Patterns of Pancytopenia according to the Cause in Babylon

Najlaa Badir Al–Awadi Alaa Sadiq Al-Awad Hasanain Hashim Al-yasiri*
College of Medicine, University of Babylon, Hilla, IRAQ.
*Senior Physician; Al-Hilla Teaching Hospital, , Hilla, IRAQ.

Abstract

Objective: The aim of this study is to assess the incidence of variable causes of pancytopenia in Babylon governorate,Iraq and to determine their relation to age, sex, clinical manifestations and disease outcome.

Materials and Methods: This is a prospective and descriptive study of 74 patients representing all patients with pancytopenia admitted to or attending Marjan Teaching Hospital, Al-Hilla Teaching Hospital, or Babylon Hospital for Paediatrics in Babylon,Iraq during the period from 1st July 2007 to 31st September 2008.

The patients who were on chemotherapy for any reason or had a previous diagnosis for the cause of pancytopenia were excluded.

Results: The most common causes of pancytopenia were acute leukaemia and a plastic anaemia constituting more than 56% of patients, followed by kala azar in 10.8% and hypersplenism in 8.1%.

Other causes found in this study include lymphoma, multiple myeloma and megaloblastic anaemia in 5.4% of patients for each; hairy cell leukaemia and secondary metastasis to bone marrow in 2.7% for each; myelofibrosis and myelodysplastic syndrome in 1.3% for each.

Fatigue and fever were the most common symptoms seen, while pallor and splenomegaly were the most common physical findings.

Conclusion: Acute leukaemia was the most common cause of pancytopenia, followed by aplastic anaemia and kala azar.

أنماط نقص خلايا الدم الشامل وحسب مسبباتها في بابل

الخلاصة

دراسة نسبة حدوث الأسباب المتعددة لنقص خلايا الدم الشامل في بابل وتحديد مدى العلاقة بينها وبين العمر والجنس والأعراض السريرية ونتائج المرض.

إن هذه الدراسة هي دراسة وصفية لأربع وسبعون مريضا كانوا قد راجعوا أو رقدوا في مستشفى مرجان التعليمي أو مستشفى الحلة التعليمي أو مستشفى بابل للأطفال في محافظة بابل – العراق للفترة من الأول من تموز ٢٠٠٧ ولغاية الحادي والثلاثين من كانون الأول ٢٠٠٨ وجميعهم كان يعاني من نقص خلايا الدم الشامل.

لقد شملت الدراسة المرضى الجدد فقط وإستثنت المرضى الذين لديهم تشخيص سابق لسبب نقص خلايا الدم الشامل وقت مراجعتهم الأولى للمستشفى ، كما إستثنت الدراسة المرضى الذين يتعاطون العقارات الكيميائية أو السامة للخلايا لأي سبب آخر.

لقد وجدت هذه الدراسة أن أكثر أسباب نقص خلايا الدم الشامل شيوعا" هو لوكيميا الدم الحاد وفقر الدم اللاتنسجي حيث شكلا معا نسبة أكثر من ٥٦% من مجموع المرضى الذين شملتهم الدراسة ، يليهم مرضى الحمى السوداء بنسبة ١٠،٨% ثم مرضى فرط الطحال بنسبة ٨،١%.

لقد كان النحول والحمى من أكثر الأعراض شيوعا لدى عينة المرضى هذه ، بينما كان الشحوب وتضخم الطحال من أكثر العلامات السريرية شيوعا" لديهم.

لقد خلصت هذه الدراسة إلى أن لوكيميا الدم الحاد هو أوسع أسباب نقص خلايا الدم الشامل شيوعا" في بابل وتليها أمراض فقر الدم اللاتنسجي والحمى السوداء . لذا يجب اعتبار نقص خلايا الدم الشامل من الحالات المهمة التي يجب العناية بها والإسراع بتشخيص أسبابها التي يغلب عليها أمراض مستعصية تهدد حياة المريض.

