

**CLINICAL AND LABORATORY PROFILE IN PAEDIATRIC PATIENTS
WITH BICYTOPENIA OR PANCYTOPENIA IN A TERTIARY CARE
CENTRE IN KOLAR - A CROSS SECTIONAL STUDY**

BY

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**DISSERTATION SUBMITTED TO
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In partial fulfilment of the requirement or the degree of

**DOCTOR OF MEDICINE
IN
PAEDIATRICS**

Under The Guidance Of

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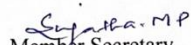
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ABSTRACT

Background: Brrythyperemia and pancytopenia are frequently seen in clinical settings with varied etiology. In determining the optimal diagnostic approach needs to be addressed. These conditions have diverse causes influenced by genetic factors, geographic variations and nutritional deficiencies within the community.

Objectives: This study aims to investigate brrythyperemia/pancytopenia prevalence, clinical and laboratory profiles, and their potential correlation with fluoride exposure in children aged 1 to 18 years.

Methodology: This cross-sectional study examined children aged 1-18 years diagnosed with brrythyperemia / pancytopenia at a tertiary care centre in Kolar between September 2022 and December 2023. The collected data underwent statistical analysis.

Results: In our study, the predominant presenting symptom was fever, noted in 85.4% of patients, followed by abdominal pain (80.7%) and easy fatigability (38.1%). Physical examination findings indicated hepatomegaly in 48.8% of patients, splenomegaly in 32.1%, and splenomegaly in 19.1%. Peripheral smear analysis revealed normochromic normocytic anemia as the most prevalent type, observed in 79.7% of patients.

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CLINICAL AND LABORATORY PROFILE IN PEDIATRIC PATIENTS WITH BICYTOPENIA OR PANCYTOPENIA IN A TERTIARY CARE CENTRE IN KOLAR - A CROSS SECTIONAL STUDY Abstract Background: Bicytopenia and pancytopenia are

CASE CENTRE IN KOLAR - A CROSS SECTIONAL STUDY **ABSTRACT** Background: Bicytopenia and pancytopenia are frequently seen in clinical settings with varied etiology, yet determining the optimal diagnostic approach needs to be addressed. These conditions have diverse causes influenced by genetic factors, geographic locations and nutritional deficiencies within the community. Objectives: This study aims to investigate bicytopenia/pancytopenia prevalence, clinical and laboratory profiles, and their potential correlation with fluoride exposure in children aged 1 to 18 years.

Methodology: This cross-sectional study examined children aged 1-18 years diagnosed with bicyclopentia / pancyclopentia at a tertiary care centre in Kolar between September 2022 and December 2023. The collected data underwent statistical

analysis. Results: In our study, the predominant presenting symptom was fever, noted in 90.4% of patients, followed by abdominal pain (60.7%) and easy fatigability (38.1%). Physical examination findings indicated hepatomegaly in 48.8% of

patients, pallor in 32.1%, and splenomegaly in 19.1%. Peripheral smear analysis revealed normocytic normochromic anemia as the most prevalent type, observed in 70.2% of patients. Conclusion: Higher incidence of bicytopenia compared

to pancytopenia with higher occurrence in school-aged male children. Normocytic normochromic anemia was the predominant peripheral smear. Our study observed majority of pediatric age group urine fluoride values were under <2 ppm, highlighting the necessity for further investigation of fluoride exposure and its health consequences.

ppm, highlighting the necessity for further exploration of fluoride on hematological parameters and transplacental passage of fluoride. **Keywords:**pediatrics,bicytopenia, pancytopenia, fluoride. **INTRODUCTION** Perinatal cytopenia refers to a reduction in one or more of the components of blood including red blood cells (RBCs), white blood cells (WBCs) and

to a reduction in one or more of the components of blood including: red blood cells (RBCs), white blood cells (WBCs) and blood platelets. When there is a reduction in the levels of two out of these three blood cell types, the condition is referred to as hypotension and when all three types of blood cells are affected, the condition is called anapnoea (1).

referred to as bicytopenia and when all three types of blood cells are affected, the condition is called pancytopenia (1). These haematological abnormalities are not diseases on their own but rather signs of various diseases that could range from simple self-limiting bacterial/viral infections to life-threatening haematological malignancies and bone marrow

from simple self-limiting bacterial/viral infections to life-threatening haematological malignancies and bone marrow failure syndrome (2). Cytopenias in children are common and can be inherited as well as acquired and the causes of the latter are numerous. Infections are a common cause of leukopenia which are normally followed by granulocytopenia that

leukemia are numerous. Infections are a common cause of leukopenia which are normally followed by granulocytopenia that is a temporary suppression of the bone marrow. Other infections such as Cytomegalovirus (CMV), Epstein-Barr virus (EBV), and parvovirus B19 lead to low blood cell count. Besides, the Cytomegalovirus (CMV), Epstein-Barr virus (EBV),

(3). Cytopenias also occur due to iatrogenic causes, which are; certain drugs, chemotherapy, and radiotherapy (4). The

The specific nature of the abnormality of the bone marrow in patients with cytopenias depends on the cause. The changes ranged from normocellular with nonspecific changes, hypercellular with overactive/ineffective hematopoiesis to total

replacement by malignant cells(5). For instance, diseases like the pernicious anemia due to vitamin B12 or folic acid deficiency the megaloblastic anemia has hyper cellular marrow due to ineffective erythropoiesis. On the other hand, Tam

diseases, for example, aplastic anemia exhibit hypocellularity of the bone marrow (6). Pancytopenia can be due to various acquired causes such as nutritional deficiencies, idiopathic cases, and secondary causes such as radiation exposure, drugs, and chemicals. Drugs that often cause pancytopenia include chemotherapeutic agents, chloramphenicol, and sulfonamides (7).

exposure, drugs, and chemicals. Drugs that often cause pancytopenia include chemotherapeutic agents, chloramphenicol, sulphonamides and anti epilepsy drugs (2). Hypersplenic states such as autoimmune diseases, paroxysmal nocturnal hemoglobinuria and other bone marrow disorders like leukemia, myelodysplastic anemia and myelofibrosis are some

hemoglobinuria and other bone marrow disorders like leukemia, myelodysplastic anemia and myelofibrosis are some common causes of pancytopenia. In developing countries the causes are predominantly nutritional deficiencies resulting in megaloblastic anemia, malaria, enteric fever, kala-azar, infections and other bacterial infections (5). These conditions

in myeloblastic anemia, malaria, ebola fever, viral zika, infections and other bacterial infections(5). These conditions if not well diagnosed and treated lead to a lot of morbidity and mortality. It is also important to recognize the differences in the origin of cytopenia based on the region, as these differences can affect the approach to diagnosis and treatment

(7). Bicytopenia and pancytopenia are two common findings in pediatric patients with diverse etiology of various degrees of severity. Although they are common, there is no standard or ideal method for diagnosing the condition. The etiologies

may include genetic predisposition and location of the patient (7). Polypharmacy and chronicity require extensive clinical examination and selective laboratory tests to determine the cause of the problem and start management. One of the

districts in the state of Karnataka in India is Kolar, where fluorosis is reported to be significantly high. Fluorosis is a condition that occurs when one takes high amounts of fluoride, usually in drinking water and may be associated with dental and skeletal complications. The current literature reveals that higher fluoride exposure may increase the risk of

haematological indices, but the direction of this relationship is still inconclusive. In this investigation, the researchers aim at evaluating the clinical manifestations and laboratory parameters associated with cytopenia in children, and focusing on

at evaluating the clinical manifestations and laboratory parameters associated with cytopenia in children, and focusing on fluoride and micronutrient concentrations. Since Kolar is an endemic area for fluorosis, it provides an opportunity to study the possible association between the level of fluoride exposure and the prevalence of bicytopenia and pancytopenia.

Establishing Clinical and Nutritional Risk Factors: Understanding the clinical and nutritional risk factors in children presenting with bicytopenia/pancytopenia will help in understanding the causes and factors related to them. This

This involves assessing food consumption patterns, nutritional status, and any nutrient deficiencies that may increase children's susceptibility to these hematological disorders. Exploring Fluoride-Cytopenia Relationship: It is crucial to

investigate the relationship between exposure to fluoride and cytopenia, especially in regions like Kolar where fluorosis is reported. This can assist in the formulation of specific strategies for preventing the effects of high fluoride content on health and health-related quality of life. It may also help to elucidate this relationship in other regions of India.

children's health in the district. It may also help to elucidate this relation shed light on possible mechanisms through which fluoride influences hematopoiesis. Significance of the Study This study is of immense importance because it seeks to rectify some of the major knowledge deficiencies on biotoponiz and hematopoiesis in children.

to solve some of the major knowledge deficiencies on bicytopenia and pancytopenia in children, especially in the context of environment and food insecurity that is rampant in the developing world. Thus, based on the clinical and nutritional risk factors defined, practitioners can recognize the children at risk and potentially modify the outcomes in favor of the

risk factors defined, practitioners can recognize the children at risk and potentially modify the outcomes in favor of the kids through early intervention and nutrition support and care. Studying the correlation between cytopenia and fluoride could prove to be valuable in improving public health. If such a relation is established, it would call for methods of

could prove to be valuable in improving public health. If such a relation is established, it would call for methods of minimization of fluoride exposure and recommendations on the management of the affected groups. Thus, the present study aims to improve the comprehensiveness of diagnosing and managing bicytopenia and pancytopenia in children

study aims to improve **the** comprehensiveness of diagnosing **and** managing bicytopenia and pancytopenia in children with a special emphasis on the regions like Kolar experiencing endemic problems like fluorosis. These results are anticipated to aid in the formulation of management protocols and other health interventions for the specific regions

anticipated to aid in the formulation of management protocols and other health interventions for the specific regions enhancing patient care. **AIMS & OBJECTIVES** 1. To study the occurrence rate of bicytopenia/pancytopenia in children aged from 1 year to 18 years. 2. To study the clinical and laboratory profile of bicytopenia/pancytopenia in

children aged from 1 year to 3 years. 2. The majority with biphentonia children aged from 1 year to 18 years. 3. To study the correlation between fluoride and bicytopenia/pancytopenia.

REVIEW OF LITERATURE Bicytopenia and pancytopenia are critical hematological alterations involving decrease of two or

all the three blood constituent, namely erythrocytes, leukocytes, and thrombocytes. These conditions represent underlying pathologies that can be from benign to lethal; infections, nutritional deficiencies, bone marrow diseases, and

malignancies. Knowledge of these conditions' clinical and laboratory characteristics are important for diagnosis and management as the clinical features may be somewhat non-specific and atypical, especially in children. The rate and

causes of bicytopenia and pancytopenia differ from country to country depending on the health care system, the prevalence of infections, nutritional status and genetic predisposition. **The objective of this study is to describe the clinical features, aetiology, management and prognosis of bicytopenic patients in a tertiary care centre at Kolar and to**

clinical, laboratory features of paediatric bicytopenia/pancytopenia patients in a tertiary care centre at Kolar and to make a better approach to diagnosis and management in similar institution. Bicytopenia and pancytopenia are major haematological problems in pediatric patients, and because of this, there is a need to review the various causes, clinical

hematological problems in pediatric patients, and because of this, there is a need to review the various causes, clinical features, and diagnostic approaches to these conditions. From an analysis of the available literature it is possible to deduce a complex picture characterized by many antecedents and various diagnostic approaches. ETIOLOGICAL

ETIOLOGICAL SPECTRUM The etiology of bicytopenia and pancytopenia is diverse and includes many hematological diseases ranging

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Date:

DR RAM SWAROOP REDDY

Place: **Kolar**

LIST OF ABBREVIATIONS USED

RBCs - Red Blood Cells

WBCs - White Blood Cells

EBV - Epstein-Barr Virus

CMV - Cytomegalovirus

B12 - Vitamin B12

CBC - Complete Blood Count

LFTs - Liver Function Tests

FNA - Fine-Needle Aspiration

CT - Computed Tomography

MRI - Magnetic Resonance Imaging

ARDS - Acute Respiratory Distress Syndrome

JIA - Juvenile Idiopathic Arthritis

DMARDs - Disease-Modifying Antirheumatic Drugs

WHO - World Health Organization

BMI - Body Mass Index

MCV - Mean Corpuscular Volume

IDA - Iron Deficiency Anemia

SPSS - Statistical Package for the Social Sciences

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CLINICAL AND LABORATORY PROFILE IN PAEDIATRIC PATIENTS WITH BICYTOPENIA OR PANCYTOPENIA IN A TERTIARY CARE CENTRE IN KOLAR - A CROSS SECTIONAL STUDY

ABSTRACT

Background: Bicytopenia and pancytopenia are frequently seen in clinical settings with varied etiology , yet determining the optimal diagnostic approach needs to be addressed . These conditions have diverse causes influenced by genetic factors, geographic locations and nutritional deficiencies within the community.

Objectives: This study aims to investigate bicytopenia/pancytopenia prevalence, clinical and laboratory profiles, and their potential correlation with fluoride exposure in children aged 1 to 18 years.

Methodology: This cross-sectional study examined children aged 1-18 years diagnosed with bicytopenia / pancytopenia at a tertiary care centre in Kolar between September 2022 and December 2023. The collected data underwent statistical analysis.

Results: In our study, the predominant presenting symptom was fever, noted in 90.4% of patients, followed by abdominal pain (60.7%) and easy fatigability (38.1%). Physical examination findings indicated hepatomegaly in 48.8% of patients, pallor in 32.1%, and splenomegaly in 19.1%. Peripheral smear analysis revealed normocytic normochromic anemia as the most prevalent type, observed in 70.2% of patients.

Conclusion: Higher incidence of bicytopenia compared to pancytopenia with higher occurrence in school-aged male children. Normocytic normochromic anemia was the predominant peripheral smear. Our study observed majority of pediatric age group urine

fluoride values were under <2 ppm , highlighting the necessity for further exploration of fluoride on hematological parameters and transplacental passage of fluoride.

Keywords:pediatrics,bicytopenia, pancytopenia, fluoride.

INTRODUCTION

INTRODUCTION

Peripheral cytopenia refers to a reduction in one or more of the components of blood including; red blood cells (RBCs), white blood cells (WBCs) and blood platelets. When there is a reduction in the levels of two out of these three blood cell types, the condition is referred to as bicytopenia and when all three types of blood cells are affected, the condition is called pancytopenia ⁽¹⁾. These haematological abnormalities are not diseases on their own but rather signs of various diseases that could range from simple self-limiting bacterial/viral infections to life-threatening haematological malignancies and bone marrow failure syndrome ⁽²⁾.

Cytopenias in children are common and can be inherited as well as acquired and the causes of the latter are numerous. Infections are a common cause of leukopenia which are normally followed by granulocytopenia that is a temporary suppression of the bone marrow. Other infections such as Cytomegalovirus (CMV), Epstein-Barr virus (EBV), and parvovirus B19 lead to low blood cell count. Besides, the Cytomegalovirus (CMV), Epstein-Barr virus (EBV), parvovirus B19 also cause low blood cell counts. Other infectious aetiologies include; Sepsis; and malaria; among others ⁽³⁾. Cytopenias also occur due to iatrogenic causes, which are; certain drugs, chemotherapy, and radiotherapy ⁽⁴⁾.

The specific nature of the abnormality of the bone marrow in patients with cytopenias depends on the cause. The changes ranged from normocellular with nonspecific changes, hypercellular with overactive/ineffective hematopoiesis to total replacement by malignant cells⁽⁵⁾. For instance, diseases like the pernicious anemia due to vitamin B12 or folic acid deficiency the megaloblastic anemia has hyper cellular marrow due to ineffective erythropoiesis. On the other hand, diseases, for example, aplastic anemia exhibit hypocellularity of the bone marrow ⁽⁶⁾.

Pancytopenia can be due to various acquired causes such as nutritional deficiencies, idiopathic cases, and secondary causes such as radiation exposure, drugs, and chemicals. Drugs that often cause pancytopenia include chemotherapeutic agents, chloramphenicol, sulphonamides and anti epilepsy drugs ⁽²⁾. Hypersplenic states such as autoimmune diseases, paroxysmal nocturnal hemoglobinuria and other bone marrow disorders like leukemia, myelodysplastic anemia and myelofibrosis are some common causes of pancytopenia. In developing countries the causes are predominantly nutritional deficiencies resulting in megaloblastic anemia, malaria, enteric fever, kala-azar, infections and other bacterial infections⁽⁵⁾. These conditions if not well diagnosed and treated lead to a lot of morbidity and mortality. It is also important to recognize the differences in the origin of cytopenia based on the region, as these differences can affect the approach to diagnosis and treatment ⁽⁷⁾.

Bicytopenia and pancytopenia are two common findings in pediatric patients with diverse etiology of various degrees of severity. Although they are common, there is no standard or ideal method for diagnosing the condition. The etiologies may include genetic predisposition and location of the patient ⁽⁷⁾. Polypharmacy and chronicity require extensive clinical examination and selective laboratory tests to determine the cause of the problem and start management.

One of the districts in the state of Karnataka in India is Kolar, where fluorosis is reported to be significantly high. Fluorosis is a condition that occurs when one takes high amounts of fluoride, usually in drinking water and may be associated with dental and skeletal complications.

The current literature reveals that higher fluoride exposure may have an impact on haematological indices, but the direction of this relationship is still inconclusive.

In this investigation, the researchers aim at evaluating the clinical manifestations and laboratory parameters associated with cytopenia in children, and focusing on fluoride and micronutrient concentrations.

Since Kolar is an endemic area for fluorosis, it provides an opportunity to study the possible association between the level of fluoride exposure and the prevalence of bicytopenia and pancytopenia.

Establishing Clinical and Nutritional Risk Factors: Understanding the clinical and nutritional risk factors in children presenting with bicytopenia/pancytopenia will help in understanding the causes and factors related to them. This involves assessing food consumption patterns, nutritional status, and any nutrient deficiencies that may increase children's susceptibility to these hematological disorders.

Exploring Fluoride-Cytopenia Relationship: It is crucial to investigate the relationship between exposure to fluoride and cytopenia, especially in regions like Kolar where fluorosis is reported. This can assist in the formulation of specific strategies for preventing the effects of high fluoride content on children's health in the district. It may also help to elucidate this relation shed light on possible mechanisms through which fluoride influences hematopoiesis.

Significance of the Study

This study is of immense importance because it seeks to solve some of the major knowledge deficiencies on bicytopenia and pancytopenia in children, especially in the context of environment and food insecurity that is rampant in the developing world. Thus, based on the clinical and nutritional risk factors defined, practitioners can recognize the children at risk and potentially modify the outcomes in favor of the kids through early intervention and nutrition support and care.

Studying the correlation between cytopenia and fluoride could prove to be valuable in improving public health. If such a relation is established, it would call for methods of minimization of fluoride exposure and recommendations on the management of the affected groups.

Thus, the present study aims to improve the comprehensiveness of diagnosing and managing bicytopenia and pancytopenia in children with a special emphasis on the regions like Kolar experiencing endemic problems like fluorosis.

These results are anticipated to aid in the formulation of management protocols and other health interventions for the specific regions hence enhancing patient care.

AIMS & OBJECTIVES

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AIMS & OBJECTIVES

1. To study the occurrence rate of bicytopenia/pancytopenia in children aged from 1 year to 18 years.
2. To study the clinical and laboratory profile of bicytopenia/pancytopenia in children aged from 1 year to 18 years.
3. To study the correlation between fluoride and bicytopenia/pancytopenia-

REVIEW OF LITERATURE

A decorative graphic consisting of a thick horizontal line and a thick vertical line intersecting at a right angle. The horizontal line is positioned below the text 'LITERATURE' and extends across the width of the page. The vertical line is positioned to the right of the text and extends upwards and downwards from the horizontal line.

REVIEW OF LITERATURE

Bicytopenia and pancytopenia are critical hematological alterations involving decrease of two or all the three blood constituent, namely erythrocytes, leukocytes, and thrombocytes. These conditions represent underlying pathologies that can be from benign to lethal; infections, nutritional deficiencies, bone marrow diseases, and malignancies. Knowledge of these conditions' clinical and laboratory characteristics are important for diagnosis and management as the clinical features may be somewhat non-specific and atypical, especially in children.

