Original Article

Etiological Heterogeneity of Pancytopenia without Organomegaly and Lymphadenopathy from A Tertiary Care Hematology Centre of Eastern India

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Most common cause of Pancytopenia without organomegaly and lymphadenopathy in pediatric age and adolescent group is Acute Leukemia. Hypoplastic Anemia is the most common cause in adult population. Elderly patients were least affected (6.66%) in this study.The sample size is small because of restricting ourselves to only Pancytopenia and no orgnomegaly, longer duration of follow up is not possible due to varied educational status of our patients and last but not the least, the COVID-19 pandemic was a huge deterrent for many patients to attend specialized health care facilities

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Pancytopenia is an important clinico-hematological entity encountered in our day-to-day clinical practice. Pancytopenia is not a disease entity but a triad of findings in which all blood cell lineages ie, Leukocytes, Erythrocytes and Platelets are reduced in blood[1]. Presenting symptoms are usually attributable to anaemia, leucopenia or thrombocytopenia. Anaemia leads to fatigue, dyspnoea and cardiac symptoms. Thrombocytopenia leads to bruising, mucosal bleeding and neutropenia to sharply increased susceptibility to infection[2]. The common clinical manifestations of Pancytopenia are usually Fever (86.7%), Fatigue (76%), Dizziness (64%), Weight loss (45.3%), Anorexia (37.3%), Night sweats (28%), Pallor (100%), Bleeding (38.7%), Splenomegaly (48%), Hepatomegaly (21.3%) and Lymphadenopathy (14.7%)[3]. Etiological causes of Pancytopenia often vary by geographical region, age, and gender[4]. Nutritional megaloblastic anemia, caused by folate or Vitamin B12 deficiency, is one of the leading causes of Pancytopenia in developing countries[5]. The Bone Marrow picture may vary depending on the aetiology, from normocellular with non-specific changes to hypercellular being replaced completely by malignant cells. The marrow is generally hypocellular in cases of Pancytopenia caused by a primary production defect[6]. Cytopenia resulting from ineffective haematopoiesis, increased peripheral utilization or destruction of cells and Bone Marrow invasive processes are usually associated with a normocellular or hypercellular marrow[7]. It is recommended that Bone Marrow Aspiration (BMA) and Biopsy be done simultaneously in cases of Pancytopenia. Aspiration smears are superior for morphological details while Biopsy provides a more reliable index of cellularity and often reveals Bone Marrow Infiltration, Fibrosis and Granulomas[8]. Although Pancytopenia is a common clinical finding with extensive differential diagnosis, there is a paucity of data on patients without lymphadenopathy and organomegaly. This study has been undertaken to identify common causes of Pancytopenia in age based groups of such population.

Editor's Comment :

- It's not uncommon to encounter pancytopenia in clinical practices, the next step we do is an in detail clinical examination but when no organomgaly or lymphadenopathy is found, a clinician need to go deeper and in most cases.
- A bone marrow study needs to be performed and across different age groups acute leukaemia is most common and needs urgent attention.

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Materials and Methods

It is a descriptive cross-sectional study estimating the prevalence of the etiological causes of Pancytopenia without organomegaly and lymphadenopathy in four subgroups of patients stratified on the basis of age (pediatric ie, <12 years, adolescents and young ie, 13 -24 years, adults ie, 25-65 years and elderly ie, >65 years) over a period of one year from June, 2020-May, 2021. A total of 60 patients attending the OPD in NRS Medical College & Hospital from April 2021 to September 2021 presenting with Pancytopenia were analyzed. All patients were clinically examined in detail for palpable lymph nodes, hepatomegaly and splenomegaly. Peripheral blood samples were run on Sysmex XP 100 three part differential cell counter and pancytopenia was screened. Pancytopenia was defined as Hb <10gm/dl, WBC <4000/ml, Platelet Count<1, 00,000/ml. Peripheral Blood Smear (PBS) examination and morphological study of Bone Marrow Aspiration and Biopsy were done for all patients of Pancytopenia. The Peripheral Blood Smear (PBS) & Bone Marrow Aspirate (BMA) smears were stained by Leishman Giemsa (LG) stains and the Biopsy sections were stained with routine Hemotoxylin and Eosin (H&E). Iron status was assessed on the BMA smears with Perls stain where possible. Subsequently etiological causes of Pancytopenia were analyzed,peripheral smear were analyzed for Red Blood Cell (RBC) shape and size, any circulating immature White Blood Cells (WBC) and also exact platelet count. Reticulocyte count was also done with new methylene blue in all patients. Vitamin B12 & folic acid were done in all patients with Chemiluminescent Immunoassay Technology (CLIA) assay; the cut off blast percentage for diagnosis of acute leukaemia was taken as more than equal to 20%.Cytogenetics was sent for all patients and it was outsourced as this facility was unavailable in our lab. An Ultrasonography of abdomen was done to rule out hepato-splenomegaly.

