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A Case Study on Systemic Lupus Erythematous With Anaemia

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ABSTRACT

A 25 years female patient was admitted in hospital 5days before, she complained that she was apparently normal 4months back then she developed round over left foot due to slipper bite which gradually increased in size, associated with whitish discharge from the wound, non foul swelling and polyarimalgia. Hyperpigmented rashes all over the body since 15days associated with itching, initially started over the face and whole body. Pain abdomen since 15days, burning and over epigastric area, radiating to back, aggregates after taking food. Cough since 15days associated with sputum productive scanty, low grade fever since 15days.

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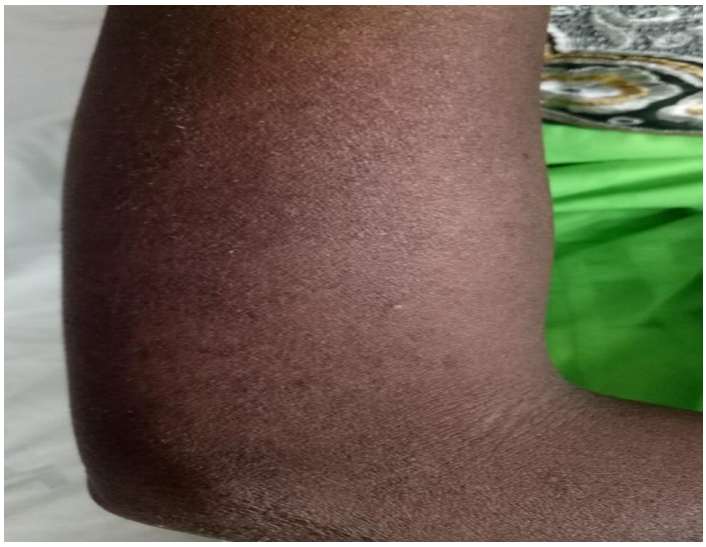
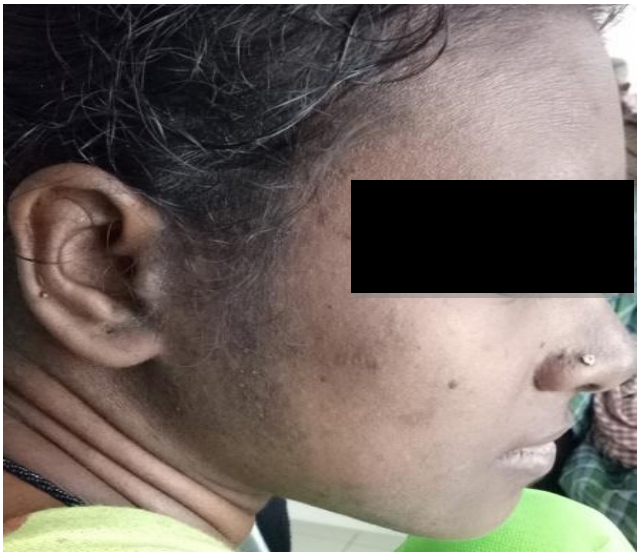




INTRODUCTION:

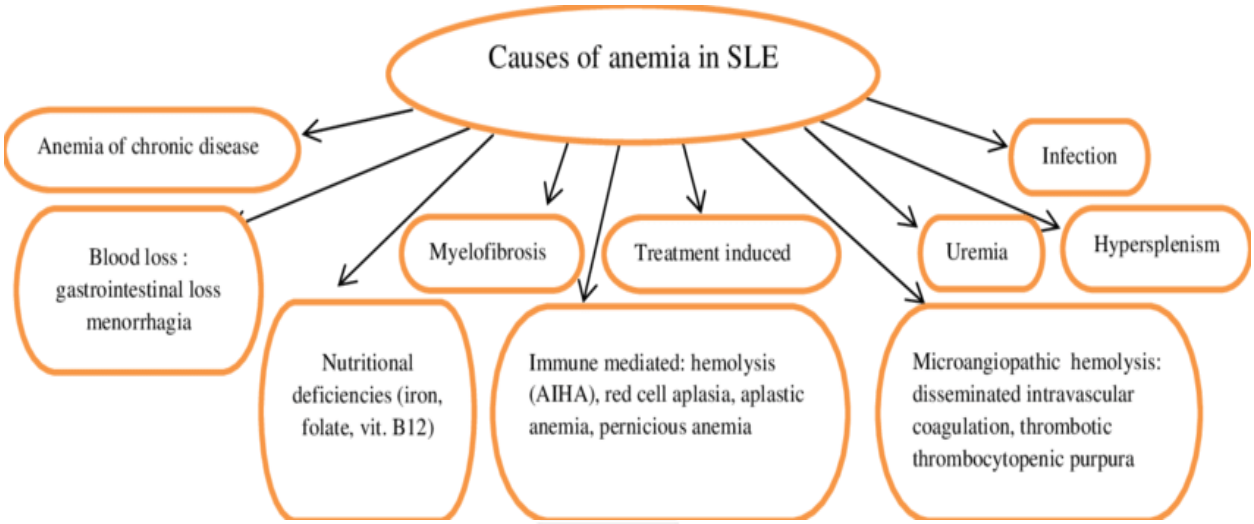
Systemic lupus erythematosus (SLE) is an autoimmune disease of unknown etiology characterized by the presence of autoantibodies and immune complex deposition. Hematological manifestations are very common and are one of the classification criteria of the American College of Rheumatology (ACR). Thrombocytopenia occurs in 25–50% of the patients, leucopenia in approximately 50% and Coombs' positive hemolytic anemia in about 10%.The cytopenias can occur singly or in combination. They are usually the result of autoantibody-mediated peripheral destruction with associated hypercellular bone marrow. Although hematological manifestations are common, they are seldom the sole presenting feature of the disease. Most often, cytopenias appear during the course of the disease, but occasionally aplastic anemia is the initial manifestation of SLE.This may be underestimated due to the presumed peripheral destruction of the blood cells. In this paper, we describe 2 adolescents with aplastic anemia as the presenting feature of pediatric SLE.

MATERIALS AND METHODS

Samples of 5 newly diagnosed ANA positive SLE patients were taken. Complete blood counts, ESR, reticulocyte count, coagulation studies, diluted Russel Viper Venom Test (dRVVT), mixing studies, serological tests, high sensitivity CRP along with iron profile, transferrin saturation, soluble transferrin receptor (sol TFR) levels, anti-beta2 glycoprotein1, direct and indirect Coomb’s test were estimated in cases diagnosed as SLE. Clinical symptoms were co-related with and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) was estimated.

CLASSIFICATION OF SLE

Systemic lupus erythematosus has been classified according to types depending on where they are found. Generally, when the word lupus alone is used, it refers to the systemic lupus erythematosus. Other types have been reported namely: Neonatal lupus which is very rare but occurs in one third of mothers with systemic lupus erythematosus who carry the anti SS A (Ro) antibody. It was reported that this maternal antibody attack the fetus causing skin rash, liver problems and low blood counts. This type resolves by the age of 3 to 6 months



DERMATOLOGICAL MANIFESTATIONS

Past researchers reported that as many as 20% of patients present with dermatological symptoms such as malar rash which develops after sunlight exposure (Schur, 2001). Vasculopathy: Arterial and venous thrombosis is a sequel to chronic inflammatory events triggered by autoantibodies. This has been documented to occur in the form of petechiae, purpura or ecchymoses in the skin or swollen medium sized vessels causing tender nodules, seizures, stroke or behavioral changes. Renal: There could be renal involvement, nephritic syndrome or renal failure. Painless haematuria or proteinuria may be the only presenting symptoms. This may take place in about 35% of the patients.