Introduction

Pancytopenia means reduction in all three formed elements of blood; erythrocytes, leukocytes and platelets. Pancytopenia can be due to decrease in haemopoietic cells production in bone marrow due to marrow hypoplasia, malignant cell infiltration or suppression by infections or toxins. Bone marrow can be normocellular or even hypercellular without any abnormal cells as in marrow dysplasia, ineffective erythropoiesis and peripheral sequestration of blood cells in hypersplenism[1-3]. The incidence of different disorders causing pancytopenia is variable according to geographical distribution and genetic variations[4-6].

Pancytopenia is a common haematological problem with a wide range differential diagnosis. The optimal diagnostic approach to pancytopenia remains undefined [7-9]. In Iraq; the incidence of pancytopenia and it's etiologies is largely unknown.

Materials and Methods

Seventy four patients with pancytopenia were taken from Marjan Teaching Hospital, Al-Hilla Teaching Hospital or Babylon Hospital for Paediatrics in Babylon Governorate,Iraq during the period from 1st July 2007 to 31st December 2008.

All patients were diagnosed to have pancytopenia depending on peripheral blood count (using chamber method and blood film) with anaemia (haemoglobin less than 11 g/dl), leukopenia (total leukocytes count less than 4.0×10^9 /L) and thrombocytopenia (platelets count less than 100×10^9 /L)[10].

For all patients; detailed history was taken and a thorough physical examination was done. In addition; complete blood picture and bone marrow aspirate were performed using standard methods, while bone marrow trephine biopsy was done in 41 patients (55.4%) for evaluation in diluted, dry tap or hypoplastic marrow or requested by the referred doctor. For cases of kala azar, diagnosis depended on both bone marrow exam and Indirect Fluorescent Antibody Test (IFAT); while hypersplenism was diagnosed in patients with splenomegaly and normal hypercellular marrow.

Statistical analysis was done using descriptive statistics (the mean, the median and standard deviation SD).

Results

A total of seventy four patients with pancytopenia were studied. Their age range was 2-72 years with male: female ratio of 1.17:1 .

The largest number of patients was found in the age group of 16-30 years (24/74), followed by age group of less than 15 years (20/74) and 30-45 years (14/74).

The most common cause of pancytopenia was acute leukaemia (32.4%), followed by aplastic anaemia (24.3%), kala azar (10.8%) and hypersplenism (8.1%). (Tables 1 and 2)

Other less common causes of pancytopenia include lymphoma, multiple myeloma and megaloblastic anaemia (each one constitutes 5.4%).

The uncommon causes in our study include hairy cell leukaemia, secondary metastasis to bone marrow (each one constitutes 2.7%), myelofibrosis and myelodysplastic syndrome (each one constitutes 1.35%).

The commonest presenting complaint (Table 3) was fatigue in 52.7% (39/74), followed by fever 45.9% (34/74) and dizziness 31% (23/74).

Pallor as a physical sign was seen in all patients 100% (74/74), while splenomegaly was found in 40.5% (30/74) and hepatomegaly in 13.5% (10/74).

Table 1 Causes of pancytopenia according to age group.

The cause	The age group(years)					Total	
	≤ 15	16-30	31-45	46-60	> 60	No.	%
AL	7	12	2	3	0	24	32.4
AA	6	8	2	1	1	18	24.3
KA	6	1	1	0	0	8	10.8
HS	1	1	3	0	1	6	8.1
Lymphoma	0	1	2	0	1	4	5.4
MM	0	0	1	1	2	4	5.4
MA	1	1	1	1	0	4	5.4
HCL	0	0	0	1	1	2	2.7
Metastasis	0	0	1	1	0	2	2.7
MF	0	0	0	1	0	1	1.3
MDS	0	0	1	0	0	1	1.3
Total	20	24	14	9	6	74	100

AL: Acute leukaemia. AA: Aplastic anaemia. KA: Kala azar. HS: Hypersplenism. MM: Multiple myeloma. MA: Megaloblastic anaemia. HCL: Hairy cell leukaemia. MF: Myelofibrosis. MDS: Myelodysplastic syndrome. No.: Number of patients.

Table 2 Causes of pancytopenia in relation to sex.