Inclusion Criterion :

- Pancytopenic patients as defined
- Without any associated lymphadenopathy, splenomegaly & hepatomegaly

Exclusion Criterion :

- Less than 1 year of age
- Any associated lymphadenophathy
- Any associated splenomegaly & hepatomegaly
- Unwilling for bone marrow study
- Patients with chronic liver disease
- Pregnancy

Results

In Table 1,baseline parameters of the patients were mentioned, patients with Pancytopenia without organomegaly were divided into four age groups notably, pediatrics with age group less than equal to 12 years, adolescent and young adults, adults and elderly .Mean age in each group are 6,17,44 & 73 years respectively. There is male preponderance in each group. The Complete Blood Count (CBC) comprising of hemoglobin, total leucocyte count, platelet counts, absolute neutrophil counts and reticulocyte count depicts pancytopenia like blood picture at baseline.

Overall out of 60 patients 21 patients (35%) were diagnosed as acute leukemia, 28 patients (48 %) as hypoplastic anemia, 4(6%) as MDS, 1 (1.5%) as megaloblastic anemia and as lymphoma infiltrate each, lastly hemophagocytosis 5 (8%) (Fig 1).

Age and etiology of pancytopenias were further analyzed, it was noted that acute leukaemis are more

Table 1 — *Baseline parameters of patients (N=60)*

Pediatric (<12 years) n=16	Mean values	Range
Mean age	6 years	1-12 years
Sex(male:female)	11:5	-
Hemoglobin(Hb)	6.3 g/dl	4.3-8.1 g/dl
Total Leucocyte Count (TLC)	2300/cmm	1100-3200/cmm
Absolute Neutrophil Count (ANC)	800/cmm	400-1100/cmm
Total Platelet Count	53000/cmm	12000-80000/cmm
Reticulocyte Count	0.6%	0.4-1.1%
Adolescent & Young (13-24 years) n=11		
Mean age	17 years	13-24 years
Sex(male:female)	8:3	-
Hemoglobin(Hb)	7.6 g/dl	3.6-9.2 g/dl
Total Leucocyte Count (TLC)	1600/cmm	900-3400/cmm
Absolute Neutrophil Count (ANC)	400/cmm	300-700/cmm
Total Platelet Count	47000/cmm	10000-77000/cmm
Reticulocyte Count	0.6%	0.4-1.2%
Adults (25-65 years) n=29		
Mean age	44 years	25-65 years
Sex (male : female)	19:10	-
Hemoglobin (Hb)	6.2 g/dl	3.5-8.6 g/dl
Total Leucocyte Count (TLC)	2300/cmm	1000-3700/cmm
Absolute Neutrophil Count (ANC)	600/cmm	200-1200/cmm
Total platelet Count	52000/cmm	15000-84000/cmm
Reticulocyte Count	0.8%	0.6-1.4%
Elderly (>65 years) n=4		
Mean age	73 years	66-77 years
Sex (male : female)	3:1	-
Hemoglobin (Hb)	7.8 g/dl	4.4 -8.3 g/dl
Total Leucocyte Count (TLC)	1800/cmm	1100-2300/cmm
Absolute Neutrophil Count (ANC)	600/cmm	400-900/cmm
Total platelet Count	35000/cmm	8000-43000/cmm
Reticulocyte Count	0.6%	0.4-1.2%

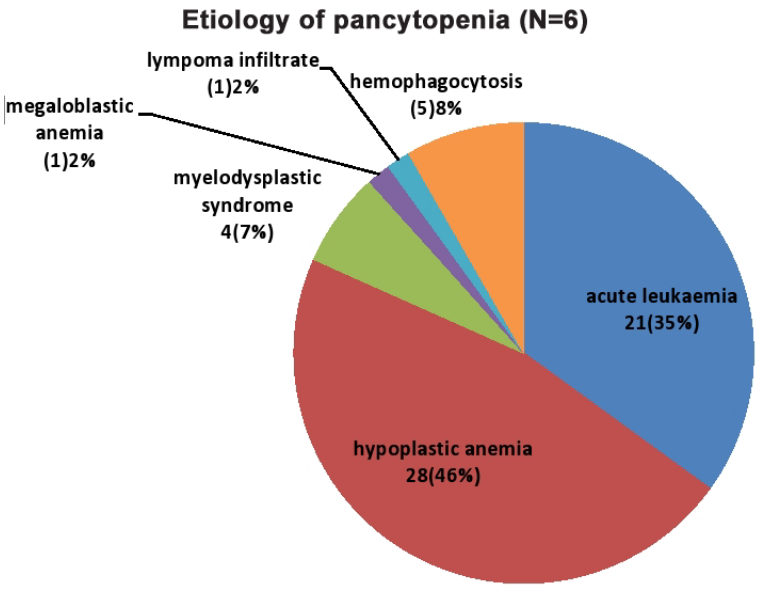

Fig 1 — Etiological distribution of 60 patients with Pancytopenia

common in the age group of paediatric and adolescents, compared to adults. Hypoplastic anemias were more common in the adults and other rarer etiologies as shown were more common in adults and elderly (Fig 2).