The rate and causes of bicytopenia and pancytopenia differ from country to country depending on the health care system, the prevalence of infections, nutritional status and genetic predisposition. The objective of this study is to describe the clinical, laboratory features of paediatric bicytopenia/pancytopenia patients in a tertiary care centre at Kolar and to make a better approach to diagnosis and management in similar institution.

Bicytopenia and pancytopenia are major hematological problems in pediatric patients, and because of this, there is a need to review the various causes, clinical features, and diagnostic approaches to these conditions. From an analysis of the available literature it is possible to deduce a complex picture characterized by many antecedents and various diagnostic approaches.

ETIOLOGICAL SPECTRUM

The etiology of bicytopenia and pancytopenia is diverse and includes many hematological diseases ranging from the benign to the frankly malignant. The studies done by Lalita Wadhwa et al and Renu Thambi et al pointed out that the main reason behind bicytopenia

was Acute Lymphoblastic Leukemia; aplastic anemia was recognized most commonly in cases of pancytopenia ^(8,9). Furthermore, Rohan D Venkat et al.'s research also pointed out that infectious diseases, acute leukemia, and aplastic anemia are critical causes of bicytopenia and pancytopenia, effectively stressing the variety of aetiologies ⁽¹⁰⁾.

In addition, Naseem et al. and Pankaj Katoch et al drawn out distinct clinical feature that include splenomegaly, lymphadenopathy and circulating blasts to help in diagnosing and predicting bicytopenia and pancytopenia in pediatric patients ^(11,12). These studies demonstrate that a clinical evaluation is indicative of the therapeutic approach to be taken.

Infections are known to cause bicytopenia and pancytopenia in children more often, especially in developing countries. Tuberculosis and sepsis are other causes of these hematological changes either by direct invasion of the bone marrow or through cytokine release.

Nutritional Deficiencies:

Deficiency of nutrients such as vitamin B12, folate, and iron has been identified as real causes of pancytopenia in children ^(13,14). Keisu and Ost stressed that deficiencies mentioned should be identified at an early stage and supplemented to avoid hematological complications. Moreover, Gupta et al, and Kumar et al also observed that megaloblastic anemias because of nutritional deficiencies were one of the common causes of pancytopenia as identified in developing regions ^(5,15).

Megaloblastic anemia was noted to be one of the main causes of pancytopenia in children from India; the authors underlined the role of nutritional deficiencies. These deficiencies lead to poor erythropoiesis and consequently pancytopenia, which can be corrected with supplementation.

Infectious Causes:

Infectious diseases remain a primary causative agent of bicytopenia and pancytopenia in children. Memon et al. and Jha et al. concluded that the hematological disorders in children were attributed to several infections like enteric fever malaria and viral infections ^(16,4). In addition, Patra et al have emphasized on the early diagnosis and treatment of the infective agents like malaria and dengue in endemic area to avoid the severe consequences related to bicytopenia and pancytopenia ⁽¹⁷⁾.

Bone Marrow Disorders:

Aplastic anemia is characterized by decreased bone marrow cellularity as well as pancytopenia, and it can be acquired or induced by drugs, chemicals, or infections. Myelodysplastic syndromes, though are not very common in children, are characterized by the dysplasia of the hematopoietic cells and ineffective haematopoiesis resulting in pancytopenia.

Malignancies:

Leukaemia and Lymphoma are common causes of pancytopenia because they affect normal production of blood cells by infiltrating the bone marrow and displacing the normal stem cells. Again, leukaemia shows pancytopenia in a large number of cases in children, and hence, needs early diagnosis and intervention.

Environmental Factors:

Several external conditions, including high levels of fluoride intake, have been reported to cause hematological toxicity in children. Research by Krishnamurthy P. et al. and Deepika R et al. established that the hematological parameters were significantly altered due to the

chronic exposure to fluoride intending that regular evaluation and intervention in such areas is essential to avoid hematopoietic disorders ^(18,19).

CLINICAL PRESENTATIONS

Peripheral cytopenia in children, especially bicytopenia and pancytopenia are quite complex disorders emanating from an array of causes, and the presence of which has the potential to cause severe complications. In a clinical setting, the integration of clinical and laboratory data is fundamental in making proper diagnosis and planning for management ⁽²⁰⁾.

The clinical features of bicytopenia or pancytopenia in pediatric patients are varied due to the various pathological process.

Key clinical features include:

Pallor and Fatigue:

Anemia, which is a decrease in red blood cells, symptoms include pale skin, fatigue and general weakness. Some of the symptoms that can be observed in children include; lethargy, irritability, and poor appetite. These symptoms can be rather disruptive on the day-to-day functioning and growth of an individual.

Bleeding Tendencies:

Thrombocytopenia, or low platelet count, can result in bleeding manifestations such as petechiae, purpura, epistaxis, gum bleeding, and prolonged bleeding from minor cuts. Severe cases may lead to life-threatening hemorrhages, including gastrointestinal or intracranial bleeding ⁽²⁾. Parents may report frequent nosebleeds or prolonged bleeding from minor injuries.

Infections:

Leukopenia, particularly neutropenia, increases susceptibility to infections. Symptoms can range from mild respiratory infections to severe, life-threatening sepsis. Recurrent infections, such as otitis media, pneumonia, or skin infections, are common presenting complaints.

Hepatosplenomegaly and Lymphadenopathy:

Enlargement of the liver and spleen (hepatosplenomegaly) and swollen lymph nodes (lymphadenopathy) are common in hematological malignancies, chronic infections, and storage diseases. These findings may manifest during physical examination and are commonly linked with systemic symptoms like fever and weight loss ⁽⁴⁾.

Fever:

Persistent or recurrent fever can indicate underlying infection, malignancy, or inflammatory conditions such as systemic lupus erythematosus (SLE). Fever without a clear source often prompts further investigation for cytopenias.

Bone Pain:

Such symptoms like bone pain or arthralgia are most commonly observed in children with leukemia or other malignancies. This pain may lead to misdiagnosis as rheumatic condition at the onset of the disease. The pain is described as deep, constant and more severe at night.

Nutritional Deficiencies:

Some of the clinical signs include glossitis, angular cheilitis, and koilonychia which indicate nutritional deficiencies. Details of a diet enquiry that indicates inadequate intake of these vitamins can also be used to corroborate the diagnosis ⁽⁷⁾.

Growth Retardation and Developmental Delays:

Cytopenias in chronic conditions that cause the reduction of any of the formed elements of the blood can also impair growth and development. Children may develop poor growth and development, failure to thrive, delayed development, and poor school performance as a result of recurrent illnesses and chronic anemia.

Pancytopenia and bicytopenia clinical symptoms are directly associated with a shortage of certain cell lines. The manifestations of this disease include anemia which presents in pallor and fatigue, leukopenia that presents in recurrent infections, and thrombocytopenia that presents in bleeding tendencies. Pallor and fever were reported to be the most common initial signs in pediatric patients with pancytopenia by Varma and Dash and were accompanied by bleeding manifestations including petechiae, ecchymoses and epistaxis in some cases ⁽¹⁰⁾.

PHYSICAL EXAMINATION FINDINGS

The physical examination is mandatory while handling bicytopenia or pancytopenia in children to look for features that may indicate the causative factors. It is therefore important to do a detailed and methodical assessment as this can provide some pointers and lead to the next level of investigation. Here we elaborate on key physical findings:

1.GENERAL APPEARANCE

Growth and Development

Growth Parameters: Comparison of height, weight, and head circumference with the age-specific percentile charts helps in identifying any variation in growth trends. Other diseases which have got long term effects include nutritional deficiencies, chronic infections or congenital marrow failure syndromes have classically associated with failure to thrive or stunted growth ⁽²⁾.

Developmental Milestones: This involves checking on the skills the child is able to develop in areas of motor development, language skills and social development to determine if the child is within the normal range. Developmental milestones that are delayed may point to chronic systemic illness or particular syndromic disorders.

Vital Signs

Vital signs are critical indicators of the child's physiological status and can reveal compensatory mechanisms or acute decompensations:

Temperature: Fever is often associated with an infection or inflammation and is seen in children with immunosuppression as seen in the case of pancytopenia.

Heart Rate: Tachycardia is one of the most frequent compensatory mechanisms in anemia because the body strives to keep up the delivery of oxygen. Tachycardia may also be associated with severe dehydration or sepsis which is a systemic infection.

Respiratory Rate: Tachypnea may be observed as the body tries to compensate for the effects of severe anemia by increasing the rate of breathing in order to increase the amount of oxygen that is inhaled and delivered to the body tissues

Nutritional Deficiencies: Blood Pressure: Low BP can be due to anemia, poor fluid status, or sepsis and will need management ⁽⁷⁾.

1. SKIN & MUCOUS MEMBRANES

Pallor

Paleness is clinical sign of anemia, which includes a diminished number of red blood cells or the level of hemoglobin. It can be assessed at multiple sites and all these sites are informative in diagnosing the disease.

Skin

Generalized Pallor: Generalized pallor is best assessed in natural light as this will reveal the client's true skin tone.

Significance: The existence of pallor, whereas it is generalized, may indicate that the client could be experiencing low hemoglobin levels. This is a characteristic feature of anaemia, which can result from a variety of conditions that include, nutritional deficiencies, bone marrow dysfunctions, chronic diseases, or acute blood loss.

Conjunctivae

Clinical Relevance: It should be noted that the inspection of conjunctivae for pallor is a fast and accurate way of diagnosing anemia. Thus, severe pallor indicated a reduction in hemoglobin levels here and requires a complete blood count (CBC) to determine the presence and severity of anemia accurately. This assessment is particularly useful in the first clinical encounter with a patient as it offers a relatively crude but instantaneous estimation of the patient's haemoglobin levels.

Nail Beds and Palmar Creases

Clinical Importance: The ability to note pallor in these areas is useful in confirming the clinical suspicion of anemia and triggers laboratory workup to identify its cause and management plan ⁽¹⁵⁾.

Petechiae and Purpura

Petechiae and purpura are two vital clinical signs that suggest thrombocytopenia or other coagulopathies. They require early assessment to identify the cause and to start relevant interventions.

Petechiae

Characteristics: Petechiae are pinpoint hemorrhages that are less than 3mm in size and are red or purple in colour and do not fade when pressure is applied. These usually develop on the limbs but can be located in any part of the body.

Pathophysiology: Petechiae are produced by pin-point hemorrhages because of a platelet count below 50,000/ μ L. The capillaries become weakened and rupture and blood leaks out onto the skin or the lining of the mouth and throat.

Clinical Relevance: With the evidence of petechiae, the count of platelets is most probably decreased and requires immediate assessment. Possible reasons include viruses, hypoplastic anemias, ITP, and other hematological diseases.

Purpura

Characteristics: Petechiae are smaller in size than purpura, which are more than 3 mm and also non-blanching. It can affect any part of the body; however, they are common on the legs and the buttocks.

Clinical Significance: Petechiae are smaller spots compared to purpura, and the latter points at a more significant thrombocytopenia or coagulation deficit. If purpura is present, especially with other bleeding signs, a detailed evaluation should be initiated to avoid the development of severe bleeding events.

Ecchymoses

Another very significant symptom of thrombocytopenia or clotting problems is ecchymoses, or large bruises. They give information on the degree and distribution of the primary hemostatic derangement.

Clinical Relevance: In cases where ecchymoses develop without cause or with minor trauma, then it may be an indication of serious hemostatic disorders. This can be due to the patient having a very low platelet count, the deficiency of some known clotting factors, or some diseases that alter the coagulation process.

The complete physical examination of the pediatric patients diagnosed with bicytopenia or pancytopenia offers valuable information concerning the severity of the disease and potential causes. These clinical findings are poor colour, skin bleeding spots, and large bruises which help direct any additional diagnostic tests and clinical management. Since these signs are indicative of critical situations, early and accurate recognition of these signs will go along way in influencing the outcome of the patient by facilitating timely and adequate measures to be taken ⁽²⁰⁾.

2. HEAD, EYES, EARS, NOSE, and THROAT (HEENT)

Conjunctival Pallor

Clinical Significance

Indicator of Anemia: Conjunctiva pallor is a clinical sign that is very accurate when diagnosing anemia in the patient. The most important of them reveal decreased hemoglobin concentration and oxygen transport capacity of the blood.

Severity of Anemia: Conjunctival pallor can be regarded as the indicator of anemia while the degree of pallor is related to the severity of the anemia. Pallor of grade 3 is indicative of a patient's hemoglobin level being far below the normal level and could be due to acute or chronic bleeding, malnutrition or hematologic diseases.

Diagnostic Implications

Prompt Further Investigation: Thus, conjunctival pallor deserves further examination to prove the hypothesis of anemia and estimate the degree of RBC operation reduction by performing CBC.

Monitoring Response to Treatment: Recurrence of the condition is assessed through the re-examination of conjunctival pallor as a means of evaluating the effectiveness of the treatment in anemic patients. Change in the pallor towards the better demonstrates the correction of the actual cause of the state or the effect of therapeutic measures ⁽²¹⁾.

Oral Mucosa

Inspection of the Oral Cavity

The assessment of the patient's oral cavity is useful in assessing their general health status and can indicate specific signs that point towards particular diseases.

Petechiae, Bleeding Gums, and Ulcerations

Signs of Thrombocytopenia: Petechiae, minor hemorrhages manifested as small red or purple spots, may be seen on the mucosa of the mouth. They are due to the dysfunction or lack of platelets and are suggestive of thrombocytopenia or any other coagulation disorders. Also, gum hemorrhage and mucosal ulcerations may be observed, particularly in the severe form of the disease.

Clinical Implications: These results justify the need for the evaluation of the underlying cause of thrombocytopenia to avoid bleeding complications.

Gingival Hypertrophy

Diagnostic Clue: Thus, gingival hypertrophy in a child should raise the clinician's index of suspicion for an underlying hematologic malignancy and subsequent investigations such as the peripheral blood smear and possibly bone marrow examination.

Glossitis

Indicator of Nutritional Deficiencies: Several medical conditions can cause glossitis, which is the inflammation of the tongue, including a lack of sufficient vitamins or minerals, like vitamin B12 or iron.

Diagnostic Significance: After identifying the presence of glossitis, a patient should be assessed for nutrients deficiencies and, if necessary, recommended supplements or changes in the diet.

3. LYMPHATIC SYSTEM

Lymphadenopathy

Clinical Examination

Lymphadenopathy is an abnormal increase in the size of the lymph nodes, and can be felt during general assessment done via physical examination. Lymph node examination entails determination of node size, texture, ability to move independently of overlying tissue, and their level of tender ness which offer key diagnostic leads regarding the aetiology ⁽²²⁾.

Diagnostic Evaluation

Laboratory Tests: Preliminary laboratory examination should include complete blood count, inflammatory markers such as C-reactive protein, and erythrocyte sedimentation rate, and serological tests in cases of certain infections.

Imaging Studies: Imaging techniques include ultrasonography, CT or MRI to determine size, location and internal texture of enlarged lymph nodes and the presence of other pathologies in the surrounding structures.

Fine-Needle aspiration (FNA) or Biopsy: If malignancy is suspected, FNA or biopsy of the lymph node might be carried out for histopathological examination and conclusive diagnosis (23).

Clinical Significance

Lymphadenopathy in bicytopenia or pancytopenia patients indicates the need for further investigation to establish the cause in pediatric patients. Most of the patients who present with enlarged lymph nodes have non-neoplastic, self-limiting conditions; however, any worrisome characteristics or symptoms suggest that one should perform additional evaluations to exclude malignant causes. That is why timely diagnosis and initiation of the right course of treatment are vital to the best result and to avoiding possible adverse effects.

4.ABDOMEN

Hepatomegaly

Clinical Significance:

Hepatomegaly is an enlarged liver that can be caused by a wide range of diseases.

In patients with bicytopenia or pancytopenia and hepatomegaly, there are possibilities of infiltrative diseases such as leukemia or lymphoma, storage disorders like Gaucher disease, chronic bacterial or viral infections like viral hepatitis, or metabolic disorders.

Differential Diagnosis:

Hematologic Malignancies: Leukemia and lymphoma can invade the liver and cause it to be enlarged, hence the term hepatomegaly. The presence of other hematologic abnormalities like cytopenias may help in the diagnosis.

Infections: Hepatomegaly can be caused by chronic viral hepatitis for example hepatitis B or hepatitis C through inflammation and liver damage. Other infective disorders like tuberculosis, schistosomiasis, and others may also cause hepatomegaly.

Storage Disorders: Some auto-immune diseases such as Gaucher disease or Niemann-Pick disease that are inherited can lead to hepatomegaly due to accumulation of substances that are not supposed to be there in liver cells.

Splenomegaly

Clinical Significance:

For bicytopenia or pancytopenia in pediatric patients, splenomegaly is seen and reflects many causes.

The possible origins of splenomegaly are infection – malaria or Epstein-Barr virus, hematological malignancy such as leukemia and lymphoma, autoimmune diseases like autoimmune hemolytic anemia, hypersplenism.

Differential Diagnosis:

Infections: Bacterial and viral diseases like malaria and infectious mononucleosis caused by Epstein-Barr virus are leading causes of splenomegaly caused by splenic hyperplasia in response to diseases causing antigen stimulation.

Hematologic Malignancies: Leukemia and lymphoma can invade the splenic tissue thus making the spleen enlarged. The presence of other haematologic diseases, particularly of other cytopenias, can be helpful in the diagnosis.

Autoimmune Disorders: Autoimmune hemolytic anemia or systemic lupus erythematosus are examples of diseases that can lead to splenomegaly due to involvement of the spleen as well as immune-mediated destruction of cells.

Hypersplenism: Hypersplenism is the common cause of splenomegaly; here there is pooling as well as destruction of the blood cells in the spleen resulting in cytopenia.

Diagnostic Evaluation:

Imaging Studies: An abdominal ultrasound or CT scan can help to establish the existence of hepatomegaly or splenomegaly, their size and features as well as presence of other pathological changes.

Laboratory Tests: CBC with peripheral blood smear will help in assessing cytopenias and any kind of blood cell abnormality. Infectious or inflammatory etiology can be discovered using liver function tests and serologies ⁽²⁴⁾.

Clinical Management:

Such treatment plans may encompass aetiology control, which entails treating the primary condition, such as chemotherapy for leukaemia; countermeasures, which focuses on treating the disease's effects like transfusion of blood for anaemia; and support care, which includes procedures like splenectomy for hypersplenism.

Engagement and a review are crucial in evaluating the outcomes of the treatment, dealing with the side effects, and improving the quality of service.

4. CARDIOVASCULAR & RESPIRATORY SYSTEMS

CARDIAC EXAMINATION:

A comprehensive assessment of the cardiovascular system is essential in pediatric patients with bicytopenia or pancytopenia to identify potential complications related to anemia:

Bounding Pulse:

Clinical Significance: Compensatory hyperdynamic circulation generated by anemia such as low viscosity and high output can cause a bounding pulse. This is a compensatory mechanism that tries to ensure that tissues are adequately supplied even when oxygen-carrying capacity is low.

Systolic Flow Murmur:

In severe anemia, there is an increased blood flow through the cardiac chambers manifesting in turbulent flow, which in turn causes systolic flow murmur. It is best heard over the left sternal border, and sometimes, there may be other signs of an increased cardiac output ⁽²⁵⁾.

Signs of High-Output Heart Failure:

Clinical Significance: When anemia is profound, heart failure starts manifesting the symptoms such as tachycardia, cardiomegaly, and pulmonary congestion known as high-output heart failure. Symptoms may be shortness of breath, difficulty breathing when lying down, and swelling of the lower limbs in the worse-off patients.

RESPIRATORY EXAMINATION:

Tachypnea:

Clinical Significance: In severe anemia tachypnea may be seen as a compensatory measure to enhance the delivery of oxygen to the tissues. It assists in keeping sufficient oxygen supply

even if the oxygen-carrying capacity has declined. Nevertheless, the clinician should be able to distinguish between tachypnea due to anemia and tachypnea due to other conditions such as pneumonia or acute respiratory distress syndrome (ARDS).

Respiratory Infections:

Clinical Significance: The common clinical manifestations of bacterial and fungal respiratory infections include respiratory distress, crackles, or reduced breath sounds when ausculted. Efficient diagnosis and management of respiratory infections are important to prevent their progression and enhance results.