HAEMATOLOGIC FEATURES

Anemia secondary to chronic inflammation, iron deficiency and hemolysis may develop in as many as half of SLE patients. Thrombocytopenia and leucopenia may be due to SLE or side effects of pharmacologic treatment. Patients may have an association with antiphospholipid

antibody syndrome (a thrombotic disorder) where auto antibodies to phospholipids are present in the patient's serum. Abnormalities associated with antiphospholipids antibody syndrome include a paradoxical prolonged prothrombin time (which usually occurs in hemorrhagic disorders) and a positive test for antiphospholipid antibodies, the combination of such finding have earned the term" Lupus" "anticoagulant positive". Another autoantibody finding in lupus is the anticardiolipin antibody which can cause a false positive test for syphilis

ANEMIA

It is a common hematological abnormality in SLE that is defined as hemoglobin levels of < 12g/dL for women and <13.5 g/dL for men. It is categorized into the following: anemia of chronic disease (ACD), which is the most common form (60%-80%), iron deficiency anemia (IDA), autoimmune hemolytic anemia (AIHA), and anemia due to chronic renal insufficiency. In a cohort comprising 132 anemic patients with SLE, ACD was found in 37.1% of the cases, IDA in 35.%, AIHA in 14.4% and other causes of anemia in 12.9% of the patients. ACD results from suppressed erythropoiesis secondary to chronic inflammation (normocytic and normochromic, with a relatively low reticulocyte count, low to normal serum iron, adequate bone marrow iron stores and elevated serum ferritin level.Low levels of erythropoietin due to chronic inflammation or renal insufficiency and presence of anti-erythropoietin auto antibodies which are associated with European Consensus Lupus Activity Measurement (ECLAM) high score are found in some patients.IDA is defined by serum ferritin below 20 μg/dl. it is common and may be the result of menorrhagia or increased gastrointestinal blood loss because of long term use of corticosteroids. AIHA is characterized by elevated reticulocyte counts, low haptoglobin levels; increased indirect bilirubin concentration and a positive direct Coombs' test.It has been noted in up to 10% of patients with SLE. The presence of hemolytic anemia may associate with manifestations of severe disease such as renal disease, seizures and serositis. The presence of both immunoglobulin and complements on red blood cells is usually associated with some degree of hemolysis, while presence of complements alone (C3 and /or C4) is often not associated with hemolysis.Other types of anemia in SLE are rare. Pure red cell aplasia (PRCA), pernicious anemia (PA), and aplastic anemia have been reported in these patients. PRCA is characterized by antibodies directed against either erythropoietin or bone marrow erythroblasts, aplastic anemia is mediated by auto antibodies against one marrow precursors.

Furthermore, drugs, myelofibrosis, sideroblastic anemia, hemophagocytic syndrome and thrombotic microangiopathy are also implicated in the causation of SLE anemia. Microangiopathic hemolytic anemia (MAHA) is manifested by schistocytes on peripheral blood smear, elevated serum levels of lactate dehydrogenase and bilirubin. Many affected patients also have thrombocytopenia, renal involvement, fever and neurologic symptoms. These features are compatible with a diagnosis of thrombotic thrombocytopenic purpura (TTP). However, the pathogenesis of TTP in these patients is likely heterogeneous, as it may reflect vasculitis or antiphospholipid syndrome as well.

LAB INVESTIGATIONS:

POLYMORPHS - 50%	HB – 5.4gml/dl
EOSINOPHILLS - 03 %	TWBC - 2800 /cmm
LYMPHOCYTES – 43%	T R B C – 1.8mill/cmm
MONOCYTES - 04%	ESR - 45 mm/hr
BASOPHILLS - 00%	PCV – 1.6%
MCV - 86 FL	MCH – 28pg
MCHC - 33%	PLATELETS- 72000/cmm

RETICULOCYTE COUNT- 0.1%

AN APPROACH TO THE INVESTIGATIONS OF HEMATOLOGICAL DISORDERS IN SLE

A detailed history is essential, including symptoms of anemia, bleeding tendencies, and particular attention should be given to drugs such as statin, antibiotic and angiotensin converting enzyme inhibitor use. Leucopenia and thrombo- cytopenia may complicate treatment with azathioprine, methotrexate and rarely, cyclosporine mycophenolatemofetil or hydroxychloroquine. Neutropenia may follow pulsed cyclophosphamide. Macrophage activation syndrome should be considered if cytopenia develops rapidly, especially in juvenile SLE. If neutropenia with pyrexia >38.0o C is present, blood cultures and samples from other sites should be sent for microbiological examination. In cases of pancytopenia or

