



St. Paul Hospital Millennium Medical College

Post Graduate Study Program

**ASSESSMENT OF PATTERNS AND POSSIBLE RISK FACTORS OF
PANCYTOPENIA IN CHILDREN TREATED IN SAINT PAUL'S
HOSPITAL FROM AUGUST 2021-2024**

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ADDIS ABABA, ETHIOPIA

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St. Paul Hospital Millennium Medical College

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**A THESIS TO BE SUBMITTED TO DEPARTMENT OF PEDIATRICS
AND CHILD HEALTH, SAINT PAUL'S HOSPITAL MILLENNIUM
MEDICAL COLLEGE IN PARTIAL FULFILMENT OF THE
REQUIREMENTS FOR THE CERTIFICATE IN PEDIATRICS AND
CHILD HEALTH.**

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Research Thesis Submission Form

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Acronyms

BMA- bone marrow aspiration

IHRERC- Institutional Health Research Ethics Review Committee

OPD-out patient department

PICT- Provider initiative counseling and testing

PICU – pediatric intensive care unit

PM- peripheral morphology

SPHMMC – St. Paul’s Hospital Millennium Medical College

SPSS – Statistical Package for Social Science

Key words

Pancytopenia , Bicytopenia , Anemia ,Neutropenia ,thrombocytopenia ,Leukemia

1 Abstract

Background: pancytopenia is a common clinical condition among paediatric patients. It is a reduction of all three classes of formed elements of the blood: erythrocytes, leucocytes, and platelets. It is not a disease entity but a triad of findings that may result from a number of disease processes. The risk factors may vary in different patients and in different areas of the world. Assessing the risk factors helps to identify gaps and suggest possible interventions for policymakers.

Objective: It was aimed to determine the pattern and risk factors of pancytopenia among children treated in Saint Paul's hospital over a 3-year period from August 2021 to August 2024.

Methods: A 3-year retrospective facility-based descriptive study was carried out at the Department of Paediatrics and Child Health at Saint Paul's Hospital. Retrospectively, a chart review was done for the children who were treated at our hospital from August 2021 to August 2024. The diagnosis of pancytopenia was considered based on their laboratory values showing neutropenia, anaemia, and thrombocytopenia. A total of 89 patients' were included in the study according to the inclusion criteria.

Results: pancytopenia mostly affected children who were between one and five years of age. Most common clinical symptoms were decreased Appetite followed by generalised fatigability and fever, and the sign was lymphadenopathy. The most common underlying aetiology was aplastic anaemia, followed by ALL and infection.

Conclusion: The most common cause of pancytopenia was aplastic anemia and ALL which is a different picture from other studies. Most of children presented with generalised fatigability decreased appetite,, and fever. The disease processes signify underlying causes, which warrant thorough workup.

2 Introduction

2.1 Background

Pancytopenia is a medical disorder characterized by a decrease in peripheral blood cell lineages, including platelets, leukocytes, and erythrocytes, in the blood. Alterations in peripheral blood counts resulting in pancytopenia are commonly encountered in pediatric practice. (1)

Pancytopenia is a medical condition that generally exists among children in which the peripheral blood cell lineages are found to reduce in blood. The condition is diagnosed as a common haematological problem with an extensive differential diagnosis and varies according to the geographical distribution and genetic mutation. The condition is reversible and easily treatable if identified at the earliest (2).

Pancytopenia is a relatively common entity. However, it has received inadequate attention. A study of pancytopenia using easily available diagnostic techniques is therefore relevant. Bone marrow aspiration (BMA) and biopsy is an important diagnostic tool in hematology to evaluate various causes of pancytopenia (3).

2.2 Statement of the problem

Pancytopenia, characterized by a simultaneous reduction in red blood cells, white blood cells, and platelets, poses significant challenges in paediatric healthcare. Despite advances in medical science, the aetiology and management of pancytopenia in children remain complex and multifaceted. In the context of Saint Paul's Hospital there is a need to comprehensively assess the patterns and potential risk factors associated with pancytopenia among paediatric patients.

Protein energy malnutrition (PEM) is a syndrome that often results in immunodeficiency coupled with pancytopenia (4). Acute leukaemia and bone marrow failure were identified as the most common causes of pancytopenia in children (5).

