S MI & RC, Pipariya. Tal. Waghodia. District Vadodara.

Ph. No.- 7573096316

પરિચય

મારું નામ AVIRAL ચંદ્ર છે. હું એક ડૉક્ટર પેથોલોજીસ્ટ (રોગ અને તપાસ અભ્યાસ જે ડોક્ટર) અહીંયા ધીરજ જનરલ હોસ્પિટલ અને તાલીમ કામ કરું છું. હું મારા તાલીમ ભાગ તરીકે એક અભ્યાસ હાથ ધર્યો છું.

આ અભ્યાસમાં દર્દી તબીબી તપાસ કરવામાં આવશે અને લેબોરેટરી પરીક્ષણો કરવામાં આવશે. ઉંમર, ક્લિનિકલ ચિહ્નો અને લક્ષણો વિવિધ હેમેટોલોજીકલ પરિમાણો, અને મજ્જા મહાપ્રાણ (દર્દીને મજ્જા મહાપ્રાણ માટે સંમતિ આપે તો) જેવી વિગતો Performa માં રેકોર્ડ કરવામાં આવશે.

તમે આ અભ્યાસમાં ભાગ લેવા માટે સંમત હોય તો તમે લખવા માટે સમર્થ નહિં હોય, તો તમે તેને સંમતિ પત્રક પર સહી અથવા વ્યક્તિની ઓળખ માટે લેવાતી તેના અંગૂઠાની છાપ કરવાની જરૂર પડશે. તમે જેથી કોઈપણ કારણોસર માંગો છો અને બાળક સારવાર કોઈપણ રીતે અસર થશે નહીં, તો અભ્યાસ પરથી પાછી ખેંચી માટે મુક્ત છે.

તમે અભ્યાસ માં ભાગ લેવા માટે સંમત તો કોઈ ચૂકવણી અથવા ઓફર ભેટ હશે કે કૃપા કરીને નોંધ રાખો.

દર્દીઓ આરોગ્ય અને ગુપ્ત રાખવામાં આવશે જો કોઈ હોય તો અન્ય વ્યક્તિગત હકીકતો સંબંધિત માહિતી.

વધારાની જાણકારી મેળવી:

જરૂરિયાત ઊભી થાય તો, દર્દી ભૂતકાળ, વ્યક્તિગત અને કુટુંબ ઇતિહાસ વિશે પૂછપરછ સંપર્ક કરી શકે છે. પણ ધાર્મિક પૃષ્ઠભૂમિ, સામાજિક રિવાજો, વગેરે માન્યતાઓ તપાસ કરી શકાય છે.

1. આ અભ્યાસ હેતુ શું છે?

આ અભ્યાસ સારી આયોજન pancytopenia સાથે દર્દીઓમાં ડાયગ્નોસ્ટિક એન્ડ ઉપચારાત્મક અભિગમ મદદ કરશે

2. હું શા માટે પસંદ કરવામાં આવી છે?

તમારી તબીબી અને લેબોરેટરી તારણો વધુ સારી મૂલ્યાંકન મદદ કરી શકે છે કે જે અભ્યાસ સાથે સંબંધ ધરાવે છે.

3. મારે ભાગ લેવા માટે હોય છે?

ભાગીદારી સ્વૈચ્છિક પ્રકૃતિ છે.

4. લાંબા કેવી રીતે અભ્યાસ ચાલશે?

અભ્યાસ એક વર્ષમાં ચાલશે.

5. હું ભાગ લેવા હોય તો મને શું થશે?

ક્લિનિકલ પરીક્ષા અને લેબોરેટરી તપાસ પછી કોઈ વધુ સક્રિય ભાગીદારી જરૂરી છે. જરૂરિયાત ઊભી થાય તો, તમે જાણ કરવામાં આવશે.

6. હું શું છે?

તમે ક્લિનિસિયનની મુખ્ય ફરિયાદો સાથે સંપૂર્ણ તબીબી ઇતિહાસ આપી છે.

પણ રક્ત નમૂનો પ્રયોગશાળામાં તપાસ માટે આપવામાં આવશે. તમે અસ્થિ માટે સંમતિ આપી છે, તો

મજ્જા બાયોપ્સી, તે સારી પરિણામો માટે કરી શકાય છે.

7. ડ્રગ શું પરીક્ષણ કરવામાં આવી રહી છે?

કોઈ દવા આ અભ્યાસમાં પરીક્ષણ કરવામાં આવશે.

8) અભ્યાસ ના લાભો શું છે?

આ અભ્યાસ વ્યક્તિગત અને સમુદાય લાભ ધરાવે છે. તે સારી રીતે આયોજન pancytopenia સાથે દર્દીઓમાં

ડાયગ્નોસ્ટિક એન્ડ ઉપચારાત્મક અભિગમ મદદ કરશે.