suspected pure red cell aplasia, parvovirus B19 serology should be performed. Reticulocyte index is the major step for determination of the cause of anemia.If the reticulocyte count is high, a hemolytic process or acute bleeding should be suspected, if it is low, anemia of chronic disease or nutritional deficiencies namely IDA, folate and vitamin B12 deficiency should be suspected .Examination of peripheral blood film stained with Wright's stain provides clues in the diagnosis of anemia's, leucopenia and thrombocytopenia. Other tests are specific according to the presenting problems. Ferritin is necessary for diagnosing IDA. Concentrations greater than 20µg/dL, excludes IDA and a bone marrow examination may be considered; however, because ferritin is an acute phase reactant, it can be elevated in any inflammatory process of any cause. Direct Coomb's test, serum lactate dehydrogenase, liver function tests, immunoglobulin's and serum protein electrophoresis have to be measured in AIHA.

RESULTS AND DISCUSSION:

Anemia has been described in patients with SLE and is most commonly seen following the diagnosis of SLE while presentation before or at the time of diagnosis of SLE is unusual and only a limited number of patients are reported in the pediatric medical literature. Where in the anemia preceded the diagnosis of SLE in only 18% of the cases. Since that report, there has been one additional case of anemia with SLE reported at the time of diagnosis in a 25-year-old.

In patients with SLE, the immune-mediated cytopenia is secondary to antibodies directed to one or more cell lines resulting in peripheral destruction. However, in our cases and in the previously reported cases of anemia secondary to bone marrow failure, studies have failed to demonstrate peripheral destruction and in most cases the etiology of the bone marrow failure was not defined. Different mechanisms of anemia have been considered in the literature. An IgG complement-dependent antibody or a non-complement-dependent antibody suppressing early hematopoietic progenitor cells but also an auto-immune cellular process inhibiting bone marrow progenitor cells or a cytotoxic lymphocyte activation suppressing the hematopoiesis have been proposed. Two large studies examined bone marrows of SLE patients with cytopenias. One showed either global hypocellularity or granulocytic hypoplasia while the other showed stromal bone marrow damage, bone marrow necrosis and dysplasia of all hematopoietic lineages. The latter study did not find a correlation of the severity of peripheral cytopenias with the cellularity and distribution of individual hematopoietic lineages.

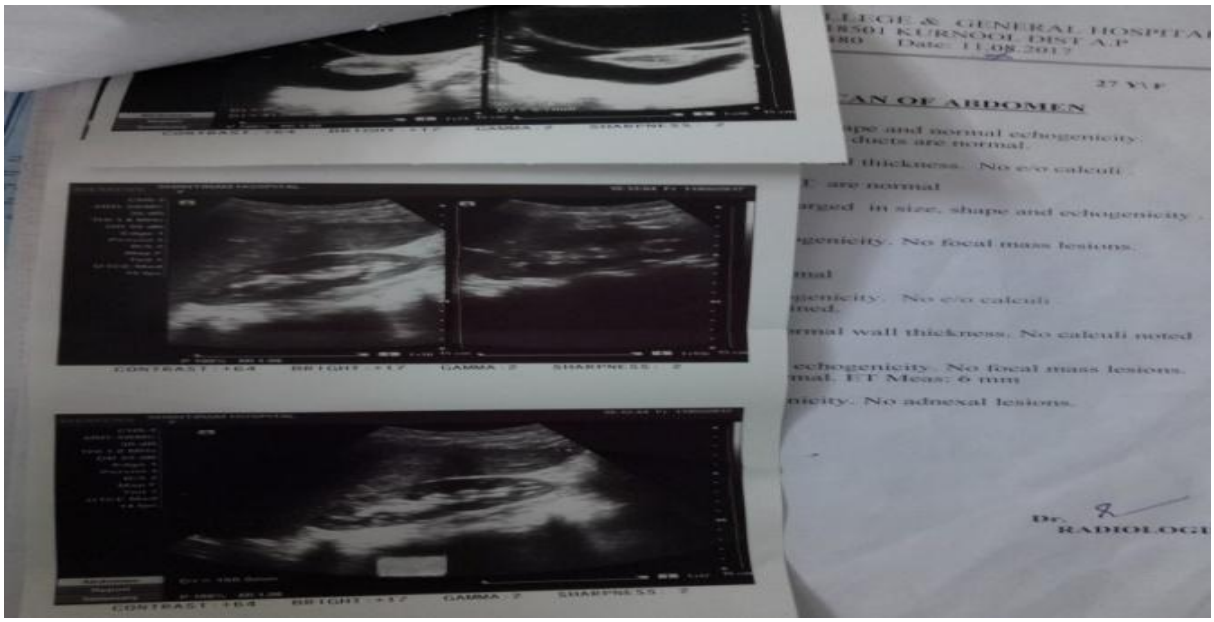
Although cyclosporine and anti-thymocyte globulin are commonly used in idiopathic anemia; its use in anemia associated with SLE is very limited and as suggested by our patients, intensive immunotherapy may not be required for SLE patients. Our patients, with mild pancytopenia, responded to hydroxychloroquine and moderate doses of prednisone and hydroxychloroquine, respectively. This is in contrast to the previous reports in the literature which showed that the majority of cases required a second immunosuppressive agent in addition to oral corticosteroids or pulse methylprednisolone to obtain a response in children, plasmapheresis has been used in addition to corticosteroids, while in adults also cyclophosphamide, azathioprine, and oxymetholone have been used.