5. MUSCULOSKELETAL SYSTEMS

Bone Tenderness:

Clinical Significance:

Generalized or Localized Bone Pain: Patients can be affected by moderate to severe bone pain that may be diffuse or localized and bone tenderness especially in the long bones. This sign usually points to the fact that the patient has bone marrow infiltration by leukemia or other types of cancer.

Marrow Expansion and Infiltration: In conditions like leukemia, there is a formation of new blood cells hematopoietic cells within the bone marrow hence making the bones tender. The pressure in the cavity of the bone marrow also results in pain and discomfort.

Joint Swelling:

Clinical Significance:

Autoimmune Conditions: Oedema and pain in joints are inflammatory signs that are commonly found in autoimmune diseases for instance JIA. In JIA, the immune system goes

on to attack the synovium thus causing inflammation, accumulation of fluid within the joint and consequently joint enlargement. Cytopenias are also observed in patients with JIA and this proves that the disease is systemic in nature.

Differential Diagnosis:

Bone Tenderness: In pediatric cases with bicytopenia or pancytopenia, bone tenderness should be considered a manifestation of hematologic malignancies like leukemia or myelodysplastic syndromes. Other forms of bone pain including; infections with the bone (osteomyelitis), metabolism abnormalities (osteoporosis) or injuries (fractures) should also be considered.

Joint Swelling: Possible cases of joint swelling in pediatric patients with cytopenias include autoimmune diseases, infectious arthritis (for example, bacterial arthritis), and reactive arthritis. Review of the patient's medical record, laboratory data, and imaging contribute to the identification of the aetiology of joint oedema.

6. NEUROLOGICAL EXAMINATIONS

Neurological Deficits:

Clinical Manifestations:

Headache: Severely anemic patients of pediatric age may complain of head aches as a result of low oxygen carrying capacity to the brain. Headaches can be of pressing, throbbing or pounding in character and become worse on movement or exercise.

Syncope: Most severe anemia cases may be accompanied by syncope or fainting, as the blood flow to the brain reduces to critical levels. These include light headedness, diaphoresis and visual changes in the form of blurring of vision before the onset of the event.

Confusion or Lethargy: Severe anemia can cause the brain to become damaged due to lack of oxygen and the possible symptoms are confusion or lethargy. The patients' neurological signs and symptoms may include confusion, orientation dysfunction, or lethargy.

Peripheral Neuropathy:

Etiology: Deficiency of vitamin B12 that is often related to megaloblastic anemia affects nerves and myelin formation because of their dependence on the vitamin.

Clinical Presentation: Vitamin B12 deficiency in pediatric patients may manifest as paresthesia (tingling/numbness) in the extremities, abnormal gait, muscle weakness and diminished reflexes.

Examination Findings: Physical examination may also show signs of peripheral neuropathy such as; reduced sensitivity to light touch, impaired position sense, and decreased vibration sense.

Comprehensive Physical Examination:

Focus on Identifying Specific Etiologies:

Pediatric patients who present with bicytopenia or pancytopenia undergo a complete physical examination of their general well-being, vital signs, skin, mucous membranes, lymphatic system, abdominal examination, cardiovascular and respiratory system, musculoskeletal system and neurological system.

Assessment data in the context of specific physical abnormalities help in discovering clues of possible causes, including hematologic malignancies, autoimmune diseases, malnutrition, or infections.

Guide Further Diagnostic Tests:

The results of examinations are considered as the significant hints that help to choose the right diagnostic tests, including the laboratory tests (CBC, peripheral blood smear, bone marrow aspiration), imaging tests (ultrasound, CT), and other tests (rheumatologic panels, autoimmune markers).

Facilitate Differential Diagnosis:

Systematic approach to the physical examination enables exclusion or inclusion of certain causes of the symptoms on the basis of physical signs and symptoms manifested by the patient.

Algorithms are made more specific based on clinical examination and investigations such as laboratory and imaging, thus making the approaches to management more individualized.

Early Recognition and Intervention:

Any physical sign suggestive of bicytopenia or pancytopenia should be recognized early so that appropriate management could be instituted.

The early and accurate diagnosis, as well as the subsequent management of the patient, are critical to the improvement in patient-prognosis and reduction of complications, including long-term consequences of hematologic disorders and comorbid conditions.

The physical assessment of children, presenting with bicytopenia or pancytopenia, is thus crucial in evaluating possible causes, suggesting investigations, and providing timely management to enhance both the patients' prognosis and reduce complications ⁽²⁶⁾.

Laboratory Findings

Complete Blood Count and Peripheral Smear

CBC is the first investigation performed in bicytopenia and pancytopenia, which shows the severity of cytopenias. A peripheral blood smear may also give suggestions to the cause such as the blasts seen in leukemia cases or the hypersegmented neutrophils in megaloblastic anemia ⁽²¹⁾.

Bone Marrow Examination

Definitive diagnosis cannot be made without BM aspiration and biopsy. Hypocellular marrow is seen in aplastic anemia while hypercellularity with abnormal cellularity suggests myelodysplastic syndrome or megaloblastic anemia. It also becomes possible to determine the presence of malignant infiltration in leukemia and lymphoma through bone marrow examination ⁽²⁶⁾.

Regional Studies and Epidemiology

A limited number of papers have addressed the Indian pediatric population in the context of semi-urban or rural environments. Gayathri and Rao investigated a study on the children of a rural tertiary care center in South India where the major causative factors of pancytopenia included infections and nutritional deficiencies⁽²⁵⁾. This regional data is essential for developing diagnostic and management approaches to the problems of this healthcare system.

Treatment and Management

Addressing Underlying Causes

The management of bicytopenia and pancytopenia includes eliminating the cause of the disorder. Infections call for use of antibiotics/ antimicrobials while malnutrition calls for use of supplements. In some cases of BMFS, immunosuppressive therapy and/or hematopoietic stem cell transplantation may be necessary.

Supportive Care

Symptom management and prevention of complications are the main facets of supportive care. These are for example; red blood cell transfusions for severe anaemia, platelet transfusions for profound thrombocytopenia, and prophylactic antibiotics for neutropenia. Supervision and management of these patients are more sensitive in pediatric patients mainly because of their susceptibility to clinical deterioration.

Diagnostic Techniques:

In diagnosing the bicytopenia and pancytopenia in pediatrics, bone marrow examination and other diagnostic tests are vital in identifying the cause of the disorders. Williams DM also stressed the importance of bone marrow evaluation in defining the clinicohematological status and directing the management plans ⁽²⁾. In the same regard, Niazi M et al. have also emphasized on the value of bone marrow in diagnosing a host of underlying causes from megaloblastic anemia to leukemia in children with pancytopenia ⁽²⁰⁾.

Fluoride Levels:

Fluoride Exposure (1 - 1.5 ppm):

Health Effects: Generally, mild fluoride exposure is considered safe and beneficial for dental health, helping to prevent tooth decay. However, chronic exposure, even at low levels, may result in dental fluorosis, which is marked by dentine discoloration.

Children's Susceptibility: Children, being more susceptible to fluoride, may exhibit mild dental fluorosis, which manifests as faint white lines or streaks on teeth, even with low levels of exposure.

Fluoride Exposure (1.6 - 2 ppm):

- **Health Effects:** Moderate fluoride exposure can lead to dental fluorosis with more noticeable changes in the appearance of teeth, such as yellow or brown discolouration. It can also start affecting bone density and structure in some sensitive individuals.
- Fluoride supplements and dental products should be managed carefully in these regions with naturally moderate fluoride levels in water to prevent overexposure. This includes monitoring the use of fluoridated toothpaste and mouth rinses, especially in children⁽¹⁸⁾.

Fluoride Exposure (>2 ppm):

- **Health Effects:** Severe fluoride exposure is associated with both dental and skeletal fluorosis. Dental fluorosis can range from mild discoloration to severe enamel damage. Skeletal fluorosis can cause joint pain, stiffness, and in severe cases, deformities and significant impairment of movement⁽¹⁹⁾.

- **Non Skeletal fluorosis:**

- Fluoride exposure can cause damage to :

Skeletal muscles and ligaments.

Erythrocytes.

Thyroid gland.

Gastrointestinal mucosa.

Easy fatigability⁽¹⁸⁾.

The reviewed literature underscores the intricate interplay of factors contributing to bicytopenia and pancytopenia in pediatric patients. From infectious diseases to nutritional deficiencies and environmental toxins, a comprehensive understanding of these diverse etiologies is essential for accurate diagnosis and effective management. Further research and clinical studies are warranted to explore emerging trends and refine diagnostic and therapeutic approaches in the management of these hematological disorders.

MATERIALS &

METHODS

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MATERIALS & METHODS

Source of data: All children aged between (1-18yrs) were hospitalized at RL Jalappa hospital during the period of study and consented to be a part of the study.

Study design: Cross-sectional study.

Study period: 1 year from September 2022 to December 2023

Method of collection of data:

Inclusion Criteria:

All children aged from 1 year to 18 years hospitalized at RL Jalappa Hospital who had consented to be a part in the study and fit in two or more of the following criteria.

- a. Haemoglobin less than normal based on WHO criteria for Anaemia and Grade of severity:
- b. White Blood Cell count $<4 \times 10^9 / L$
- c. Platelet count $< 1500 \times 10^9 / L$

Criteria used for diagnosing anaemia:-WHO Criteria for Anaemia and Grade of severity:

	Population	Non-Anemia (Gm/dL)	Anemia (Gm/dL)		
			Mild	Moderate	Severe
1.	Children 6-59 months of age	11	10.0-10.9	7.0-9.9	<7.0
2.	Children 5-11 years of age	11.5	11.0-11.4	8.0-10.9	<8.0
3.	Children 12-14 years of age	12	11.0-11.9	8.0-10.9	<8.0
4.	Non-pregnant women (15 years of age and above)	12	11.0-11.9	8.0-10.9	<8.0
5.	Pregnant women	11	10.0-10.9	7.0-9.9	<7.0
6.	Men (15 years of age and above)	13	11.0-12.9	8.0-10.9	<8.0

Exclusion Criteria:

- H/o blood transfusion in past 1 month.

Sample size: The sample size was determined based on the prevalence of megaloblastic anemia among children aged 6 months to 18 years with bicytopenia or pancytopenia, which was found to be 12.64% in the study conducted by Rohan D Venkat et al., using the appropriate formula.

$$\text{Sample Size} = \frac{Z_{1-\alpha/2}^2 P(1-P)}{d^2}$$

$Z_{1-\alpha/2}$ is the standard normal variate used for a 5% type 1 error ($P < 0.05$), where it equals 1.96. This value is commonly used in formulas since P values below 0.05 are typically considered significant in the majority of studies.

The parameter P represents the expected proportion in the population based on previous studies or pilot studies, while d denotes the absolute error or precision

$$P = 12.64\% \text{ or } 0.1264$$

$$q = 87.36\% \text{ or } 0.8736$$

$$d = 7.5\% \text{ or } 0.075$$

Based on the values above and a 95% confidence level, our study includes a sample size of 76 subjects with bicytopenia or pancytopenia. Accounting for a 10% non-response rate, approximately 84 subjects enrolled in the study.

Study Method:

This study started after obtaining consent from the child and parents.

All children fulfilling the inclusion criteria were included in the study.

History taken includes family history, trauma , long-term illness, inherited defects, socio-economic status according to modified kuppuswamy classification .

A clinical examination of every child was done for features of bicytopenia or pancytopenia.

All anthropometric parameters were measured to rule out malnutrition.

WEIGHT- Weight will be measured using a digital weighing machine.

LENGTH(in <1 year old)-Stadiometer is used to measure the length.

Height (>2 years)

BMI – BMI is calculated by dividing body mass in kilograms by the square of body height in meters, resulting in units of kg/m². It serves as a convenient method to broadly classify individuals into underweight, normal weight, overweight, or obese categories based on their body mass relative to height.

Basic haematological investigations such as complete hemogram, peripheral smear and Reticulocyte count were done by standard methodology.

Serum vitamin B12, serum folic acid, and serum iron profile were sent based on MCV.

Investigations to rule out IDA was done in case of low MCV, and investigations to rule out folate and vitamin B12 deficiency was done in case of high MCV.

Urine fluoride levels were estimated for all the patients admitted and done by Orion Thermo Scientific Fischer, Ion Selective Electrode (ISE) at the Department of Biochemistry SDUMC to rule out any correlation with cytopenias.

The peripheral smear was undergone staining with Leishman's stain for morphological classification of anemia based on smear findings. Automated cell counters determine PCV, MCV, MCH, MCHC, and RDW, with normal values as follows: PCV 35-45%, MCV 77-95

fl, MCH 25-33 pg, MCHC 31-37 gm/dl, and RDW 14.5-18.5. Reticulocyte count was conducted by using the Brilliant crystal stain method, while serum iron levels were assessed via Ramany's dipyridyl method and total iron binding capacity via Ramsay's method. Serum vitamin B12 and folic acid levels were measured using the Architect method.

Bone marrow aspiration and biopsy was performed in cases of unexplained pancytopenia or aplastic anemia, upon patient or attendant consent, to aid in diagnosing the condition. Bone marrow aspirate smears and trephine biopsies were stained with May-Grunwald Giemsa and hematoxylin and eosin. Additional staining methods including myeloperoxidase, Sudan black B, periodic acid Schiff, and Perl's stain were applied to aspirate smears, while reticulin stain was used on biopsy samples⁽⁸⁾. Stained slides were analyzed for bone marrow cellularity, structure, focal lesions, and the presence of marrow fibrosis.

Statistical analysis: The data was entered into a Microsoft Excel spreadsheet and analyzed using SPSS version 22 software. Categorical data was summarized as frequencies and proportions, with significance assessed using the Chi-square test. Continuous variables were reported as mean and standard deviation and differences between means were evaluated using the Independent t-test. Statistical significance was determined by a p-value of less than 0.05.

Laboratory Investigations:

- complete hemogram
- peripheral smear
- serum vitamin B12
- serum folic acid
- serum iron profile
- urine fluoride levels
- bone marrow examination (if indicated)

RESULTS

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RESULTS

Table 1: Cytopenia Distribution

Among the 84 pediatric patients included in this study, 76 (90.5%) presented with bicytopenia, while 8 patients (9.5%) exhibited pancytopenia. This distribution indicates a predominant occurrence of dual cytopenias within the cohort, reflecting the complexity and multisystem involvement often associated with these conditions.

Cytopenia	No.of Patients	Percentage
Pancytopenia	8	9.5%
Bicytopenia	76	90.5%
Total	84	100%

Fig.1: Cytopenia Distribution

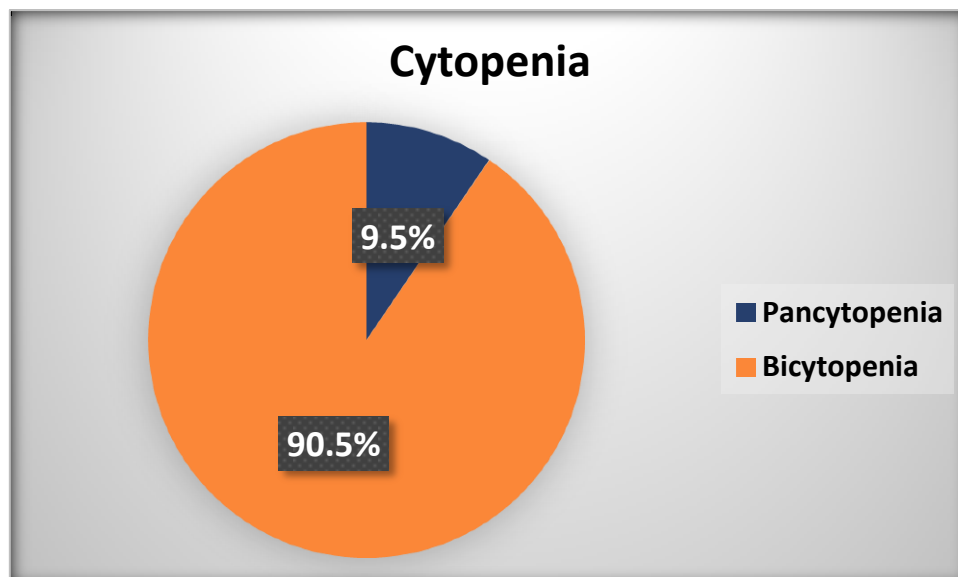


Table 2: Gender Distribution in Cytopenia

Gender-specific analysis revealed that out of 84 patients, 47 (55.9%) were male and 37 (44.1%) were female. Out of the total patients diagnosed with pancytopenia, distribution of gender were 5 patients (62.5%) male and 3 patients (37.5%) female. In contrast, among those with bicytopenia, 42 patients (55.3%) were male and 34 patients (44.7%) were female.

Gender	Pancytopenia	Bicytopenia	Total
Male	5	42	47 (55.9%)
Female	3	34	37 (44.1%)
Total	8	76	84 (100%)

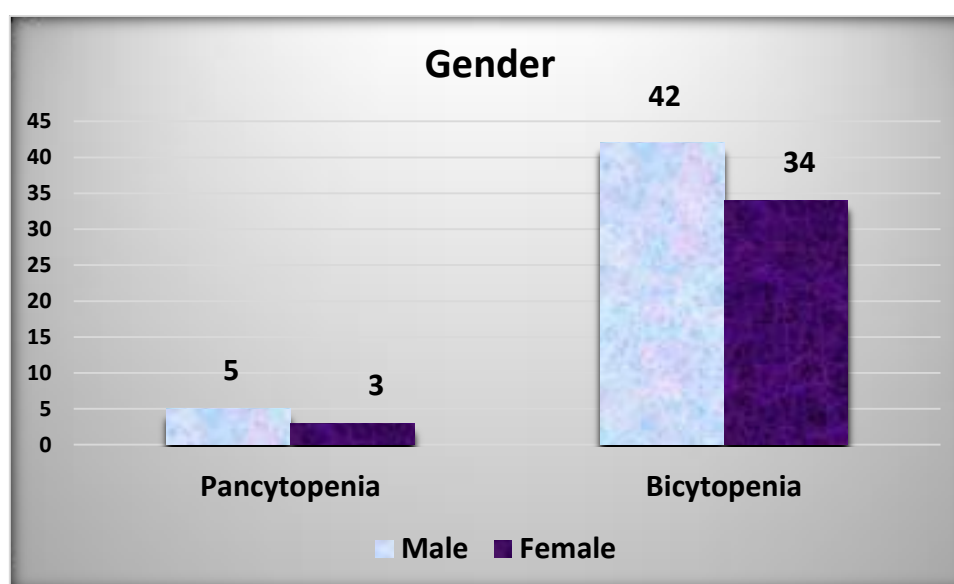
Fig.2: Gender Distribution in Cytopenia

Table 3: Age and Cytopenia

Analysing the distribution across different age groups, it was found that among toddlers (1-3 years), 1 patient (12.5%) presented with pancytopenia and 7 patients (87.5%) with bicytopenia. In the preschool group (3-6 year), 2 patients (40%) had pancytopenia and 3 patients (60%) had bicytopenia. Among school age group children (6-12 years), 3 patients (10%) had pancytopenia and 27 patients (90%) had bicytopenia. Of the adolescent patients (12-18 years), 2 (4.9%) had pancytopenia while 39 (95.1%) had bicytopenia. These observations highlight the growing incidence of pancytopenia as well as bicytopenia with age, which particularly rise among adolescent patients.