9. સારવાર માટે આ વિકલ્પો શું છે?

રક્ત મિશ્રણ અથવા તબીબી પાસું મજ્જા રિપ્લેસમેન્ટ. કોઈ સક્રિય

હસ્તક્ષેપ મારા તરફથી કરવામાં આવશે.

10. અભ્યાસ દરમિયાન પ્રાપ્ત સારવાર ની આડઅસરો શું છે?

દર્દીના સંપૂર્ણ સહકાર સાથે અભ્યાસ દરમ્યાન કોઈપણ સારવાર માટે કોઈ આડઅસર નથી.

11. નવી માહિતી ઉપલબ્ધ બને તો શું?

તે દર્દી પરિણામ એક લાભ હશે. પરંતુ અભ્યાસ માત્ર વિષય સાથે મુદ્દો ચિંતા લક્ષ્ય કરશે.

12. અભ્યાસ અટકે ત્યારે શું થાય છે?

કોઇપણ ભાગોમાં ભૂલ વિશ્લેષણ કરવામાં આવશે. ભૂલો સુધારાઈ અને અભ્યાસ આગળ વધવા માટે પ્રયાસ કરવામાં આવશે. બધા અભ્યાસ ડેટા કરતાં આ અભ્યાસ કરવામાં આવ્યો છે તે સાથે એકત્રિત કરવામાં આવશે છતાં અટકે છે. તે અર્થ, સ્થિતિ, પ્રમાણભૂત વિચલન અથવા chi- સ્ક્વેર ટેસ્ટ જેવી યોગ્ય આંકડાકીય પરીક્ષણ મદદથી વિશ્લેષણ કરવામાં આવશે.

13. શું કંઈક ખોટું થાય તો?

કોઇ સમસ્યા વિકસે તો તમે સંપર્ક કરી શકો છો:

ડો Aviral ચંદ્ર

પેથોલોજી, SBKS MI અને આરસી, Pipariya વિભાગ. તાલ. Waghodia. જિલ્લા વડોદરા.

પીએચ. નં 7573096316

14. મારા ભાગ લેવા ગુપ્ત રાખવામાં આવશે?

દર્દીના આરોગ્ય અને જો કોઈ હોય તો અન્ય વ્યક્તિગત હકીકતો સંબંધિત માહિતી, ગુપ્ત રાખવામાં આવશે.

15. હું બીજું શું જાણવું જોઈએ?

જરૂરિયાત ઊભી થાય તો, દર્દી ભૂતકાળ, વ્યક્તિગત અને કુટુંબ ઇતિહાસ વિશે પૂછપરછ સંપર્ક કરી શકે છે. પણ ધાર્મિક પૃષ્ઠભૂમિ, સામાજિક રિવાજો, વગેરે માન્યતાઓ તપાસ કરી શકાય છે.

16. વધારાની સાવચેતી

પ્રતિકૂળ અસર અથવા જોખમ અને કોઈપણ વધારાની સાવચેતી જેથી કોઈ જરૂર કોઈ મુદ્દો છે તેથી આ અભ્યાસમાં જેમ કે કોઈ પ્રયોગ દર્દી પર કરવામાં આવશે.

17 પ્રશ્નો સાથે કોને કૉલ કરવા માટે?

ડો Aviral ચંદ્ર

પેથોલોજી, SBKS MI અને આરસી, Pipariya વિભાગ. તાલ. Waghodia. જિલ્લા વડોદરા.

પીએચ. નં 7573096316

S.B.K.S MEDICAL INSTITUTE AND RESEARCH CENTRE

SUMANDEEP VIDYAPEETH UNIVERSITY

PIPARIA, TA. WAGHODIA, DIST. VADODARA. PIN – 391760

Informed Consent Form (ICF) for Participants in Research Programs involving studies on human beings

STUDY TITLE: **A CLINICO HAEMTOLOGICAL STUDY OF PANCYTOPENIA**

Study Number: SVU/SBKS/ /2013- Participants Initials: _____
Participant's Name _____

Date of Birth / Age _____ ( ) Years

I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

I understand that the investigator of this study, others working on the investigator's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records, both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I agree to this access. However, I understand that my identity will not be revealed in any information related to third party or published. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).

I agree to take part in the above study.

