ETIOLOGY AND CLINICOPATHOLOGICAL PROFILE OF PATIENTS WITH PANCYTOPENIA

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF

M.D. -BRANCH I (GENERAL MEDICINE) EXAMINATION OF THE

Dr. M.G.R. MEDICAL UNIVERSITY**, TAMIL NADU, CHENNAI**

TO BE HELD IN FEBRUARY 2006.

ETIOLOGY AND CLINICOPATHOLOGICAL PROFILE OF PATIENTS WITH PANCYTOPENIA

CERTIFICATE

This is to certify that the dissertation entitled, **"ETIOLOGY AND CLINICOPATHOLOGICAL PROFILE OF PATIENTS WITH PANCYTOPENIA**" is the bonafide original work of **Dr.Rajiv A** toward the M.D. Branch-I (General Medicine) Degree Examination of the Dr. M.G.R. Medical University, Tamil Nadu to be conducted in February,2006.

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INTRODUCTION

Pancytopenia refers to reduction in all three formed elements of blood-erythrocytes, leucocytes and platelets. It is not a disease entity, but rather a triad of findings[anemia, leucopenia, thrombocytopenia] that may result from number of disease processes.

The pattern of diseases causing pancytopenia is expected to vary in different population groups with their differences in nutritional status and prevalence of infective disorders. In India causes of pancytopenia are not well defined.

Clinical features are those due to pancytopenia per se, and those of causative disorder. The presenting symptoms are usually attributable to anaemia / thrombocytopenia. Leucopoenia is an uncommon cause of initial presentation, but can be the most serious threat to life during subsequent course of disorder. Major diagnostic problems occur when there are no specific features in blood to suggest the diagnosis, or when the clinical features are not specific to point to the cause of an associated feature such as splenomegaly or lymphadenopathy. The prognosis

depends both on the severity of pancytopenia and on the nature of underlying condition.

The most common etiology from studies in developed countries have been aplastic anaemia [1] and malignant myeloid disease. [2] A few Indian studies however report a high incidence of megaloblastic anaemia. [3,4,5] This seems to reflect the higher prevalence of nutritional anaemia in Indian subjects.It is important to investigate the etiology so as to formulate a rational approach to diagnosis and management.

AIMS AND OBJECTIVES

To study the etiology and clinicopathological profile of patients presenting with pancytopenia at Christian Medical College, Vellore during the study period.

LITERATURE REVIEW

The study of bone marrow failure is traditionally dated to 1888, when Paul Ehrlich described an young woman who died after an explosive short illness marked by severe anaemia,bleeding and high fever.[6] As a pathologist,Ehrlich was struck by absence of nucleated RBCs and the fatty quality of femoral marrow, in contrast to findings from the physiological response to severe anaemia,and he inferred from the morphology a mechanism of failed blood cell regeneration. Vaquez and Aubertin in their 1904 case report of "pernicious anaemia with yellow marrow" first named the disease and emphasized a pathophysiology of failed haematopoiesis. [7] Pancytopenia is one of the well known haematological manifestations of hypersplenism.Challfford [1907] introduced the term hypersplenism to refer to this concept.[8] Tissue from patients with early cases of aplastic anaemia could only be examined at autopsy ,and in practice, as reflected in medical literature of the early 20^{th} century, pancytopenia was often equated with aplastic anaemia.[9] Adams E B [1951] reported pancytopenia associated with idiopathic aplastic anaemia in 27 cases.He also reported pancytopenia with aleukaemic leukaemia in 3 patients.[10] Lorenz et al [1955] from Australia first described association of aplastic anaemia with viral hepatitis.[11]

Under the title of ‘familial infantile pernicious like anaemia’Fanconi[1967]described a fatal autosomal recessive disorder that was characterized by clinical picture consisting of pancytopenia,skin abnormalities,neurological and endocrine disorders,chromosomal instability and increased rate of leukaemia and other tumours.[9]

Zidal B L et al [1977] reported 7 cases of hairy cell leukaemia ,presenting as splenomegaly,pancytopenia and recurrent infection. [12] Howel R B et al [1982] reported a subset of patients with acute myelogenous leukaemia presenting as pancytopenia with predominance of granulocytopenia. [13]

HIV infection is associated with a wide range of hematological abnormalities. The peripheral blood findings and the morphological abnormalities in the bone marrow can simulate myelodysplastic syndrome, myeloproliferative disorders, and T cell lymphoma. A study of peripheral blood smear and bone marrow findings of 42 patients with HIV infection over a 3-year period with the aim of recognising the morphological findings sufficiently characteristic of HIV infection revealed salient peripheral blood smear findings of anaemia, bicytopenia and pancytopenia. The bone marrow revealed trilineage dysplasia, plasma cells and eosinophils, increased megakaryocytes, increased iron and reticulin fibrosis. In two cases the bone marrow revealed granuloma. [14] Patients with infection associated haemophagocytic syndrome have fever,severe constitutional symptoms and blood cytopenias.Pancytopenia due to haemophagocytic syndrome as the presenting manifestation of tuberculosis was described by Basu Set al. [15]

NORMAL HAEMOPOIETIC SYSTEM AND HAEMOPOIESIS

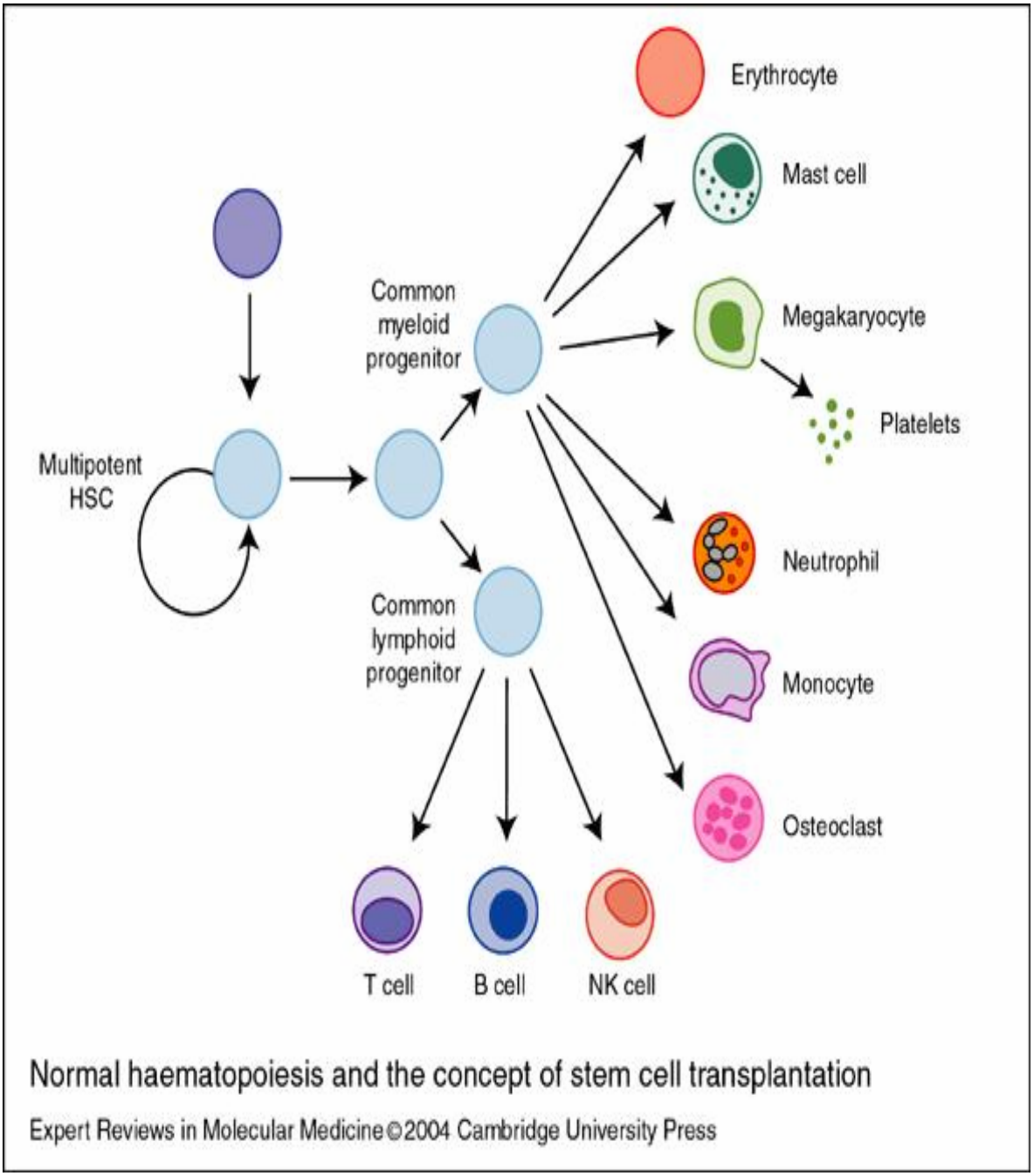
Sites of blood formation:[8]

Formation of blood cells occurs at different anatomical sites during the course of development from embryonic to adult life. Production of blood cells commences in the yolk sac of the embryo, but then shifts to the liver, and to a lesser extent to the spleen, so that these organs become the dominant sites of production between the second and seventh month of gestation. The liver and the spleen are then superceded by the bone marrow, which serves as the only important site of blood cell production after birth. An exception is lymphocyte production ,which occurs substantially in other organs, in addition to the bone marrow ,in adult life.

Haemopoietic tissue fills all of the cavities within the bones of newborn ,but with increasing age ,becomes localized in the cavities of the upper shafts of the femur and humerus,the pelvis,spine,skull and bones of the thorax.The total volume of haemopoietic tissue in adults is 1-2 litres.

Normal haematopoiesis:

The bone marrow is rich in haematopoietic stem cells (HSCs) that have the ability to differentiate into a variety of lineages. Multipotent HSCs may become committed lymphoid or myeloid precursors (common lymphoid and myeloid progenitors, respectively). The lymphoid lineage produces T cells, B cells and natural killer (NK) cells. The myeloid lineage produces erythrocytes, mast cells, megakaryocytes, neutrophils and monocytes, as well as cells not directly associated with the haematopoietic system, such as osteoclasts.



Normal haematopoiesis and the concept of stem cell transplantation

NORMAL BONE MARROW STRUCTURE [8]

The red marrow interspersed between the trabeculae of bone within the bony cavity contains specialized connective tissue cells,reticulin fibrils,blood vessels,fat cells ,nerves and macrophages in addition to cells of lymphoid and myeloid series. A supportive frame work for the components of bone marrow is provided by a network of fine reticulin fibrils.These fibrils stretch from the endosteum of the bony trabeculae to the vascular sinusoids and appear to be produced by the adventitial reticular cell.Arteriolar blood passes into the relatively large lumen of sinusoids lined by a single layer of endothelial cells. Entry of newly formed blood cells into the circulation occurs at this site.

Fat cells make up approximately half the extravascular volume of red marrow, and nearly all of the extravascular volume of yellow marrow in the more peripheral parts of the long bones. Distribution of fat cells is irregular in red marrow, and an adequate sample size is necessary in order to obtain a reliable indication of the cellularity of haemopoietic tissue.

Bone marrow biopsy:[8,16]

The advantages of aspiration are that films prepared from aspirated material can be examined almost immediately, and the morphological detail is superior to that in histological sections of core biopsies obtained by the trephine procedure. The bone marrow trephine,on the other hand, provides a more reliable index of the cellularity of haemopoietic elements, and reveals certain abnormalities such as neoplastic cells or fibrotic material which may not be dislodged from the marrow cavity by suction. The information obtained by each

procedure is therefore additive, so that combined data is of greater diagnostic value than that provided by either procedure alone.

NEEDLE ASPIRATION BIOPSY OF THE BONE MARROW[8,16]

Satisfactory samples of bone marrow can usually be aspirated from the sternum, iliac crest or anterior or posterior iliac spines. However, the sternum is no longer favoured because unless the needle is correctly inserted there is a danger of perforating the inner cortial layer and damaging the underlying large blood vessels and right atrium with serious consequences. Overlying skin at the site, is cleaned with 70% alcohol (e.g Ethanol) or 0.5% chlorhexidine . The skin, subcutaneous tissue and periosteum overlying the site selected for the puncture are carefully infiltrated with 2 % lignocaine.With a boring movement, pass the needle perpendicularly into the cavity of ilium at the posterior superior iliac spine.When the bone has been penetrated, remove the stillete and with a well-fitting 2 or 5 ml syringe suck up not more than 0.3 ml of marrow contents – bone marrow diluted with a variable amount of blood.

The posterior superior iliac spine overlies a large marrow containing area and relatively large volumes of marrow can be aspirated from the site. Posterior iliac puncture can be carried out with the patient lying prone or on his side. An advantage of puncturing the ilium rather than the sternum is that the patient can lie on his side and cannot see what is happening.

Bone marrow films.

Deliver single drops of aspirate on to slides about 1 cm from one end, place the slides on a slope to allow the blood to drain away. The irregularly

shaped marrow fragments tend to adhere to the slide and most of them will be left behind. Then make films 3 – 5 cms in length, of the marrow fragments and the remaining blood using a smooth-edged glass spreader of not more than 2 cms in width.Fix the films of bone marrow and stain them with Romanovsky dyes as for peripheral blood films. Some workers add the aspirated marrow routinely to an anti-coagulant, eg :dried EDTA, in a tube and prepare films on return to the laboratory.