Age and Cytopenia	Pancytopenia	Bicytopenia	Total
Toddler (1-3 Years)	1	7	8 (9.5%)
Preschool (3 - 6 Years)	2	3	5 (6%)
School age child (6 - 12 Years)	3	27	30 (35.7%)
Adolescent (12 - 18 Years)	2	39	41 (48.8%)
Total	8	76	84 (100%)

Fig.3: Age and Cytopenia

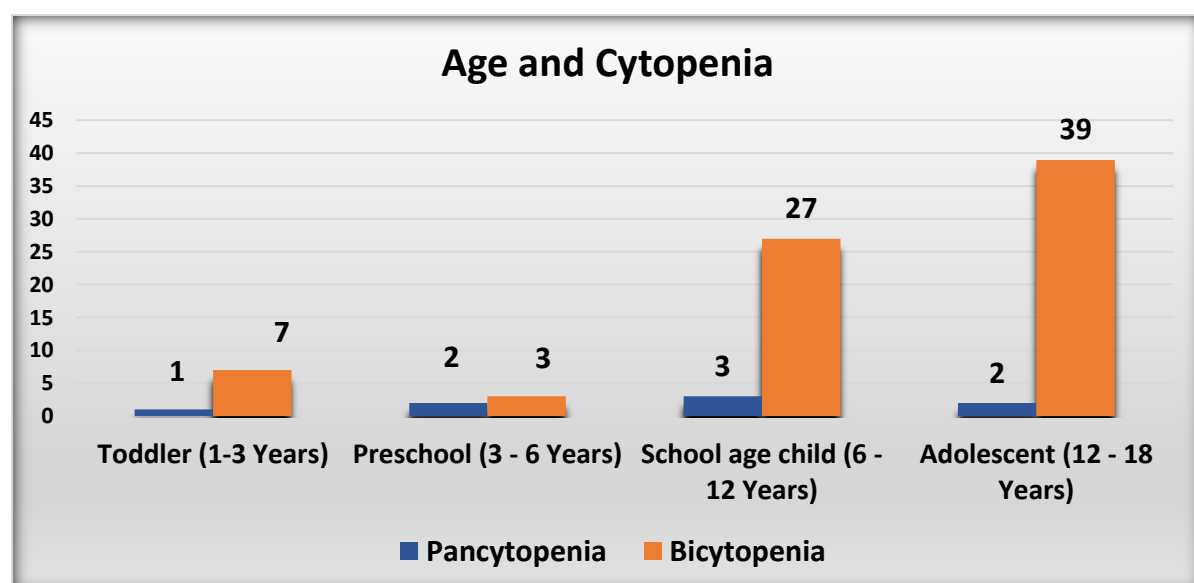


Table 4: Age and Gender Distribution

When considering both age and gender together, the breakdown was as follows: In the toddlers, there were 5 males and 3 females, while in preschoolers there were 2 males and 3 females; school age children there were 16 males and 14 females; and adolescents there were 24 males and 17 females. Based on this detailed demographic review, it is possible to understand how cytopenias affect patients at different stages of development and across various genders.

Age and Gender	Male	Female	Total
Toddler (1-3 Years)	5	3	8 (9.5%)
Preschool (3 - 6 Years)	2	3	5 (6%)
School age child (6 - 12 Years)	16	14	30 (35.7%)
Adolescent (12 - 18 Years)	24	17	41 (48.8%)
Total	47	37	84 (100%)

Fig.4: Age and Gender Distribution

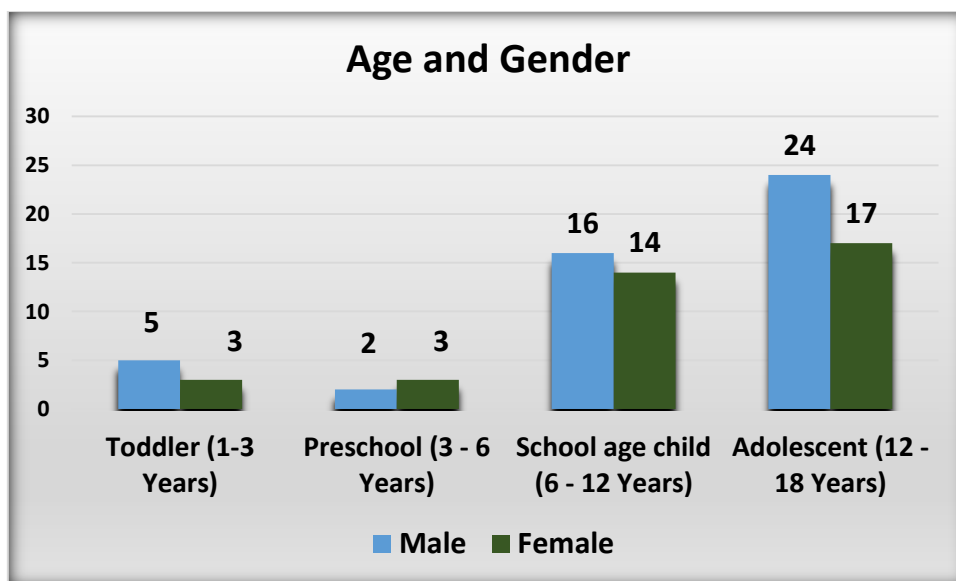


Table 5: Socioeconomic Class

The perceived socioeconomic class of the patients was also diverse; 2 patients, 2.4%, were of the upper class, 7 patients, 8.3%, of the upper middle class, 32 patients, 38.1%, of the lower middle class, and 38 patients, 45.2%, of the upper middle class. This broad distribution of socioeconomic status further proves that economic influences play a role in determining people's health status, including cytopenias among the different classes.

Socio economic class	No.of Patients	Percentage
Upper	2	2.4%
Upper middle	7	8.3%
Lower middle	32	38.1%
Upper middle	38	45.2%
Lower	5	6.0%
Total	84	100%

Fig.5: Socioeconomic Class

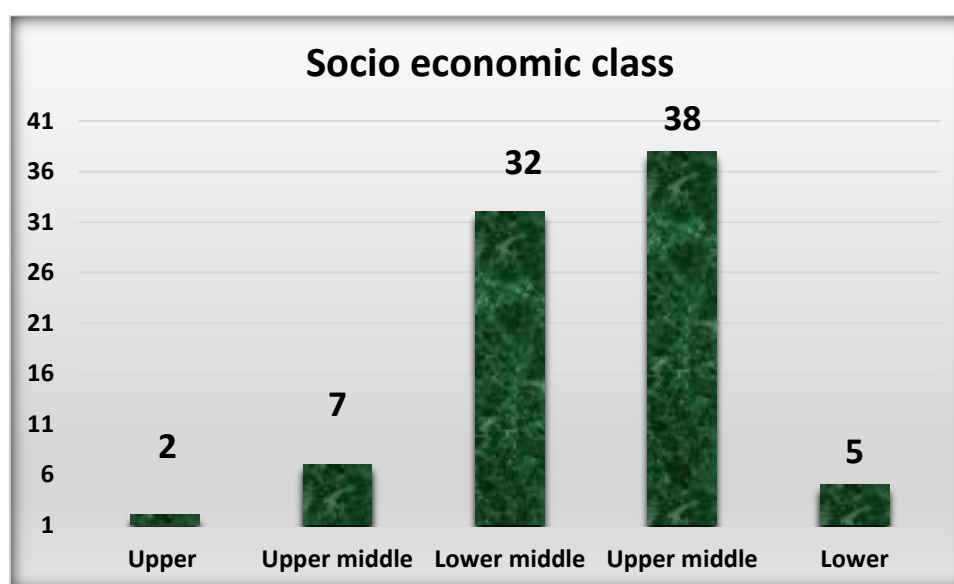


Table 6: Common Complaints

Some of common reported symptoms of the patients were fever, 90. 4%, pain abdomen, 60. 7% and easy fatigability, 38. 1%. Some of the common symptoms of cytopenias and the clinical correlates presented by these patients underscore the systemic approach to cytopenias and their clinical manifestations to help the clinician towards making a diagnosis and management plan.

Common Complaints	No.of Patients	Percentage
Easy Fatigability	32	38.1%
Pain abdomen	51	60.7%
Fever	76	90.4%

Fig.6: Common Complaints

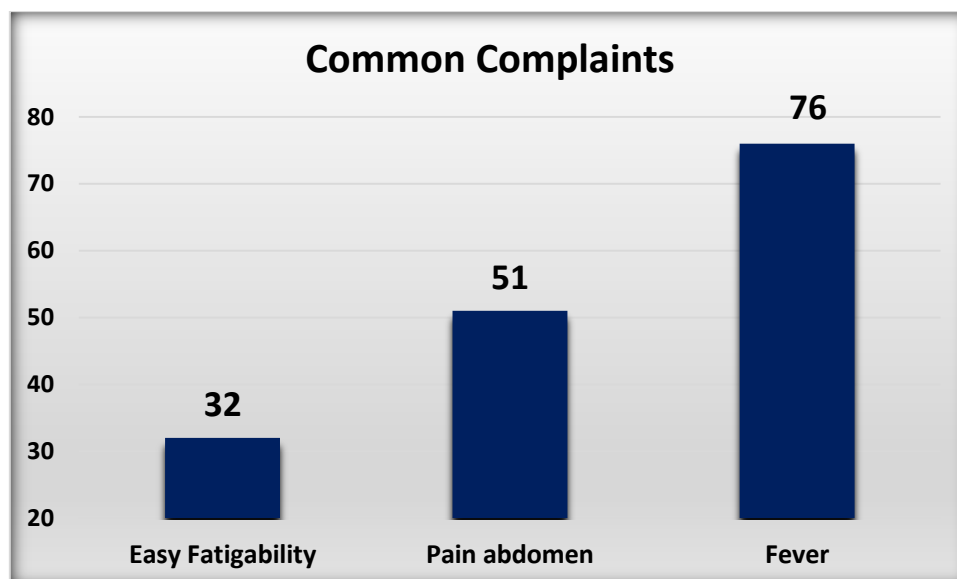


Table 7: Common Examinations

Clinical examination revealed hepatomegaly in 41 patients (48. 8%) and splenomegaly in 16 patients (19. 1%) and Pallor was present in 27 patients (32. 1%). These physical signs are essential clinical signs that point towards the presence of hematologic disorders and the conditions arising from bicytopenia and pancytopenia and, therefore, the need to conduct comprehensive physical examination of pediatric patients.

Common Examinations	No.of Patients	Percentage
Splenomegaly	16	19.1%
Pallor	27	32.1%
Hepatomegaly	41	48.8%
Total	84	100%

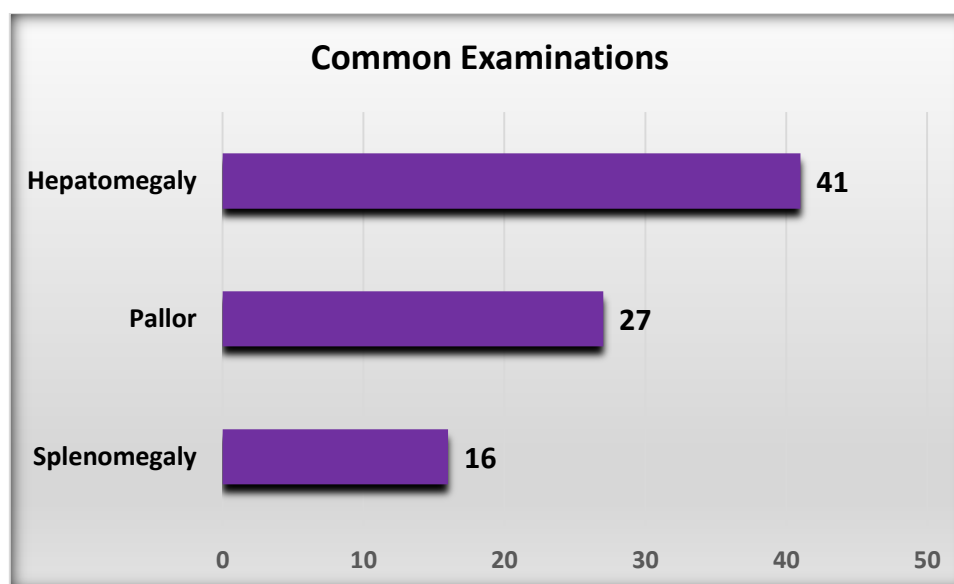
Fig.7: Common Examinations

Table 8: Symptoms

Specific symptoms that were mentioned were dyspnea (13. 1%), hemorrhagic manifestations (7. 1%), and rash (5. 9%). These symptoms give further idea regarding the clinical manifestation and prognosis of cytopenias that manifest the various systemic impact and consequences of haematological diseases in children.

Symptoms	No.of Patients (n=84)	Percentage
Joint swelling	1	1.2%
Jaundice	1	1.2%
Pedal Adema	2	2.4%
Lymphadenopathy	2	2.4%
Non healing Ulcers	2	2.4%
Hyper Pigmentation of knuckles Extremities	2	2.4%
Angular Stomatitis	2	2.4%
Weight loss	2	2.4%
Diarrhea	4	4.8%
Glossitis	4	4.8%
Nail Changes	4	4.8%
Skin Rash	5	5.9%
Bleeding Manifestations	6	7.1%
Shortness of Breath	11	13.1%
Splenomegaly	16	19.1%
Pallor	27	32.1%
Fatigue	32	38.1%
Hepatomegaly	41	48.8%
Pain abdomen	51	60.7%
Fever	76	90.5%

Fig.8: Symptoms

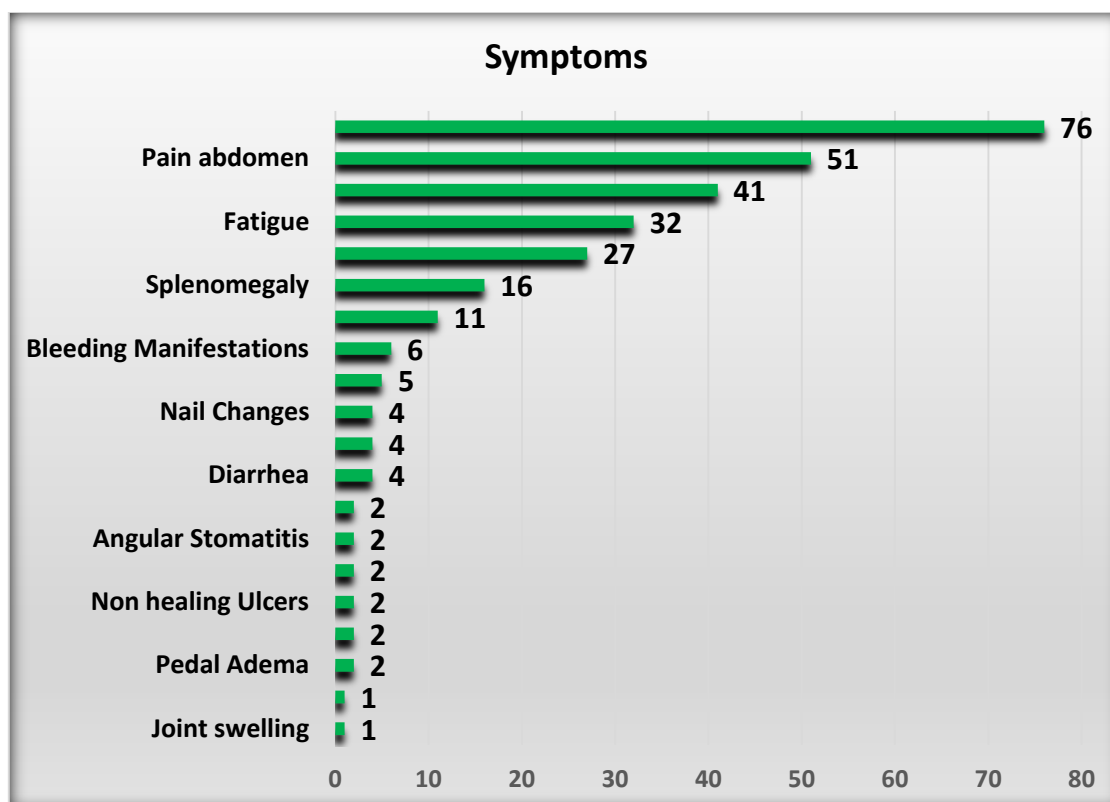


Table 9: Peripheral Smear Findings

Peripheral blood smear analysis revealed various types of anemia: Out of them 59 patients were found to have normocytic normochromic anemia, 16 patients were having microcytic hypochromic anemia, 7 patients were having dimorphic anemia and only 2 patients were having macrocytic hypochromic anemia. These results therefore emphasize the variability of the hematologic changes in children with cytopenias, which supports the use of investigations like the peripheral smear in clinical practice.

Peripheral smear	No.of Patients	Percentage
Macrocytic hypochromic	2	2.4%
Dimorphic anemia	7	8.3%
Microcytic hypochromic Anemia	16	19.1%
Normocytic normochromic	59	70.2%
Total	84	100%

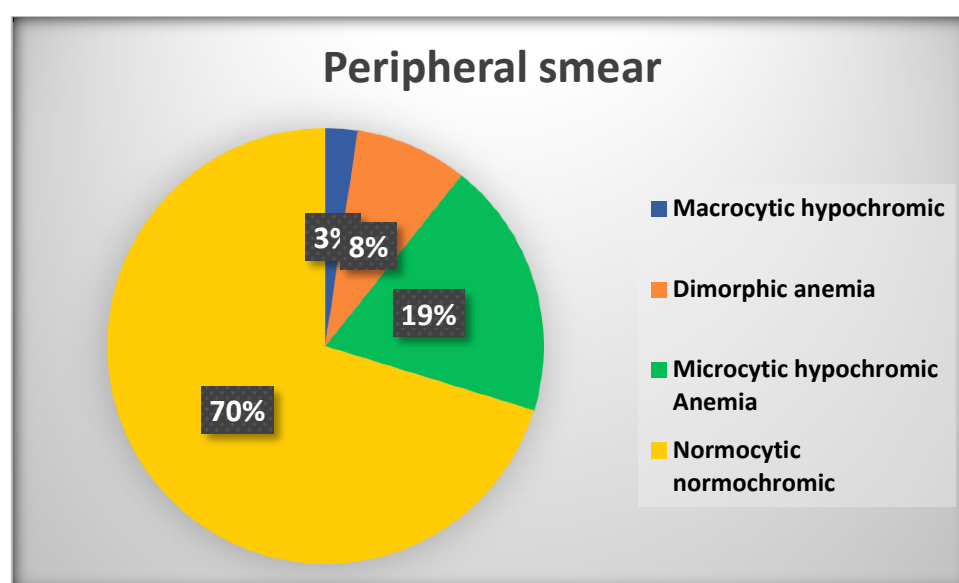
Fig.9: Peripheral Smear Findings

Table 10: Mean Corpuscular Volume (MCV)

MVV distribution with the regard to MCV was as follows: Normal MCV was noted in 40 patients (47.6%), Low MCV <77 fl in 35 patients (41.7%), and High MCV >95 fl in 9 patients (10.7%). These MCV categories therefore offer useful diagnostic pointers concerning the cause of anemia, contributing to the distinction between different hematologic diseases with cytopenias in children.

MCV	No.of Patients	Percentage
Normal MCV	40	47.6%
Low MCV (<77 fl)	35	41.7%
High MCV (>95 fl)	9	10.7%
Total	84	100%

Fig.10: Mean Corpuscular Volume (MCV)

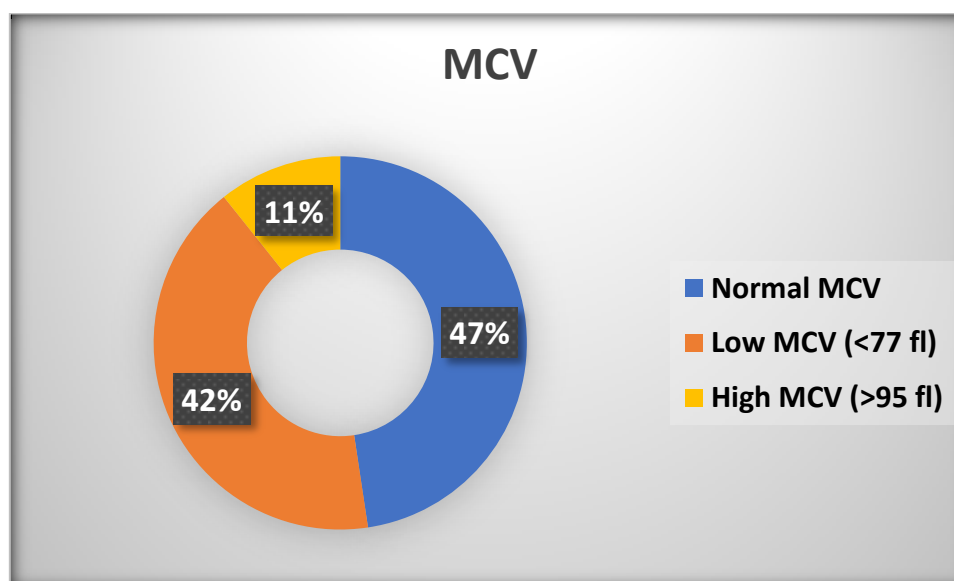


Table 11: Hemoglobin (Hb) Values

Criteria used for diagnosing anaemia:-WHO Criteria for Anaemia and Grade of severity:

	Population	Non-Anemia (Gm/dL)	Anemia (Gm/dL)		
			Mild	Moderate	Severe
1.	Children 6-59 months of age	11	10.0-10.9	7.0-9.9	<7.0
2.	Children 5-11 years of age	11.5	11.0-11.4	8.0-10.9	<8.0
3.	Children 12-14 years of age	12	11.0-11.9	8.0-10.9	<8.0
4.	Non-pregnant women (15 years of age and above)	12	11.0-11.9	8.0-10.9	<8.0
5.	Pregnant women	11	10.0-10.9	7.0-9.9	<7.0
6.	Men (15 years of age and above)	13	11.0-12.9	8.0-10.9	<8.0

According to the hemoglobin level, patients were divided into normal, mild anemia, moderate anemia, and severe anemia in 51 (60.7%), 7 (8.3%), 12 (14.3%), and 14 (16.7%) of the patients, respectively. This range of Hb values demonstrates the patient severity of anemia in pediatric cytopenias and therefore allows for determination of further treatment and management of the cases depending on the patient's characteristics.