The primary problem arises from the lack of a thorough understanding of the epidemiological trends, diagnostic approaches, and treatment outcomes specific to paediatric pancytopenia cases within the hospital's catchment area. Additionally, the identification of modifiable risk factors contributing to the development and progression of pancytopenia in children remains limited (6). This knowledge gap will compromise the overall quality of care and patient outcomes.

Furthermore, the scarcity of research focusing on paediatrics pancytopenia within the Ethiopian healthcare context exacerbates the challenge of devising evidence-based strategies for prevention, diagnosis, and management. Without a comprehensive understanding of the underlying patterns and risk factors, healthcare providers at Saint Paul's Hospital face significant hurdles in delivering personalized and targeted care to patients presenting with pancytopenia.

In addition, an early recognition of the underlying conditions will have an impact on the mortality and morbidity in vulnerable paediatrics patients. In the current study, I will try to study the clinical profile of children with pancytopenia and identify the likely aetiology in these cases.

Therefore, this study will address the following key questions:

1. What are the demographic and clinical patterns of paediatric patients diagnosed with pancytopenia at Saint Paul's Hospital from August 2021 to 2024?
2. What are the potential risk factors associated with the development and progression of pancytopenia in children treated at Saint Paul's Hospital during the specified time period?
3. How do diagnostic modalities, treatment strategies, and outcomes vary among paediatric patients with pancytopenia?

By addressing these critical questions, this research aims to contribute to the advancement of knowledge regarding paediatric pancytopenia, thereby informing evidence-based practices and improving patient care outcomes at Saint Paul's Hospital and potentially beyond.

2.3 Significance of the study

1. **Clinical Impact:** Enhances understanding of paediatric pancytopenia for improved diagnosis and treatment at Saint Paul's Hospital and beyond.
2. **Research Advancement:** Contributes new insights to pediatric pancytopenia research, aiding future studies and therapeutic developments.
3. **Public Health Implications:** Informs preventive strategies and health policies for better management of paediatrics haematological disorders.
4. **Clinical Guidelines and Policies:** Guides the development of evidence-based guidelines and protocols for standardized care.
5. **Capacity Building and Training:** Facilitates professional development and knowledge exchange among healthcare providers and researchers.

This study's findings have the potential to significantly impact clinical practice, research endeavors, public health initiatives, policy development, and professional capacity building in the field of paediatric haematology.

3 Literature review

3.1 Patterns of pancytopenia

A five year review study among in Hospitalized Children in the United States, shows a total of 64 children were identified with the diagnosis of pancytopenia. The most common diagnoses were infectious in origin (64%), followed by hematologic (28%) (7).

A research done in a tertiary hospital in India shows Megaloblastic anemia as the most common cause of pancytopenia accounting for about 75% followed by aplastic anemia which is seen in around 18%. (8) In another tertiary hospital in India, the most common etiological factors were ALL followed by Aplastic Anemia and others. (9)

A study done in India shows, from a total of 50 cytopine cases 24 patients have pancytopenia. The most common presenting symptoms were fever (87.5%) followed by lethargy (45.8%), and anorexia (41.7%) (10). Another study also shows, from a total of 990 children who were referred for bone marrow examination, 57.7% had either pancytopenia or bicytopenia (11). From 6109 hospitalized patients, 79 had pancytopenia. Pallor was found in 90.8% cases followed by hepatomegaly in 64.8% and splenomegaly in 40.8% cases (12).

A retrospective descriptive study was carried out at Department of paediatrics Rahman Medical Institute Peshawar, Pakistan, Out of 14642 patients admitted to the paediatrics department 205 (1.4%) patients were pancytopenia on their peripheral blood smear (13).

A retrospective cross-sectional study on Clinico-Pathological profiles of pancytopenia in University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia shows, 720 patients had pancytopenia. The most common presenting symptom was fatigue in 100% followed by weight loss 62.5%, fever 58%, pallor 27.8%, chills and rigor 9.7%, bleeding 8.3%. The most common presenting sign was splenomegaly 75% followed by hepatosplenomegaly 16.7% (14).

3.2 Etiologies' of pancytopenia

A retrospective study shows, out of the 24 cases, 22 (91%) had a non-malignant aetiology and malignant aetiology was seen in 2 cases only (10). Most common aetiology was acute leukaemia (66.9%) in bicytopenic children and aplastic anaemia (33.8%) in pancytopenia

children. Children with pancytopenia had underlying malignancy (26.6%) and splenomegaly (37.4%) (11).