CELLULARITY OF MARROW

The degree of cellularity can be altered within broad limits as increased, normal or reduced by inspection of a stained film containing marrow particles and for practical purposes this is all that is usually necessary. As a rough guide, if less than 25% of the particle is occupied by haemopoietic cells it is probably hypocellular, and if more than 75-80 % it is hypercellular. In one study, by means of point counting of sections from the iliac crest, the range of cellularity in children under 10 years was reported as 59 – 95% with a mean of 79% ,at 30 years mean as 50 % and at 70 Years it was 30 % with a range of 11 – 47 % .[17]

CELL COMPOSITION OF ASPIRATED NORMAL ADULT BONE MARROW

Cell Classification	Percentage of Total cells
Granulocytic series	
1. Myeloblasts	0.1 - 3.5
2.Promyelocytes	0.5 - 5
3. Myelocytes	5 - 23
4. Metamyelocytes	7 - 27
5. Band Forms	9 - 18
6. Segmented Forms	4 - 28
Erythroid series	
1. Proerythroblsats	0.1 - 1.1
2. Basophiles	0.4 - 2.4
3. Polychromatic	2 - 30
4. Orthochromatic	2 - 10
Lymphocytes	5 - 24
Plasma Cells	0 - 3.5
Monocytes	0 - 0.6
Macrophage	0 - 2
Megakaryocytes	0 - 0.5

RATIO

The M:E [myeloid:erythroid] ratio is based on a count of 200 – 500 marrow cells. In the normal adult the ratio is about 3 or 4:1.

BONE MARROW TREPHINE BIOPSY [16,18]

A trephine biopsy is usually most easily carried out on the posterior superior iliac spine, with the patient in the left or right lateral position with the knees drawn up. An alternative site is the ilium, just below the anterior superior iliac spine. Various needle designs are satisfactory including Jamshidi and Islam needles.

A trephine biopsy and aspiration biopsy can be carried out through the same skin incision but with the bone being entered at two different points, about 1 cm apart. Aspiration is performed first. It is easier to perform the least painful procedure first. Local anesthesia must be adequate with particular attention being paid to infiltrating an adequate area of the periosteum. In anxious patients sedation is useful. The trephine should be inserted by to and fro rotation through approximately 90 degree. The biopsy needle should be firmly fixed in the cortex of the bone before the trocar is removed. Ideally, the biopsy should measure at least 20mm in length after processing.

Trephine biopsies can be carried out safely on patients with severe thrombocytopenia , but prolonged pressure is indicated to achieve primary haemostasis and reduce bleeding to a minimum.

Bleeding problems are more likely in patients with coagulation defects and, if patients with severe liver disease or disseminated intravascular coagulation

require a biopsy, the coagulation defect should be corrected, as far as possible, before the procedure is undertaken.

Fix the specimen in 10 % formalin solutin buttered to pH 7. Sections of marrow should be stained as a routine by haematoxylin and eosin and by a reticulin impregnation method. H and E staining is excellent for demonstrating the cellularity and pattern of the marrow and for revealing pathological changes such as firbosis or the presence of granulomata or carcinoma.

Diagnostic utility of bone marrow sampling in HIV positive patients[19]

Bone marrow sampling has diagnostic utility in HIV infected patients with pyrexia without localising signs, pancytopenia, and staging/investigation of lymphoma; this test has little value in the investigation of afebrile patients with isolated thrombocytopenia, anaemia, or leucopenia as HIV is usually the underlying cause. Of 122 bone marrow samples taken to investigate pyrexia, 33 (27%) revealed the cause on microscopy: unexpected lymphoma in seven (6%), mycobacteriosis in 25 (20%), and toxoplasmosis in one (1%). Marrow infiltration was confirmed in 11 of 38 bone marrow samples taken for staging/investigation of lymphoma/leukaemia. In afebrile patients, of 22 with pancytopenia, bone marrow samples showed HIV associated changes in 17 and specific diagnoses in five. (Mycobacterial infection in three, haemophagocytic syndrome in one, and megaloblastic change due to vitamin B-12 deficiency in one)

PANCYTOPENIA

Pancytopenia refers to a reduction in all three formed elements of the blood- erythrocytes, leukocytes and platelets. It is not a disease entity, but rather a triad of findings that may result from a number of disease processes.

Pathophysiology:

The mechanisms by which pancytopenia develops appear to be varied.

1. Some conditions are associated with a decrease in haematopoietic cell production in bone marrow as a result of
   a) Destruction of marrow tissue by toxins (acellular or hypoplastic marrow)
   b) Replacement by abnormal or malignant tissue.
   c) Suppression of normal marrow growth and differentiation.

2. In other conditions the marrow may be normally cellular or even hypercellular, and no abnormal cells may be present. The mechanisms are

   a) Ineffective haematopoiesis with cell death in the marrow.
   b) Formation of defective cells that are rapidly removed from the circulation.
   c) Trapping of normal cells in hypertrophied and overactive reticuloendothelial system.
   d) Sequestration and/or destruction of cells by action of antibodies.

CAUSES OF PANCYTOPENIA [8]

Aplastic anaemia

Subleukaemic acute leukaemia

Administration of cytotoxic agents and antimetabolites

Radiotherapy

Myelodysplastic disorders

Bone marrow infiltration or replacement:

- Lymphoma,macroglobulinemia.
- Multiple myeloma
- Metastatic carcinoma in bone marrow
- Myelofibrosis

Hypersplenism

Megaloblastosis-vitamin B 12 and folate deficiency

Systemic lupus erythematosus

Overwhelming infection

Paroxysmal nocturnal hemoglobinuria

Miscellaneous.

Causes:[20]

The diverse causes of pancytopenia can also be classified as:

1.Pancytopenia with hypocellular bone marrow

1.Acquired aplastic anaemia

2. Inherited aplastic anaemia

3 Some Myelodyplastic syndrome

4.Rare aleukaemic leukaemia [Acute myeloid leukaemia]

5.Some acute lymphoid leukaemia.

6.Some Lymphomas of bone marrow

II.Pancytopenia with cellular bone marrow

A]Primary bone marrow diseases

1.Myelodyplastic syndromes

2.Paroxysmal nocturnal hemoglobinuria

3.Myelofibrosis

4.Some aleukaemic leukaemia's

5.Myelophthisis

6.Bone marrow lymphoma

7.Hairy cell leukaemia

B]Secondary to systemic diseases

1.Systemic lupus Erythematosus

2.Hypersplenism

3.B12, folate deficiency

4.Overwhelming infections

5.Alcohol

6.Brucellosis

7.Sarcoidosis

8.Tuberculosis

9.Leishmaniasis

III.Hypocellular bone marrow ± Cytopenia

1.Q fever

2 Legionnaires disease

3. Anorexia nervosa

4. Mycobacteria

Clincial Features:[8,9,20]

The initial clinical picture in patients with pancytopenia varies widely. The onset often is insidious. Manifestations depend on the severity of the anaemia, thrombocytopenia, or leukopenia. Sometimes pancytopenia is detected as an incidental feature in a patient who has presented with symptoms of a disorder that is capable of depressing the levels of all cellular elements in the blood. The clinical features and simple laboratory finding reflect the underlying disease process and usually serve to reduce the number of possible diagnosis quickly. Thus, the presence of splenomegaly calls attention to the possibility of leukaemia, myelofibrosis, congestive splenomegaly etc. The presence of enlarged lymph nodes further supports the possibilities of leukaemia, one of the lymphomas, or lupus erythematosus. On the other hand, lack of these signs and absence of evidence of Vitamin B12 or folate deficiency should suggest multiple myeloma or aplastic anaemia. The presence of rouleaux on the blood smear or Bence Jones protein in the Urine suggest

myeloma. Immature erythrocytes and leukocytes in the blood smear, (leukoerythroblstic blood picture) should lead the clinician to consider infiltrative disease in the bone marrow (e.g., metastatic carcinoma, leukaemia or myelofibrosis), except in the event of greatly accelerated blood formation and destruction, such as occurs in cases with frank haemolytic anaemia.

The anaemia usually is normochromic and normocytic, but occasionally,it is mildly macrocytic. The leukopenia usually results from a reduction in the absolute number of cells of the myeloid series and thus relative lymphocytosis is noted. If, however, the reduction is sufficiently great, lymphocytopenia is found as well.

Difficulties in diagnosis:

Difficulty arises when atypical features are encountered e.g: when a patient thought to have aplastic anaemia has normally cellular or even hypercellular marrow. One explanation for such a contradictory findings is that the biopsy needle entered an area in which the bone marrow is regenerating after severedamage, such as after benzene intoxication or irradiation. Another dilemma involves finding that several marrow aspirations are acellular in a patient thought to have leukaemia. In most situations, a larger marrow sample obtained by biopsy will solve the problem. With a few conditions, such as congestive splenomegaly the diagnosis is made largely by excluding the other possibilities. Finally, in a few patients, no clearly defined syndrome can be recognized.

Treatment:

The treatment of pancytopenia is dictated by the nature of the underlying disease.

APLASTIC ANAEMIA [8,9,20,21,22,23]

Definition:

Aplastic anaemia is pancytopenia with bone marrow hypocellularity.

Classification of aplastic anaemia[8,9,20]

ACQUIRED APLASTIC ANAEMIA

a. Idiopathic aplastic anaemia

b. Secondary aplastic anaemia

Irradation

Drugs and chemicals

Regular effects

Cytotoxic agents

Benzene

Idiosyncratic reactions

Chloramphenicol

Nonsteroidal anti-inflammatory drugs

Antiepileptics

Gold

Other drugs and chemicals

Virus

Ebstein-barr virus (infectious mononucleosis)

Hepatitis virus (non A, non B, non C, non G hepatitis)

Parvo virus (transient aplastic crises, some pure red cell aplasia)

HIV (Acquired Immunodeficiency Syndrome)

Immune diseases

Eosinophilic fasciitis

Hypoimmunoglobulinemia

Thymoma and thymic carcinoma

Graft-Versus-host disease in immunodeficiency

Paroxysmal nocturnal hemoglobinuria

Pregnancy

INHERITED APLASTIC ANAEMIA

Fanconi's anaemia

Dyskeratosis congenita

Shwachman – Diamond syndrome

Reticular dysgeneis

Amegakaryocytic thrombocytopenia

Familial aplastic anaemia's

Preleukaemia (monosomy, etc.)

Nonhaematologic syndromes (Down, Dubowrky, Sickle)

Pathophysiology:

Bone marrow failure results from severe damage to the haematopoietic cell compartment.Cells bearing the CD34 antigen, a marker of early haematopoietic cell, are greatly diminished; and in functional studies, committed and primitive progenitor cells are virtually absent. Aplastic anaemia does not appear to result from defective stroma or growth factor production.

Immune mediated injury

Blood and bone marrow cells of patients can suppress normal haematopoietic progenitor cell growth, and removal of T cells from aplastic anaemia bone marrow improves colony formation in vitro. Increased numbers of activated cytotoxic T cells are observed in aplastic anaemia patients and usually decline with successful immuno-suppresive therapy. Interferon and tumour necrosis factor induce Fas expression on CD34 cells, leading to apoptotic cell death.

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Clinical features

History

Aplastic anaemia can appear with seeming abruptness or have a more insidious onset. Bleeding is the most common early symptom; a complaint of days to weeks of easy bruising, oozing from the gums, nose bleeds, heavy menstrual flow and sometimes petechiae will have been noticed. Symptoms of anaemia are also frequent, including lassitude, weakness, shortness of breath and a pounding sensation in the ears. Infection is an unusual first symptom in aplastic anaemia. A striking feature of aplastic anaemia is the restriction of

symptoms to the haematologic system. History of drug use, chemical exposure and preceding viral illness must often be elicited with repeated questioning.

Physical examination

Pallor of the skin and mucous membranes is common. Petechiae and ecchymoses are often present, and retinal haemorrhages may be present. Infection on presentation is unusual but may be present if the patient has been symptomatic for few weeks. Lymphadenopathy and splenomegaly are highly atypical of aplastic anaemia. Café au lait spots and short stature suggest Fanconi's anaemia , peculiar nails Dyskeratosis congenita.

Laboratory studies

Blood

The smear shows erythrocytes and a paucity of platelets and granulocytes. Reticulocytes are absent or few, and lymphocyte numbers may be normal or reduced.

Bone marrow

The bone marrow is usually readily aspirated but appears dilute on smear, and the fatty biopsy specimen may be grossly pale on withdrawal. The biopsy is superior for dertermination of cellularity and shows mainly fat under the microscope, with haematopoietic cells occupying, by definition, <25% of the marrow space. The correlation between marrow cellularity and disease severity is imperfect.

Ancillary studies

Chromosome breakage studies of peripheral blood using diepoxybutane[DEB] or mitomycin C should be performed on children to exclude Fanconi's anaemia.Chromosomal studies of bone marrow cells are often revealing in myelodysplastic syndrome and should be negative in typical aplastic anaemia.Flow cytometric studies have replaced the Hams test for the diagnosis of PNH.Serological studies may show evidence of viral infection,especially Ebstein Barr virus and HIV.Post hepatitis aplastic anaemia is typically seronegative.

PROGNOSIS

The major prognostic determinant is the blood count. Severe disease is defined by the presence of two or three parameters, absolute neutophil count <500/ cu.mm, platelet count <20000 /cu.mm, and corrected reticulocytes count <

1%. Survival of patients who fulfill these criterial is about 20% at one year after diagnosis: patients with very severe disease, defined by an absolute neutrophil count <200/ cu.mm do even more poorly.

Treatment

Treatment includes therapies that reverse the underlying marrow failure and supportive care of the pancytopenic patient. Severe acquired aplastic anaemia can be cured by replacement of the absent haematopoietic cells by stem cell transplant, or ameliorated by suppression of the immune system to allow recovery of the patients residual bone marrow function. Haematopoietic growth factors have limited usefulness and glucocorticoids are of no value. Suspect exposures to drugs or chemicals should be discontinued.

Bone marrow transplation

This is the best therapy for the young patient with a fully histocompatible sibling donor. For allogenic transplant from fully matches siblings, long-term survival rates for children are about 80%. Transplant morbidity and mortality are increased among adults, due mainly to the increased rate of chronic graft-versus-host disease and serious infections. Survival using alternative donors is about half that of conventional sibling transplants.

