ORIGINAL ARTICLE

PANCYTOPENIA IN TWO NATIONAL ETHNIC GROUPS OF BALUCHISTAN

Saleh Muhammad Tareen, Masroor Ahmad Bajwa*, Mohammad Masood Tariq*, Shakeel Babar*, Abdul Malik Tareen*

Bolan Medical College, *Centre for Advanced Studies in Vaccinology and Biotechnology, University of Baluchistan, Quetta, Pakistan

Background: Pancytopenia is a recognisable haematological problem with common categorises diagnosis but best possible diagnostic approach is still to be defined. **Objective:** The aim of this study was to determine the frequent causes and clinical presentation of pancytopenia in relation to age and sex in different ethnic groups of two national (Pakistani and Afghan) living in Baluchistan province. **Methods:** This is a cross sectional descriptive type of study was carried out on patients (n=180) for two years (July 2009–June 2011). Cases were successively registered in 2 provincial government hospital and 2 private clinics in Quetta with diagnosis of pancytopenia. **Results:** The most frequent causes of pancytopenia in both national ethnic groups were malaria (29.44%) fallowed by tuberculosis (17.22%), leukaemia (16.67%), aplastic anaemia (13.33%), hepatitis (12.22%), other diseases (7.22%) and iron deficiency anaemia (3.89%). Overall, 63.89% male subjects were observed pancytopenia as compared to 36.11% female patients. The results also showed that patients with age >41 years were highly (50%) affected by pancytopenia followed by 21–40 years (30.66%) and <20 years (19.44%). Moreover, leukaemia cases were observed significantly higher in Afghan subjects (>41 years). The most common symptom of patients was (71.11%) fever followed by Pallor (42.22%), fatigue (38.33%), weight loss (26.11%) and dizziness (25.56%). Leukaemia and aplastic anaemia were found to be the most serious causes of pancytopenia in Afghan ethnic group. **Conclusions**: Malaria, tuberculosis, aplastic anaemia, and leukaemia were the leading causes of pancytopenia in Pakistani and Afghan ethnic groups. Severe pancytopenia has significant relation with the clinical conclusion and can be used as a prognostic marker.

Keywords: Pancytopenia, Ethnic groups, Malaria, Tuberculosis, Leukaemia

INTRODUCTION

Pancytopenia refers to a disorder in which all three elements of the blood (Erythrocytes, Leukocytes and Platelets) are lower in counts than normal**.** Pancytopenia can be due to reduction in haematopoietic cell production in the bone marrow by means of infections, toxins, over use of drugs or idiosyncratic response, malignant cells infiltration or suppression[1], congenital and autosomal, medication/ chemotherapy/alcohol/radiotherapy and parasitic infestation.[2,3] The most common cause of pancytopenia was megaloblastic anaemia, followed by aplastic anaemia, acute leukaemia, and acquired immunodeficiency syndrome (AIDS), hypersplenism, tuberculosis and hepatitis. Aplasia is also the most frequent cause of severe pancytopenia.[3] Patients with aplastic anaemia and acute leukaemia were usually children, whereas those with megaloblastic anaemia were adults. Aplasia is the most frequent cause of severe pancytopenia. Anisocytosis, poikilocytosis, macro-ovalocytosis, microcytosis, fragmentation, and teardrop erythrocytes were more prominent on the blood films of patients with megaloblastic anaemia.[4]

Many people at Hiroshima and Nagasaki died not directly from the actual explosion, but from the radiation released as a result of the explosion. The survivors have suffered physically from cataracts, leukaemia and other cancers, malformed offspring, and premature aging, and also emotionally, from social discrimination.[5] Further, there were explosions at reactor nuclear power plant at Chernobyl in Ukraine on 26 April 1986. After that the most common problems was diagnosed as thyroid cancer, lung cancer, leukaemia, cardiovascular diseases, cataract, mental health and psychological effects and reproductive disorder in the patients that lead to the heavy mortality. Similarly, French nuclear tests in Algeria (1960–67)[6], and USA military activities in Iraq in (1991)[7] have thrown huge amounts of uranium contamination over large areas of Algeria and Iraq respectively. As a result, the people, animals, and environments in these areas have been and will continue to be irradiated by ionizing radiation for long periods of time.[8] There are strong associations between the rise in the incidence of health problems (leukaemia, lung cancer, thyroid cancer, breast cancer and still birth) in Iraq and the exposure to the war environment since 1991, and also in Algeria since 1960. Similarly, in pancytopenia there could be normal cellular or even hypercellular bone marrow, without any abnormal cells, like ineffective haematopoiesis and dysplasia, maturation arrest of all cell lines and peripheral sequestration of blood cells.[9]