Discussion

In a study by Pizzo PA, *et al* from a different geographical region had shown that etiologies of Pancytopenia were quite varied, acute leukemia and Bone Marrow Failure Syndrome were well recognized causes where as infection and Megaloblastic anemia were not common in pediatric population[9]. Though the above study didn't excluded lymphadenopathy and organomegaly but their results were similar to ours.

A study from Eastern Mediterranean region conducted among adults by Nafil H, *et al* had shown that main causes of Pancytopenia were Megaloblastic Anemia (32.2%) and Acute Leukemia (23.7%) followed by Aplastic Anemia (15.2%)[10].

Another study from Karachi by Farooque R, *et al* also had shown that main cause of pancytopenia in adult was Megaloblastic Anemia (41.7%)[11]. But this study revealed main causes to be Hypoplastic Anemia followed by hypersplenism,so organomegaly was not excluded.

A study done among elderly population by Thyagaraj V, *et al* had shown that most common cause of Pancytopenia was Megaloblastic Anemia(60%) followed by aplastic anemia (7.5%) and Myelodysplastic syndrome (5%)[12]. Though a few elderly patients were included in the present study, the etiologies of Pancytopenia can be Hypoplastic Anemia and Myelodysplastic syndrome.

As etiology is concerned Megaloblastic anemia seems to be major contributing factor in different studies and it is curable. But in our study shows Hypoplastic anemia and acute Leukemia were the most common causes among younger age group and pediatric population. If Pancytopenia is associated with organomegaly such as lymphadenopathy and hepatospleomegaly as most studies across world has reported, but to report the causes of isolated Pancytopenia is unique in our study. This might be reason for our small sample size.

For any patients regardless of age Pancytopenia is a sinister finding in Complete Blood Count hence Bone Marrow studies are absolutely indicated along with other needful investigations such as immuopheotyping and cytogenetics.

It is also important to evaluate for Vitamin B12, folic acid

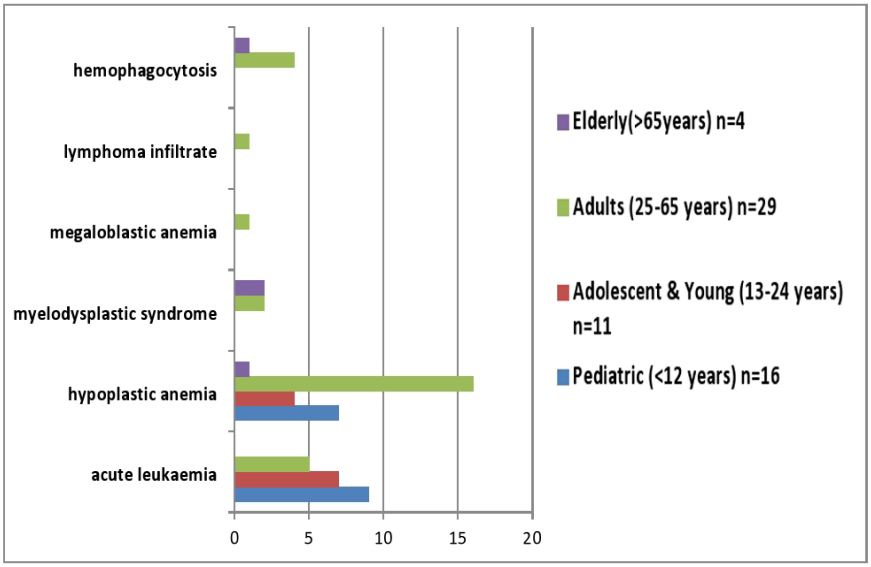

Fig 2 — Age wise etiological distribution of patients with Pancytopenia

deficiency as these are curable with replacement therapy. In our study however it was insignificant due to predominance of non- vegetarian population from Eastern India.

Such etiological knowledge is essential for clinicians in remote areas to intervene early and judicious management especially the hygiene for individual patients.

Limitations of the study :

The sample size is small because of restricting ourselves to only Pancytopenia and no orgnomegaly, longer duration of follow up is not possible due to varied educational status of our patients and last but not the least, the Covid-19 pandemic was a huge deterrent for many patients to attend specialized health care facilities.

Conclusion

Most common cause of pancytopenia without organomegaly and lymphadenopathy in pediatric age and adolescent group is acute leukemia. Hypoplastic anemia is the most common cause in adult population. Elderly patients were least affected (6.66%) in this study

Declaration of patient consent : Patient's consent not required as patients identity is not disclosed or compromised.

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