Immunosuppression

Used alone, antilymphocyte globulin (ALG) or antithymocyte globulin, (ATG) induces haematologic recovery in about 50% of patients. The addition of cyclosporine to either ALG or ATG has further increased response rates to about 70% to 80%. Combined treatement is now standard for patients with severe disease.

Horse ATG is given at 40mg/kg per day for four days, rabbit ALG is administered at 3.5 mg/kg per day for five days. Most patients are given methylprednisolone, 1 mg/kg per day for two weeks, to ameliorate the immune consequences of heterologous protein infusion. Cyclosporine is administered orally at an initial dose of 12 mg/kg per day in adults, with subsequent adjustment according to blood levels obtained every two weeks.

Other therapies

The effectiveness of androgen therapy has not been verified in controlled trials, but occasional patients will respond. For patients with moderate disease or those with severe pancytopenia who have failed immunosuppression, a 3 to 4 months trail is appropriate. Haematopoietic growth factors, G-CSF, GM-CSF and interleukin-3, are not recommended as initial therapy for severe aplastic anaemia.

Supportive care

Both platelet and erythrocyte numbers can be maintained by transfusion. Any rational regimen of prophylaxis requires transfusions once or twice weekly in order to maintain the platelet count >10,000 . Menstruation should be suppressed by oral estrogen. Red blood cells should be transfused to maintain a normal level of activity, usually at a hemoglobin value of 70 g/L (90 g/L if there is underlying cardiac or pulmonary disease), a regimen of 2 units every 2 weeks will replace normal losses in patient without a functioning bone marrow.

HYPERSPLENISM [8,9,20]

Definition

It has been known for many years that certain patients with splenomegaly secondary to a number of disorders develop neutropenia, anaemia, or thrombocytopenia, either singly or in combination and that splenectomy results in varying degrees of improvement in the peripheral blood picture, even to normal. The fact that the peripheral blood picture is corrected by splenectomy led to the concept of hypersplenism.

Etiology

Secondary

Portal hypertension with congestive splenomegaly

Lymphomas

Sarcoidosis

Felty's syndrome

Lipid storage disease – Gauchers's disease

Kala azar, Chronic Malaria, tropical splenomegaly

Bacterial infections – tuberculous, brucellosis, bacterial endocarditis,

Thalassemia

Chronic Lymphatic leukaemia

Myelofibrosis

Hairy cell leukaemia

Primary (idiopathic)

Mechanism of hypersplenism

The processes involved in depression of the red cell count is pooling of red cells within the enlarged spleen. Studies with radio-isotope labeled red cells indicate that passive pooling of red cells in the spleen has a greater impact on lowering the red cell count in the blood than accelerated destruction of entrapped red cells, although the latter can occur to some extent in some instances.

Diagnostic criteria of hypersplenism[8,24]

1. Anaemia, leukopenia or thrombocytopenia, either singly or in combination

2. Cellular or hyperplastic bone marrow

3 Splenomegaly

4. Significant improvement in the peripheral blood picture following splenectomy.

In many cases of hypersplenism, the cause of the splenomegaly is suggested by the presence of manifestations of the underlying disease, e.g portal hypertension or lymphoma and is confirmed by appropriate investigation.

Treatment

Splenectomy produces partial or complete recovery of the abnormal blood picture in otherwise uncomplicatied cases. When the effect of hypersplenism is not sufficient to cause symptoms, splenectomy offers no benefit to the patient. Splenectomy is indicated when significant problems are caused by the sole or the additional effect of hypersplenim in reducing the count of blood cells, usually anaemia of sufficient severity to cause symptoms, neutropenia predisposing to infectious, or thrombocytopenia causing spontaneous bleeding.

MEGALOBLASTIC ANAEMIA [8,9,26]

The megaloblastic anaemia's are disorders caused by impaired DNA synthesis. Cells primarily affected are those having relatively rapid turnover,especially haematopoietic precursors and gastrointestinal epithelial cells. Cell division is sluggish, but cytoplasmic development progresses normally, so megaloblastic cells tend to be large, with an increased ratio of RNA to DNA .Megaloblastic erythroid progenitors tend to be destroyed in the marrow (ineffective erythropoiesis)

Classification of the megaloblastic anaemia's

Cobalamine deficiency

I Inadequate intake - Vegetarians

II Malabsorption

A. Defective release of Cobalamine from food

1. Gastric achlorhydria
2. Partial gastrectomy
3. Drugs that block acid secretion

B Inadequate production of intrinsic factor (IF)

1. Pernicious anaemia
2. Total Gastrectromy
3. Congenital absence or functional abnormality of IF (rare)

C Disorders of terminal ileum

1. Tropical sprue
2. Non-tropical sprue
3. Regional enteritis
4. Intestinal resection
5. Neoplasma and granulomatous disorder (rare)

D Competition for Cobalamine

1. Fish Tapeworm (Diphyllobothrium latum)
2. Bacteria : “blind loop” syndrome

E .Drugs: p-amino salicyclic acid, colchicines, neomycin

III Others

A. Nitrous oxide

B. Congential enzyme defect

Folic acid deficiency

I Inadequate intake: Unbalanced diet (common in alcoholics, teenagers)

II Increased requirements

A. Pregnancy

B. Infancy

C. Malignancy

D. Increased haematopoiesis

E. Chronic exfoliative skin disorders

F. Haemodialysis

III Malabsorption

A. Tropical sprue

B Non-tropical sprue

C.Drugs: Phenytoin, barbiturate,(?) ethanol

IV Impaired metabolism

A. Inhibitors of dihydrofolate reductase: methotrexate, pyrimethamine, triamterene, pentamidine.

B. Alcohol

Other causes

I Drugs that impair DNA metabolism

A. Purine antagonists: 6-mercaptopurine , azathioprine, etc

B. Pyrimidine antagonists:5 – flurouracil, cytosine arabinoside etc.

C. Others: Procarbazine, hydroxyurea, acyclovir, zidovudin

II Metabolic disorders

A. Hereditary orotic aciduria

B. Lesch-Nyhan syndrome

III Megaloblstic anaemia of unknown eitiology

A. Refractory megaloblastic anaemia

B. Di Guglielmos syndrome

C. Congenital dyserythropoietic anaemia

Clinical features

1.Cobalamine deficiency

The clinical features of cobalamine deficiency involve the blood, the gastrointestinal tract, and the nervous system. The haematologic manifestations are almost entirely the result of anaemia, although very rarely purpura may appear, due to thrombocytopenia. Symptoms of anaemia may include weakness, light-headedness, vertigo and tinnitus, as well as palpitation, angina and the symptoms of congestive failure. On examination, the patient is pale, with slight icterus of skin and eyes. The gastrointestinal manifestation are sore tongue, which on inspection will be smooth and beefy red, anorexia with moderate weight loss, possibly accompanied by diarrhoea. The neurologic manifestations include numbness, paresthesia in the extremities, weakness and ataxia , due to demyelination, followed by axonal degeneration of peripheral nerves, the spinal cord and the cerebrum itself.

2.Folate deficiency

Patients with folic acid deficiency are more often malnourished than those with cobalamine deficiency. The haematologic and gastrointestinal

manifestations are the same as those of cobalamine deficiency. However, in contrast to cobalamine deficiency,neurologic abnormalities do not occur.

Diagnosis

The findings of significant macrocytosis (MCV > 100 fl) suggests the presence of a megaloblastic anaemia. The reticulocyte count may also be decreased particularly in severely anaemic patient. The blood smear demonstrates marked anisocytosis and poikilocytosis, together with macrovalocytes. In the white blood cell series, the neutrophils show hypersegmentation of the nucleus. Bizarre, misshapen platelets are also observed.

The bone marrow is hypercellular with a decreased myeloid/erythroid ratio. RBC precursors are abnormally large and have nuclei that appear much less mature than would be expected from the development of the cytoplasm. The nuclear chromatin is more dispersed than expected, and it condenses in a peculiar fenestrated pattern. Granulocyte precursors are also affected, many being larger than normal, including meta-myelocytes. Megakaryocytes are decreased and show abnormal morphology.Enhanced intramedullary destruction of erythroblasts results in an increase in unconjugated bilirubin and lactic acid dehydrogenase in plasma. Once cobalamine deficiency has been established, its pathogenesis can be delineated by means of Schilling test.

Treatment

Cobalamine deficiency

Apart from specific therapy related to the underlying disorder, the mainstay of treatment for cobalamine deficiency is replacement therapy.Parental treatment

begins with 1000micro g cobalamine daily for 1 week followed by weekly for eight weeks and every month later for the rest of patient's life.

Folate deficiency

As for cobalamine deficiency, folate deficiency is treated by replacement therapy. The usual dose of folate is 1 mg/d by mouth, but higher doses (upto 5 mg/d) may be required for folate deficiency due to malabsorption.

PATIENTS AND METHODS

Study Setting:

The study was carried out in subjects attending the Christian Medical College Hospital,Vellore, a tertiary care teaching hospital.

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Study Design:

Cross sectional survey of patients with pancytopenia.

Subjects:

Consecutive patients with a diagnosis of pancytopenia ,defined as [27]

Hemoglobin < 10g/dl,and

Total leucocyte count < 4000/cu.mm,and

Platelet count < 1,00,000/cu.mm.

Patients were recruited from inpatient as well as outpatient departments of General Medicine and Haematology . All newly detected cases of pancytopenia were taken up for further evaluation.Patients who had normal blood counts at first visit and subsequently had pancytopenia [secondary to drugs,radiotherapy.etc] were not included in the study.

Inclusion criteria:

All newly detected adult patients[age >12 years] with pancytopenia were included in the study.

Exclusion criteria:

1. Patients with normal blood counts at first visit and subsequently manifesting pancytopenia[secondary to drugs,radiotherapy.etc]

2. Age <12 years.

Subject enrollment:

The list of patients fulfilling the inclusion criteria were obtained daily from the Department of clinical pathology [Hospital numbers,Name and Age] and then traced for further evaluation and diagnostic work up.OPD patients who could not be seen the same day were followed up during subsequent visits.

Evaluation:

Cases enrolled were evaluated in detail by history,physical examination and relevant labarotary investigations,and the details entered in a proforma. [Appendix] Bone marrow aspiration and biopsy were planned to be undertaken in all cases. Patients with pancytopenia on whom bone marrow were not done were also included in the study.

Procedures:

Bone marrow aspiration and biopsy were done after an informed consent was obtained.Patients were premedicated with pethidine and phenargan.Local infiltration anaesthesia [2% xylocaine] was used and sterile precautions were observed.With a boring movement,bone marrow needle was passed perpendicularly into the cavity of ilium at posterior superior iliac spine.When the bone has been penetrated ,with a 5 ml syringe 0.2-0.3ml of marrow was aspirated.The aspirate was transferred to a set of slides and smeared.Slides were stained with Romanovsky dyes.Trephine biopsy was done through the same site.The trocar was removed after biopsy needle was fixed in the cortex and the needle was pushed further into the marrow.The needle was removed and the specimen transferred to 10% formalin solution.A tincture benzoin seal applied.Section of marrow was stained by Haematoxylin and eosin stain.

Diagnostic criteria for etiological conditions:

1.APLASTIC ANAEMIA:Presence of pancytopenia with a fatty,empty bone marrow and haematopoietic cells occupying, by definition, <25% of the marrow space.[8,9,20]

2. HYPERSPLENISM: A. Anaemia, leukopenia and thrombocytopenia.

B. Cellular or hyperplastic bone marrow
C. Splenomegaly

In many cases of hypersplenism, the cause of the splenomegaly was suggested by the presence of manifestations of the underlying disease, e.g portal hypertension which was confirmed by appropriate investigation.In patients whom bone marrow could not be carried out ,indirect evidence of bone marrow functioning was obtained by reticulocyte response.

3. SUBLEUKAEMIC LEUKAEMIA:Depressed leucocyte counts with >30% of the bone marrow consisting of blast cells.

4.MEGALOBLASTIC ANAEMIA:Bone marrow showing characteristic megaloblastic erythroid and granulocytic precursors and /or documented low levels of vitamin B12,folic acid.

5.MYELODYSPLASTIC SYNDROME:Bone marrow revealing dyserythropoietic changes (especially nuclear abnormalities) and ringed sideroblasts in the erythroid lineage; hypogranulation and hyposegmentation in

granulocytic precursors, with an increase in myeloblasts ; and megakaryocytes showing reduced number of disorganized nuclei.

6.SYSTEMIC LUPUS ERYTHEMATOSUS:Presence of atleast 4 of the 11 criteria. Malar rash,discoid rash,serositis,oral ulcers,photosensitivity,non erosive arthritis,renal abnormalities,neurological manifestation,presence of autoantibodies,immunological phenomenon and haematological manifestations.

7. INFILTRATIVE DISORDERS:Bone marrow examination [Documented evidence of granuloma,lymphoma,myeloma cells .etc.]

8.SEPSIS:Documented source of infection with evidence of bone marrow suppression/haemophagocytic syndrome.

The cause of pancytopenia was classified as "unknown" if it was not evident after extensive investigations or incomplete diagnostic work up of OPD patients as they were lost to follow up after the first visit.

Statistical methods:

Data entry was done using the software package ,SPSS 11. Descriptive statistics [distribution of age,sex,etc] were analysed using SPSS. Odds ratio,sensitivity and specificity were calculated using EPI INFO software and a p value less than 0.05 was considered statistically significant.

RESULTS

One hundred and fifty [150] consecutive patients with pancytopenia were studied during the period Jan 2005 to Jun 2005 at Christian Medical College Hospital,Vellore. The following data were recorded and analysed.

AGE DISTRIBUTION

TABLE SHOWING THE AGE DISTRIBUTION

Age group in years	Number of cases	Percent
13-20	17	11.3
21-30	29	19.3
31-40	34	22.7

41-50	33	22.0
51-60	14	9.3
61-70	19	12.7
71-80	4	2.7

Mean age:40.34 years,SD:15.952,Median:40, Range:13-77 (64)

In the present study,most of the patients were in the third [19.3],fourth[22.7] and fifth decade [22.0].The mean age is 40.34.