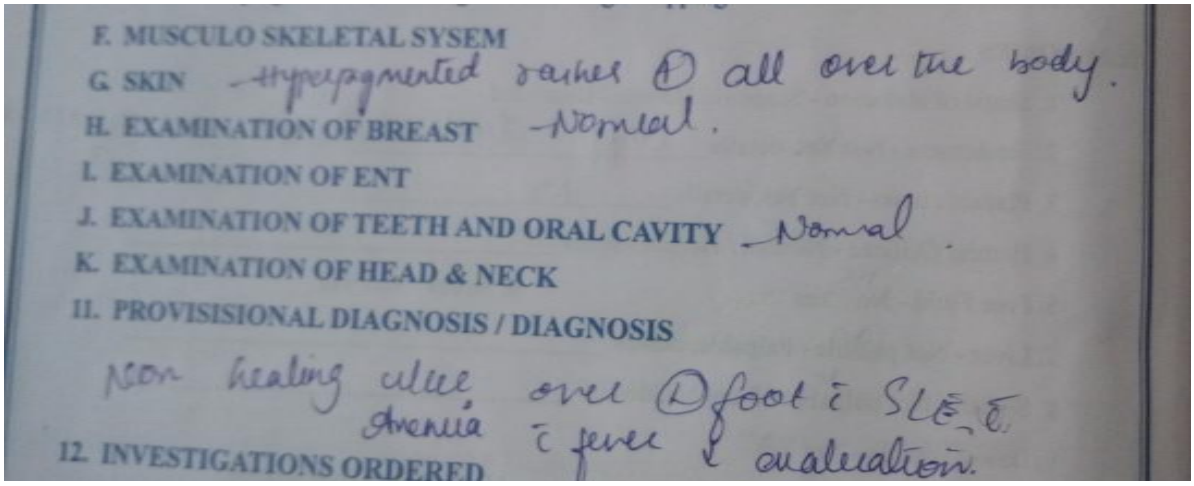
The long-term outlook after the recovery from anemia with SLE is very good, especially in comparison with idiopathic acquired anemia.

CONCLUSION:

Only limited number of cases of anemia associated with SLE are described in the literature. We suggest that this is likely the result of the presumption that the pancytopenia in SLE is always secondary to the peripheral destruction of the blood cells. We therefore suggest that SLE should be included in the differential diagnosis of a child with pancytopenia and the appropriate investigations for SLE should be undertaken. In addition, as demonstrated by our second case, patients should be serially followed for the subsequent development of SLE. Similar to what is seen in other SLE manifestations, both antibody-mediated and T lymphocyte-mediated mechanisms may lead to the bone marrow failure in SLE patients. An accurate diagnosis with the appropriate therapy is vital and can cause lasting reversal of this condition.