From 79 pancytopenia cases, infective diseases were the common causes found in 87 (50%) cases, followed by malignancies in 28 (16%) cases and megaloblastic anemia in 22 (12.64%) cases (12).

A retrospective descriptive study done in Pakistan also shows the Common etiological pattern were Aplastic anaemia 58(28.3%), Haematological malignancies 49 (23.9%), megaloblastic anaemia 40 (19.5%), idiopathic thrombocytopenic purpura 16 (7.8%), iron deficiency anaemia 9 (4.4%) (13).

A retrospective cross-sectional study done in Gondar shows, the most common cause of pancytopenia was megaloblastic anaemia 385(53.5%) followed by Hyper reactive Malarial Splenomegaly 170(23.6%), leukaemia 70(9.7%), VL 40(5.6%), aplastic anaemia and stage IV RVI per se each 20(2.8%) and others 15(2.1%) (14). Other studies also show 81.8% cases of pancytopenia had non-malignant causes. Severe malnutrition, dengue fever, malaria and others were treatable causes for pancytopenia (15).

4 Objectives

4.1 General objectives

- To assess the pattern and risk factors of pancytopenia among pediatric patients aged less than 15 years at SPHMMC's Hospital Pediatrics and child health from August 2021 to 2024.

4.2 Specific objectives

- To describe the pattern of pancytopenia among pediatric patients aged under 15 years
- To identify the possible risk factors of pancytopenia among children's aged under 15 years
- To assess the clinical pictures of pancytopenia and treatment modalities among children's aged under 15 years

5 Methodology

5.1 Study area

This study was conducted in St. Paul's Millennium Medical College paediatrics and child health department. SPHMMC is the second largest hospital in the capital, Addis Ababa, with a catchment population of more than 5 million. The hospital was established in 1969 by the late emperor Haile Selassie and is currently governed by a board under the federal ministry of health. In addition to an inpatient capacity of more than 700 beds, on average, 1200 emergency and outpatient clients are seen daily in the hospital.

The paediatric haematology oncology unit was founded in 2021 GC and is currently run by two paediatric haematology oncologists and 4 fellows. Its patients are seen at ROPD, EOPD, Paediatric Ward, and PICU and the Hemato-Oncology follow-up clinic. The paediatric haematology-oncology follow-up clinic works once weekly.

5.2 Study design and period

Institution based retrospective descriptive study (from August 1, 2021 to August 1, 2024) was conducted

The study period is from August- Feb 2025

5.3 Population

4.2.1 Source population

All pancytopenia patients aged under 15 years and treated at SPHMMC

4.2.2 Study population

Patients aged less than 15 years who were diagnosed with pancytopenia/bicytopenia at SPHMMC's Hospital Pediatrics Clinic from August 2021 to 2024.

5.4 Eligibility criteria

5.4.1 Inclusion

- All pancytopenia children less than 15 years treated from August 2021 to August 2024 at SPHMMC's Hospital Pediatrics department.

5.4.2 Exclusion Criteria

- Patients taking chemotherapy at time of Pancytopenia diagnosis
- Cases with incomplete registrations
- Lost charts were excluded.

5.5 Sample Size Determination and Sampling Technique

The study assess the patterns of pancytopenia by reviewing the medical records of all cases less than 15 years who were diagnosed with pancytopenia, received treatment and follow-up at SPHMMC's Hospital Pediatrics Clinic from August 2021 to August 2024.

On average, 3- 4 new pancytopenia patients visits our hospital pediatrics department monthly which makes our study population~124 patients over the periods of 3yrs ,so all pancytopenia patients were planned to be included in the study.

5.6 Dependent and independent variables

Dependent Variable –

- pancytopenia

Independent Variables -

Socio demographic factors

- Age
- Sex
- Place of residence

Clinical factors

- Presenting clinical symptoms
- Duration of illness
- Hematologic profile
- having comorbidity
- causes/risk factors
- Treatment received

5.7 Data Collection procedure

Data was collected by reviewing their medical records. For better management of the data collection process, 3 data collectors (Interns) were recruited. As the topic requires a good deal of closer attention, the principal investigator was involved in supervision to ensure accurate and complete data collection. To assure data quality, the team was oriented regarding the objectives, methods of data collection, and other related issues.

5.8 Data processing and Analysis

The data was checked, coded, and entered into EPI data then exported to STATA 18 statistical software for analysis. The categorical variables were analyzed using frequencies and percentages. Descriptive statistics of numeric variables was presented in means, standard deviation, median, minimum, maximum, frequency, and ratio values.