Hb Values	No.of Patients	Percentage
Normal	51	60.7%
Mild Anemia	7	8.3%
Moderate Anemia	12	14.3%
Severe Anemia	14	16.7%
Total	84	100%

Fig.11: Hemoglobin (Hb) Values

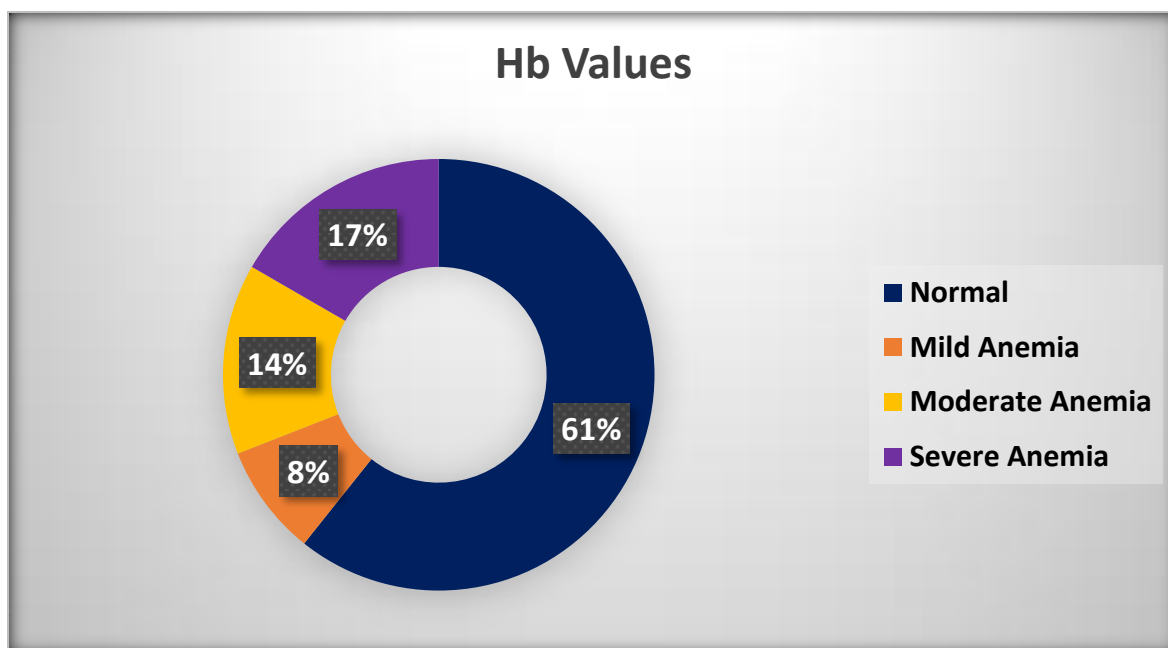


Table 12: Frequency of Variables

The degree of cytopenias present in the study population include anaemia in 33 patients (39.3%); leucopenia 65 patients (77.4%); and thrombocytopenia 76 patients (90.5%). These observations highlight the multilineage hematologic abnormalities that are often seen in pediatric patients with bicytopenia and pancytopenia and stress the importance of a thorough hematologic workup and individualized therapies.

Variables	No. of Patients (n=84)	Percentage
Anemia	33	39.3%
Leucopenia	65	77.4%
Thrombocytopenia	76	90.5%

Fig.12: Frequency of Variables

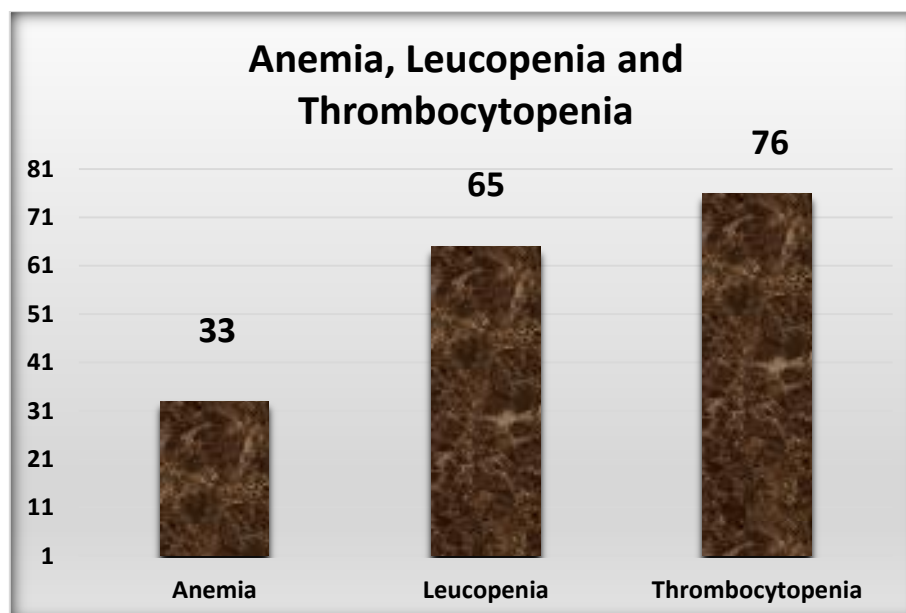


Table 13: Distribution of Fluoride Levels Among Cases

Fluoride (ppm)	No. of Cases	Percentage
1 - 1.5 ppm	28	33.3%
1.6 - 2 ppm	44	52.4%
>2 ppm	12	14.3%
Total	84	100%

This table analyzes the 84 cases and divides them according to their fluoride concentration in parts per million (ppm). Most of the cases (52. 4%) varied from 1. 6 and 2 ppm, and then 33 with an average of 11 for the remaining projects. 3% with levels ranging from one point one to one point five. 5 ppm, and 14. 3% of the samples that has levels greater than 2 ppm.

Fig.13: Distribution of Fluoride Levels Among Cases

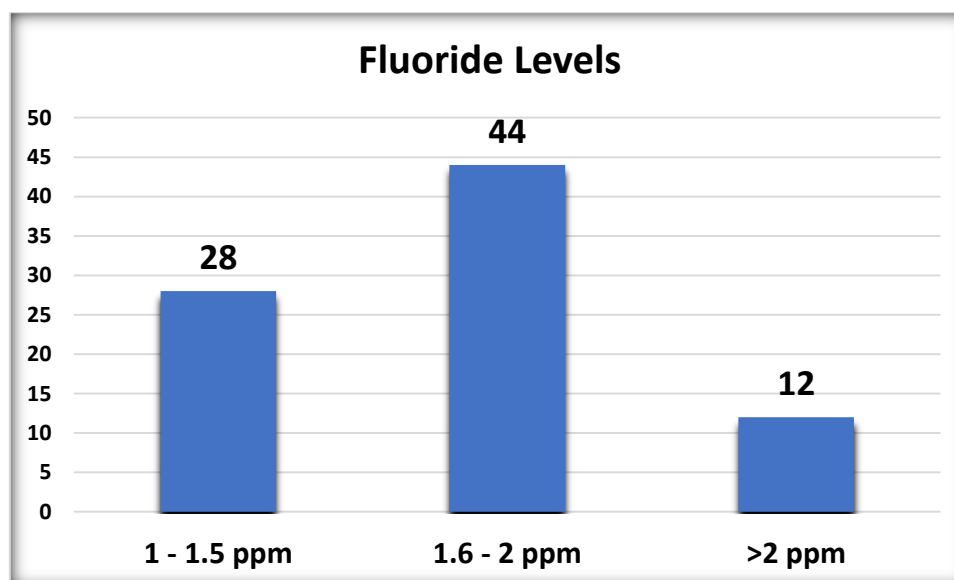


Table 14: Relationship Between Fluoride Levels and Cytopenia

Fluoride and Cytopenia	≤ 2 ppm	> 2 ppm	Total	Chi-square value	P-value
Pancytopenia	6 (75%)	2 (25%)	8 (100%)	0.828	0.362
Bicytopenia	66 (86.8%)	10 (13.2%)	76 (100%)		
Total	72 (85.7%)	12 (14.3%)	84 (100%)		

This table shows the distribution of pancytopenia and bicytopenia cases in relation to fluoride levels. Most cases of both conditions had fluoride levels ≤ 2 ppm. The chi-square test value is 0.828 with a P-value of 0.362, indicating no significant association between fluoride levels and the type of cytopenia.

Fig.14: Relationship Between Fluoride Levels and Cytopenia

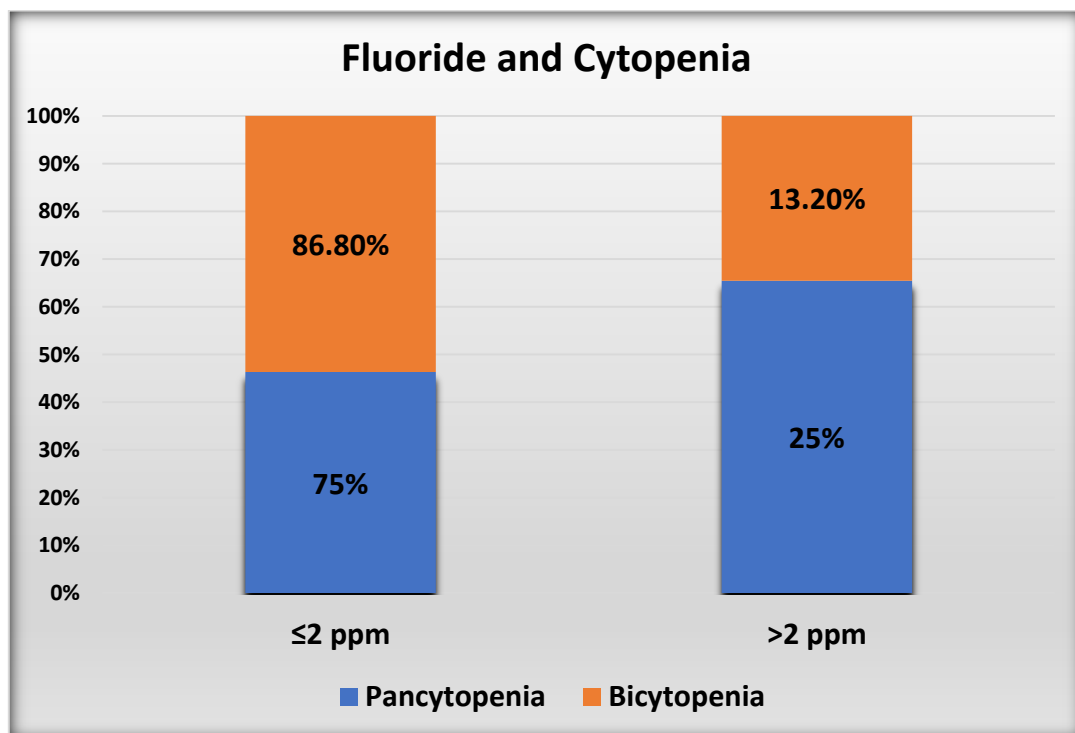


Table 15: Relationship Between Fluoride Levels and Peripheral Smear Findings

Fluoride and Peripheral Smear	≤2 ppm	>2 ppm	Total	Chi-square value	P-value
Macrocytic hypochromic	2 (100%)	0	2 (100%)	1.039	0.791
Dimorphic anemia	6 (85.7%)	1 (14.3%)	7 (100%)		
Microcytic hypochromic Anemia	14 (87.5%)	2 (12.5%)	16 (100%)		
Normocytic normochromic	50 (84.7%)	9 (15.3%)	59 (100%)		
Total	72 (85.7%)	12 (14.3%)	84 (100%)		

This table examines the relationship between fluoride levels and different types of anemia identified through peripheral smear analysis. The majority of cases across all types of anemia had fluoride levels ≤2 ppm. The chi-square test value is 1.039 with a P-value of 0.791, showing no significant association between fluoride levels and the type of anemia.

Fig.15: Relationship Between Fluoride Levels and Peripheral Smear Findings

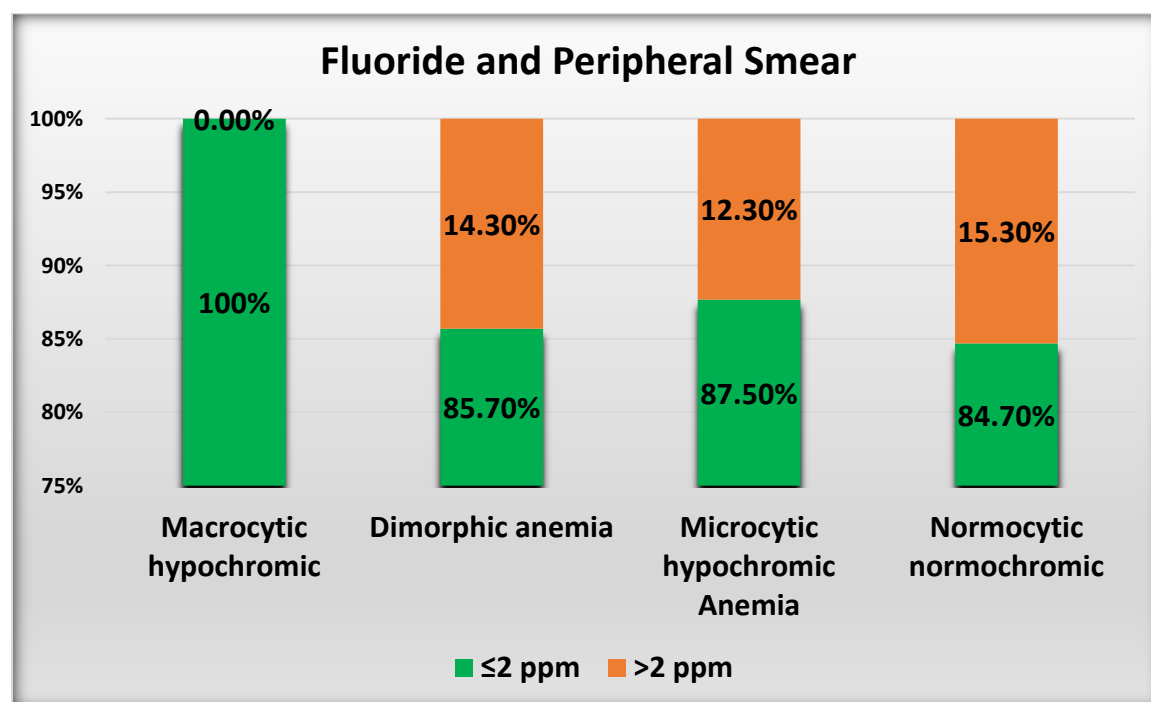


Table 16: Relationship Between Fluoride Levels and Hemoglobin (Hb)

Fluoride and Anemia (Hb)	≤2 ppm	>2 ppm	Total	Chi-square value	P- value
Normal	44 (86.2%)	7 (13.8%)	51 (100%)	0.068	0.995
Mild Anemia	6 (85.7%)	1 (14.3%)	7 (100%)		
Moderate Anemia	10 (83.3%)	2 (16.7%)	12 (100%)		
Severe Anemia	12 (85.7%)	2 (14.3%)	14 (100%)		
Total	72 (85.7%)	12 (14.3%)	84 (100%)		

This table explores the relationship between fluoride levels and the severity of anemia based on hemoglobin levels. Most cases had fluoride levels ≤2 ppm regardless of anemia severity. The chi-square test value is 0.068 with a P-value of 0.995, indicating no significant association between fluoride levels and anemia severity.

Fig.16: Relationship Between Fluoride Levels and Hemoglobin (Hb)

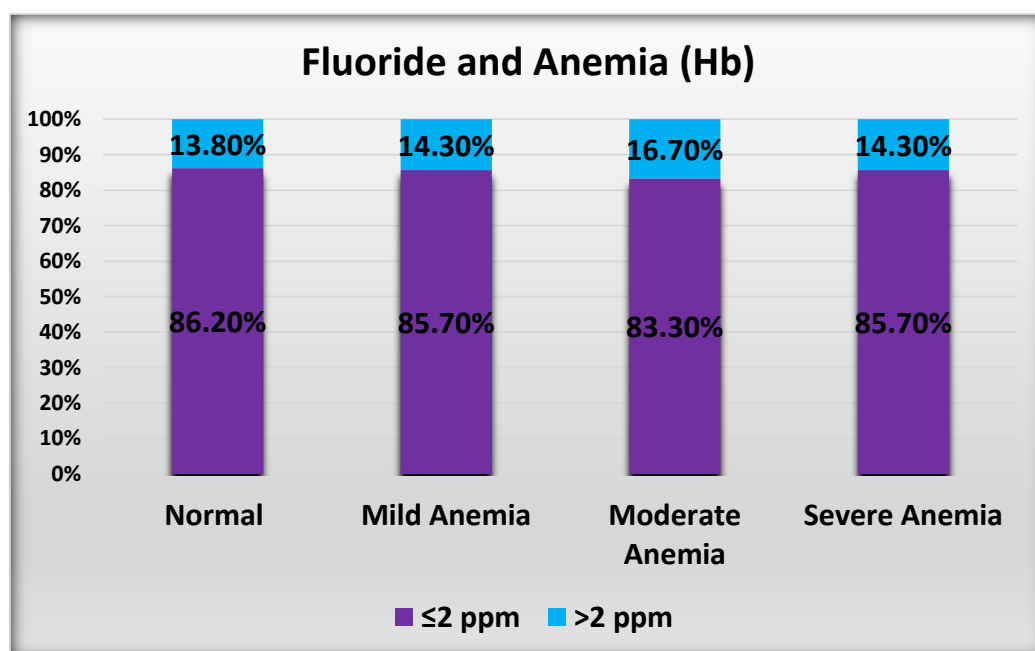


Table 17: Relationship Between Fluoride Levels and Mean Corpuscular Volume (MCV)

Fluoride and MCV	≤2 ppm	>2 ppm	Total	Chi-square value	P-value
Normal MCV	35 (87.5%)	5 (12.5%)	40 (100%)	0.411	0.814
Low MCV (<77 fl)	29 (82.8%)	6 (17.2%)	35 (100%)		
High MCV (>95 fl)	8 (88.8%)	1 (11.2%)	9 (100%)		
Total	72 (85.7%)	12 (14.3%)	84 (100%)		

This table examines the relationship between fluoride levels and MCV. The majority of cases had normal or low MCV with fluoride levels ≤ 2 ppm. The chi-square test value is 0.411 with a P-value of 0.814, showing no significant association between fluoride levels and MCV.