In Pakistan, specifically in Baluchistan, the prevalence and causes of pancytopenia are variable. However, the apparent state of affairs in relation to

pancytopenia in Afghanstan is fairly different than Pakistan. Most of Afghan people frequently visit Baluchistan (Pakistan) for job and treatment. The possible reason could be that from last thirty years the country is at war or war like situation. There has been extensive bombing during Afghan war. It is possible that due to release of different toxic chemicals in air, soil and water resources, the incidence of haematological problems may occur in Pushtoon (Afghan) higher as compared to ethnic groups living in Baluchistan. Pancytopenia is a recognizable haematological problem with widespread discriminated diagnosis but best possible diagnostic approach is still to be defined. This study is therefore aimed to identify the frequent causes and clinical presentation of pancytopenia in different ethnic groups (Pakistani and Afghan) living in Baluchistan areas.

MATERIAL AND METHODS

This was a cross sectional descriptive type of study that is carried out for two years period (July 2009–June 2011) on pancytopenia patients. All the cases admitted (n=180) in the hospitals (Sandman Provincial Hospital, Bolan Medical College Complex Hospital, Combined Military Hospital and Private Clinics in Quetta) with diagnosis of pancytopenia were consecutively enrolled in the study. Pancytopenia was diagnosed with the presence of anaemia (haemoglobin <11 g/dl), leukopenia (total leukocyte count (TLC) <4,000/mm^3), and thrombocytopenia (platelet count <150,000/mm^3).[1] Patients were included from both sex and all age (divided in to age groups <20, 21–40 and >41 years). Patients were divided according to the ethnic groups Afghan (Pushtoon, Hazara, Uzbak) and Pakistani (Pushtoon, Baloch, Hazara, Punjabi) for comparative study. Patients with cancer chemotherapy were excluded. A questionnaire including a detailed relevant history and physical examination were applied in all the patients. The following primary investigations for the pancytopenia and were done whenever possible. Haemoglobin, total leukocyte count (TLC), differential leukocyte count (DLC), total platelets count, peripheral red blood cell morphology, erythrocyte sedimentation rate (ESR), reticulocytes, and malaria parasites. blood CP, C/S of urine and sputum, chest X-ray PA view, urine re/me /stool re/me and occult blood, ultrasound of abdomen, bone marrow aspiration or biopsy according to need, Investigations apart from these, HBsAg, Anti HCV, HIV ELISA tests, DsDNA, Random blood sugar, serum electrolytes, urea, and creatinine were done absolutely on the decision of the attending physician.

Complete blood counts and bone marrow aspiration were performed in all patients, using standard methods. Bone marrow trephine biopsy was done in 25 patients for the evaluation of bone marrow in insufficient cells, dry tap or hypo-plastic bone marrow. A complete blood count obtained from venous blood was counted by an automated blood counter (PCE-170N). Microsoft Excel spreadsheet was used for entering and editing of data and making comma delimited files. Chi-test was used for analysis of data on Graph pad Prism (version 5).

RESULTS

In the present study patients total subjects were (n=180) belonged to Pakistani ethnic group (n=130) 73.33% residing in Baluchistan province (Pushtoon n=40; Baloch, n=36; Hazara n=28; Punjabi n=26) and Afghan ethnic group (n=50) 27.77% (Pushtoon n=25; Uzbek n=13 and Hazara, n=12) were registered. Majority of the patients were anticipated for pancytopenia according to the following causes, Malaria (29.44%) followed by tuberculosis 17.22%, leukaemia 16.67%, aplastic anaemia 13.33%, hepatitis 12.22%, other diseases 7.22% and iron deficiency anaemia 3.89% (Table-1). The effect of diseases causing pancytopenia in two of the ethnic groups patients were observed non significant (χ^2=11.91, df =6, p=0.0639).

The results of the present study reflects (Table-2) malaria (30%) fallowed by leukaemia (15.39%), hepatitis (15.39%),), aplastic anaemia (13.85%), tuberculosis (13.08%), other diseases (9.23%) and iron deficiency anaemia (3.08%) as probable causes of pancytopenia in the ethnic groups belonging to Baluchistan (Pakistan) origin. Malaria cases were observed higher in Pakistani ethnic group (30%) as compared to Afghanstan origin subjects (28%). Overall almost same tendency of causes of pancytopenia were observed as in both ethnic groups. However, leukaemia (26%) and tuberculosis (22%) cases were observed significantly higher in Afghan ethic group as compared to Pakistanis (15.39%) and (13.08%) respectively (Table-2 and 3). The effect of diseases causing pancytopenia in Pakistani ethnic groups patients were observed insignificant (χ^2=16.79, df =18, p=0.5374) (Table-2). There was non-significant difference (χ^2=5.297, df=12, p=0.9473) between diseases causing pancytopenia and ethnic groups of Afghan patients (Table-3).