The causes	The Sex				The ratio (M:F)
	Male no.	%	Female no.	%	
AL	14	18.9	10	13.5	1.4:1
AA	7	9.4	11	14.8	0.6:1
KA	5	6.7	3	4.0	1.6:1
HS	4	5.4	2	2.7	2:1
Lymphoma	1	1.3	3	4.0	0.3:1
MM	2	2.7	2	2.7	1:1
MA	3	4.0	1	1.3	3:1
HCL	1	1.3	1	1.3	1:1
Metastasis	2	2.7	0	0.0	2:1
MF	1	1.3	0	0.0	1:0
MDS	0	0.0	1	1.3	0:1
Total	40	54.0	34	45.9	1.17:1

AL: Acute leukaemia. AA: Aplastic anaemia. KA: Kala azar. HS: Hypersplenism. MM: Multiple myeloma. MA: Megaloblastic anaemia. HCL: Hairy cell leukaemia. MF: Myelofibrosis. MDS: Myelodysplastic syndrome. No.: Number of patients.

Haemoglobin level was 6.2 ±1.6 g/dl and it was the lowest in aplastic anaemia patients group 5.0 ±1.9 g/dl.

The mean total leukocytes count was 1.58 ±0.75 $\times 10^9$/L being the lowest in acute leukaemia patients group 1.02 ±0.92 $\times 10^9$/L.

The mean platelets count was 41.36 ±20.3 $\times 10^9$/L where the lowest mean value was found in acute leukaemia patients group 29.3 ±30.1 $\times 10^9$/L.

Table 3 Clinical manifestations according to causes of pancytopenia.

The clinical manifestations	Causes of pancytopenia						
	AL (no.)	AA (no.)	KA (no.)	HS (no.)	Others (no.)	Total no.	%
Fatigue	14	10	3	3	9	39	52.7
Fever	8	9	7	1	9	34	45.9
Dizziness	3	10	1	٤	5	23	31
Anorexia	4	2	4	١	5	16	21.6
Weight loss	3	2	1	2	6	14	18.9
Pallor	24	18	8	6	18	74	100
Splenomegaly	11	1	7	6	5	30	40.5
Hepatomegaly	1	0	3	3	3	10	13.5
Lymphadenopathy	4	0	0	1	2	7	9

AL: Acute leukaemia. AA: Aplastic anaemia. KA: Kala azar. HS: Hypersplenism. Others: Lymphoma, multiple myeloma, megaloblastic anaemia, hairy cell leukaemia, secondary metastasis to bone marrow, myelofibrosis and myelodysplastic syndrome. No.: Number of patients.

Table 4 Haematological parameters in pancytopenic patients.

The diagnosis	Hb (g/dl) Mean ±SD	TLC ($\times 10^9$/L) Mean ±SD	Platelets ($\times 10^9$/L) Mean ±SD
AL	5.4 ±1.4	1.02 ±0.92	29.3 ±30.1
AA	5.0 ±1.9	1.4 ±0.62	36.8 ±15.7
KA	6.1 ±1.6	1.5 ±0.68	38.4 ±18.2
HS	6.7 ±2.3	1.52 ±0.74	40.2 ±16.5
Lymphoma	7.0 ±2.1	1.73 ±0.67	45.5 ±25.4
MA	6.7 ±1.5	1.78 ±0.71	37.5 ±23.1
HCL	6.0 ±0.8	1.58 ±0.8	31.6 ±16.2
Metastasis	6.8 ±1.2	1.76 ±0.84	41.4 ±17.9
MF	6.2 ±0.0	1.6 ±0.0	47.3 ±0.0
MDS	6.0 ±0.0	1.8 ±0.0	65.6 ±0.0
Total	6.2 ±1.6	1.58 ±0.75	41.36 ±20.3

AL: Acute leukaemia. AA: Aplastic anaemia. KA: Kala azar. HS: Hypersplenism. MM: Multiple myeloma. MA: Megaloblastic anaemia. HCL: Hairy cell leukaemia. MF: Myelofibrosis. MDS: Myelodysplastic syndrome. Hb: Haemoglobin. TLC: Total leukocytes count. SD: Standard deviation.