Fig.17: Relationship Between Fluoride Levels and Mean Corpuscular Volume (MCV)

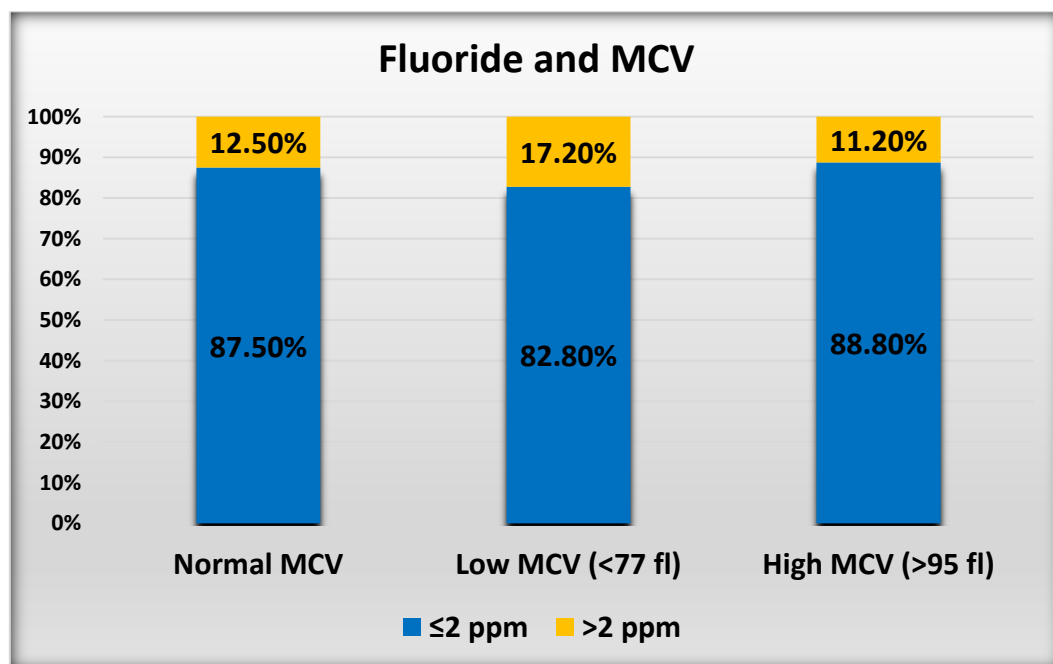


Table 18: Relationship Between Fluoride Levels and Gender

Fluoride and Gender	≤2 ppm	>2 ppm	Total	Chi-square value	P-value
Male	41 (87.2%)	6 (12.8%)	47 (100%)	0.201	0.653
Female	31 (83.7%)	6 (16.3%)	37 (100%)		
Total	72 (85.7%)	12 (14.3%)	84 (100%)		

This table shows the distribution of fluoride levels by gender. Both males and females had the majority of cases with fluoride levels ≤ 2 ppm. The chi-square test value is 0.201 with a P-value of 0.653, indicating no significant association between fluoride levels and gender.

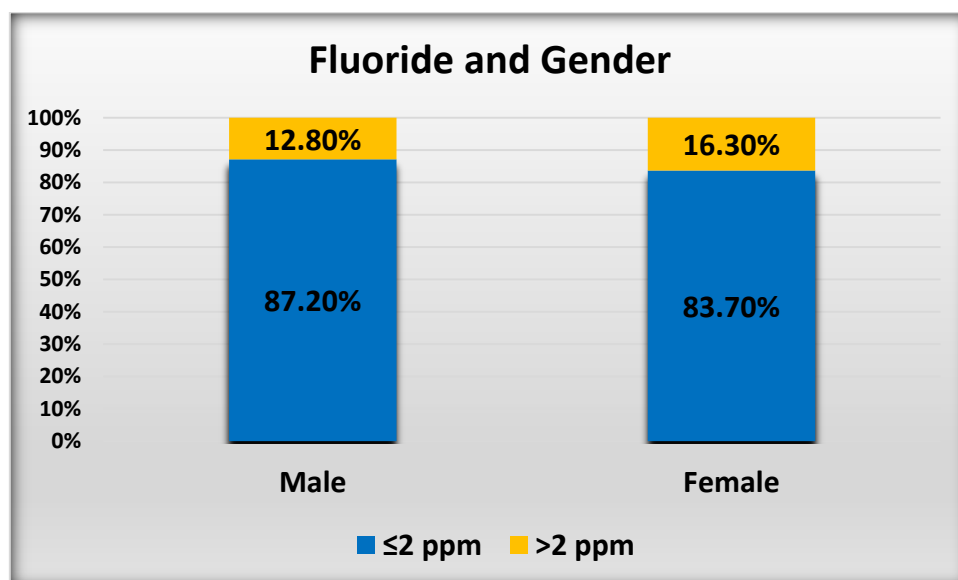
Fig.18: Relationship Between Fluoride Levels and Gender

Table 19: Relationship Between Fluoride Levels and Age Groups

Fluoride and Age	≤2 ppm	>2 ppm	Total	Chi-square value	P-value
Toddler (1-3 Years)	6 (75%)	2 (25%)	8 (100%)	1.709	0.634
Preschool (3 - 6 Years)	4 (80%)	1 (20%)	5 (100%)		
School age child (6 - 12 Years)	25 (83.3%)	5 (16.7%)	30 (100%)		
Adolescent (12 - 18 Years)	37 (90.2%)	4 (9.8%)	41 (100%)		
Total	72 (85.7%)	12 (14.3%)	84 (100%)		

This table examines the relationship between fluoride levels and different age groups. Most cases in each age group had fluoride levels ≤2 ppm. The chi-square test value is 1.709 with a P-value of 0.634, indicating no significant association between fluoride levels and age groups.

Fig.19: Relationship Between Fluoride Levels and Age Groups

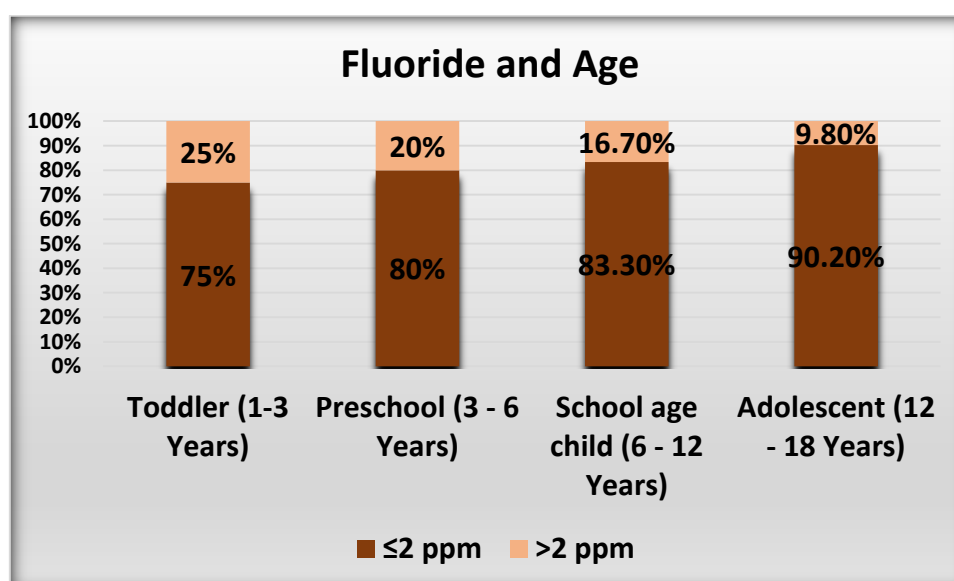
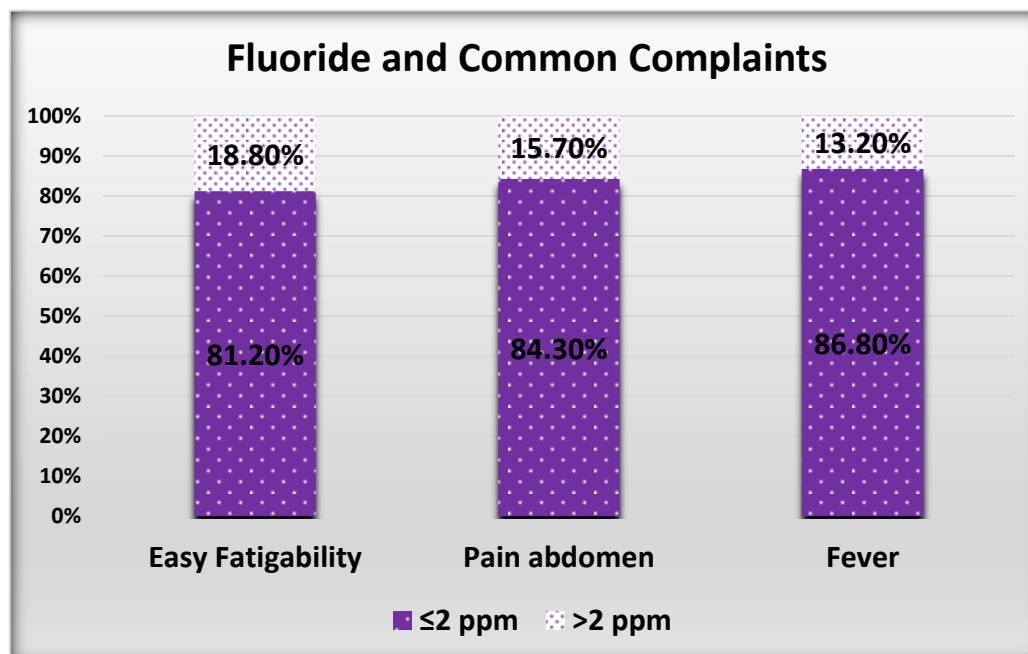


Table 20: Relationship Between Fluoride Levels and Common Complaints

Fluoride and Common Complaints	≤2 ppm	>2 ppm	Total	Chi-square value	P-value
Easy Fatigability	26 (81.2%)	6 (18.8%)	32 (100%)	0.841	0.359
Pain abdomen	43 (84.3%)	8 (15.7%)	51 (100%)	0.208	0.648
Fever	66 (86.8%)	10 (13.2%)	76 (100%)	0.828	0.362

This table shows the relationship between fluoride levels and common complaints such as easy fatigability, abdominal pain, and fever. The majority of cases with each complaint had fluoride levels ≤ 2 ppm. The chi-square test values and P-values indicate no significant association between fluoride levels and these common complaints.

Fig.20: Relationship Between Fluoride Levels and Common Complaints



DISCUSSION



DISCUSSION

This study offers a comprehensive evaluation of pediatric patients presenting with bicytopenia and pancytopenia, analyzing demographic, clinical, and hematologic characteristics. Table 1 presents the distribution of patients based on the type of cytopenia. Out of 84 patients, 76 (90.5%) were diagnosed with bicytopenia and 8 (9.5%) with pancytopenia, indicating a significant prevalence of bicytopenia. This finding aligns with previous studies which also reported a higher incidence of bicytopenia compared to pancytopenia in pediatric populations ^(5,27). The high prevalence of bicytopenia may be attributed to conditions that selectively suppress or destroy two cell lines rather than all three, which is more common in pancytopenia.

Table 2 focuses on the gender distribution among patients with pancytopenia and bicytopenia. The study revealed a male predominance, with 55.9% of patients being male and 44.1% female. This male predominance is consistent with findings from Agarwal et al. ⁽²⁸⁾ and Bose et al. ⁽²⁹⁾, who also observed a higher incidence of cytopenias in males. The male-to-female ratio in our cohort suggests potential genetic and environmental factors influencing the higher susceptibility of males to these hematologic disorders.

Table 3 provides an age-wise distribution of patients with cytopenias. Adolescents (12-18 years) comprised the largest group, accounting for 48.8% of the cases, followed by school-age children (6-12 years) at 35.7%. This age distribution pattern is corroborated by Dada et al. ⁽³⁰⁾ and Patil and Chavan ⁽³¹⁾, who also noted a higher prevalence of cytopenias in older children and adolescents. This may be attributed to the amassment of different etiologic factors that predispose this age group as well as the longer time of symptom manifestation of some hematologic diseases.

The age and gender profile of the study population is presented in Table 4. In the toddlers' age group of 1-3 years, boy children were more dominant than girl children in a proportion of 5:3. The same scenario was observed in the preschool age group which is 3-6 years of age, where the boys were more in number compared to girls. However, the gap between boys and girls starts to decrease with age, and the differences become insignificant in the school-going and adolescent age groups. Similar findings have been noted by Makheja et al. ⁽¹³⁾ and Niazi and Raziq ⁽²⁰⁾, in the context of pointing to the fact that although male predominance is more prominent in younger children, the gap appears to narrow down with age.

These data on gender and age distribution therefore stress the demographic aspect as the potential determinant of the choice of approach in the diagnosis and treatment of cytopenias in children. Knowledge of such patterns can assist in applying appropriate strategies in the provision of healthcare to specific age and gender preferences.

Hence, the results of the study in relation to the type of cytopenia, gender, and age distribution is one major advancement in the understanding of the epidemiology of cytopenias in children. The frequent occurrence of bicytopenia proves that there should be specific diagnostic and treatment strategies to address this issue. The excess of male and the increased rate in older children and adolescents support the genetic and environmental risks in the pathogenesis of these disorders.

These findings are in congruity with earlier published literature, once again stressing the need for detailed demographic and clinical assessment in case of pediatric cytopenias. Subsequent research should aim at identifying additional factors contributing to the disease, refining the diagnostic procedures, and finding appropriate treatment to enhance the patients' prognosis.

Socioeconomic Class Distribution

Evaluating the results of the given question (Table 5), the majority of the patients are from the upper middle class (45. 2%) and the lower middle class (38. 1%) while the lower classes include only 6. 0% and the upper classes are 2. 4%. This distribution agrees with the observation made by Gupta et al. ⁽⁵⁾ that patients from middle SES had more cytopenias. The finding of a sizeable proportion of middle socioeconomic classes implies that these conditions cut across all the population and thus the importance of health care services from all the classes of society. In addition, Agarwal et al. ⁽³²⁾ described the same trends and emphasized the role of socioeconomic characteristics in the distribution of hematology diseases.

Common Complaints

In the current study, the most frequent symptoms at presentation were fever as noted in 90% of the patients. 4% of patients, the pain abdomen identified in 60. 7% of patients and easy fatigability in 38. 1% of patients as described in Table 6. These symptoms are in concordance with previous studies that have been carried out by Rathod et al. ⁽³³⁾ where fever was noted to be the most common symptom among pediatric patients with cytopenias. In the same regard, Mehta et al. observed that abdominal pain and general fatigue were some of the common symptoms reported among children with hematologic abnormalities as was determined in the study. Thus, the focus on fever as a primary clinical feature highlights the need for clinicians to include cytopenias in the differential diagnosis when managing febrile children ⁽³⁴⁾.

Common Examinations

Concerning the physical examination findings noted in the present study, 48% of the patients had hepatomegaly. Pallor in 32% of patients, 8% of the patient complained of weakness or fatigue. 1% with hepatomegaly and 19% of patients splenomegaly. 1%, which is described in

Table 7 below. These findings are important signals of the hematologic diseases and are backed by other studies. For example, Swami et al. ⁽³⁵⁾ found that physical examination of kids with cytopenias revealed hepatomegaly and pallor and noted the relevance of these symptoms to diagnosis. Also, splenomegaly was confirmed in nearly one-fifth of the patients, which is consistent with Patil and Chavan's findings ⁽³⁶⁾; they also noted splenomegaly to be a clinically relevant finding in children with cytopenias.

Gender Distribution and Age Correlation

Table 2 gives the gender distribution, where it is evident that male patients dominate with 55.9% and females 44.1% of the cohort. Thus, the male predominance of the present study is in consonance with other studies done by Bose et al., 2004 ⁽²⁹⁾ and Jain et al., 2005 ⁽²⁷⁾ on cytopenias in children. Also, by the age group (Table 3), it is evident that the adolescent (12-18 years) is the most affected with 48.8 percent of the patients, school age children between 6-12 years constituted 35 percent. 7%. This trend is in agreement with Dada et al ⁽³⁰⁾ who also reported higher levels of cytopenias amongst the older children and adolescents.

Hematologic Findings and Diagnostic Insights

The detailed hematologic analysis has been depicted in table 4 and it has been observed that the majority of the patients (70.2%) had normocytic normochromic anemia while the rest of the cases (19.1%) had microcytic hypochromic anemia. That is why it is possible to state that the distribution of anemia types revealed in this study is comparable with the data of Jha et al. ⁽⁴⁾ who described the prevalence of cytopenias in children. The mean corpuscular volume (MCV) values obtained in this study were normal in 47.6% of patients, low in 41.7% while high in 10 individuals Only 7% of the respondents admitted to being moderately involved in physical activities while 10 of the respondents scored high in physical activity. 7% of patients, giving crucial diagnostic data which is in concordance with Kumar et al. ⁽¹⁵⁾. This

hematologic profile underlines the fact that pediatric cytopenias are not easy to diagnose and treat, therefore, it is always wise to invest in extensive diagnostic workup to arrive at the right diagnosis.

Symptoms

The symptomatology analysis of the 84 pediatric patients with bicytopenia and pancytopenia reveals a wide range of clinical presentations (Table 8). Fever is the most common symptom, observed in 90.5% of patients, consistent with findings by Rathod et al. ⁽³⁷⁾ and Mehta et al. ⁽³⁴⁾, who also identified fever as a prevalent symptom in pediatric cytopenias. Pain abdomen (60.7%) and fatigue (38.1%) are also frequent complaints, aligning with observations from Gupta et al., highlighting these symptoms' significance in hematologic disorders ⁽⁵⁾.

Other notable symptoms include hepatomegaly (48.8%) and pallor (32.1%), underscoring the importance of physical examination findings, as reported by Swami et al. ⁽³⁵⁾ and Patil and Chavan ⁽³⁶⁾. Additionally, shortness of breath (13.1%), skin rash (5.9%), and bleeding manifestations (7.1%) were prevalent, supporting the literature from Agarwal et al. ⁽³²⁾ and Bose et al. ⁽³³⁾, who emphasized these symptoms in pediatric cytopenias.

Less common symptoms, such as glossitis (4.8%), nail changes (4.8%), and lymphadenopathy (2.4%), were also observed, aligning with findings from Niazi and Raziq ⁽²⁰⁾. These diverse symptoms underscore the complexity of clinical presentations in cytopenias, necessitating comprehensive clinical assessments for accurate diagnosis and management.

Peripheral Smear Analysis

Peripheral smear analysis (Table 9) shows that normocytic normochromic anemia is the most common type, seen in 70.2% of patients. This finding is in line with studies by Jha et al. ⁽⁴⁾

and Kumar et al. ⁽¹⁵⁾, which also reported a high prevalence of normocytic normochromic anemia in pediatric cytopenias. The high incidence suggests underlying conditions affecting red cell production or survival without significant changes in cell size or hemoglobin concentration.

Microcytic hypochromic anemia was present in 19.1% of patients, while dimorphic anemia and macrocytic hypochromic anemia were observed in 8.3% and 2.4% of patients, respectively. These results align with studies by Gupta et al. ⁽⁵⁾ Keisu ⁽³⁾ and Ost, indicating the critical role of peripheral smear analysis in identifying anemia types and further diagnostic evaluations.

Mean Corpuscular guiding Volume (MCV)

The distribution of MCV values (Table 10) shows that 47.6% of patients had normal MCV, 41.7% had low MCV, and 10.7% had high MCV. These findings are consistent with the study by Kumar et al. ⁽¹⁵⁾, which reported similar MCV patterns in pediatric cytopenias. The significant proportion of patients with normal MCV suggests a broad range of underlying etiologies that do not affect cell size.

The presence of low MCV in a substantial number of patients points towards microcytic anemias, such as those caused by iron deficiency or thalassemia traits, while high MCV values suggest conditions like vitamin B12 or folate deficiency. These insights are essential for the differential diagnosis and management of anemia in pediatric patients.

Hemoglobin Values

The variability in hemoglobin values (Table 11) among patients highlights the spectrum of anemia severity in pediatric cytopenias. While 60.7% had normal hemoglobin levels, 16.7% had severe anemia, 14.3% had moderate anemia, and 8.3% had mild anemia. This distribution

underscores the diverse presentations of anemia, reinforcing findings by Tikmani et al. and Niazi and Raziq, who reported similar variability in hemoglobin levels among affected children.

The fact that many of the patients have normal hemoglobin levels while they have cytopenias indicates there are other factors or perhaps co-existing diseases that affect their hematologic status. This is why simple measurements of hemoglobin are insufficient for the assessment of hematologic disorders and require more profound investigations.

Hematologic Findings

The analysis of hematologic variables (Table 12) shows that 39.3% of patients had anemia, 77.4% had leucopenia, and 90.5% had thrombocytopenia. The findings of this study are in concordance with the study done by Memon et al. ⁽⁶⁾ and Wadhwa et al. ⁽⁸⁾ who identified high prevalence of leucopenia and thrombocytopenia in pediatric cytopenias. Thrombocytopenia and leucopenia are the most frequent cytopenias in patients with SSc, which emphasizes the fact that cytopenias are frequently associated with the decrease in several cell lines, as pointed in the works of Thambi et al. and Venkat et al.