SEX DISTRIBUTION:

Sex	Frequency	Percent
Male	93	62.0
Female	57	38.0
Total	150	100.0

In the present study the male:female ratio was 1.62:1.

CLINICAL PROFILE:

TABLE SHOWING SYMPTOMS AND SIGNS AT PRESENTATION

Clinical profile	FREQUENCY	PERCENTAGE
Easy fatiguability	119	79.3
Breathlessness	20	13.4
Fever	50	33.3
Bleeding manifestations	48	32.0
Pallor	150	100.0
Icterus	16	10.7
Lymphadenopathy	8	5.3
Hepatomegaly	18	12.0
Splenomegaly	42	28.0
Peripheral neuropathy	7	4.7

The most common presenting symptoms were that of easy fatiguability [79.3%] followed by fever [33.3%] and bleeding manifestations [32.%].Examination wise pallor was a universal finding followed by splenomegaly [28%] and hepatomegaly. [12%] .

HAEMATOLOGICAL PARAMETERS

	Hemoglobin g/dl	Total WBC count cells/cu.mm	Platelet count cells/cu.mm
Mean	6.963	2378.00	34926.67
Median	7.400	2350.00	24000.00
Std. Deviation	2.0460	781.916	29983.686
Range	2 – 10	500 - 4000	1000 – 100000

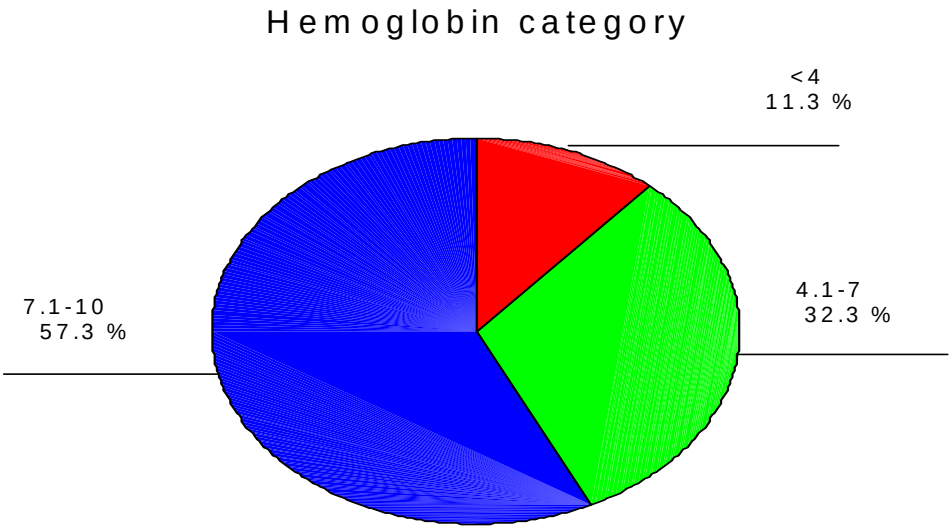
In the present study the mean hemoglobin percentage was 6.96 g/dl, total WBC count ***2378 cells/cu.mm and platelet count was 34926 cells/cumm.***

Distribution of Hemoglobin in patients with Pancytopenia

HEMOGLOBIN CATEGORY G/DL	Frequency	Percent
1-4	17	11.3

4.1-7	47	31.3
7.1-10	86	57.3
Total	150	100.0

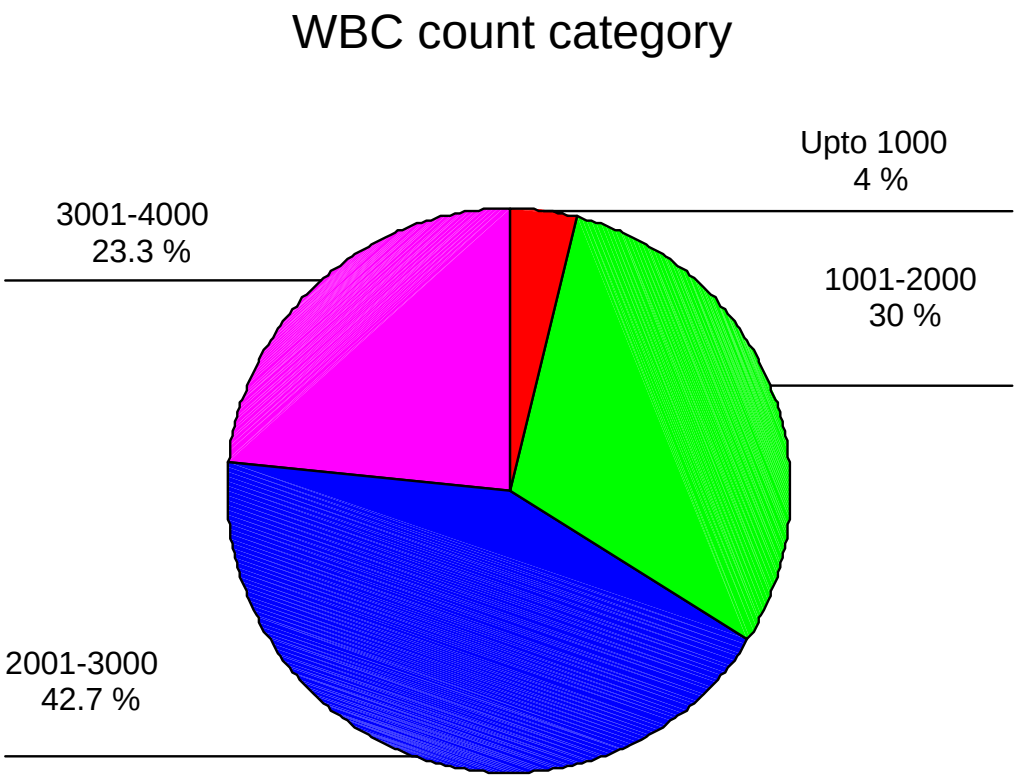
The hemoglobin varied from 2.0 to 10 g/dl. Majority of the patients had hemoglobin ranging from 7.1 to 10 g/dl .[57.3%] 94% of the patients who had Hemoglobin<4g/dl had symptoms of easy fatiguability,in contrast with 32.3% of patients with hemoglobin in the range 7.1-10 g/dl.



Range of total WBC count in patients with pancytopenia

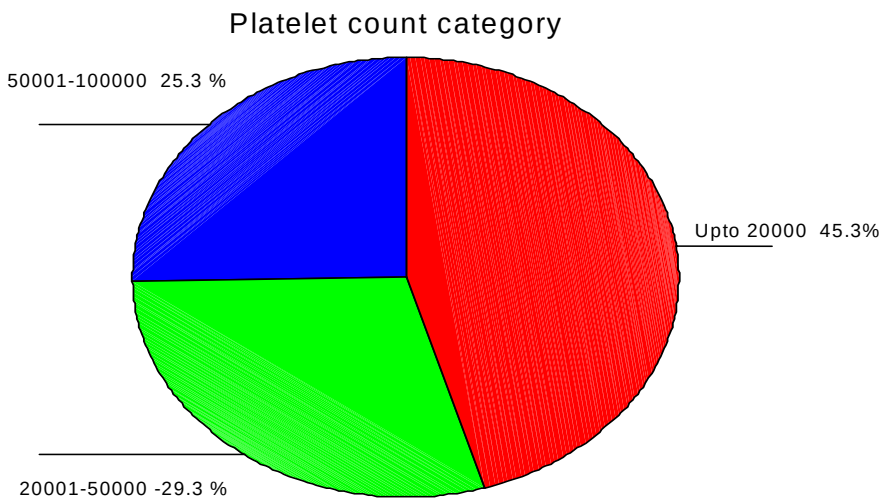
The total WBC count ranged from 400 cells/cu.mm to 3900 cells /cu.mm.Majority of the patients were in the range between 2001-3000 cells/cu.mm.[42.7%]

TOTAL **Total WBC Count (cells/cu.mm)**	**Frequency**	**Percent**
Upto 1000	6	4.0
1001-2000	45	30.0
2001-3000	64	42.7
3001-4000	35	23.3
Total	150	100.0



Range of platelet count in patients with pancytopenia

Platelet count cells/cu.mm	Frequency	Percent
Upto 20000	68	45.3
20001-50000	44	29.3
50001-100000	38	25.3
Total	150	100.0



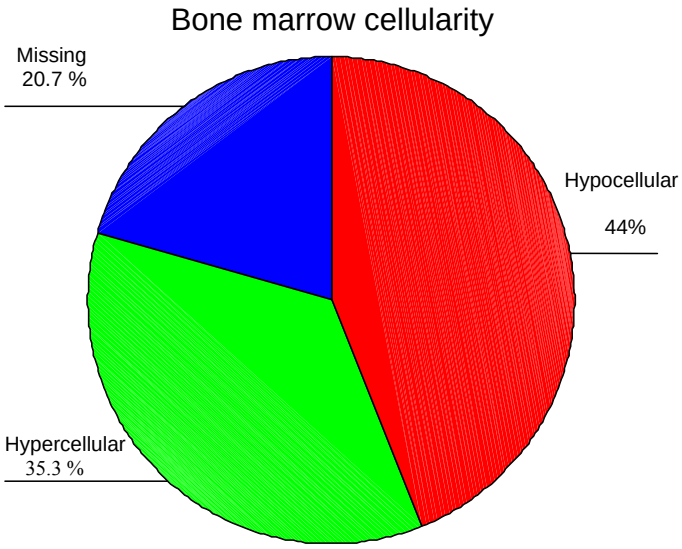
In the present study,platelet count ranged from 1000 to 1 lakh/cu.mm.Majority of the patients were in the range between 1000-20000.[45.3%] 35 [73%]of the 48 patients who presented with bleeding manifestations had platelet count less than 20000.

BONE MARROW CELLULARITY

In the present study,majority of the patients had a hypocellular marrow [44 %].Bone marrow examination could not be carried out in 31[20.7%] participants due to various reasons.[Lack of consent-17,obvious diagnosis on noninvasive testing-low B12 levels-1, evidence of portal hypertension with splenomegaly-19, blasts on blood picture-2]

	Frequency	Percent

Hypocellular	66	44.0
Hypercellular	53	35.3
Not done	31	20.7
Total	150	100



ETIOLOGY OF PANCYTOPENIA

	Frequency	Percent
Aplastic anaemia	41	27.3
Myelodysplastic syndrome	14	9.3
Subleukaemic leukaemia	19	12.6
Hypersplenism	38	25.3
Megaloblastic anaemia	8	5.3
Infiltrative disorders	13	8.7
Sepsis	2	1.3
Systemic lupus erythematosus	2	1.3
Unknown	13	8.7

Infiltrative disorders included tuberculosis, nonhodgkins lymphoma, multiple myeloma and cryptococcosis. The most common cause of pancytopenia in this study is *aplastic anaemia[27.3%] followed by hypersplenism[25.3%] and*

subleukaemic leukaemia[12.6%]. Rare causes include sepsis[1.3%] and systemic lupus erythematosus.[1.3%]

PANCYTOPENIA WITH APLASTIC ANAEMIA

In the present study,most common cause of aplastic anaemia was idiopathic[92.7%]. There were 3 cases of drug induced aplastic anaemia.[Azothioprine,busulfan and imatinib].

ETIOLOGY	**FREQUENCY (%) N=41**
IDIOPATHIC	38 (92.7)
DRUG INDUCED	3 (7.3)

65 % [27/41]of the patients were in the third ,fourth and fifth decade of life.

Male:Female ratio was 1.73.(Male –26 Female –15)

TABLE SHOWING THE AGE DISTRIBUTION IN PATIENTS WITH APLASTIC ANAEMIA

Age category	Frequency (%) N = 41
13-20	6 (15)
21-30	10 (24)
31-40	7 (17)
41-50	10 (24)
51-60	3 (7)
61-70	4 (10)
71-80	1 (3)

Mean age-37.93 years,Median-37, Standard deviation-16.041, Range-15-75.

TABLE SHOWING SYMPTOMS AND SIGNS OF PATIENTS WITH APLASTIC ANAEMIA

Clinical profile	**FREQUENCY**	**PERCENTAGE**

Easy fatiguability	35	85
Breathlessness	6	14.6
Fever	11	26.8
Bleeding manifestations	28	68.2
Pallor	41	100.0

The most common presenting symptoms were that of easy fatiguability [85 %] followed by bleeding manifestations [68.2.%] and fever [26.8 %] and examination wise none of the patients had hepatosplenomegaly. Symptomatic thrombocytopenia was more common in the aplastic anaemia group [68.2%] as compared overall.[32%]

HAEMATOLOGICAL PARAMETERS IN PATIENTS WITH APLASTIC ANAEMIA

	Hb g/dl	Total WBC cells/ cu.mm	Platelets cells/cu.mm
Mean	6.495	2446.34	8365.85
Median	6.800	2400.00	7000.00
Std. Deviation	2.0118	670.111	5252.409
Range	2 – 9.9	200 – 3900	1000 – 23000

The mean platelet count in the aplastic anaemia group was only 8365 cells/cu.mm as compared with overall mean of 34296 cells/cu.mm.