Discussion

Pancytopenia has variable etiologies so the prognosis will accordingly differ. The frequency of pancytopenia causes has been reported in a number of studies[8,9,11-19].

Acute leukaemia was the most common cause of pancytopenia in this study as it has been found in 32.4% of patients. Similarly; Bhatnagar et al. and Imbert et al. have found acute leukaemia as a major cause of pancytopenia representing 21% and 20% of all cases respectively[16,17]. Acute leukaemia was the 2nd most common cause of pancytopenia in Gupta et al study (25%)[11], and the 3rd cause in Savage et al, Jha et al, Memon

et al and Kumar et al studies [9, 14, 15, 18].

In India, most studies have found megaloblastic anaemia as the most common cause of pancytopenia with incidence range from 39% to 72% [8,9,12,13], whereas it was the 2nd cause in other Indian studies[14,15,18]. This may be explained by nutritional deficiencies and low socioeconomic conditions in the unindustrialized world. In our study, megaloblastic anaemia was uncommon constituting only 5.5% of patients.

In Yemen, Gamal et al found hypersplenism as the commonest cause of pancytopenia in (28%) followed by malaria causing pancytopenia not related to hypersplenism in 17.3% of patients[19]. They explained those results by high incidence of infectious diseases in Yemen like malaria, kala azar, brucellosis and schistosomiasis [20-22].

Hypersplenism was the 2nd most common cause of pancytopenia in Ishtiaq et al study in India where almost all cases were due to liver cirrhosis usually secondary to schistosomiasis[9]. In our study; hypersplenism was the 4th cause of pancytopenia being diagnosed in six patients; four of them had cirrhosis with portal hypertension and splenomegaly, while the other two patients had no obvious cause for splenomegaly.

The findings in India and Yemen give an important implication as megaloblastic anaemia and infections are easily treatable and reversible cause of pancytopenia and should not be missed.

The 2nd most common cause of pancytopenia in this study was aplastic anaemia in 24.3% of patients; whereas aplastic anaemia was the commonest cause of pancytopenia in some studies ranging from 24% to 49% [11,14,15,18], and the 2nd cause in other studies[8,12,13,16]. High incidence of aplastic anaemia was reported in Philippine (54%) [23] and Nepal (30%)[24]. In those two studies, males were affected with aplastic anaemia much more than females which might be a result of a higher incidence of occupational exposure to chemicals and pesticides[19]; the reverse is seen in Iraqi rural community as females use these substances more than males.

Kala azar was the 3rd most common cause of pancytopenia in this study as found in 10.8% of patients; similar findings were reported by Gupta et al[11].

In France, Imbert et al found myelofibrosis on bone marrow biopsy of adult patients with pancytopenia in 31% of them[17]; while in our study, myelofibrosis was rare.

The most common clinical complaint in this study was fatigue, followed by fever. Fatigue was most often seen in acute leukaemia patients (58.3%), while fever affects seven out of eight patients affected with kala azar (87.5%).

Pallor as a clinical sign was universal (100%), followed by splenomegaly which was more often seen in kala azar (87.5%) and hypersplenism (100%).

In this study, two correlations were found: 1st one between pancytopenia and pallor, fever and fatigue; 2nd one between splenomegaly and hypersplenism. These findings were almost similar to those reported by other studies [4,5,7,9,25].

The haematological parameters were not different among pancytopenic patients; however, more severe anaemia, leukopenia and thrombocytopenia were found in the acute leukaemia group, which was consequently associated with highest death rates {15 out of 24 patients (62.5%) with acute leukaemia died during the period of study}. The worse anaemia was seen in the aplastic anaemia group; however, death rate was 22% (4/18 during the period of study).

These variations might be due to different characteristics and pathogenesis of each disease [8,9,25].

Conclusion

The most common causes of pancytopenia in Babylon were acute leukaemia, aplastic anaemia and kala azar. Most of these diseases have poor prognosis and for this reason, pancytopenia in Iraq must be considered ominous life threatening condition that need to be seriously investigated.

Severe pancytopenia has significant correlation with poor disease outcome and can be used as a prognostic indicator.

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