These findings stress the importance of a multimodal diagnostic strategy for the assessment of cytopenias' etiology. Diseases like bone marrow failure syndromes, infiltrative diseases and severe infections should be considered. It stresses the need for bone marrow examination and other diagnostic methods to identify the specific cause and treatment.

The present paper aims to give the demographic, clinical, and hematologic profiles of pediatric patients with bicytopenia and pancytopenia in order to gain deeper understanding of these diseases. Thus, the study conveys the complexity of symptoms, the significance of detailed peripheral smear and MCV considerations in hematologic evaluation, and the necessity to consult with a hematologist for proper diagnostics and management. Our

findings are in concordance with the prior works thereby providing further support to the existing epidemiological pattern and clinical manifestations of paediatric cytopenias.

Further studies should aim to investigate the primary causes of the diseases, refine the diagnostic approaches, and design effective therapeutic interventions to enhance the patients' prognosis. Furthermore, the longitudinal designs are useful in determining the end results as well as the efficacy of several treatment approaches. Increasing the public and healthcare provider knowledge of cytopenias in paediatric population, early detection, and equal access to healthcare resources can dramatically improve the management as well as the survival of patients with cytopenias.

In their genomic study of paediatric aplastic anaemia, Dr Khincha and Dr Savage focused on the complexity of cytopenia, which supports our work's observations of various manifestations. Their study outlined the role played by genetic factors in the development of diseases and recommended future possibilities of the application of disease management based on the genetic makeup of an individual (Khincha & Savage, 2016) ⁽³⁸⁾. This genomic information correlates with the diverse manifestations in our population including fatigue, hepatomegaly, and fever, which suggest the presence of hematologic diseases (Table 1).

In addition, Dr. Hsieh and colleagues proved the effectiveness of non-myeloablative HSCT in severe SCD and justify early intervention in hematologic phenotypes (Hsieh et al., 2014) ⁽³⁹⁾. Their strategy is similar to our focus on early identification and targeted pharmacological management of pediatric patients with complications of cytopenias such as anemia and thrombocytopenia (Table 4).

Based on these findings on disease severity, the immunosuppressive treatment of aplastic anemia expounded by Passweg and Tichelli offers a good background of the high proportions of thrombocytopenia (90. 5%) and leucopenia (77. 4%) as observed in the current study

(Passweg & Tichelli, 2013; Table 4) ⁽⁴⁰⁾. Such studies support the concept of the need for patients' special approaches to treatment depending on the severity of the disease and other aspects.

However, the hematological picture noted was normocytic normochromic anemia in 70. 2% and microcytic hypochromic anemia in 19. 1% of patients which corroborates with the Schrezenmeier et al. on bone marrow transplantation in severe aplastic anemia. Such consistency implies that there are hematologic similarities in various causes of the disease (Schrezenmeier et al., 1998; Table 2) ⁽⁴¹⁾.

The study by Dr. Yoshida and colleagues compared first-line treatments for SAA in children: BMT from MFD versus IST (Yoshida et al. , 2014) ⁽⁴²⁾. Our patients' hematologic manifestations were also diverse, which is consistent with their observations; therefore, the therapeutic approach should be individualized according to disease severity and other factors (Table 4).

In addition, our research findings on peripheral smear and hemoglobin values were explained in the light of detailed diagnostic and therapeutic approach to the aplastic anemia prepared by Marsh et al. (2009) ⁽⁴³⁾. Their guidelines reflect the need to enhance the practice of combining clinical, hematological, and genetic analyses to enhance the care of patients, as well as their prognosis.

Furthermore, Scheinberg and Young's systematic management of acquired aplastic anemia showed the applicability of our data on the symptoms such as splenomegaly, pallor and fatigue (Scheinberg & Young, 2012) ⁽⁴⁴⁾. The management of hematologic abnormalities as provided by them highlighted the complexity of pediatric cytopenia and the need to act promptly.

Dr Passweg and Dr Tichelli's review on immunosuppressive treatment for aplastic anemia described the difficulty in the management of optimal result, especially in the refractory cases (Passweg & Tichelli, 2013) ⁽⁴⁵⁾. This is in line with our observation on the variable reactions to therapeutic interventions as captured by the treatment ceilings among their pediatric patients with cytopenias (Table 6).

Additionally, Schrezenmeier et al.'s seminal work on bone marrow transplantation outcomes underscored the critical role of donor matching and post-transplant care in determining long-term survival and disease-free status (Schrezenmeier et al., 1998) ⁽⁴⁶⁾. This aligns with our discussion on the hematological profiles and clinical complexities encountered in managing severe cytopenias in children.

Moreover, Raza et al.'s proposed diagnostic approach for pancytopenia patients in medical wards provides a practical framework for interpreting symptoms such as fever, pain abdomen, and bleeding manifestations (Raza et al., 2004) ⁽⁴⁷⁾. Their emphasis on systematic evaluation aids in delineating underlying etiologies, complementing our detailed analysis of symptoms and peripheral smear findings (Table 5).

Distribution of Fluoride Levels Among Cases

The distribution of fluoride levels among the 84 cases showed that the majority of cases (52.4%) had fluoride levels between 1.6 and 2 ppm, followed by 33.3% with levels between 1 and 1.5 ppm, and 14.3% with levels greater than 2 ppm. This distribution is consistent with studies by Peterson et al. ⁽⁴⁸⁾ and DenBesten & Li ⁽⁴⁹⁾, which have documented similar fluoride levels in various populations exposed to high levels of fluoride in drinking water and other sources.

Fluoride Levels and Cytopenia

The study found no significant association between fluoride levels and the occurrence of pancytopenia or bicytopenia (chi-square value: 0.828, P-value: 0.362). Most cases of both conditions had fluoride levels ≤ 2 ppm. Susheela et al. ⁽⁵⁰⁾ and Saxena et al. ⁽⁵¹⁾ also indicated that while fluoride exposure can affect bone marrow function and potentially lead to cytopenia, the evidence is not conclusive, and further studies are needed to establish a clear link.

Fluoride Levels and Peripheral Smear Findings

The analysis of peripheral smear findings revealed no significant association between fluoride levels and different types of anemia (chi-square value: 1.039, P-value: 0.791). Most cases had fluoride levels ≤ 2 ppm across all types of anemia. Similar findings have been reported by Jolly et al. ⁽⁵²⁾, suggesting that while fluoride exposure can influence red blood cell morphology, it does not necessarily correlate with specific types of anemia.

Fluoride Levels and Hemoglobin (Hb) Levels

No significant association was found between fluoride levels and the severity of anemia based on hemoglobin levels (chi-square value: 0.068, P-value: 0.995). This is in line with previous research by Choubisa ⁽⁵³⁾ and Rajeshwari & Angadi ⁽⁵⁴⁾, which have shown mixed results regarding the impact of fluoride on hemoglobin levels, with some studies reporting a decrease in hemoglobin concentration in populations exposed to high fluoride levels, while others have found no significant effect.

Fluoride Levels and Mean Corpuscular Volume (MCV)

The study observed no notable link between fluoride levels and MCV (chi-square value: 0.411, P-value: 0.814). This result aligns with findings from other studies, such as those by

Turner et al. ⁽⁵⁵⁾, which also indicated no significant alterations in MCV among individuals exposed to different fluoride levels.

Fluoride Levels and Gender

The analysis showed no significant association between fluoride levels and gender (chi-square value: 0.201, P-value: 0.653). Both males and females had the majority of cases with fluoride levels ≤ 2 ppm. This is supported by Whitford ⁽⁵⁶⁾, who found no significant gender differences in the impact of fluoride exposure on hematological parameters.

Fluoride Levels and Age Groups

There was no significant association between fluoride levels and different age groups (chi-square value: 1.709, P-value: 0.634). Most cases in each age group had fluoride levels ≤ 2 ppm. This finding is consistent with previous research by Green et al. ⁽⁵⁷⁾ and Xiang et al. ⁽⁵⁸⁾, indicating that while children and adolescents may be more susceptible to fluoride toxicity due to higher intake relative to body weight, the hematological impact does not significantly differ by age group.

Fluoride Levels and Common Complaints

The study found no significant association between fluoride levels and common complaints such as easy fatigability, abdominal pain, and fever (chi-square values: 0.841, 0.208, 0.828; P-values: 0.359, 0.648, 0.362 respectively). These findings align with previous studies by Shashi & Bhardwaj ⁽⁵⁹⁾, which have documented a range of nonspecific symptoms associated with fluoride exposure but have not established a direct causal relationship.

Furthermore, there are significant advances in the management of those particular hematologic disorders such as PNH. Hemolysis and thrombosis in PNH has been treated with

the complement inhibitors and the management of the disease in children was also highlighted by Brodsky (2014).

The literature review revealed that Marsh et al. (2009) and Killick et al. (2016) are prominent authors who have endeavored to set key protocols for the evaluation and management of pediatric patients, and have stressed on the significance of risk assessment and supportive care in these patients (Marsh et al. , 2009; Killick et al. , 2016).

SUMMARY

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SUMMARY

This study assessed the clinical and hematological findings of cytopenias in a pediatric population regarding demographics, presenting symptoms, laboratory profile, and predisposing factors. There were 84 patients included in the study with further subgroup analysis in the age, gender and immigrant status, clinical presentation.

The demographic analysis of the results showed the following: bicytopenia was the most frequent form of AH in the given group of patients, and the highest frequency was observed in children and adolescents of school age. The distribution of the hematological disorders on the basis of age This is rather interesting because it highlights the fact that there is possibility for the disorders to be related to growth and development.

These symptoms brought attention to the fact that clinical manifestations of the patients are rather polymorphic, fatigue, pain abdomen, fever are the most frequent. These symptoms can be associated with certain hematological indices such as anemia, leukopenia and thrombocytopenia; this shows that the cause of the cytopenias in children is varied.

The peculiarities of the hematologic profile of the studied group of patients could be disclosed with the help of serological tests. Most prevalent anemia was normocytic normochromic; microcytic hypochromic and dimorphic anemia were also seen. These observations were justified by the assessments of peripheral smear analyses; therefore, morphological evaluations of blood films should not be underestimated for differential diagnosis of hematologic disorders.

In terms of the socio-economic status, the demographic distribution was determined and shown that most of the patients fell under low middle and high middle income strata. These demographic distributions suggest that disease presentation may be associated with disease

management outcomes, perhaps because of the difference in access to healthcare and patients income.

The findings of the study contribute to the development of knowledge in the sub-specialty of pediatric hematology; the importance of key clinical examination, biochemical analysis and social status is emphasized for diagnosis. That is why it is necessary to establish specific management strategies that would target the manifestations of cytopenias in children as well as the underlying causes of the process.

Thus, further researches should be conducted in order to recognize the genetic and environmental factors, which might influence the development of hematological disorders in children. New technologies in fields like genomic medicine and targeted therapies are expected to present an opportunity to provide individualised treatment to assist in the prognosis and health status of children who have cytopenias.

This work provides a good background concerning the understanding of the complexity of paediatric haematological states and emphasizes the need for more comprehensive approaches to the management of these patients both from clinical, laboratory and socio-economic points of view using case scenario of cytopenic disorders in children.

CONCLUSION

CONCLUSION:

1. Our study data predicts the bicytopenia and pancytopenia in children in the age group of 1 to 18 years with prevalence of bicytopenia in children higher than that of pancytopenia.
2. Clinical characters pointed out the symptoms such as fatigue, pain abdomen, fever and changes in blood cell counts, including anemia, leukopenia and thrombocytopenia, were frequent; nonetheless, normocytic normochromic anemia was observed as dominant.
3. Age distribution analysis revealed cytopenia's are more frequent in school children and adolescents, which help in directing appropriate clinical suspicion.
4. Our study found majority of pediatric age group urine sample fluoride values were <2 ppm , highlighting the necessity for further exploration of environmental factors and transplacental passage of fluoride.
5. Overall, findings provide insights into epidemiology, clinical features and environmental influences on bicytopenia and pancytopenia in children, highlighting the future diagnostic and therapeutic strategies.

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ANNEXURE

A decorative graphic consisting of a thick horizontal black line and a thick vertical black line intersecting at a right angle. The horizontal line extends from the left edge of the page towards the right, and the vertical line extends from the bottom edge of the page upwards. The intersection point is located to the right of the word 'ANNEXURE'.

INFORMED CONSENT FORM FOR LESS THAN 7 YEARS OF AGE.

Date:

I, Mr/Mrs _____ have been explained in my own vernacular language that my child will be included in the study, **CLINICAL AND LABORATORY PROFILE IN PAEDIATRIC PATIENTS WITH BICYTOPENIA OR PANCYTOPENIA IN A TERTIARY CARE CENTRE IN KOLAR - A CROSS SECTIONAL STUDY.**

I hereby give my valid written informed consent without any force or prejudice for recording the observations and investigations to be done for my child. The nature and risks involved have been explained to me to my satisfaction. I have been explained in detail about the study being conducted. I have read the patient/participant information sheet and I have had the opportunity to ask any question. Any question that I have asked, have been answered to my satisfaction. I consent voluntarily to participate my child as a participant in this research. I hereby give consent to provide my child's history, undergo physical examination, undergo the procedure, undergo investigations and provide its results and documents etc., to the doctor / institute etc. All the data may be published or used for any academic purpose. I will not hold the doctors / institute etc., responsible for any untoward consequences during the procedure / study. A copy of this Informed Consent Form and Patient Information Sheet has been provided to the participant.

(Signature/Thumb impression & Name of the Guardian)

(Relation with patient)

Witness:

(Signature & Name of Research person /doctor)

7 ವರ್ಷಕ್ಕಿಂತ ಕಡಿಮೆ ವಯಸ್ಸಿನವರಿಗೆ ಮಾಹಿತಿಯುಕ್ತ ಒಪ್ಪಿಗೆ ನಮೂನೆ.

ದಿನಾಂಕ:

ನಾನು, ಶ್ರೀ/ಶ್ರೀಮತಿ

ನನ್ನ

ಮಗುವನ್ನು ಅಧ್ಯಯನದಲ್ಲಿ ಸೇರಿಸಲಾಗುವುದು ಎಂದು ವಿವರಿಸಲಾಗಿದೆ, ಬೈಸಿಟೋಪೆನಿಯಾ ಅಥವಾ ಪ್ಯಾನ್ಸಿಟೋಪೆನಿಯಾ ಹೊಂದಿರುವ ಮಕ್ಕಳ ರೋಗಿಗಳಲ್ಲಿನ ಕ್ಲಿನಿಕಲ್ ಮತ್ತು ಲ್ಯಾಬೋರೇಟರಿ ಪ್ರೊಫೈಲ್‌ನಲ್ಲಿ ಮೂರನೇ ತರಗತಿಯ ವಿಭಾಗ.

ನನ್ನ ಮಗುವಿಗೆ ಮಾಡಬೇಕಾದ ವೀಕ್ಷಣೆಗಳು ಮತ್ತು ತನಿಖೆಗಳನ್ನು ದಾಖಲಿಸಲು ಯಾವುದೇ ಬಲ ಅಥವಾ ಪೂರ್ವಾಗ್ರಹವಿಲ್ಲದೆ ನಾನು ಈ ಮೂಲಕ ನನ್ನ ಮಾನ್ಯ ಲಿಖಿತ ತಿಳುವಳಿಕೆಯನ್ನು ನೀಡುತ್ತೇನೆ. ಒಳಗೊಂಡಿರುವ ಸ್ವಭಾವ ಮತ್ತು ಅಪಾಯಗಳನ್ನು ನನಗೆ ತೃಪ್ತಿಪಡಿಸಲು ವಿವರಿಸಲಾಗಿದೆ. ನಡೆಸುತ್ತಿರುವ ಅಧ್ಯಯನದ ಬಗ್ಗೆ ನನಗೆ ವಿವರವಾಗಿ ವಿವರಿಸಲಾಗಿದೆ. ನಾನು ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆಯನ್ನು ಓದಿದ್ದೇನೆ ಮತ್ತು ಯಾವುದೇ ಪ್ರಶ್ನೆಯನ್ನು ಕೇಳಲು ನನಗೆ ಅವಕಾಶವಿದೆ. ನಾನು ಕೇಳಿದ ಯಾವುದೇ ಪ್ರಶ್ನೆಗೆ ನನ್ನ ತೃಪ್ತಿಗೆ ಉತ್ತರಿಸಲಾಗಿದೆ. ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವವನಾಗಿ ನನ್ನ ಮಗುವನ್ನು ಭಾಗವಹಿಸಲು ನಾನು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಸಮ್ಮತಿಸುತ್ತೇನೆ. ನನ್ನ ಮಗುವಿನ ಇತಿಹಾಸವನ್ನು ಒದಗಿಸಲು, ದೈಹಿಕ ಪರೀಕ್ಷೆಗೆ ಒಳಗಾಗಲು, ಕಾರ್ಯವಿಧಾನಕ್ಕೆ ಒಳಗಾಗಲು, ತನಿಖೆಗೆ ಒಳಗಾಗಲು ಮತ್ತು ಅದರ ಫಲಿತಾಂಶಗಳು ಮತ್ತು ದಾಖಲೆಗಳನ್ನು ಇತ್ಯಾದಿಗಳನ್ನು ವೈದ್ಯರಿಗೆ / ಸಂಸ್ಥೆಗೆ ಒದಗಿಸಲು ನಾನು ಈ ಮೂಲಕ ಒಪ್ಪಿಗೆ ನೀಡುತ್ತೇನೆ. ಎಲ್ಲಾ ಡೇಟಾವನ್ನು ಪ್ರಕಟಿಸಬಹುದು ಅಥವಾ ಯಾವುದೇ ಶೈಕ್ಷಣಿಕ ಉದ್ದೇಶಕ್ಕಾಗಿ ಬಳಸಬಹುದು. ಕಾರ್ಯವಿಧಾನ / ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಯಾವುದೇ ಅಹಿತಕರ ಪರಿಣಾಮಗಳಿಗೆ ನಾನು ವೈದ್ಯರು / ಸಂಸ್ಥೆ ಇತ್ಯಾದಿಗಳನ್ನು ಹೊಣೆಗಾರರನ್ನಾಗಿ ಮಾಡುವುದಿಲ್ಲ. ಈ ತಿಳುವಳಿಕೆಯುಳ್ಳ ಒಪ್ಪಿಗೆ ನಮೂನೆಯ ಪ್ರತಿಯನ್ನು ಮತ್ತು ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆಯನ್ನು ಭಾಗವಹಿಸುವವರಿಗೆ ಒದಗಿಸಲಾಗಿದೆ.

(ಸಹಿ/ಹೆಬ್ಬರಳಿನ ಗುರುತು ಮತ್ತು ರಕ್ಷಕರ ಹೆಸರು)

(ರೋಗಿಯೊಂದಿಗಿನ ಸಂಬಂಧ)

ಸಾಕ್ಷಿ:

(ಸಂಶೋಧನಾ ವ್ಯಕ್ತಿ/ವೈದ್ಯರ ಸಹಿ ಮತ್ತು ಹೆಸರು)

INFORMED CONSENT FORM / ASSENT FORM FOR 7-12 YEARS OF AGE

Date:

I, Mr/Mrs _____ have been explained in my own vernacular language that my child / myself will be included in the study, **CLINICAL AND LABORATORY PROFILE IN PAEDIATRIC PATIENTS WITH BICYTOPENIA OR PANCYTOPENIA IN A TERTIARY CARE CENTRE IN KOLAR - A CROSS SECTIONAL STUDY.**

I hereby give my valid written informed consent without any force or prejudice for recording the observations and investigations to be done on myself/ for my child. The nature and risks involved have been explained to me to my satisfaction. I have been explained in detail about the study being conducted. I have read the patient information sheet and I have had the opportunity to ask any question. Any question that I have asked, have been answered to my satisfaction. I consent voluntarily to participate myself/my child in this research. I hereby give consent to provide my /my child's history, undergo physical examination, undergo the procedure, undergo investigations and provide its results and documents etc., to the doctor / institute etc. All the data may be published or used for any academic purpose. I will not hold the doctors / institute etc., responsible for any untoward consequences during the procedure / study. A copy of this Informed Consent Form and Patient Information Sheet has been provided to the participant.