Signature (or thumb impression) of the participant / guardian

Legally acceptable representative _____

Signatory's Name _____ Date _____

Signature of the investigator _____ Date _____

Study Investigator's Name _____

Signature of the impartial witness _____ Date _____

Name of the witness _____

S.B.K.S તબીબી સંસ્થા એન્ડ રિસર્ચ સેન્ટર

SUMANDEEP વિદ્યાપીઠ યુનિવર્સિટી

PIPARIA, તા. WAGHODIA, જિ. વડોદરા. PIN - 391760

મનુષ્ય પર અભ્યાસ સંડોવતા સંશોધન કાર્યક્રમો માં ભાગ લેનારા માટે (ICF) માહિતીપૂર્ણ સંમતિ પત્રક

અધ્યયન શીર્ષક: PANCYTOPENIA ઓફ CLINICO PATHOLOGICAL મૂલ્યાંકન અભ્યાસ

અભ્યાસ સંખ્યા: SVU / SBKS / / 2013- સહભાગીઓ ટૂંકાક્ષરો: ____

સહભાગી નામ _____

જન્મ / ઉંમર _____ તારીખ ( ) વર્ષો

હું વાંચી અને ઉપર અભ્યાસ માટે ક માહિતી શીટ _____ સમજી અને પ્રશ્નો પૂછી તક મળી છે છે કે તેની ખાતરી કરો. હું અભ્યાસ મારો સહયોગ સ્વૈચ્છિક છે અને હું મારા તબીબી સંભાળ કર્યા વગર, કોઇ કારણ આપ્યા વગર, કોઈપણ સમયે પાછી ખેંચી મુક્ત છું અથવા કાનૂની અધિકારો પર અસર થઈ રહી છે કે જે સમજે છે.

હું આ અભ્યાસના તપાસનીસ, તપાસનીસ વતી કામ અન્ય એથિક્સ સમિતિ અને નિયમનકારી સત્તાવાળાઓ વર્તમાન અભ્યાસ આદર અને હાથ ધરવામાં કરી શકાય છે કે જે કોઈપણ વધુ સંશોધન બંને મારા આરોગ્ય રેકોર્ડ જોવા માટે મારા પરવાનગી જરૂર નથી કે જે સમજે છે તે સંબંધમાં, હું અભ્યાસ ખસી તો પણ. હું આ ઍક્સેસ કરવા માટે સંમત થાય છે. જો કે, હું મારી ઓળખ ત્રીજી વ્યક્તિ અથવા પ્રકાશિત સંબંધિત કોઈ માહિતી જાહેર કરવામાં આવશે નહીં કે સમજે છે. હું જેમ કે ઉપયોગ માત્ર વૈજ્ઞાનિક હેતુ (ઓ) માટે પૂરી પાડવામાં આ અભ્યાસ પરથી ઊભી છે કે જે કોઈપણ માહિતી અથવા પરિણામો ઉપયોગ મર્યાદિત કરવા સંમત છો.

હું ઉપર અભ્યાસ માં ભાગ લેવા માટે સંમત થાય છે.

સહભાગી ની સહી (અથવા અંગૂઠાની છાપ) / ગાર્ડિયન
કાયદાકીય રીતે સ્વીકાર્ય પ્રતિનિધિ _____
સહી નામ _____ તારીખ _____
તપાસનીસ _____ તારીખ હસ્તાક્ષર _____
તપાસનીશ નામ અભ્યાસ _____
આ નિષ્પક્ષ સાક્ષી _____ તારીખ હસ્તાક્ષર _____
સાક્ષી નામ _____

MASTER CHART

Data					Clinical details											Complete hemogram									
Sl No	BM No	Age	Sex	Fever	Generalised Weakness	Breathlessness	Bone Pain	Weight loss	Dyspnea	Bleeding	Pallor	Hepatomegaly	Splenomegaly	Lymphadenopathy	Hb %	TLC cells/mm3	PLT cells/mm3	MCV	MCH	MCHC	RBC	Peripheral smear	Bone marrow aspiration	Bone Marrow Biopsy	Final diagnosis
1	4/16	42	M	+	+	-	-	-	-	-	+	-	-	-	4.5	3800	82000	98.4	34.6	32.4	1.3	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
2	7/16	3	F	+	+	-	-	-	-	-	+	+	+	-	8.2	3600	140000	84.4	29.1	31.8	2.82	Normocytic anemia	Leukemia	Hypercellular	Subleukemic leukemia
3	9/16	18	M	-	+	-	-	-	-	-	+	-	-	-	7.2	3000	100000	104.2	30	33	2.4	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
4	12/16	42	F	+	+	-	-	-	-	+	+	-	-	-	3	3600	120000	78.2	24.5	31.5	3.4	Dimorphic anemia	Normal erythroid hyperplasia	Normocellular	Dimorphic anemia
5	14/16	28	F	-	+	-	-	-	-	+	+	-	-	-	5.8	3400	10000	104.2	36.7	35	1.58	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
6	17/16	64	M	-	+	+	+	-	-	-	+	-	-	-	5.4	3000	100000	101.4	29.2	31.4	1.8	Macrocytic anemia	Plasma Cell Dyscrasis	Hypercellular withPlasma Cells	Multiple Myeloma
7	18/16	63	M	-	+		-	-	-	-	+	-	-	-	7.2	3700	30000	106.6	32.7	33	2.2	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
8	26/16	57	M	+	+	+	-	-	-	-	+	-	-	-	5.6	900	10000	99.4	35	34.2	1.6	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
9	29/16	38	M	-	+	-	-	-	-	-	+	-	-	-	5.4	2000	44000	118.2	34.1	35	1.58	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
10	30/16	8	F	+	+	-	-	-	-	+	+	-	-	-	6.2	3200	25000	101.4	34.4	33.6	1.8	Normocytic hypochromic	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
11	36/16	62	F	+	+	-	-	-	-	-	+	-	-	-	8.4	3100	10000	98.8	36.2	34.1	2.3	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
12	39/16	16	F	+	+	-	-	-	-	-	+	-	+	-	6.3	1500	36000	99.4	28.6	32.8	2.2	Macrocytic anemia	Erythroid hyperplasia	Hypercellular with P. Falciparum	Malaria
13	44/16	20	M	-	+	-	-	-	-	-	+	-	-	-	7.2	3300	98000	117.4	34.2	33	2.1	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
14	47/16	22	F	+	+	-	-	-	-	-	+	-	-	-	5.3	1000	10000	67.8	24.1	31.6	2.2	Dimorphic anemia	Normal erythroid hyperplasia	Hypercellular	Dimorphic anemia
15	49/16	37	F	+	+	-	-	-	-	-	+	+	-	-	8.2	2400	88000	100.4	35.6	35	2.3	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
16	50/16	27	M	+	+	-	-	-	-	-	+	+	+	-	5.3	3200	134000	108.4	33.1	32.8	1.6	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia

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Data					Clinical details											Complete hemogram									
Sl No	BM No	Age	Sex	Fever	Generalised Weakness	Breathlessness	Bone Pain	Weight loss	Dyspnea	Bleeding	Pallor	Hepatomegaly	Splenomegaly	Lymphadenopathy	Hb %	TLC cells/mm3	PLT cells/mm3	MCV	MCH	MCHC	RBC	Peripheral smear	Bone marrow aspiration	Bone Marrow Biopsy	Final diagnosis
17	66/16	39	F	+	+	-	-	-	-	-	+	-	-	-	6.4	3600	89000	116.2	34.4	32.6	1.86	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
18	68/16	60	M	+	+	-	-	-	-	-	+	+	-	-	6.8	2800	124000	99.6	34	33	2	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
19	72/16	62	M	-	+	-	-	-	+	-	+	-	-	-	8	2800	20000	102.6	28.6	35.2	2.8	Macrocytic anemia	Dry Tap	Hypoplastic marrow	Aplastic Anemia
20	74/16	52	M	+	+	-	-	-	-	-	+	-	-	-	4.8	3600	95000	102.8	32.4	34.4	1.48	Dimorphic anemia	Megalobastic anemia	Hypercellular	Megaloblastic anemia
21	79/16	19	M	+	+	-	-	-	+	-	+	-	-	-	9.6	3200	85000	110.4	33.1	36	2.9	Dimorphic anemia	Megalobastic anemia	Hypercellular	Megaloblastic anemia
22	83/16	30	M	-	+	-	-	-	-	-	+	+	-	-	4.4	3000	146000	100.4	26.8	31.8	1.64	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
23	84/16	22	M	+	+	-	-	-	-	-	+	+	-	-	5.8	3600	72000	97.4	32.2	32	1.8	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
24	86/16	50	F	-	+	-	-	-	+	-	+	+	-	-	3.8	3100	140000	102.6	33.9	31.2	1.12	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
25	92/16	17	M	-	+	-	-	-	-	-	+	-	-	-	4.8	3800	55000	112.6	35.2	33.2	1.36	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
26	94/16	40	M	+	+	-	-	-	+	-	+	-	-	-	6.2	2800	56000	91.2	31.4	30	1.9	Normocytic hypochromic	Hypoplasia	Hypoplastic marrow	Aplastic Anemia
27	96/16	73	F	+	+	-	-	-	+	-	+	-	-	-	8.2	3300	134000	107.4	37.2	34.8	2.2	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
28	97/16	35	F	+	+	-	-	-	-	-	+	-	-	-	1.8	3200	140000	106.8	22.5	30.5	0.8	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
29	101/16	30	F	-	+	-	-	-	+	-	+	-	-	+	6.8	3400	128000	72.4	28.3	31.8	2.4	Dimorphic anemia	Micronormoblasts with megaloblast	Hypercellular with micronormoblasts with megaloblast	Dimorphic anemia
30	103/16	21	M	-	+	-	-	-	-	-	+	-	-	-	8.4	3800	114000	98.6	33.6	34.7	2.5	Dimorphic anemia	Megaloblastic anaemia	Hypercellular	Megaloblastic anemia
31	105/16	21	F	+	+	-	-	-	-	-	+	-	-	-	6.2	3600	136000	112.8	34.4	33.6	1.8	Dimorphic anemia	Megaloblastic anaemia	Hypercellular	Megaloblastic anemia