MCV IN PATIENTS WITH APLASTIC ANAEMIA

Mean	90.941
Median	88.400
Std. Deviation	9.0339
Range	74.8-112.1

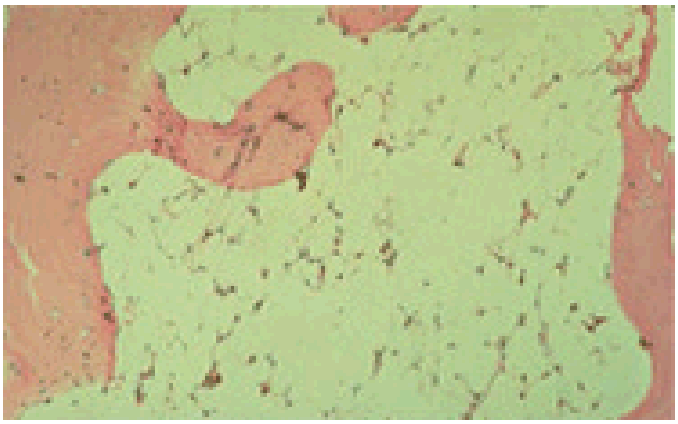
BLOOD PICTURE IN PATIENTS WITH APLASTIC ANAEMIA

	FREQUENCY N = 40
Normocytic normochromic	20 (48.7 %)
Microcytic Hypochromic	8 (19.5 %)
Macrocytosis	12 (29.2 %)

The most common blood picture in patients with aplastic anaemia was normocytic normochromic [48.7%].

All patients[41] with aplastic anaemia had a hypocellular marrow.

Low-power,H&E stained bone marrow biopsy from a patient with severe aplastic anaemia



HYPERSPLENISM

The most common cause of hypersplenism is portal hypertension .[71%] Other causes included kala-azar,hemolytic anaemia,malaria and hairy cell leukaemia.The cause of hypersplenism was considered idiopathic in 5 patients in whom no cause was found after extensive investigations.

ETIOLOGY	**FREQUENCY (%) N =38**

PORTAL HYPERTENSION	27 (71)
IDIOPATHIC	5 (13)
KALA AZAR	2 (5)
HEMOLYTIC ANAEMIA	2 (5)
MALARIA	1 (3)
HAIRY CELL LEUKAEMIA	1 (3)

TABLE SHOWING THE AGE DISTRIBUTION IN PATIENTS WITH HYPERSPLENISM

Age category	Frequency (%) N = 38
13-20	4 (10)
21-30	5 (13)
31-40	11 (29)
41-50	6 (16)
51-60	6 (16)
61-70	5 (13)
71-80	1 (3)

Mean age-42.71 years, Median-40 , Standard deviation-16.050, Range- 15-72. Male:Female ratio is 1.71:1. [Male-24, Female-14]

TABLE SHOWING SYMPTOMS AND SIGNS IN PATIENTS WITH HYPERSPLENISM

Clinical profile	FREQUENCY	PERCENTAGE
Easy fatiguability	27	71
Breathlessness	2	5
Fever	8	21
Bleeding manifestations	9	24
Pallor	38	100.0
Icterus	10	26
Hepatomegaly	6	16
Splenomegaly	38	100

Easy fatiguability was the most common symptom [71%] and splenomegaly was a universal finding on examination in patients with hypersplenism.

HAEMATOLOGICAL PARAMETERS IN PATIENTS WITH HYPERSPLENISM

	Hb g/dl	TC cells/ cu.mm	Platelets cells/cu.mm

Mean	7.174	2342.11	51078.95
Median	7.550	2350.00	46500.00
Std. Deviation	2.1355	720.222	23284.819
Range	3.1 – 10	1000 – 3800	9000 - 99000

MCV IN PATIENTS WITH HYPERSPLENISM

Mean	80.243
Median	79.100
Std. Deviation	12.495
Range	51.6 – 106.7

BLOOD PICTURE IN PATIENTS WITH HYPERSPLENISM

	FREQUENCY N = 27
Normocytic normochromic	5 (18.5 %)
Microcytic Hypochromic	17 (63 %)
Macrocytosis	5 (18.5 %)

The most common blood picture in patients with hypersplenism was microcytic hypochromic [63%] probably secondary to gastrointestinal blood loss due to portal hypertension. All the patients [19] on whom bone marrow was done showed a hypercellular picture.

HYPERSPLENISM AND HBSAG INFECTION

	HYPERSLENISM	
HBSAG	PRESENT	ABSENT
POSITIVE	6	3
NEGATIVE	29	83

Fisher's exact *p* value:0.017

Odds ratio[OR]=5.7. [95% CI 1.3,24.4] *p*=0.018

Patients with hypersplenism were more likely to be having chronic HBV infection.[OR=5.7. 95% CI 1.3,24.4. *p*=0.018]

HYPERSPLENISM AND HCV INFECTION

HCV	HYPERSLENISM	
	PRESENT	ABSENT
POSITIVE	3	2
NEGATIVE	31	82

Fisher's exact *p* value:0.143

Odds ratio[OR]=3.97 [95% CI 0.6-24.8] *p*=0.141

Patients with hypersplenism were more likely to be having HCV infection.

INFILTRATIVE DISORDERS

In the present study,tuberculosis [54 %] is the most common infiltrative disorder responsible for pancytopenia..Other causes included non hodgkins lymphoma[31 %], multiple myeloma and cryptococcosis.

ETIOLOGY	**FREQUENCY (%) N = 13**
TUBERCULOSIS	7 (54)
NON HODGKINS LYMPHOMA	4 (31)
MULTIPLE MYELOMA	1 (7.5)

CRYPTOCOCCOSIS	1 (7.5)

INFILTRATIVE DISORDERS AND HIV INFECTION

HIV	INFILTRATIVE DISORDER	
	PRESENT	ABSENT
POSITIVE	6	5
NEGATIVE	7	104

HIV testing not done in 28 patients

Fisher's exact *p* value[0.0000]

Odds ratio[OR]=18.95 [95% CI 4.3,73.2] p=0.000

Patients with bone marrow infiltrative disorders were much more likely to be HIV infected.

[OR=18.95. 95% CI 4.3,73.2. p=0.000]

HIV INFECTION AND PANCYTOPENIA

11 of the 122 patients who were tested for HIV were positive.[7.3%] Etiological workup in these patients revealed tuberculosis in 45.4% of the individuals [5/11].There was one case of disseminated cryptococcosis. Other 5 causes of pancytopenia were attributed to HIV infection per se after excluding drug induced aplasia,opportunistic infections and malignancy.

HIV	Frequency	Percent
Positive	11	7.3

Negative	111	74.0
Total	122	81.3

HIV testing not done in 28 patients.

ETIOLOGY OF PANCYTOPENIA IN HIV INFECTED INDIVIDUALS

ETIOLOGY	**FREQUENCY (%) N = 11**
TUBERCULOSIS	5 (45.5)
IDIOPATHIC	5 (45.5)
CRYPTOCOCCOSIS	1 (9)

TUBERCULOSIS AND HIV INFECTION

HIV	TUBERCULOSIS	
	PRESENT	ABSENT
POSITIVE	5	6
NEGATIVE	3	108

Fisher's exact *p* value[0.0000]

Odds ratio[OR]=30.95 [95% CI 5.8,156.3] *p*=0.000

Patients with tuberculosis were much more likely to be HIV infected.

[OR=30.95. 95% CI 45.8,156.3. p=0.000]

SUBLEUKAEMIC LEUKAEMIA

ETIOLOGY	FREQUENCY (%) N = 19
AML	15 (79)
ALL	4 (21)

Subleukaemic leukaemia was surprisingly the third most common cause of pancytopenia.15 of them were categorized as having AML[78.9%] and the rest as ALL[21.1%].

TABLE SHOWING THE AGE DISTRIBUTION IN PATIENTS WITH SUBLEUKAEMIC LEUKAEMIA

Age category	Frequency (%) N = 19
13-20	4 (21)
21-30	6 (31.5)
31-40	2 (10.5)
41-50	3 (15.75)
61-70	3 (15.75)
71-80	1 (5.5)

Mean age:34.79 years, Median:24, Standard deviation:18.677,Range:13-72. Male:Female ratio was 1.375:1. [Male-11, Female-8]

TABLE SHOWING SYMPTOMS AND SIGNS IN PATIENTS WITH SUBLEUKAEMIC LEUKAEMIA

Clinical profile	FREQUENCY	PERCENTAGE
Easy fatiguability	13	68.4
Breathlessness	2	10.5
Fever	10	52.6
Bleeding manifestations	6	31.5
Pallor	19	100.0
Splenomegaly	2	10.5

The proportion of patients presenting with fever [52.6%] was significantly higher in patients with subleukaemic leukaemia as compared overall.[33.3%]

HAEMATOLOGICAL PARAMETERS IN PATIENTS WITH SUBLEUKAEMIC LEUKAEMIA

	Hb g/dl	TC cells/ cu.mm	Platelets

			cells/cu.mm
Mean	7.026	2152.63	28052.63
Median	7.600	2200.00	17000.00
Std. Deviation	2.3909	723.701	23051.810
Range	2.3 – 9.9	1000 - 3500	2000 - 89000

MCV IN PATIENTS WITH SUBLEUKAEMIC LEUKAEMIA

Mean	91.276
Median	90.800
Std. Deviation	5.1800
Range	82.7 – 101.5

BLOOD PICTURE IN PATIENTS WITH SUBLEUKAEMIC LEUKAEMIA

	FREQUENCY N = 18
Normocytic normochromic	4 (22.2 %)
Microcytic Hypochromic	1 (5.5 %)
Macrocytosis	4 (22.2%)

Blasts	9 (50%)

50% of patients with subleukaemic leukaemia showed presence of blasts in blood picture. 11 [64.7 %] of the 17 patients with subleukaemic leukaemia had a hypocellular marrow.

MEGALOBLASTIC ANAEMIA :

Megaloblastic anaemia formed only a small group among the patient population with pancytopenia.[5.3%]All the 8 patients were characterized as having B12 deficiency. [serum B12 levels <200 pg/ml] Peripheral neuropathy was noted in 5 out of the 8 patients.[62.5%]

MEGALOBLASTIC ANAEMIA AND PERIPHERAL NEUROPATHY

PERIPHERAL NEUROPATHY	MEGALOBLASTIC ANAEMIA	
	YES	NO
PRESENT	5	2
ABSENT	3	140

Fishers exact *p* value: 0.000

Odds ratio [OR]: 116.7 , CI: 15.8-861.4, *p* value:0.000

Peripheral neuropathy was much more likely to be present in those patients with megaloblastic anaemia, than in those without megaloblastic anaemia .[OR:116.7 , CI: 15.8-861.4, *p* value:0.000]

SENSITIVITY AND SPECIFICITY OF MCV FOR MEGALOBLASTIC ANAEMIA

MCV	MEGALOBLASTIC ANAEMIA	
	YES	NO
> 100	4	14
< 100	4	107

Fisher's exact *p* value[0.013]

Sensitivity:50% Specificity:88%

Positive predictive value:22% Negative predictive value:96%

Mean Corpuscular Volume as a screening test for megaloblastic anaemia is more specific,but less sensitive.Negative predictive value is 96% indicating that if the MCV ≤ 100,the probabililty of patient having megaloblastic anaemia is only 4 %.

SENSITIVITY AND SPECIFICITY OF HYPERSEGMENTED POLYMORPHS FOR DIAGNOSIS OF MEGALOBLASTIC ANAEMIA

HYPERSEGMENTED PMN	MEGALOBLASTIC ANAEMIA	
	YES	NO
PRESENT	4	6
ABSENT	4	125

PMN – Polymorphonuclear cells

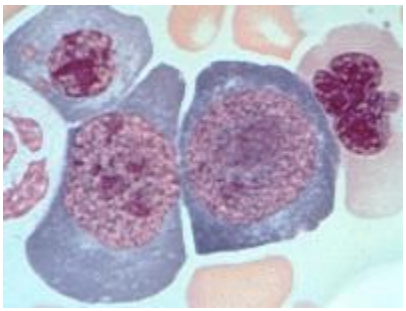
Fisher's exact *p* value[0.009]

Sensitivity:50% Specificity:95%

Positive predictive value:40% Negative predictive value:97%

Hypersegmented polymorphs as a screening test for megaloblastic anaemia is more specific,but less sensitive.Negative predictive value is 97% indicating that if hypersegmented polymorphs are absent, the probability of patient having megaloblastic anaemia is only 3 %.

Bone marrow aspirate from a patient with Megaloblastic maturation



DISCUSSION

Peripheral pancytopenia may be a manifestation of a wide variety of disorders which primarily or secondarily affect the bone marrow.The pattern of disease leading to pancytopenia is expected to vary in different population groups with their differences in nutritional status, and prevalence of infective disorders.[1,3] In India the causes of pancytopenia are not well defined.

In the present study ,150 cases of age varying from 13 years to 77 years were studied of which 93 were males and 57 were females.The incidence of pancytopenia was high in the third,fourth and fifth decades. The commonest causes of pancytopenia in our patients were aplastic anaemia [27.3%] followed by hypersplenism [25.3%] and subleukaemic leukaemia. [12.6%]. The most common presenting symptoms were that of easy fatiguability [79.3%] followed by fever [33.3%] and bleeding manifestations [32.%].Examination wise pallor was a universal finding. Peripheral neuropathy was much more likely to be present in those patients with megaloblastic anaemia, than in those without megaloblastic anaemia. MCV>100 fl and presence of hypersegmented polymorphs as a screening test have high specificity[88% and 95 % respectively] and negative predictive value[96% and 97% respectively] for patients with megaloblastic anaemia. Patients with tuberculosis and bone marrow infiltrative disorders were much more likely to be HIV infected.. [OR:30.95. CI 5.8,156.3. p=0.000 and OR:18.95 CI 4.3,73.2. p=0.000 respectively].The above data obtained from our study are compared with some other published studies.