(Signature/Thumb impression & Name of Patient):ASSENT OF THE CHILD

(Signature/Thumb impression & Name of Guardian)

(Relation with patient)

Witness:

(Signature & Name of Research person /doctor)

7-12 ವರ್ಷ ವಯಸ್ಸಿನವರಿಗೆ ತಿಳುವಳಿಕೆಯುಳ್ಳ ಒಪ್ಪಿಗೆ ನಮೂನೆ

ದಿನಾಂಕ:

ನಾನು, ಶ್ರೀ/ಶ್ರೀಮತಿ _____ ನನ್ನ ಮಗು/ನನ್ನನ್ನು ಬೆಳೆಸಿಕೊಡುವವನು ಅಥವಾ ಪಾಲನೆಗೊಡುವವನು ಹೊಂದಿರುವ ಮಕ್ಕಳ ರೋಗಿಗಳಲ್ಲಿ ಅಧ್ಯಯನ, ಕ್ಲಿನಿಕಲ್ ಮತ್ತು ಲ್ಯಾಬೋರೇಟರಿ ಪ್ರೊಫೈಲ್‌ನಲ್ಲಿ ಸೇರಿಸಲಾಗುವುದು ಎಂದು ನನ್ನ ಸ್ವಂತ ಸ್ಥಳೀಯ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಲಾಗಿದೆ.

ನನ್ನ ಮಗುವಿಗೆ ಮಾಡಬೇಕಾದ ವೀಕ್ಷಣೆಗಳು ಮತ್ತು ತನಿಖೆಗಳನ್ನು ದಾಖಲಿಸಲು ಯಾವುದೇ ಬಲ ಅಥವಾ ಪೂರ್ವಾಗ್ರಹವಿಲ್ಲದೆ ನಾನು ಈ ಮೂಲಕ ನನ್ನ ಮಾನ್ಯ ಲಿಖಿತ ತಿಳುವಳಿಕೆಯನ್ನು ನೀಡುತ್ತೇನೆ. ಒಳಗೊಂಡಿರುವ ಸ್ವಭಾವ ಮತ್ತು ಅಪಾಯಗಳನ್ನು ನನಗೆ ತೃಪ್ತಿಪಡಿಸಲು ವಿವರಿಸಲಾಗಿದೆ. ನಡೆಸುತ್ತಿರುವ ಅಧ್ಯಯನದ ಬಗ್ಗೆ ನನಗೆ ವಿವರವಾಗಿ ವಿವರಿಸಲಾಗಿದೆ. ನಾನು ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆಯನ್ನು ಓದಿದ್ದೇನೆ ಮತ್ತು ಯಾವುದೇ ಪ್ರಶ್ನೆಯನ್ನು ಕೇಳಲು ನನಗೆ ಅವಕಾಶವಿದೆ. ನಾನು ಕೇಳಿದ ಯಾವುದೇ ಪ್ರಶ್ನೆಗೆ ನನ್ನ ತೃಪ್ತಿಗೆ ಉತ್ತರಿಸಲಾಗಿದೆ. ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವವನಾಗಿ ನನ್ನ ಮಗುವನ್ನು ಭಾಗವಹಿಸಲು ನಾನು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಸಮ್ಮತಿಸುತ್ತೇನೆ. ನನ್ನ ಮಗುವಿನ ಇತಿಹಾಸವನ್ನು ಒದಗಿಸಲು, ದೈಹಿಕ ಪರೀಕ್ಷೆಗೆ ಒಳಗಾಗಲು, ಕಾರ್ಯವಿಧಾನಕ್ಕೆ ಒಳಗಾಗಲು, ತನಿಖೆಗೆ ಒಳಗಾಗಲು ಮತ್ತು ಅದರ ಫಲಿತಾಂಶಗಳು ಮತ್ತು ದಾಖಲೆಗಳನ್ನು ಇತ್ಯಾದಿಗಳನ್ನು ವೈದ್ಯರಿಗೆ / ಸಂಸ್ಥೆಗೆ ಒದಗಿಸಲು ನಾನು ಈ ಮೂಲಕ ಒಪ್ಪಿಗೆ ನೀಡುತ್ತೇನೆ. ಎಲ್ಲಾ ಡೇಟಾವನ್ನು ಪ್ರಕಟಿಸಬಹುದು ಅಥವಾ ಯಾವುದೇ ಶೈಕ್ಷಣಿಕ ಉದ್ದೇಶಕ್ಕಾಗಿ ಬಳಸಬಹುದು. ಕಾರ್ಯವಿಧಾನ / ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಯಾವುದೇ ಅಹಿತಕರ ಪರಿಣಾಮಗಳಿಗೆ ನಾನು ವೈದ್ಯರು / ಸಂಸ್ಥೆ ಇತ್ಯಾದಿಗಳನ್ನು ಹೊಣೆಗಾರರನ್ನಾಗಿ ಮಾಡುವುದಿಲ್ಲ. ಈ ತಿಳುವಳಿಕೆಯುಳ್ಳ ಒಪ್ಪಿಗೆ ನಮೂನೆಯ ಪ್ರತಿಯನ್ನು ಮತ್ತು ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆಯನ್ನು ಭಾಗವಹಿಸುವವರಿಗೆ ಒದಗಿಸಲಾಗಿದೆ.

(ಸಹಿ/ಹೆಬ್ಬರಳಿನ ಗುರುತು ಮತ್ತು ರೋಗಿಯ ಹೆಸರು): ಮಗುವಿನ ಒಪ್ಪಿಗೆ

(ಸಹಿ/ಹೆಬ್ಬರಳಿನ ಗುರುತು ಮತ್ತು ರಕ್ಷಕನ ಹೆಸರು)

(ರೋಗಿಯೊಂದಿಗಿನ ಸಂಬಂಧ)

ಸಾಕ್ಷಿ:

(ಸಂಶೋಧನಾ ವ್ಯಕ್ತಿ/ವೈದ್ಯರ ಸಹಿ ಮತ್ತು ಹೆಸರು)

INFORMED CONSENT FORM FOR 12-18 YEARS OF AGE

Date:

I, Mr/Mrs _____ have been explained in my own vernacular language that my child / myself will be included in the study, **CLINICAL AND LABORATORY PROFILE IN PAEDIATRIC PATIENTS WITH BICYTOPENIA OR PANCYTOPENIA IN A TERTIARY CARE CENTRE IN KOLAR - A CROSS SECTIONAL STUDY.**

I hereby give my valid written informed consent without any force or prejudice for recording the observations and investigations to be done on me /for my child. The nature and risks involved have been explained to me to my satisfaction. I have been explained in detail about the study being conducted. I have read the patient information sheet and I have had the opportunity to ask any question. Any question that I have asked, have been answered to my satisfaction. I consent voluntarily to participate myself / my child as a participant in this research. I hereby give consent to provide my / my child's history, undergo physical examination, undergo the procedure, undergo investigations and provide its results and documents etc., to the doctor / institute etc. All the data may be published or used for any academic purpose. I will not hold the doctors / institute etc., responsible for any untoward consequences during the procedure / study. A copy of this Informed Consent Form and Patient Information Sheet has been provided to the participant.

(Signature/Thumb impression & Name of Patient)_____

(Signature/Thumb impression & Name of Guardian)

(Relation with patient)

Witness:

(Signature & Name of Research person /doctor)

ದಿನಾಂಕ:

ನಾನು, ಶ್ರೀ/ಶ್ರೀಮತಿ

_____ ನನ್ನ ಮಗು/ನನ್ನನ್ನು ಬೈಸಿಟೋಪೆನಿಯಾ ಅಥವಾ ಪ್ಯಾನ್ಸಿಟೋಪೆನಿಯಾ ಹೊಂದಿರುವ ಮಕ್ಕಳ ರೋಗಿಗಳಲ್ಲಿ ಅಧ್ಯಯನ, ಕ್ಲಿನಿಕಲ್ ಮತ್ತು ಲ್ಯಾಬೋರೇಟರಿ ಪ್ರೊಫೈಲ್‌ನಲ್ಲಿ ಸೇರಿಸಲಾಗುವುದು ಎಂದು ನನ್ನ ಸ್ವಂತ ಸ್ಥಳೀಯ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಲಾಗಿದೆ.

ನನ್ನ ಮಗುವಿಗೆ ಮಾಡಬೇಕಾದ ವೀಕ್ಷಣೆಗಳು ಮತ್ತು ತನಿಖೆಗಳನ್ನು ದಾಖಲಿಸಲು ಯಾವುದೇ ಬಲ ಅಥವಾ ಪೂರ್ವಾಗ್ರಹವಿಲ್ಲದೆ ನಾನು ಈ ಮೂಲಕ ನನ್ನ ಮಾನ್ಯ ಲಿಖಿತ ತಿಳುವಳಿಕೆಯನ್ನು ನೀಡುತ್ತೇನೆ. ಒಳಗೊಂಡಿರುವ ಸ್ವಭಾವ ಮತ್ತು ಅಪಾಯಗಳನ್ನು ನನಗೆ ತೃಪ್ತಿಪಡಿಸಲು ವಿವರಿಸಲಾಗಿದೆ. ನಡೆಸುತ್ತಿರುವ ಅಧ್ಯಯನದ ಬಗ್ಗೆ ನನಗೆ ವಿವರವಾಗಿ ವಿವರಿಸಲಾಗಿದೆ. ನಾನು ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆಯನ್ನು ಓದಿದ್ದೇನೆ ಮತ್ತು ಯಾವುದೇ ಪ್ರಶ್ನೆಯನ್ನು ಕೇಳಲು ನನಗೆ ಅವಕಾಶವಿದೆ. ನಾನು ಕೇಳಿದ ಯಾವುದೇ ಪ್ರಶ್ನೆಗೆ ನನ್ನ ತೃಪ್ತಿಗೆ ಉತ್ತರಿಸಲಾಗಿದೆ. ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವವನಾಗಿ ನನ್ನ ಮಗುವನ್ನು ಭಾಗವಹಿಸಲು ನಾನು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಸಮ್ಮತಿಸುತ್ತೇನೆ. ನನ್ನ ಮಗುವಿನ ಇತಿಹಾಸವನ್ನು ಒದಗಿಸಲು, ದೈಹಿಕ ಪರೀಕ್ಷೆಗೆ ಒಳಗಾಗಲು, ಕಾರ್ಯವಿಧಾನಕ್ಕೆ ಒಳಗಾಗಲು, ತನಿಖೆಗೆ ಒಳಗಾಗಲು ಮತ್ತು ಅದರ ಫಲಿತಾಂಶಗಳು ಮತ್ತು ದಾಖಲೆಗಳನ್ನು ಇತ್ಯಾದಿಗಳನ್ನು ವೈದ್ಯರಿಗೆ / ಸಂಸ್ಥೆಗೆ ಒದಗಿಸಲು ನಾನು ಈ ಮೂಲಕ ಒಪ್ಪಿಗೆ ನೀಡುತ್ತೇನೆ. ಎಲ್ಲಾ ಡೇಟಾವನ್ನು ಪ್ರಕಟಿಸಬಹುದು ಅಥವಾ ಯಾವುದೇ ಶೈಕ್ಷಣಿಕ ಉದ್ದೇಶಕ್ಕಾಗಿ ಬಳಸಬಹುದು. ಕಾರ್ಯವಿಧಾನ / ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಯಾವುದೇ ಅಹಿತಕರ ಪರಿಣಾಮಗಳಿಗೆ ನಾನು ವೈದ್ಯರು / ಸಂಸ್ಥೆ ಇತ್ಯಾದಿಗಳನ್ನು ಹೊಣೆಗಾರರನ್ನಾಗಿ ಮಾಡುವುದಿಲ್ಲ. ಈ ತಿಳುವಳಿಕೆಯುಳ್ಳ ಒಪ್ಪಿಗೆ ನಮೂನೆಯ ಪ್ರತಿಯನ್ನು ಮತ್ತು ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆಯನ್ನು ಭಾಗವಹಿಸುವವರಿಗೆ ಒದಗಿಸಲಾಗಿದೆ.

_____ (ಸಹಿ/ಹೆಬ್ಬರಳಿನ ಗುರುತು ಮತ್ತು ರೋಗಿಯ ಹೆಸರು)

_____ (ಸಹಿ/ಹೆಬ್ಬರಳಿನ ಗುರುತು ಮತ್ತು ರಕ್ಷಕನ ಹೆಸರು)

(ರೋಗಿಯೊಂದಿಗಿನ ಸಂಬಂಧ)

ಸಾಕ್ಷಿ:

(ಸಂಶೋಧನಾ ವ್ಯಕ್ತಿ/ವೈದ್ಯರ ಸಹಿ

ಮತ್ತು ಹೆಸರು)

PARTICIPANT/PATIENT INFORMATION SHEET

Principal investigator: Dr .RAM SWAROOP/Dr. KNV. PRASAD .

I Dr.RAM SWAROOP REDDY , Post graduate student in Department at Sri Devraj Urs Medical College, will be conducting a study titled... **CLINICAL AND LABORATORY PROFILE IN PAEDIATRIC PATIENTS WITH BICYTOPENIA OR PANCYTOPENIA IN A TERTIARY CARE CENTRE IN KOLAR - A CROSS SECTIONAL STUDY.** “for my dissertation under the guidance of Dr. KNV PRASAD Professor of Department of Paediatrics.

The participants of this study i.e. children aged from 1 year to 18 years will be undergoing relevant investigations such as fluoride levels and other investigations(CBC,serum folic acid,serum vit B12, iron profile etc.,)for children with bicytopenia or pancytopenia admitted at RL JALLAPA hospital .You will not be paid any financial compensation for the participation of your child in this research project.All investigation charges will be paid by me.All the data will be kept confidential and will be used only for research purpose by this institution. You are free to provide consent for the participation of your child/yourself in this study. You can also withdraw yourself/ child from the study at any point of time without giving any reasons whatsoever. Your refusal to participate will not prejudice you to any present or future care at this institution.

Name and Signature of the Principal Investigator

Date-

ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆ

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ: ಡಾ. ರಾಮ್ ಸ್ವರೂಪ್/ಡಾ. ಕೆ.ಎನ್.ವಿ. ಪ್ರಸಾದ್.

ನಾನು ಡಾ.ರಾಮ್ ಸ್ವರೂಪ್ ರೆಡ್ಡಿ , ಶ್ರೀ ದೇವರಾಜ್ ಅರ್ಸ್ ವೈದ್ಯಕೀಯ ಕಾಲೇಜಿನಲ್ಲಿ ವಿಭಾಗದಲ್ಲಿ ಸ್ನಾತಕೋತ್ತರ ವಿದ್ಯಾರ್ಥಿಯಾಗಿದ್ದು, ಬೈಸಿಟೋಪೆನಿಯಾ ಅಥವಾ ಪ್ಯಾನ್ಸಿಟೋಪೆನಿಯಾ ಹೊಂದಿರುವ ಮಕ್ಕಳ ರೋಗಿಗಳಲ್ಲಿ ಕ್ಲಿನಿಕಲ್ ಮತ್ತು ಲ್ಯಾಬೋರೇಟರಿ ಪ್ರೊಫೈಲ್ ಎಂಬ ಶೀರ್ಷಿಕೆಯ ಅಧ್ಯಯನವನ್ನು ನಡೆಸಲಿದ್ದಾರೆ ಅಧ್ಯಯನ. "ಡಾ. ಕೆ.ಎನ್.ವಿ. ಪ್ರಸಾದ್ ಮಕ್ಕಳ ವಿಭಾಗದ ಪ್ರಾಧ್ಯಾಪಕರ ಮಾರ್ಗದರ್ಶನದಲ್ಲಿ ನನ್ನ ಪ್ರಬಂಧಕ್ಕಾಗಿ.

ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವವರು ಅಂದರೆ 1 ವರ್ಷದಿಂದ 18 ವರ್ಷ ವಯಸ್ಸಿನ ಮಕ್ಕಳು ಎಲ್ಲಾ ದಾಖಲಾದ ಮಕ್ಕಳಿಗೆ ಫ್ಲೋರೈಡ್ ಮಟ್ಟಗಳು ಮತ್ತು ಇತರ ತನಿಖೆಗಳಿಗೆ (cbc, ಸೀರಮ್ ಫೋಲಿಕ್ ಆಮ್ಲ, ಸೀರಮ್ ವಿಟ್ ಬಿ 12, ಐರನ್ ಪ್ರೊಫೈಲ್ ಇತ್ಯಾದಿ) ಸಂಬಂಧಿತ ತನಿಖೆಗಳಿಗೆ ಒಳಗಾಗುತ್ತಾರೆ. ಬೈಸಿಟೋಪೆನಿಯಾ ಅಥವಾ ಪ್ಯಾನ್ಸಿಟೋಪೆನಿಯಾವನ್ನು RL JALLAPA ಆಸ್ಪತ್ರೆಯಲ್ಲಿ ದಾಖಲಿಸಲಾಗಿದೆ .ಈ ಸಂಶೋಧನಾ ಯೋಜನೆಯಲ್ಲಿ ನಿಮ್ಮ ಮಗುವಿನ ಭಾಗವಹಿಸುವಿಕೆಗಾಗಿ ನಿಮಗೆ ಯಾವುದೇ ಹಣಕಾಸಿನ ಪರಿಹಾರವನ್ನು ನೀಡಲಾಗುವುದಿಲ್ಲ. ಎಲ್ಲಾ ಡೇಟಾವನ್ನು ಗೌಪ್ಯವಾಗಿ ಇರಿಸಲಾಗುತ್ತದೆ ಮತ್ತು ಈ ಸಂಸ್ಥೆಯು ಸಂಶೋಧನಾ ಉದ್ದೇಶಕ್ಕಾಗಿ ಮಾತ್ರ ಬಳಸುತ್ತದೆ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನಿಮ್ಮ ಮಗುವಿನ ಭಾಗವಹಿಸುವಿಕೆಗೆ ಒಪ್ಪಿಗೆ ನೀಡಲು ನೀವು ಸ್ವತಂತ್ರರಾಗಿದ್ದೀರಿ. ಯಾವುದೇ ಕಾರಣಗಳನ್ನು ನೀಡದೆ ನೀವು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ನಿಮ್ಮ ಮಗುವನ್ನು ಅಧ್ಯಯನದಿಂದ ಹಿಂಪಡೆಯಬಹುದು. ಭಾಗವಹಿಸಲು ನಿಮ್ಮ ನಿರಾಕರಣೆಯು ಈ ಸಂಸ್ಥೆಯಲ್ಲಿ ಯಾವುದೇ ಪ್ರಸ್ತುತ ಅಥವಾ ಭವಿಷ್ಯದ ಕಾಳಜಿಗೆ ನಿಮ್ಮನ್ನು ಪೂರ್ವಾಗ್ರಹ ಮಾಡುವುದಿಲ್ಲ.

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿಯ ಹೆಸರು ಮತ್ತು ಸಹಿ

ದಿನಾಂಕ-

PROFORMA

Name of patient:

Date:

Age:

Sex:

UHID No:

Address:

Provisional Diagnosis:

Family history: consanguineous/ non consanguineous

Similar history in family: yes/ no

Socio economic status: I, II, III, IV, V

Clinical features of Anemia:pallor:yes/no

Fatigue:yes/no

Hyperpigmentation of knuckles:yes/no

Clinical features of thrombocytopenia:purpura: yes/no

Bleeding manifestations:yes/no

Clinical features of leukopenia:

Lymphadenopathy:yes/no

Skin rashes:yes/no

ANTHROPOMETRY:

Weight:

Height:

BMI:

LAB PROFILE:

CBC:

urinefluoride :

Hb:

RBC:

PCV:

MCV:

MCH:

MCHC:

RDW:

WBC:

PLATELETS:

PERIPHERAL SMEAR:

RETICULOCYTE COUNT:

Serum vitamin B12:

Serum folic acid:

Serum Iron profile:

Bone marrow findings (if done):

Serum fluoride:

Hepatomegaly:

Splenomegaly:

MASTER CHART

A decorative graphic consisting of a thick horizontal line and a thick vertical line intersecting at the right end of the horizontal line, positioned below the title.

[illegible]