5.9 Data Quality Assurance

Data quality was improved by taking suggestions and instructions from advisors before data collection. Throughout the data collection, supervision was made by the supervisor. The data collector checked for completeness of each checklist at the end of the data collection from each patient card and identified those uncompleted. Data quality was improved by taking suggestions and instructions from advisors before data collection. Throughout the data collection, supervision was made by the supervisor. The data collector checked for completeness of each checklist at the end of the data collection from each patient card and identified those uncompleted.

5.10 Result Dissemination Plan

The results of the research will be presented to SPHMMC's department of pediatrics and child health. The findings will be sent for publication on relevant scientific journals and disseminated online so that they can be of use for other academic researchers and clinical practitioners. The data can also serve as a base line for future studies

5.11 Ethical Consideration

A support letter for the research work was obtained from the Institutional Health Research Ethics Review Committee (IHRERC) of SPMMC and a formal permission letter was obtained and taken to the concerned body before data collection. Confidentiality was ensured

throughout the accomplishment of the study. All the information taken from the card was used for research purposes only.

5. RESULTS

6.1 Socio-demographic Variables

During the study period, there were 97 children treated for pancytopenia in SPHMMC according to HMIS documentation. From this, 89 were accessed according to inclusion criteria with a response rate of 91.75%. Among them, forty-five patients (50.56%) were males and 44 (49.44%) were females, aged between 3 months and 15 years. The mean age of the study population was found to be 5.98, with an SD (± 4.20) years, and the majority of the children (44.94%) were in the range of 1-5 years.

Table 1: Socio-demographic characteristics of pancytopenia patients(N=89)

Variable		Frequency (N)	Percent (%)
Age in years	< 1 year	11	12.36
	1-5 year	40	44.94
	5-10 year	21	23.60
	10-15 year	17	19.10
Gender	Male	45	50.56
	Female	44	49.44

6.2 Clinical Profile

The mean duration of illness before treatment was 2.67 weeks, with an SD (± 3.44) weeks. Most of the children presented with generalized fatigability (64%) and decreased appetite (58.43%) followed by fever 36 (40.45%). 44 (49.44%) participants had physical findings; the most common clinical findings were lymphadenopathy, splenomegaly, and body rash.

The diagnosis of pancytopenia was made on the basis of physical findings, complete blood count, peripheral morphology, bone marrow aspiration, B12 and folate levels, and some genetic tests. All of the patients had a peripheral complete blood count. The mean white cell

count was a leukocyte count of $2.8573 \times 10^9/L$, neutrophil count of $0.7124 \times 10^9/L$ (SD=328.9) with a range of 43 to 5,400 / μL . 31 patients had absolute neutrophil counts less than 500 / μL at the initial presentation. The mean haemoglobin was 6.55 g/dL (SD=2.13), ranging between 2.4 and 11 g/dL. 83 of the patients (92%) had severe anaemia (haemoglobin < 8 g/dL). The mean platelet count was 30,770 / μL (SD=28.61) with a range of 1,000 to 93,000. Eighteen patients had had a count of less than 20,000 / μL .

Peripheral morphology was determined for 78 patients out of 89, and bone marrow aspiration was performed for 57 patients.

Pancytopenia accounts for 60 cases (67.42%) in this study, and the remaining 29 patients are bicytopenic (32.58%).

With regard to comorbidities, seventeen patients had comorbidities like severe acute malnutrition, tuberculosis, chronic kidney disease, and hepatoblastoma, NHL, malaria, and HIV.

Table 2 Presenting clinical symptoms of patients Treated for pancytopenia.

Symptoms		Frequency (n)	Percent (%)
Generalized fatigability	Yes	57	64.01
	No	32	35.09
	Total	89	100
Decreased appetite	Yes	52	58.43
	No	37	41.57
	Total	89	100
Weight loss	yes	47	52.8
	no	42	47.2
	total	89	100
Fever	Yes	36	40.45
	No	53	59.55
	Total	89	100
Headache	Yes	29	32.58
	No	60	67.42
	Total	89	100

Epistaxis	Yes	27	30.34
	No	62	69.66
	Total	89	100
Mucosal bleeding	Yes	22	24.72
	No	67	75.28
	Total	89	100
Abdominal pain	yes	31	34.8
Abdominal swelling	Yes	28	31.46
	No	61	68.54
	Total	89	100
Other symptoms	Yes	11	12.3