SPECTRUM OF DISEASES CAUSING PANCYTOPENIA

STUDY	***COUNTRY***	***YEAR***	***CASES***	***COMMONEST CAUSE***
1. International Agranulocytosis and aplastic Anaemia study	Israel, Europe.	1987	387	Aplastic anaemia [57.7%]
2. Imbert et al	France	1989	213	Malignant myeloid Disease [42%]
3. Hussain M A et al	Bangladesh	1992	50	Aplastic anaemia
4. Sen et al	Rohtak	1996	191	Megaloblastic anaemia [39%]
5. Sauage et al	Zimbabwe	1999	134	Megaloblastic anaemia [35.02%]
6. Kumar et al	Chandigarh	2001	166	Aplastic anaemia [29.5%]

There are limited number of studies on the frequency of various causes of pancytopenia.Limited data has been reported from the Indian subcontinent.The variation in the frequency of various diagnostic entities causing pancytopenia has been attributed to differences in methodology and stringency of

diagnostic criteria ,geographic area, period of observation ,genetic differences and varying exposure to myelotoxic agents.[1,3]

The prevalence of aplastic anaemia varies from 10% to 52.7% .[1,3,28,29] of all pancytopenic patients.Our prevalence of aplastic anaemia was 27.3%.The prevalence of hypersplenism in the present study was 25.3%,compared to Kumar et al series where prevalence was 11.4%.

The commonest cause of pancytopenia ,reported from various studies throughout the world has been aplastic anaemia.[1,17] Most Indian studies however report a high prevalence of megaloblastic anaemia. Kale et al [4] from Mumbai in a study of 65 pancytopenic patients detected megaloblastic anaemia in 25.4% of cases. Sen et al [5] from Rohtak found megaloblastic anaemia to be the commonest cause [39%] in a study of 191 pancytopenic patients. Tilak et al[3] found megaloblastic anaemia in 68% of the patients.This seems to reflect the higher prevalence of nutritional anaemia in Indian subjects.This is in sharp contrast with the results of our study where the commonest cause of pancytopenia was aplastic anaemia and the prevalence of megaloblastic anaemia was only 5.3%. This may indicate improved nutritional status accounting for the same. The prevalence of megaloblastic anaemia varies from 0.8% to 68% [1,3,28,29] of all pancytopenic patients.

AIDS was diagnosed in 25.1% of the study cases in patients with multilineage blood cytopenia and is now the commonest clinical condition associated with it in a central referral hospital in Zimbabwe.[30] In our study 7.3% of the patients were found to be HIV seropositive,and the odds of having tuberculosis and infiltrative disorders were significantly higher as compared to non-HIV infected individuals.Other causes of pancytopenia in HIV infection

include drug induced aplasia,cryptococcosis [31] and toxoplasmosis [32]. Hence, with increasing incidence of HIV infection ,a careful search for tuberculosis and other infiltrative disorders is mandatory in immunocompromised individuals.

The mean age in the present study was 40.34 years.Most of the patients were in the third,fourth and fifth decade.Similar observations was made in Kumar et al.[33], but the mean age was 30.6 years.The maximum number of patients were seen under the age of 20 years [32.47%] in Tilak et al [3]series because they have included paediatric patients in their series.

The platelet count was less in aplastic anaemia group,as compared with other groups.This observation was also noted with Kumar et al [33] study.Bleeding manifestations were also more common in aplastic anaemia group and platelet count in these patients were <23000 cells/cu.mm.

Bone marrow was predominantly hypocellular[44%] in contrast with Imbert et al [2] where 66% of the subjects had hypercellular marrow.This is probably explained by the lower prevalence of aplastic anaemia [10%] in the study population.

The role of MCV and hypersegmented neutrophils as screening test for megaloblastic anaemia were more specific and had a high negative predictive value. Sensitivity was only 50% , in contrast to the study done by Osama Ishtiaq where it was 82% and 92.3% respectively. [34]

Limitations of the study:

1. This study was carried out in a tertiary care setting ; hence the various etiological conditions for pancytopenia may not reflect the prevalence in the general population.

2. Bone marrow aspiration and biopsy could not be carried out in all subjects which is an essential investigation in patients with pancytopenia.

SUMMARY AND CONCLUSIONS

1. The commonest causes of pancytopenia in our patients were aplastic anaemia [27.3%] followed by hypersplenism [25.3%] and subleukaemic leukaemia. [12.6%]

2. Symptom of anaemia [easy fatiguability] was the commonest presenting complaint. Pallor was a universal finding in all the patients.

3. Patients with tuberculosis and bone marrow infiltrative disorders were much more likely to be HIV infected.

4. Peripheral neuropathy was much more likely to be present in those patients with megaloblastic anaemia, than in those without megaloblastic anaemia .

5. A normal MCV and absence of hypersegmented neutrophils makes the diagnosis of megaloblastic anaemia very unlikely.[NPV of MCV≤ 100 =96% and absence of hypersegmented neutrophils=97 %]

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APPENDIX

PROFORMA

Serial Number: **Hospital Number**:

Name

AGE/SEX

Occupation

Address

Presenting complaints:

	Present/Absent	**Duration**
1. *Easy fatigability*		
2. *Breathlessness*		

3. *Palpitation*
4. *Chest pain*
5. *Swelling of limbs*
6. *Fever*
7. *Sore throat*
8. *Bone pains*
9. *Bleeding tendencies*
10. *Others*

Past History:

Drug intake

Blood transfusions

Jaundice

Radiation exposure

Similar complaints

Admission to hospital

Family History:

Similar complaints

Bleeding tendencies

Personal History:

Diet *Appetite* *Habits* *Bowel/Bladder*

Consanguinity

Menstrual cycle

Obstetric History [Miscarriage/IUGR]

GENERAL EXAMINATION:

Built Nourishment Pallor Icterus Edema Lymphadenopathy

Bone tenderness Gum hypertrophy Glossitis Koilonychia

Bleeding manifestations Hyper-pigmented knuckles

Vitals:

SYSTEMIC:

Abdomen: Organomegaly/Free fluid

CVS

RS

CNS: Reflexes

Plantar

Sensory system

INVESTIGATIONS:

Essential investigations in all cases-

Hemoglobin Total count Differential count

Platelets

Blood picture

Reticulocytes

MCV

Bone marrow

Others:

Creatinine	*RBS*	*Urine routine*
LDH	*LFT*	
B12	*Folic acid*	
HIV	*ANA/Anti-ds DNA*	
Hams test	*Protein electrophoresis*	
Chest x ray	*U/S A bdomen*	

CONSENT FORM.

Title of study: A study of etiology and clinicopathological profile of pancytopenia. [Descriptive study]

Institution: Department of Medicine, CMC Hospital.

Purpose of study: You are being asked to take part in a clinical study to know the cause of decrease in blood components-red blood cells, white blood cells and platelets.

Confidentiality: Your records and all details obtained in this study will remain strictly confidential at all times, but will need to be available to the doctor conducting the study. Your identity will not otherwise be revealed. Your personal data collected will be only in connection with this study .You will not be referred to by name or identified in any report or publication.

Consent: I have read the above information before signing this consent form.

Signature of subject

GLOSSARY TO MASTER CHART

Sn-Serial Number hn-Hospital Number name-Name age-Age

agec-Age Category 1. 13-20 2. 21-30 3. 31-40 4. 41-50 5. 51-60

6.61-70 7. 71-80

sex-Sex (1.Male,2.Female)

A. ef-Easy fatiguability B.bpn-Bony pain C.sot-Sore throat D.pap-Palpitation E.boe-Breathlessness on exertion F.fev-Fever G.btn-bleeding tendency H. low-Loss of weight I.phd- past history of drugs J.pal-Pallor K.ict-Icterus L.lne.Lymphadenopathy M.ede-Edema N.hep-Hepatomegaly.O.spl-Splenomegaly P.asc-Ascitis Q.pn-Peripheral Neuropathy

A – Q 1.Present 2.Absent

hcat-Hemoglobin category (<4)-1 (4.1-7) –2 (7.1-10)- 3

hb-Hemoglobin in g/dl

tcat-Total Leucocyte count category (<1000)-1 (1001-2000)-2 (2001-3000)-3 (3001-4000)-4

tc- Total Leucocyte count per Cubic millimeter

pcat-Platelet count category (<20000)-1 (21000-50000)-2 (51000-100000)-3

bpic-Blood picture (1)-Normocytic Normochromic (2)-Microcytic Hypochromic (3)-Macrocytosis

(4)-Blasts

ret-Reticulocyte count mcv-Mean corpuscular volume in fl

bm-Bone marrow (1)-Hypocellular (2)-Hypercellular

R.hiv –HIV ELISA S.hbs-HBSAg T.hcv-HCV antibody U.hms-Hams acid serum test

R – U 1 Positive 2 –Negative

V. b12-Serum vitamin B12 W.fa-Serum Folic acid V – W 1-Normal 2-Low

etio-Etiology of Pancytopenia 1- Aplastic anaemia 2. Myelodysplastic syndrome

3. Subleukaemia leukaemia 4. Hypersplenism 5. Megaloblastic anaemia 6. Infiltrative disorders

7. Sepsis 8. Systemic lupus erythematosus 9. Unknown

dsis-Diagnosis 1-Idiopathic Aplastic anaemia 2.Drug induced Aplastic anaemia 3.Systemic lupus erythematosus 4.Myelodysplastic syndrome 5.Acute myeloid leukaemia 6. Acute lymphoid leukaemia 7. Hairy cell leukaemia 8.Portal Hypertension 9. Kala azar 10. Hemolytic anaemia 11.B12 deficiency 12.Tuberculosis 13.Non Hodgkins lymphoma. 14.Multiple myeloma