PATIENT IMAGES AND REPORTS:





F. MUSCULO SKELETAL SYSEM

G. SKIN -Hyperpigmented rashes @ all over the body.

H. EXAMINATION OF BREAST -Normal.

I. EXAMINATION OF ENT

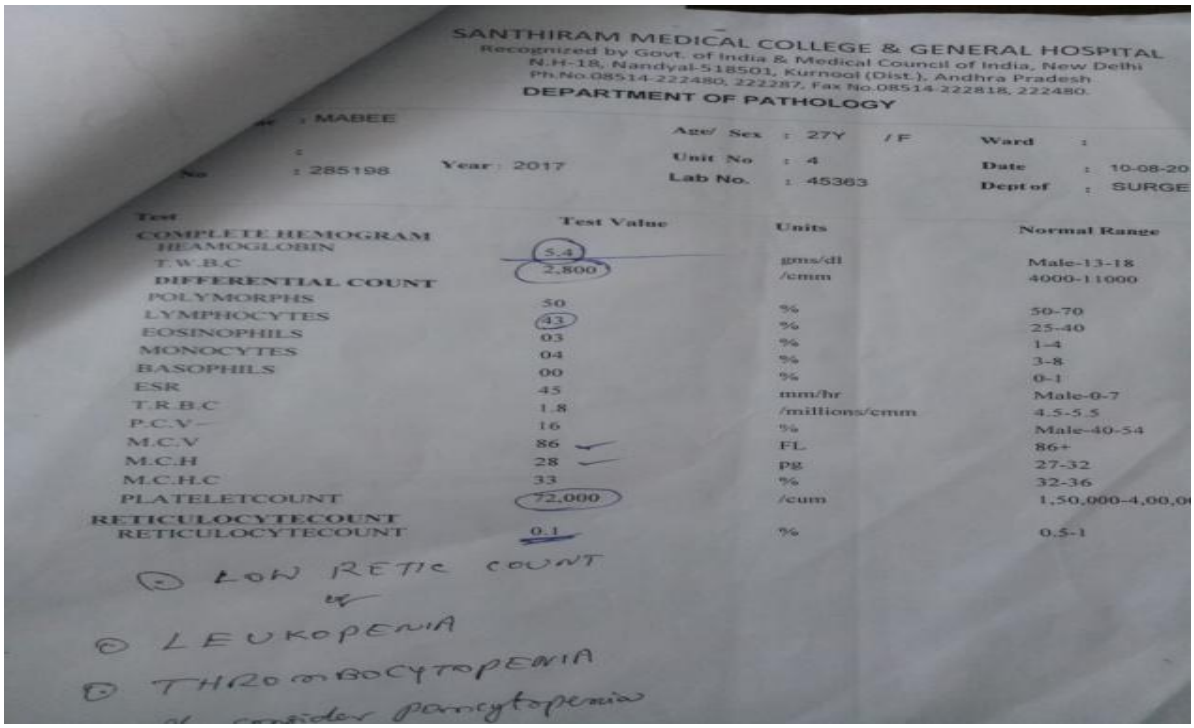
J. EXAMINATION OF TEETH AND ORAL CAVITY -Normal.

K. EXAMINATION OF HEAD & NECK

II. PROVISISIONAL DIAGNOSIS / DIAGNOSIS

Non healing ulcer over @ foot i SLE, E. Anemia i fever ? evaluation.