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Data					Clinical details											Complete hemogram									
Sl No	BM No	Age	Sex	Fever	Generalised Weakness	Breathlessness	Bone Pain	Weight loss	Dyspnea	Bleeding	Pallor	Hepatomegaly	Splenomegaly	Lymphadenopathy	Hb %	TLC cells/mm3	PLT cells/mm3	MCV	MCH	MCHC	RBC	Peripheral smear	Bone marrow aspiration	Bone Marrow Biopsy	Final diagnosis
32	106/16	66	M	-	+	-	-	-	-	-	+	+	+	+	8.4	3200	148000	68.8	24.7	33.8	3.4	Normocytic	Dry Tap	Hypocellular with metastatsis	Metastasis
33	107/16	36	M	+	+	-	-	-	-	-	+	-	-	-	5.8	3800	72000	106.2	35.2	32.5	1.65	Macrocytic anemia	Megaloblastic anaemia	Hypercellular	Megaloblastic anemia
34	111/16	60	M	+	+	-	-	-	+	-	+	-	-	+	5.2	2000	146000	104.8	38.2	32.1	1.36	Macrocytic anemia	Megaloblastic anaemia	Hypercellular	Megaloblastic anemia
35	112/16	24	M	-	+	-	-	-	-	-	+	+	-	+	7.8	4000	128000	103.6	32.5	33.6	2.4	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
36	116/16	16	M	-	+	-	-	-	-	-	+	-	-	-	6.6	4000	30000	92.2	32.4	31	2.2	Normocytic	Hypocellular	Hypoplasia	Aplastic Anemia
37	118/16	60	F	+	+	-	-	-	+	-	+	+	+	+	7.4	3400	100000	99.4	33	35.1	2.94	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
38	123/16	18	F	+	+	-	-	-	+	-	+	-	-	+	7.2	3600	149000	71.8	27.9	36.2	2.58	Dimorphic anemia	Micronormoblasts with megaloblast	Hypercellular with micronormoblasts with megaloblast	Dimorphic anemia
39	124/16	61	M	+	+	-	-	-	+	-	+	+	-	+	8.4	3200	110000	105.9	33.6	35.8	2.5	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
40	128/16	16	F	+	+	-	-	-	+	-	+	-	-	+	8.2	2500	132000	110.6	35.7	31	2.3	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
41	132/16	50	M	-	+	-	-	-	-	-	+	-	-	+	6.2	3500	142000	102.4	32	34.3	1.94	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
42	136/16	14	F	+	+	-	-	+	+	-	+	+	+	+	6.4	2400	24000	82.2	32.2	34.1	1.8	Normocytic Normochromic	Necrosis	Hypocellular with epitheloid Granuloma	Granulomatous Infection
43	139/16	18	F	+	+	-	-	-	+	-	+	-	-	-	7.9	1500	47000	86	31	33.4	2.4	Normocytic hypochromic	Dry Tap	Hypoplastic marrow	Aplastic Anemia
44	140/16	18	F	+	+	-	-	-	-	-	+	-	-	-	8.9	3800	140000	109.8	37.1	32	2.4	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
45	142/16	50	M	-	+	-	-	-	-	-	+	+	+	-	6.3	900	50000	101.8	35.4	33.9	1.78	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
46	144/16	26	M	-	+	-	-	-	+	-	+	+	+	+	7.6	2200	117000	100.9	34.2	34.5	2.22	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia

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Data					Clinical details											Complete hemogram									
Sl No	BM No	Age	Sex	Fever	Generalised Weakness	Breathlessness	Bone Pain	Weight loss	Dyspnea	Bleeding	Pallor	Hepatomegaly	Splenomegaly	Lymphadenopathy	Hb %	TLC cells/mm3	PLT cells/mm3	MCV	MCH	MCHC	RBC	Peripheral smear	Bone marrow aspiration	Bone Marrow Biopsy	Final diagnosis
47	149/16	24	M	-	+	-	-	-	-	-	+	-	+	-	7.2	2900	119000	110.4	34	33.8	2.12	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
48	150/16	28	M	-	+	-	-	-	-	-	+	-	-	-	6.5	3900	66000	106.8	32.5	32.8	2	Macrocytic anemia	Megalobloastic anemia	Hypercellular	Megaloblastic anemia
49	154/16	18	F	+	+	-	-	-	+	-	+	-	-	+	5.2	3800	47000	104.5	32.5	31.8	1.6	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
50	157/16	14	M	-	+	-	-	-	-	-	+	-	-	+	8.4	2100	75000	98.4	29.6	34.7	2.84	Dimorphic anemia	Micrormoblasts with Megaloblasts	Hypercellular with micronormoblasts with megaloblast	Dimorphic anemia
51	158/16	24	M	+	+	-	-	-	-	-	+	+	-	+	4.8	2500	34000	99.2	34.3	31.4	1.4	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
52	161/16	16	M	+	+	-	-	-	-	-	+	-	-	-	7.2	2700	54000	109.5	34.3	32.5	2.1	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
53	162/16	16	F	+	+	-	-	-	+	-	+	+	+	+	7.4	2000	44000	88.4	30.2	32.6	2.4	Macrocytic anemia	Dry Tap	Hypoplastic marrow	Aplastic Anemia
54	165/16	4	F	-	+	-	-	-	+	-	+	-	-	-	9.6	1600	65000	118.2	32.9	33.6	2.92	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
55	166/16	40	F	+	+	-	-	-	+	-	+	-	-	+	8.8	3400	78000	102.4	33.8	34.8	2.6	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
56	170/16	18	F	+	+	-	-	-	-	+	+	-	+	-	8.2	1500	66000	74.8	25.6	32.7	3.2	Normocytic Normochromic	Erythroid hyperplasia	Hypercellular with P. Falciparum	Malaria
57	174/16	18	F	+	+	-	-	-	-	-	+	-	-	-	4.8	2000	70000	58.2	26.7	31.4	1.8	Microcytic Anemia	Hypoplasia	Hypocellular	SLE
58	179/16	21	M	-	+	-	-	-	-	-	+	+	+	-	6.2	2800	126000	67.4	25.8	30.8	2.4	Dimorphic anemia	Micrormoblasts with Megaloblasts	Hypocellular with micronormoblasts with megaloblast	Dimorphic anemia
59	182/16	35	F	+	+	-	-	-	-	-	+	-	-	-	7.4	3600	148000	100.8	33	32.6	2.24	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
60	183/16	28	M	-	+	-	-	-	-	-	+	-	-	+	6.1	2400	35000	102.6	33.2	33.1	1.84	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia

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Data					Clinical details											Complete hemogram									
Sl No	BM No	Age	Sex	Fever	Generalised Weakness	Breathlessness	Bone Pain	Weight loss	Dyspnea	Bleeding	Pallor	Hepatomegaly	Splenomegaly	Lymphadenopathy	Hb %	TLC cells/mm3	PLT cells/mm3	MCV	MCH	MCHC	RBC	Peripheral smear	Bone marrow aspiration	Bone Marrow Biopsy	Final diagnosis
61	186/16	25	M	-	+	-	-	-	-	-	+	+	-	-	8.4	1700	34000	100.4	32.3	35.8	2.6	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
62	188/16	48	M	-	+	-	-	-	-	-	+	+	-	-	7.7	4000	38000	106.4	33.5	34.6	2.3	Dimorphic anemia	Megaloblastic Anemia	Hypercellular	Megaloblastic anemia
63	194/16	19	M	+	+	-	-	-	+	-	+	+	+	-	7.4	4000	45000	104.2	40.2	33.7	1.84	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
64	197/16	26	M	-	+	-	-	-	-	-	+	-	-	-	6.9	2800	92000	100.6	34.5	32.4	2	Normocytic Hypochromoic	Hypoplasia	Hypocellular	Aplastic Anemia
65	198/16	52	F	+	+	-	-	-	+	-	+	+	+	-	8.8	3700	88000	80.4	29.3	30	3	Normocytic Normochromic	Normocellular	Normocellular	Infection
66	199/16	50	F	+	+	-	-	-	+	-	+	-	-	-	4.5	3400	138000	71.4	25.4	31.8	1.77	Dimorphic anemia	Micrormoblasts with Megaloblasts	Hypocellular with micronormoblasts with megaloblast	Dimorphic anemia
67	202/16	20	F	+	+	-	-	-	-	-	+	-	-	+	7.9	3600	52000	110.8	31.6	32.2	2.5	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
68	208/16	25	F	-	+	-	-	-	-	-	+	-	-	-	8.2	3500	90000	107.6	34.2	34.4	2.4	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
69	209/16	45	M	-	+	-	-	-	+	-	+	+	+	-	8.8	1100	40000	103.6	32.4	33.8	2.72	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
70	211/16	50	M	+	+	-	-	-	+	-	+	-	-	-	5	1200	34000	104.8	35.7	32.3	1.4	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
71	212/16	4	F	-	+	-	-	-	+	-	+	+	-	-	2.8	4000	70000	120.4	35	32.2	0.8	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
72	2/17	70	M	+	+	-	-	-	+	-	+	+	-	-	6.4	2400	30000	82.2	33.2	32.4	2.6	Dimorphic anemia	Hypoplasia	Hypocellular	Aplastic Anemia
73	4/17	19	F	+	+	-	-	-	-	-	+	-	-	-	3.9	1000	28000	106.8	35.5	33.1	1.1	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
74	7/17	28	F	-	+	-	-	-	-	-	+	-	-	-	8.4	4000	126000	73.8.8	24.7	35.4	3.4	Dimorphic anemia	Micrormoblasts with Megaloblasts	Hypocellular with micronormoblasts with megaloblast	Dimorphic anemia
75	11/17	55	M	+	+	-	-	-	+	-	+	-	-	-	8.2	3600	90000	101.4	30.4	33.9	2.7	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia

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Data					Clinical details											Complete hemogram									
Sl No	BM No	Age	Sex	Fever	Generalised Weakness	Breathlessness	Bone Pain	Weight loss	Dyspnea	Bleeding	Pallor	Hepatomegaly	Splenomegaly	Lymphadenopathy	Hb %	TLC cells/mm3	PLT cells/mm3	MCV	MCH	MCHC	RBC	Peripheral smear	Bone marrow aspiration	Bone Marrow Biopsy	Final diagnosis
76	13/17	65	M	+	+	-	-	-	+	-	+	-	-	-	6.4	3900	134000	100.8	32	33.4	2	Macrocytic Anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
77	18/17	18	F	-	+	-	-	-	-	-	+	-	-	+	8.2	2600	68000	91.4	33.6	34	2.8	Normocytic anemia	Hypocellular	Hypoplasia	Aplastic Anemia
78	23/17	19	F	-	+	-	-	-	-	-	+	-	-	-	7.8	4000	24000	106.4	23.6	31.1	3.3	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
79	26/17	12	M	-	+	-	-	-	+	-	+	-	-	-	6.4	4000	53000	102.8	26.7	32	2.4	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
80	29/17	66	F	+	+	-	+	-	+	-	+	-	-	-	8.8	2900	20000	97.8	26.7	34.4	3.3	Macrocytic anemia	Plasma Cell Dyscrasis	Hypercellular with plasma cells	Multiple Myeloma
81	30/17	60	M	-	+	-	-	-	+	+	+	-	-	-	4.6	3800	24000	101.8	35.4	32.4	1.3	Dimorphic anemia	Hypercellular	Hypercellular	Megaloblastic anemia
82	31/17	25	F	+	+	-	-	-	-	-	+	-	-	+	8.4	4000	124000	72.2	30	35.4	2.8	Dimorphic anemia	Micrormoblasts with Megaloblasts	Hypocellular with micronormoblasts with megaloblast	Dimorphic anemia
83	33/17	39	M	+	+	-	-	-	-	-	+	-	-	-	6.8	4000	114000	99.3	32.2	33.7	2.6	Dimorphic anemia	Erythroid hyperplasia	Hypercellular with areas of necrosis surrounded by fibroblasts	Dimorphic anemia
84	36/17	70	M	+	+	-	-	-	+	-	+	-	-	-	6.7	2700	89000	104.8	35.3	32.1	1.9	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
85	38/17	45	M	+	+	-	-	-	-	-	+	-	-	-	7.8	3100	69000	108.4	35.5	33.6	2.2	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
86	41/17	49	M	-	+	-	-	-	-	-	+	-	-	-	8	4000	114000	100.2	33.3	34.8	2.4	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
87	42/17	46	M	+	+	-	-	-	-	-	+	-	-	-	7.4	4000	78000	106.8	35.2	32.6	2.1	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
88	46/17	35	F	+	+	-	-	-	-	-	+	-	-	-	6.6	1200	44000	80.4	19.4	33.9	3.4	Dimorphic anemia	P.falciparum with eosinophilia	Hypercellular with P. Falciparum	Malaria
89	49/17	17	F	-	+	-	-	-	-	-	+	-	-	-	6.4	4000	104000	109.4	32.8	32.4	2.8	Macrocytic Anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia

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Data					Clinical details											Complete hemogram									
Sl No	BM No	Age	Sex	Fever	Generalised Weakness	Breathlessness	Bone Pain	Weight loss	Dyspnea	Bleeding	Pallor	Hepatomegaly	Splenomegaly	Lymphadenopathy	Hb %	TLC cells/mm3	PLT cells/mm3	MCV	MCH	MCHC	RBC	Peripheral smear	Bone marrow aspiration	Bone Marrow Biopsy	Final diagnosis
90	52/17	19	M	-	+	-	-	-	-	-	+	+	+	-	6.1	3400	89000	107.6	33.9	33	1.8	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
91	55/17	14	M	+	+	-	-	-	+	-	+	+	-	-	3.4	1400	24000	103.4	37.8	32.2	0.9	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
92	58/17	50	F	-	+	-	-	-	-	-	+	-	-	-	5.2	1600	123000	108.4	34.7	33.9	1.5	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
93	59/17	51	M	-	+	-	-	-	+	-	+	-	-	-	6.4	3600	89000	101.4	32	34.3	2	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
94	61/17	38	F	+	+	-	-	-	-	-	+	+	+	-	6.4	2400	138000	74.2	18.8	32.1	3.4	Microcytic Anemia	Scanty Cellularity	Hypocellular with fibrosis	Myelofibrosis
95	62/17	4	M	+	-	-	-	-	-	-	+	+	+	-	4.2	2800	46000	79.8	30	33	1.4	Normocytic anemia	Leukemia	Hypercellular	Subleukemic Leukemia
96	64/17	51	M	+	+	-	-	-	+	-	+	-	-	-	6.6	2800	94000	96.2	32.4	35	2.9	Normocytic anemia	Hypoplasia	Hypocellular	Aplastic Anemia
97	69/17	32	F	-	+	-	-	-	-	-	+	-	-	-	8.8	2600	107000	110.4	32.6	34.1	2.7	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
98	74/17	18	F	+	+	-	-	-	+	-	+	-	-	+	5.5	1200	45000	101.8	32.4	33.8	1.7	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
99	75/17	22	F	+	+	-	-	-	+	-	+	-	-	-	5.2	2300	28000	108.4	37.1	34.2	1.4	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
100	77/17	60	F	+	+	-	-	-	-	-	+	-	-	-	4.9	3300	54000	98.6	35	31.4	1.4	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
101	82/17	18	F	-	+	-	-	-	-	-	+	-	-	+	8.7	1500	35000	108.6	36.3	35.2	2.4	Macrocytic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
102	84/17	47	M	-	+	-	-	-	+	-	+	+	+	-	6.4	3200	128000	104.2	34.4	32.4	2.1	Normocytic anemia with dysplastic changes	Hypercellular with dysplastic erythropoiesis	Hypercellular	Myeloid Dysplastic Syndrome
103	88/17	22	F	+	+	-	-	-	+	-	+	-	-	-	4.1	1000	18000	103.8	37.3	32.4	1.1	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
104	91/17	45	F	-	+	-	-	-	+	-	+	-	-	-	7.6	3800	42000	84.8	31.8	34.2	3	Normocytic anemia	Dry Tap	Hypocellular	Aplastic Anemia
105	93/17	25	M	-	+	-	-	-	+	+	+	-	-	-	4.2	4000	128000	71.8	23.3	32	1.8	Dimorphic anemia	Normal erythroid hyperplasia	Normocellular	Dimorphic anemia

MASTER CHART

Data					Clinical details											Complete hemogram									
Sl No	BM No	Age	Sex	Fever	Generalised Weakness	Breathlessness	Bone Pain	Weight loss	Dyspnea	Bleeding	Pallor	Hepatomegaly	Splenomegaly	Lymphadenopathy	Hb %	TLC cells/mm3	PLT cells/mm3	MCV	MCH	MCHC	RBC	Peripheral smear	Bone marrow aspiration	Bone Marrow Biopsy	Final diagnosis
106	94/17	80	M	+	+	-	-	-	+	-	+	-	-	-	7.9	4000	37000	104.2	37.6	35.7	2.1	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
107	96/17	16	M	-	+	-	-	-	-	-	+	-	+	-	7.6	3200	128000	100.4	33	33	2.3	Macrocytic Anemia	Erythroid hyperplasia	Hypercellular with P. Falciparum	Malaria
108	98/17	28	M	+	+	-	-	-	+	-	+	-	+	-	6.8	2000	30000	91.4	30.9	33	2.2	Normocytic anemia	Hypoplasia	Hypocellular	Aplastic Anemia
109	106/17	36	M	-	+	-	-	-	+	-	+	-	-	-	7.5	3600	82000	106.8	31.3	32.6	2.4	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
110	109/17	28	M	+	+	-	-	-	-	-	+	-	-	-	8.7	2800	134000	72.4	31.1	34.6	2.8	Dimorphic anemia	Micronormoblasts with megaloblast	HypercellularMicronormoblasts and megaloblast	Dimorphic anemia
111	112/17	52	M	+	+	-	-	-	-	-	+	+	+	-	7.8	2400	110000	94.6	31.2	30.4	2.9	Normocytic Anemia with dysplastic changes	Hypercellular with dysplastic erythropoiesis	Hypercellular	Myeloid Dysplastic Syndrome
112	114/17	28	M	-	+	-	-	-	-	-	+	-	-	-	6.9	1900	94000	111.8	36.3	33.8	1.9	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia
113	118/17	20	M	+	+	-	-	-	-	-	+	-	-	-	8.6	3900	123000	69.6	22.6	34.9	3.8	Dimorphic anemia	Micronormoblasts with megaloblast	HypercellularMicronormoblasts and megaloblast	Dimorphic anemia
114	119/17	40	M	-	+	-	-	-	-	-	+	+	+	-	8.4	2300	34000	115.6	34.6	34.2	2.43	Dimorphic anemia	Megaloblastic anemia	Hypercellular	Megaloblastic anemia