15.Cryptococcusis 16.HIV infection 17.Idiopathic 18.HCV positive

sn	hn	name	age	agec	sex	ef	bpn	sot	pap	boe	fev	btn	low	phd	pal	ict	lne	ede	hep	spl	asc	pn	hcat	hb	tcat	tc	pcat	plt	bpic	ret	mcv	bm	hiv	hbs	hcv	hms	b12	fa	etio	dsis
1	602025	CHAYA	56	5	1	2	2	2	2	2	2	1	2	2	1	2	2	2	2	1	2	2	3	7.5	2	1800	2	50000	1	2.62	91.6	2	2	2	2	.	.	.	4	8
2	626477	JHUMA	16	1	2	2	2	2	2	2	1	1	2	2	1	2	2	2	2	2	2	2	2	4.4	2	2000	1	5000	2	2.64	83.4	1	2	2	2	.	.	.	1	1
3	612282	S RAJA	71	7	1	2	2	2	2	2	1	2	2	2	1	2	2	2	2	2	2	2	1	3.8	2	1300	1	18000	3	3.26	95.4	2	2	.	.	.	2	1	5	11
4	612840	SARAV	23	2	1	2	2	2	2	2	1	2	2	2	1	2	2	2	2	2	2	2	2	4.8	3	2300	1	7000	2	2.21	81.8	1	2	1	.	.	.	.	2	4
5	600998	JEYA	24	2	2	1	2	2	2	2	2	1	1	2	1	2	2	2	2	2	2	2	1	2.3	1	1000	1	2000	4	2.28	93.6	1	.	.	.	.	.	.	3	5
6	614459	V LAXM	34	3	2	1	2	2	2	2	1	2	2	2	1	2	2	2	2	2	2	2	1	3.9	3	2300	1	12000	3	5.3	94.1	1	.	.	.	.	.	.	3	5
7	617259	GANES	77	7	1	1	2	2	2	1	2	2	2	2	1	2	2	1	2	1	2	2	1	3.1	3	2900	3	99000	2	2.27	63	2	.	.	.	.	.	.	4	17
8	617215	CHAND	15	1	2	1	2	2	2	2	2	2	2	1	1	2	2	2	2	1	2	2	1	4	2	2000	2	46000	2	.	73.4	2	2	2	2	2	.	.	4	17
9	618710	AHMED	41	4	1	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	6.4	3	2700	1	5000	1	0.99	85.6	1	2	2	2	2	.	.	1	1
10	625941	MUTHU	28	2	1	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	3	7.7	3	2600	1	12000	3	1.62	96.6	1	2	2	2	.	.	.	1	1
11	626061	PRERA	17	1	2	1	2	2	2	2	2	2	2	1	1	2	2	2	2	2	2	2	3	9.7	3	2800	2	44000	.	.	.	1	.	.	.	.	.	.	3	6
12	627356	RATAN	41	4	1	1	2	2	2	2	1	1	1	2	1	2	1	2	1	1	1	1	3	9.2	3	2200	1	14000	2	2.67	68.7	1	2	2	2	.	.	.	7	17
13	628111	MANUV	42	4	1	1	2	2	2	2	2	2	2	2	1	2	1	1	2	2	1	2	2	6.1	3	2400	3	96000	2	4.05	72.5	2	1	2	.	.	.	.	6	12
14	630077	BISWA.	18	1	1	1	2	2	2	2	2	2	2	2	1	1	2	1	1	1	2	2	2	5	3	2300	1	14000	2	1.05	76.7	2	2	2	2	2	.	.	4	10
15	629619	SHAHN	35	3	2	1	2	2	2	2	1	2	2	2	1	1	2	2	1	1	2	2	1	3.6	1	900	3	61000	3	3.67	110.4	2	2	2	2	.	.	.	2	4
16	628610	ASHA	24	2	2	1	2	2	2	2	2	2	1	1	1	2	2	2	2	2	2	2	3	8.4	3	2400	1	15000	1	1.14	83.3	2	2	2	2	.	.	.	3	5
17	628618	SONAM	47	4	2	1	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	3	9.5	3	2100	1	9000	1	0.52	86.9	1	2	2	2	.	.	.	1	1
18	612459	SHIV K	24	2	1	1	2	2	2	2	2	2	1	2	1	2	2	2	2	2	2	2	2	5.4	3	2900	1	8000	3	3.67	106.4	1	2	2	2	.	.	.	2	4
19	581614	JALEEL	54	5	1	1	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	3	8.4	4	3700	1	6000	1	0.64	95.8	1	2	2	2	.	.	.	1	1
20	580846	BAL B (	45	4	1	1	2	2	2	2	1	2	2	2	1	2	2	2	2	2	2	2	3	8.1	3	2600	1	20000	3	2.03	99.2	1	2	2	2	.	.	.	1	1
21	602111	SHOBA	60	5	2	2	2	2	2	2	2	2	2	2	1	2	2	2	1	1	2	2	3	9.1	3	3000	3	96000	2	.	84.4	2	2	2	2	.	.	.	4	17
22	579487	SALMA	24	2	2	1	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	3	8.1	3	2200	1	4000	1	1.38	92.5	1	2	2	2	.	.	.	1	1
23	586126	NAGAI/	72	7	1	1	2	2	2	2	2	2	1	2	1	2	2	2	2	2	2	2	2	6.8	2	2000	2	49000	4	0.86	90.8	.	2	.	.	.	.	.	3	5
24	636017	RAJES\	65	6	2	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	3	4.4	2	1800	1	2000	1	.	92.9	1	.	.	.	.	.	.	1	1
25	635029	GANDH	43	4	2	1	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	1	3.8	3	2400	1	3000	2	1.77	75.1	1	2	2	2	.	.	.	1	1
26	631093	S VANI	29	2	2	2	2	2	2	2	2	1	2	2	1	2	2	1	2	1	1	2	2	4.3	2	1500	2	33000	2	1.91	70.8	2	2	2	2	.	.	.	4	17
27	633734	PINJRA	60	5	2	1	2	2	2	2	1	2	1	2	1	2	2	2	2	1	2	2	3	8.7	4	3200	3	71000	1	.	82.8	2	2	2	2	.	.	.	6	13
28	626811	PULMA	55	5	2	1	2	2	2	1	2	1	2	2	1	2	2	2	2	2	2	2	3	8.1	3	2300	1	10000	1	1.97	84.7	1	2	2	2	.	.	.	1	1
29	630520	BABU	31	3	1	2	2	2	2	1	1	2	1	2	1	2	2	2	2	2	2	2	3	7.2	4	3500	3	99000	.	.	.	2	1	2	2	2	2	.	9	16
30	630724	SORNA	64	6	2	1	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	3	9.9	3	2300	1	10000	.	.	.	1	2	2	2	.	.	.	1	1
31	625234	SUBHA	42	4	1	2	2	2	2	2	2	1	2	2	1	2	2	2	2	1	2	2	3	9.8	2	1200	1	14000	2	2.74	87.5	2	2	2	2	.	.	.	4	8
32	626592	ANU DE	25	2	2	1	2	2	2	2	1	1	2	2	1	2	2	2	2	2	2	2	1	2.2	3	2700	1	8000	1	4.12	92.8	1	2	2	2	2	.	.	1	1
33	621181	P SING	37	3	1	1	2	2	2	2	1	2	2	2	1	1	2	1	2	1	1	2	3	8.1	2	1700	1	9000	2	4.25	67.5	2	2	2	2	.	.	.	4	17
34	628267	RANI B.	64	6	2	1	2	2	2	2	2	1	2	1	2	2	2	1	1	2	2	2	3	7.1	2	1600	1	18000	2	1.36	79.5	2	2	2	2	.	.	.	6	13
35	600623	GOWRI	25	2	2	1	2	2	2	2	1	1	2	1	1	2	2	2	2	2	2	2	3	8	2	1200	1	16000	1	.	88.1	1	2	2	2	.	.	.	1	2
36	602440	NONGS	30	2	1	1	2	2	2	2	2	2	1	2	1	2	2	2	2	2	2	2	3	8.1	2	1400	3	69000	1	3.22	92.7	1	1	2	2	.	1	1	9	16
37	606567	LOCHA	29	2	1	2	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	2	5.8	3	2100	1	3000	3	1.33	93.9	1	2	2	2	.	.	.	1	1
38	611136	EBASE	15	1	1	2	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	2	6.3	3	2500	1	5000	2	3.23	86.9	1	2	2	2	.	.	.	1	1
39	589469	S RAYU	38	3	1	1	2	2	2	2	1	2	2	2	1	2	2	2	2	2	2	1	2	6.4	3	2100	2	32000	3	.	95.7	2	.	.	.	.	.	.	5	11
40	593003	S DEVI	32	3	2	1	2	2	2	2	2	2	2	2	1	2	2	2	2	1	2	2	2	4.8	2	1800	3	51000	2	.	70	2	2	2	2	.	.	.	4	8
41	595540	S KUNI	13	1	2	2	2	2	2	2	1	1	1	2	1	2	2	2	2	2	2	2	3	9.6	3	2200	2	27000	4	0.3	85.8	2	2	2	2	.	.	.	3	6
42	595281	M DEBI	59	5	1	1	2	2	1	2	2	2	2	2	1	2	2	1	2	2	2	2	2	6.5	3	2700	2	41000	.	.	.	2	2	2	2	.	.	.	9	17
43	600811	M SING	63	6	1	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	3	8.6	2	1400	1	8000	1	2.32	87.9	1	2	2	2	.	.	.	3	5
44	611280	SHAFE	17	1	2	1	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	3	8.9	3	2600	1	8000	3	0.33	100.2	1	2	2	2	.	.	.	1	1
45	609514	BASHA	49	4	2	1	2	2	1	2	2	1	2	2	1	2	2	2	2	2	2	2	3	8.4	4	3200	1	16000	3	3.93	.	1	2	2	1	.	.	.	1	1
46	614464	S RAJV	42	4	1	1	2	2	2	1	2	2	2	2	1	2	2	2	2	2	2	2	3	7.4	2	1500	3	100000	2	1.73	79.1	2	2	2	2	.	.	.	2	4
47	614481	A MALL	18	1	2	1	2	2	2	1	2	2	2	2	1	2	2	1	2	2	2	2	2	5.9	2	1900	2	58000	2	3.79	77.3	1	2	2	2	.	.	.	8	3
48	615515	RAMAD	47	4	2	1	2	2	2	2	1	2	2	2	1	2	2	2	2	2	2	2	3	7.7	4	3500	1	6000	1	1.34	88.3	1	2	2	2	.	.	.	1	1
49	617645	H DAS	40	3	1	1	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	2	5.4	2	1300	1	7000	2	1.44	82.1	1	2	2	2	.	.	.	2	4
50	618504	S DEVI	70	6	2	2	2	2	2	1	2	2	2	2	1	2	2	2	2	2	2	2	3	8.4	3	2800	1	11000	1	.	.	1	2	2	2	.	.	.	9	12
51	619290	SAROJ.	49	4	2	1	2	2	2	2	2	2	2	2	1	2	2	2	2	1	2	2	3	7.6	3	2300	3	59000	2	1.3	79.1	2	2	2	2	.	.	.	4	8
52	619567	KAVITH	19	1	2	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	1	1	3.4	4	3300	2	29000	3	2.46	115.8	2	.	.	.	.	2	1	5	11
53	619551	K PURT	45	4	2	1	2	2	2	2	1	2	1	2	1	2	1	1	1	1	2	2	2	4.6	4	3400	2	29000	2	2.34	79	2	2	2	2	.	.	.	6	13
54	621869	HAZI M	64	6	1	1	2	2	2	1	1	2	2	2	1	2	2	2	2	2	2	2	2	4.7	4	3100	2	24000	3	2.31	94.2	2	2	2	2	.	.	.	3	5
55	622278	R SWA	53	5	1	1	2	2	2	2	2	2	2	1	1	2	2	2	2	2	2	2	2	6.6	2	1800	1	17000	2	.	83.4	1	2	2	2	.	.	.	1	2
56	621611	RAJAN	48	4	1	1	2	2	2	1	2	2	2	2	1	2	2	2	2	2	2	2	3	9.6	3	2300	2	41000	1	3.79	89.2	2	2	2	2	.	.	.	5	11
57	625674	R MAIT	19	1	1	1	2	2	2	1	2	2	2	2	1	2	2	2	2	2	2	2	2	5.5	3	2500	2	23000	3	4.39	110.3	1	.	.	.	2	1	1	1	1