Table 3 Hematological profile of the pancytopenia patients

Hematologic parameter	Mean $\pm$ SD
Hemoglobin (g/dL)	6.55 $\pm$ 2.13
Platelet count (1×10^9)/ μ L	30.77 $\pm$ 28.60
Leukocyte count (1×10^9) / μ L	2.8573 $\pm$ 1638
Neutrophil count (1×10^9) / μ L	0.7312 $\pm$ 838

In this study aplastic anaemia were found to be the major cause of pancytopenia in children. Fanconi anaemia cases were 5 of which genetically confirmed case is one and the others are clinically suspected, and one case with suspected dyskeratosis congenital is identified. With this congenital causes accounts for 8% of the total cases. Second most common cause of pancytopenia was ALL and followed by infection. No specific identifiable causes were noted in 16 (17.98%) out of 89 cases.

Table 4 Casual profile of pancytopenia

Cause	Frequency	Percentage (%)
Aplastic anemia	20	22.47%
ALL	18	20.22%
Infectious(n=14)	malaria (n= 6)	6.75%
	HIV (n= 4)	4.49%
	SEPSIS (n= 4)	4.49%
Megaloblastic anemia (n=7)	B12 Deficiency (n= 4)	4.50%
	folate Deficiency(n=3)	3.37%
SLE	4	4.49%
AML	5	5.62%
NHL	3	3.37
ITP	2	2.25%
Unknown cause	16	17.98%

Table 5 Etiological profile difference of children with bicytopenia and Pancytopenia

Cause		Bicytopenia		Pancytopenia	
		frequency	percent	frequency	Percent
Aplastic anemia		2	6.89	18	30.00
ALL		8	27.58	10	16.66
Megaloblastic	B12 Deficiency	1	3.44	3	5.00
	folate Deficiency	3	10.34	0	0.00
Infectious	Malaria	3	10.34	3	5.00
	HIV	0	0.00	4	6.67
	SEPSIS	2	6.88	2	3.33
SLE		0	0.00	4	6.67
AML		2	6.88	3	5.00
NHL		2	6.88	1	1.67
ITP		1	3.44	1	1.67
Unknown cause		5	17.24	11	18.33
Total		29	100.00	60	100.00

6.3 Treatment and complication of pancytopenia:

53 of patients require PRBC transfusion, 49 patients were transfused with platelet more than one times. Underlying causes were treated for thirty-eight patients, and they were given chemotherapy drugs, antibiotics, and antimalarial medications. Twenty patients received other supportive treatments like tranexamic acid injections, blood transfusions, and others. 36 (40.45%) patients developed complications like neuropenic fever treatment complications (58.33%), bleeding (36.11%), and transfusion-related complications (5.56%).