12. INVESTIGATIONS ORDERED



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DEPARTMENT OF PATHOLOGY

: MABEE

: 285198 Year : 2017 Age/ Sex : 27Y / F Unit No : 4 Lab No. : 45363 Ward : Date : 10-08-20 Dept of : SURGE

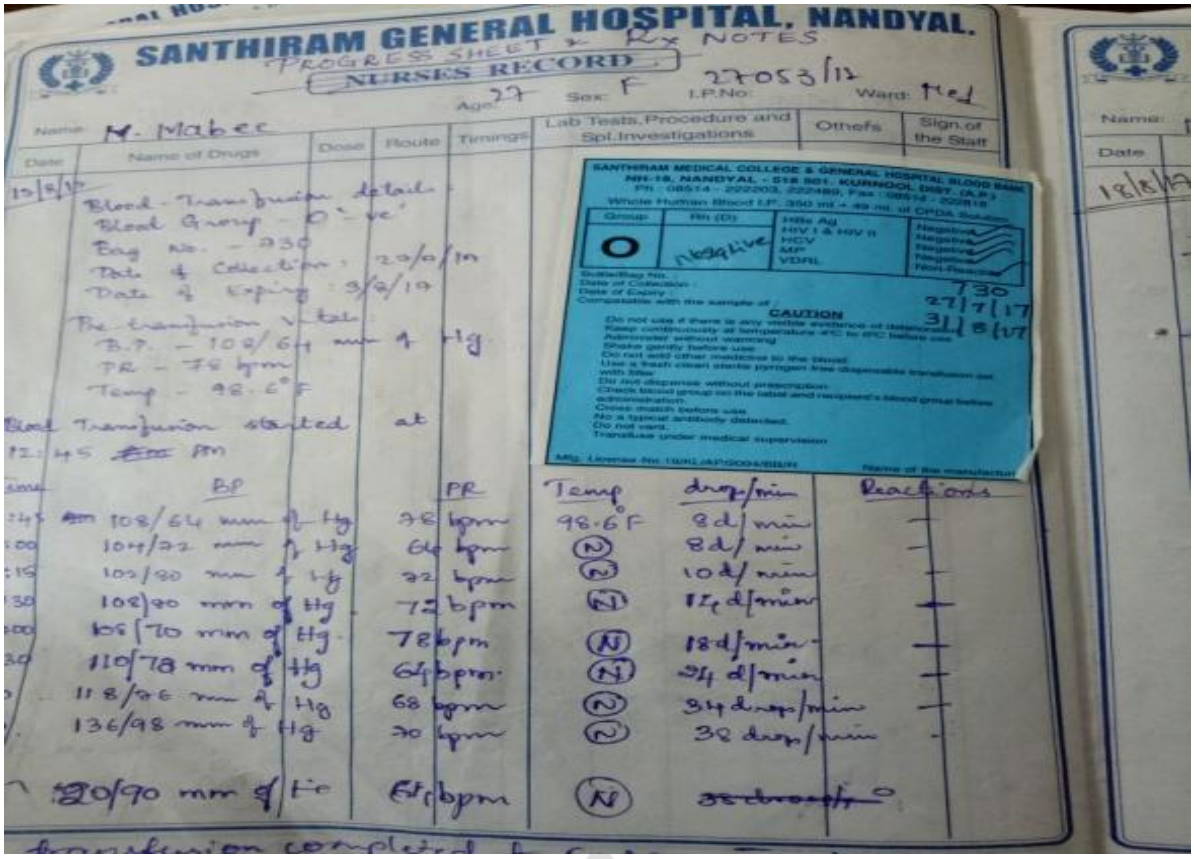
Test	Test Value	Units	Normal Range
COMPLETE HEMOGRAM			
HEAMOGLOBIN	5.4	gms/dl	Male-13-18
T.W.B.C	2,800	/cmm	4000-11000
DIFFERENTIAL COUNT			
POLYMORPHS	50	%	50-70
LYMPHOCYTES	43	%	25-40
EOSINOPHILS	03	%	1-4
MONOCYTES	04	%	3-8
BASOPHILS	00	%	0-1
ESR	45	mm/hr	Male-0-7
T.R.B.C	1.8	/millions/cmm	4.5-5.5
P.C.V-	16	%	Male-40-54
M.C.V	86	FL	86+
M.C.H	28	pg	27-32
M.C.H.C	33	%	32-36
PLATELETCOUNT	72,000	/cum	1,50,000-4,00,0
RETICULOCYTECOUNT			
RETICULOCYTECOUNT	0.1	%	0.5-1

@ LOW RETIC COUNT

@ LEUKOPENIA

@ THROMBOCYTOPENIA

consider pancytopenia



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