58	608669	RADHA	23	2	1	2	2	2	2	2	1	2	2	2	1	2	2	2	2	2	2	2	3	7.2	2	1200	1	17000	4	0.88	89.1	1	2	2	2	.	.	.	3	5
59	609495	N TAM/	32	3	1	1	2	2	2	2	2	1	2	1	2	2	2	2	2	2	2	2	3	9.4	3	2700	3	98000	1	0.37	91.6	2	1	2	2	.	1	1	9	16
60	607974	F MAH/	45	4	1	1	2	2	2	2	1	2	1	2	1	2	2	2	2	2	2	2	3	7.3	4	3400	3	86000	2	.	.	2	2	2	2	.	.	.	6	14
61	609073	MANOJ	25	2	1	1	2	2	2	2	1	2	2	2	1	2	2	2	2	2	2	2	2	5.1	3	2200	1	10000	2	1.87	86.8	1	2	2	2	2	.	.	1	1
62	609629	J PAUL	25	2	2	1	2	2	2	2	2	2	2	2	1	1	2	1	2	1	1	2	3	7.7	2	1300	2	31000	3	5.57	94.5	2	2	2	2	.	.	.	4	8
63	610411	DAYAL/	35	3	1	2	2	2	2	2	1	2	2	2	1	2	2	2	2	2	2	2	2	4.4	2	1300	1	7000	3	3.37	112.1	1	2	2	2	.	.	.	1	1
64	607505	JAGAT	37	3	1	1	2	2	2	2	2	2	2	2	2	1	2	2	1	2	1	1	2	2	4.7	2	1200	2	30000	.	.	81.4	2	2	1	2	.	.	.	4	8
65	610371	K C KA	65	6	1	2	2	2	2	1	2	2	2	2	1	2	2	2	2	2	2	2	2	5.6	3	2800	2	46000	2	.	68.4	2	2	2	1	.	.	.	9	18
66	600339	KUYAR	35	3	1	1	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	3	8.9	2	1800	1	13000	3	0.57	92.1	1	2	2	2	.	.	.	1	1
67	600596	JOSEP	27	2	1	1	2	2	2	1	1	2	1	2	1	2	1	1	1	1	2	2	2	5.5	4	3100	3	87000	2	6.35	77.2	2	1	2	2	.	.	.	6	12
68	606233	AHAMA	45	4	1	1	2	2	2	1	2	2	2	2	1	2	2	2	1	2	2	2	3	8.9	1	1000	2	27000	1	0.62	88.6	2	2	2	2	.	.	.	2	4
69	603889	KARAN	22	2	1	1	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	3	8.2	3	2600	1	9000	1	0.94	87.7	1	2	2	2	.	.	.	1	1
70	604806	C DAS	28	2	2	1	2	2	2	2	2	2	2	2	1	1	2	2	2	2	2	2	3	9	3	2500	3	98000	3	4.96	102.5	2	.	.	.	.	.	.	5	11
71	608437	SS PRA	65	6	1	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	5.8	3	2700	1	7000	1	1.23	80.3	1	2	2	2	.	.	.	1	1
72	598203	BASUD	61	6	1	1	2	2	2	2	2	2	1	2	1	2	2	2	2	2	2	2	3	8.5	2	1300	3	89000	3	2.65	101.5	1	.	.	.	.	.	.	3	5
73	579886	M BISW	62	6	1	1	2	2	2	2	1	2	2	2	1	1	2	2	2	1	2	2	3	10	3	2800	3	55000	1	0.93	89.1	2	2	2	2	.	.	.	4	7
74	578509	PZ BEC	44	4	2	1	2	2	2	1	2	1	2	2	1	1	2	2	1	2	2	2	2	4.7	2	1600	1	9000	3	5.38	97	2	2	2	2	2	.	.	2	4
75	587609	G DEVI	22	2	2	2	2	2	2	2	1	2	1	2	1	2	2	2	2	1	2	2	2	5.9	3	2100	3	83000	2	.	79.1	2	.	.	.	.	.	.	4	9
76	587557	M GOR	32	3	2	1	2	2	2	1	2	1	2	2	1	2	2	2	2	2	2	2	2	5.8	4	3300	1	10000	3	2.55	95.7	1	.	.	.	.	.	.	1	1
77	586512	D NATH	65	6	1	1	2	2	2	1	2	2	1	2	1	2	2	1	1	1	1	2	2	6.8	4	3100	2	29000	2	.	.	2	2	2	2	.	.	.	4	8
78	586472	S SARI	37	3	1	2	2	2	2	1	2	1	2	2	1	2	2	2	2	2	2	2	3	7.1	4	3900	1	6000	3	3.26	103.6	1	2	2	2	.	.	.	1	1
79	586452	ARCHA	22	2	2	2	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	3	9.9	3	2100	2	46000	4	0.9	90.1	2	2	2	2	.	.	.	3	5
80	594857	ITTOOF	75	7	1	1	2	2	2	2	1	1	2	2	1	2	2	2	2	2	2	2	3	8.9	3	2200	1	15000	1	.	88.4	1	.	.	.	.	.	.	1	1
81	596709	S GHO	48	4	2	1	2	2	2	2	1	1	2	1	1	2	2	2	2	2	2	2	2	4.2	2	1600	1	6000	2	0.6	77.1	1	.	.	.	.	.	.	1	2
82	595695	BABI D	21	2	1	1	2	2	1	2	1	1	1	2	1	2	2	2	2	2	2	2	2	6.8	2	1700	1	3000	1	0.32	85.6	1	.	.	.	.	.	.	1	1
83	597355	MUMM	63	6	1	1	2	2	2	1	2	2	2	2	1	2	2	2	2	2	2	2	3	7.4	4	3600	1	11000	1	1.9	90.4	1	2	2	2	.	.	.	1	1
84	601930	M DAS	38	3	1	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	3	7.3	4	3300	1	7000	3	1.5	108.3	1	2	2	2	.	.	.	1	1
85	601709	S MALL	38	3	1	1	2	2	2	2	1	1	2	2	1	2	2	2	2	1	2	2	3	8.6	4	3200	1	4000	1	0.99	90.3	1	2	2	2	.	.	.	2	4
86	601698	JAFAR	23	2	1	1	2	2	2	2	1	2	2	2	1	2	2	2	2	2	2	2	1	3.7	3	2600	1	3000	1	3.1	92.6	1	2	2	2	.	.	.	1	1
87	601677	AMLA	16	1	2	2	2	2	2	1	2	2	2	1	2	2	2	2	1	2	2	3	8.7	4	3500	1	16000	4	.	92.2	2	2	2	2	.	.	.	3	6
88	628362	P DAS	43	4	2	1	2	2	2	2	2	2	2	2	1	2	2	2	2	1	2	2	3	7.5	4	3800	2	43000	2	4.46	77.2	2	2	2	2	.	.	.	4	8
89	601033	SIVA S	21	2	1	1	2	2	2	2	1	1	1	2	1	2	2	2	2	2	2	2	1	4	2	1200	1	6000	1	1.24	84.9	1	2	2	2	.	.	.	1	1
90	625310	MS HO	48	4	1	1	2	2	2	2	2	1	2	2	1	2	2	1	2	2	2	2	3	8.3	3	2900	1	5000	1	1.3	87.6	1	2	2	2	.	.	.	1	1
91	629061	SHANT	20	1	2	1	2	2	2	2	2	2	2	2	1	2	2	1	2	1	2	2	2	4.2	2	1700	3	83000	2	2.69	58.6	2	2	2	2	.	.	.	4	8
92	629279	SHAMA	40	3	1	2	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	3	8.1	4	3400	1	4000	1	2.62	91.8	1	2	2	2	.	.	.	1	1
93	633224	SIVAKU	34	3	1	1	2	2	2	2	2	2	1	2	1	2	1	2	2	2	2	2	2	6.7	2	1200	3	57000	.	0.78	.	2	1	2	2	.	.	.	6	15
94	634369	SANWA	18	1	1	1	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	1	2.3	3	2600	1	5000	1	2.75	91.4	1	2	2	2	.	.	.	3	5
95	636097	SUDAK	37	3	1	1	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	1	2	3	2400	1	1000	3	.	95.2	1	.	.	.	.	.	.	1	1
96	637149	P RAJU	69	6	1	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	3	8.4	2	1500	2	22000	1	2.06	83.9	2	.	.	.	.	.	.	2	4
97	586082	L BISW	45	4	2	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	1	3.8	3	2300	1	6000	2	3.61	107.7	1	2	2	2	.	.	.	1	1
98	581999	A BHAI	45	4	1	1	2	2	2	2	1	2	1	2	1	1	2	1	2	2	2	2	3	9.6	3	2300	1	5000	1	0.37	87.3	1	2	2	2	.	.	.	6	13
99	599144	S BUNC	33	3	2	1	2	2	2	2	2	2	1	2	1	1	2	1	2	2	1	2	3	9.3	3	2800	2	22000	.	.	88.3	2	1	1	2	.	.	.	6	12
100	596141	R MAH/	60	5	1	1	2	2	2	2	1	2	2	2	1	2	2	1	2	1	2	2	3	7.4	2	1700	3	54000	2	2.46	81.9	2	2	2	2	.	.	.	4	9
101	593302	M RAJ	47	4	1	1	2	2	2	2	1	2	2	2	1	2	2	2	2	2	2	2	3	8.3	4	3500	2	22000	1	.	91.4	1	2	2	2	.	.	.	6	12
102	595543	V RAO	31	3	1	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	3	9	4	3500	3	100000	1	1.89	90.7	2	2	2	2	.	.	.	2	4
103	590058	MUTHU	56	5	1	2	2	2	2	2	1	1	2	2	1	1	2	2	2	2	2	2	3	9.9	1	400	3	79000	1	0.51	83.2	1	.	.	.	.	.	.	2	4
104	589090	C SEKA	51	5	1	1	2	2	2	2	2	2	2	2	1	2	2	1	2	2	2	1	1	3.7	3	2300	2	38000	3	1.48	106	2	.	.	.	.	2	2	5	11
105	597169	J KUM/	23	2	1	2	2	2	2	1	1	1	2	2	1	2	2	2	2	2	2	2	3	7.6	3	2500	3	66000	4	0.67	.	2	.	.	.	.	.	.	3	5
106	581342	K KUKI	49	4	1	1	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	3	7.4	3	2100	2	18000	1	0.37	84.7	1	2	2	2	2	.	.	1	1
107	589289	NATRA	67	6	1	1	2	2	2	2	1	2	2	2	1	2	2	2	1	2	2	2	2	6.9	4	3400	1	6000	1	0.86	89.2	2	.	.	.	.	.	.	2	4
108	586330	ROHIT	17	1	1	1	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	2	5.4	3	2700	1	3000	1	0.88	82.7	1	2	2	2	.	.	.	1	1
109	591341	PRAMC	56	5	1	1	2	2	2	2	2	2	2	2	1	2	2	2	2	1	2	2	3	9.6	3	3000	2	48000	3	2.62	106.7	.	2	2	2	.	.	.	4	8
110	591325	KAMAL	40	3	2	1	2	2	2	2	2	2	2	2	1	2	2	1	2	1	1	2	3	9.2	3	2500	3	70000	.	.	.	.	2	1	2	.	.	.	4	8
111	592453	R JAN I	29	2	2	1	2	2	2	2	2	2	1	2	1	2	2	2	1	1	2	2	1	3.9	3	3000	3	99000	.	.	.	.	2	2	2	.	.	.	4	8
112	611309	MAYA I	58	5	2	1	2	2	2	2	2	1	1	2	1	2	2	1	2	1	2	2	3	7.8	3	2900	3	76000	.	.	97.1	.	2	2	1	.	.	.	4	8
113	592943	H MON	38	3	1	2	2	2	2	2	1	2	1	2	1	2	2	1	2	1	2	1	1	2	3	8.8	3	2800	2	34000	3	2.6	95.3	.	2	1	2	.	.	.	4	8
114	603685	PADMA	38	3	2	1	2	2	2	2	2	2	2	2	1	2	2	1	2	1	2	1	3	7.6	4	3400	3	84000	3	3.98	104	.	.	.	.	.	2	1	5	11
115	599267	BALA S	50	4	1	1	2	2	2	1	2	2	2	2	1	2	2	2	2	2	2	2	2	4.4	4	3300	1	9000	1	3.98	93.3	.	2	2	2	.	.	.	9	17

116	597744	M KAUI	35	3	2	1	2	2	2	2	2	1	1	2	1	2	2	2	2	1	2	2	2	6.5	4	3700	3	74000	1	.	.	.	2	2	2	.	.	.	4	8
117	594398	P DUTT	34	3	1	1	2	2	2	2	1	2	2	2	1	1	2	2	2	1	2	2	2	5.7	2	1700	2	35000	1	2.25	79.1	.	2	2	1	.	.	.	4	10
118	587564	K LAMA	40	3	1	1	2	2	2	2	2	2	1	2	1	1	2	1	1	1	2	3	9.6	2	2000	2	42000	3	2.41	105.6	.	2	1	2	.	.	.	4	8
119	593186	R SING	40	3	2	1	2	2	2	2	2	2	2	2	1	2	2	1	2	2	2	2	3	7.8	4	3700	3	93000	.	.	.	.	.	2	.	.	.	.	8	3
120	586041	A DUTT	65	6	1	1	2	2	2	2	2	1	2	2	1	2	2	1	2	1	2	2	3	8.9	3	2700	2	41000	.	.	68.3	.	2	2	1	.	.	.	4	8
121	600556	CINAKI	63	6	2	2	2	2	2	1	1	2	2	2	1	2	2	2	2	2	2	2	3	9	3	2300	2	50000	.	0.97	79	.	.	.	.	.	.	.	7	19
122	607310	D SWA	65	6	1	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2	1	2	2	3	7.2	3	2400	2	34000	.	.	73.3	.	2	2	2	.	.	.	4	8
123	610103	SETUA	50	4	2	1	2	2	2	2	1	2	2	2	1	2	2	2	2	2	2	2	3	8.7	4	3300	3	70000	2	.	82.9	.	1	2	2	.	.	.	9	16
124	610380	R AHMI	27	3	1	2	2	2	2	2	2	1	2	2	1	1	2	2	2	1	2	2	3	8.5	2	2000	2	40000	.	.	73	.	2	2	2	.	.	.	4	8
125	582523	A KANT	58	5	1	1	2	2	2	2	2	2	1	2	1	2	2	1	2	1	2	2	3	9.8	4	3800	2	27000	.	.	.	.	2	2	2	.	.	.	4	8
126	637802	SENTH	18	1	1	2	2	2	2	2	1	1	2	2	1	2	2	2	2	1	2	2	3	8.5	3	2700	2	45000	.	.	.	.	2	2	2	.	.	.	4	8
127	599200	S REDI	25	2	1	1	2	2	2	2	2	2	1	2	1	2	2	2	2	1	2	2	3	8.6	4	3800	1	10000	3	5.55	109.3	1	2	2	2	2	.	.	9	17
128	625876	J KARJ	48	4	1	2	2	2	2	2	2	2	1	2	1	1	2	1	2	2	1	2	3	8.9	3	2700	3	80000	.	.	77.9	.	2	2	2	.	.	.	4	8
129	620612	A RANI	52	5	2	1	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	3	8.2	3	2100	2	43000	.	.	.	.	2	1	2	.	.	.	9	20
130	614983	R REDI	43	4	1	1	2	2	2	2	2	2	1	2	1	2	2	2	2	2	2	2	3	8.8	4	3600	3	76000	2	.	74.2	.	1	2	2	.	.	.	6	12
131	612747	S DEVI	30	2	2	1	2	2	2	2	2	2	2	2	1	2	2	1	2	2	1	2	2	6.4	2	1800	3	90000	.	.	.	.	2	2	2	.	.	.	9	17
132	633820	SWAPA	43	4	1	2	2	2	2	2	2	2	2	2	1	2	2	1	2	1	1	2	3	8.5	1	1000	2	45000	.	.	.	.	2	2	2	.	.	.	4	8
133	626565	VALAR	37	3	2	1	2	2	2	2	2	2	2	2	1	2	2	1	2	1	1	2	2	4.1	2	1900	2	34000	2	1.72	55.1	.	.	.	.	.	.	.	4	8
134	629415	SHANK	39	3	1	1	2	2	2	2	2	1	2	2	1	2	2	1	2	1	1	2	1	3.4	3	2400	3	55000	2	3.92	82.6	.	2	2	2	.	.	.	4	8
135	608389	N C PA	65	6	1	1	2	2	2	2	2	1	2	1	1	2	1	2	1	2	2	2	3	9.4	4	3100	2	47000	3	.	96.7	.	2	1	2	.	.	.	4	8
136	610103	SETUA	50	4	2	1	2	2	2	2	2	2	1	2	1	2	2	2	1	1	2	2	3	8.7	4	3300	1	15000	2	.	82.9	.	1	2	2	.	.	.	9	16
137	611173	JENIFA	17	1	2	2	2	2	2	2	1	2	1	2	1	2	2	2	2	2	2	2	3	8.3	2	1600	2	50000	2	.	.	.	2	2	2	.	.	.	6	12
138	580590	D RAJ	50	4	1	1	2	2	2	2	2	2	1	2	1	1	2	2	2	1	2	2	3	9.9	2	2000	3	67000	2	1.54	77.2	.	2	1	2	.	.	.	4	8
139	646138	BADRU	40	3	2	1	2	2	2	2	1	2	2	2	1	2	2	2	2	2	2	2	2	4.7	1	700	2	24000	2	2.35	60.4	2	.	.	.	.	.	.	9	17
140	646275	SETAM	62	6	2	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	3	9.2	4	3200	1	20000	3	2.64	106.2	1	2	2	2	.	.	.	2	4
141	646613	R MEH	37	3	1	1	2	2	2	2	2	2	2	2	1	2	2	2	2	1	2	1	3	8.2	2	1600	3	95000	2	2.41	66.1	2	2	2	2	.	.	.	5	11
142	642656	C RAO	44	4	1	1	2	2	2	2	1	1	2	2	1	2	2	2	2	2	2	2	2	5.5	2	1900	1	16000	1	.	88.5	1	2	2	2	.	.	.	3	5
143	645213	S MANS	47	4	1	1	2	2	2	2	2	1	2	2	2	1	2	2	2	2	2	2	2	5.2	3	2300	1	11000	3	0.96	94.8	1	2	2	2	.	.	.	3	5
144	645318	D DAS	32	3	1	1	2	2	2	2	2	1	2	1	2	1	2	2	2	2	2	2	3	8.3	2	1700	2	21000	4	.	101.1	.	2	2	2	.	.	.	3	5
145	642717	B MANI	42	4	1	1	2	2	2	2	2	2	1	2	1	2	2	2	2	1	2	2	3	7.3	2	1300	1	16000	2	2.19	82.7	1	.	.	.	.	.	.	3	6
146	641731	P K DA	34	3	1	1	2	2	2	2	1	2	1	2	1	2	1	1	1	1	2	1	2	6.1	2	1100	3	69000	2	1.92	.	2	1	2	2	.	.	.	6	12
147	641854	IZARAL	29	2	1	2	2	2	2	2	1	2	2	2	1	2	2	2	2	2	2	2	2	6.9	3	2500	3	69000	1	4.75	90.7	2	2	2	2	.	.	.	4	21
148	641312	A PRIY	22	2	2	2	2	2	2	2	1	2	1	2	1	2	2	2	2	2	2	2	3	9	4	3300	2	49000	4	3.8	90.6	1	2	2	2	.	.	.	3	5
149	643243	K ROY	18	1	1	1	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	2	5.5	2	1700	1	5000	2	2.72	74.8	1	2	2	2	.	.	.	1	1
150	642499	NAGAR	24	2	1	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	5	4	3500	1	9000	3	2.5	97	1	.	.	.	.	.	.	2	4