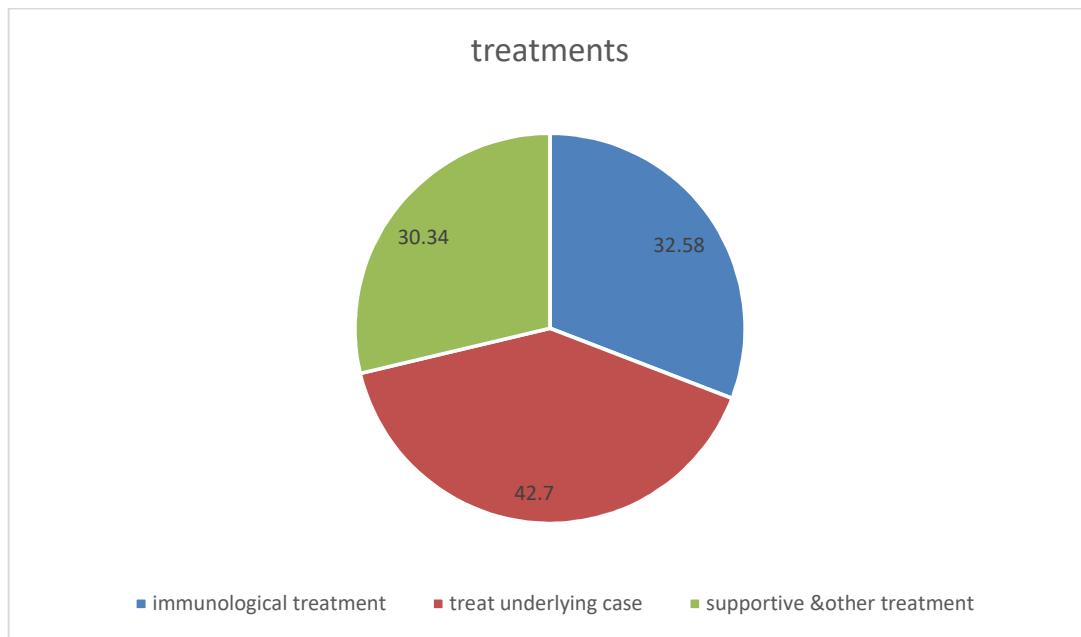


Figure 1 treatments of pancytopenia patients

7 Discussion

Pancytopenia is a common case faced in pediatric age group. In this study there were 89 Pancytopenia patients treated over a period of three years at SPHMMC. An increase in incidence of Pancytopenia cases had reported by different studies. The current study showed marked variation in the age groups affected which supported by different studies.

in our study, Females were affected by pancytopenia equivalent with males which was different with the study done by (16) (17). Which may be due to variations in the the sample size distribution.

In the current study most of the children presented with decreased Appetite and generalized fatigability and fever which was comparable with studies done by (17) ,(16), (18). This may be due to the similarity between the natures of the illness.

In the current study the most common cause of pancytopenia was aplastic anaemia followed by ALL and infections. some of the studies showed the common causes as megaloblastic and infection. The difference may be due to the fact that they included only admitted patients with pancytopenia and the sample also from different units from our study.

7.1 Limitation of the study

This study has some limitations. First, as a retrospective review, our data collection, analysis and reporting were restricted to that available in hospital databases or logbooks. Thus, for some years of data, incomplete patient information precluded further analysis.

7.2 Strength

No single study in this topic in pediatric population in the country in the previous time. The result is crucial bases for the future studies

8. Conclusion and Recommendation

The most common cause of pancytopenia was aplastic anaemia followed by ALL and infections. The children presented with decreased appetite, generalised fatigability, and fever. Of all the studies available, bone marrow aspiration seems the most useful.

An extensive differential diagnosis should be taken into account and a detailed history, examination and basic diagnostic tests were rewarding for the diagnosis, so treatable causes are identified without delay and the patient is benefited. As retrospective studies have significant limitations, pancytopenia required a prolonged prospective study with detailed registration of their investigation results and their outcome. This will help in setting up a management protocol that is relevant to our particular setting and identifying specific etiologies with details of sensitivity patterns and predisposing factors to improve the prevention of pancytopenia before occurrence.

It is recommended for the future investigators to conduct a prospective multi-centre study which includes prevalence and focusing the outcome of patients for better generalization and treatment purpose.

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9 Checklist to assess pancytopenia in pediatrics

Chart number			
Pt name			
Age			
Sex			
Address			
Initial symptoms	Headache		Duration of symptoms
	Generalized fatigability		
	Epistaxis		
	Mucosal bleeding/ gum		
	Decreased appetite		
	Fever		
	Abdominal swelling		
	Other symptom Bone pain,,rash		
Physical findings	Lymphadenopathy		If yes sites
	Splenomegaly		
	Hepatomegaly		
	Body Rash		
	Other finding	spec ify	Type of rash?
Initial Investigations	Initial CBC		
	WBC		
	ANC		
	HGB		
	HCT		
	RBC Indices		
	MCV		
	MCH		
	MCHC		
	RDW		
	Platelet count		
	Progression to pancytopenia(for bicytopenic patients)		
	VITAMIN B 12		
	FOLATE		
Reticulocyte count			

	Peripheral morphology result			
	BM aspiration/Biopsy result			
	Genetic tests			If yes what?
Comorbidity	yes		no	If yes what?
Identified risk factor /causes				
Congenital cause				If yes what
Acquired cause	malignancy	Yes		If yes what
		No		
	PICT			
	HBV			
	HCV			
	Others			
Treatments	Blood Transfusion		Platelet	How many times
			Packed RBC	How many times
	Immunosuppressive therapy			
	Treating underlying cause			
	Other therapy			
Any complication	Neutropenic fever treatment			
	Bleeding			If yes mention sites
	Transfusion related complication			

DECLARATION

I hereby declare that; this thesis report is my original work and has not presented for a degree by another person in this or any other university and all source material used for this thesis have been acknowledged.

Name: _____

Signature _____

Date _____

Name of Advisor: _____

Signature _____

Date _____