The results (Table-4 and 5) revealed that, in general male (63.89%) subjects were affected more than female (36.11%). The results further depicted that malaria, leukaemia, and tuberculosis cases are significantly higher in male. There was insignificant difference observed among sex, male (χ^2=20.38, df=24, p=0.6747) and female (χ^2=31.47, df=24,

p=0.1407) patients of ethnic groups and diseases causing pancytopenia.

The results (Table-6, 7 and 8) showed that highly affected age of patients are >41 years (50%) fallowed by 21–40 years (30.66%) and <20 years (19.44%)**.** The results revealed that, common cause of pancytopenia in all age groups of ethnic communities was malaria followed by leukaemia, tuberculosis, aplastic anaemia and hepatitis, However, leukaemia cases were observed significantly higher at age (>41 years) in Afghan subjects as compared to Pakistani ethnic groups. Statistically non-significant difference was observed among age groups in both ethnic communities in relation to diseases causing pancytopenia <20 years (χ^2=23.30, df=24, p=0.5019), (>40) years (χ^2=23.18, df=24, p=0.5092), 21–40 years age (χ^2=32.87, df=24, p=0.1068).

The results of clinical manifestation according to causes of pancytopenia in all the patients reflected major complaint for fever (71.11%) followed by Pallor (42.22%), fatigue (38.33%), weight loss (26.11%) and dizziness (25.56%) (Table-9). Statistically highly significant difference (χ^2=144.2, df 72, p<0.0001) was observed between diseases causing pancytopenia and clinical manifestations. Overall results of haematological parameters in pancytopenic patients are presented (Table-10) showing lot of variation in parameters among different diseases.

Table-1: Comparison of patients of based on ethnic groups Afghan and Pakistani nationals

Causes	Afghan	Pakistani	Total	%
Malaria	14	39	53	29.44
LK	11	20	31	17.22
TB	13	17	30	16.67
AA	6	18	24	13.33
Hepatitis	2	20	22	12.22
OD	1	12	13	7.22
IDA	3	4	7	3.89
Total	50	130	180	100

LK=Leukaemia; TB=Tuberculosis; AA=Aplastic anaemia; OD=other diseases (Hodgkin's and Non-Hodgkin's Lymphoma=2; Hypersplenism=3; Kalazar=2; Sepsis; Congo virus=2; Enteric fever=4); IDA=iron deficiency anaemia

Table-2: Pakistani ethnic groups patients in Baluchistan

Causes	Pushtoon	Bloch	Punjabi	Hazara	Total	%
Malaria	9	12	8	10	39	30.00
Hepatitis	11	4	3	2	20	15.39
LK	8	6	2	4	20	15.39
AA	4	5	4	5	18	13.85
TB	6	4	5	2	17	13.08
OD	1	5	3	3	12	9.23
IDA	1	0	1	2	4	3.08
Total	40	36	26	28	130	100

LK=Leukaemia AA=Aplastic anaemia, TB=Tuberculosis, OD=Other diseases; IDA=Iron deficiency anaemia

Table-3: Afghan ethnic groups patients in Baluchistan

Causes	Pushtoon	Uzbek	Hazara	Total	%
Malaria	5	4	5	14	28.00
LK	7	3	3	13	26.00
TB	6	3	2	11	22.00
AA	3	2	1	6	12.00
IDA	1	1	1	3	6.00
Hepatitis	2	0	0	2	4.00
OD	1	0	0	1	2.00
Total	25	13	12	50	100

Table-4: Causes of pancytopenia in relation to male patients in ethnic groups

Causes	Afghan	Pushtoon	Bloch	Punjabi	Hazara	Total	%
Malaria	10	6	7	5	6	34	18.89
LK	9	5	2	4	1	21	11.67
TB	6	4	5	2	2	19	10.56
AA	4	3	3	3	3	16	8.889
Hepatitis	2	6	3	2	0	13	7.222
OD	1	1	3	0	3	8	4.444
IDA	1	1	0	1	1	4	2.222
Total	33	26	23	17	16	115	63.89

Table-5: Causes of pancytopenia in relation to female patients in ethnic groups

Causes	Afghan	Pushtoon	Bloch	Punjabi	Hazara	Total	%
Malaria	4	3	5	3	4	19	10.56
TB	5	4	1	0	2	12	6.67
LK	4	1	2	1	1	9	5.00
Hepatitis	0	5	1	1	2	9	5.00
AA	2	1	2	1	2	8	4.44
OD	0	0	2	3	0	5	2.78
IDA	2	0	0	0	1	3	1.67
Total	17	14	13	9	12	65	36.11

Table-6: Causes of pancytopenia according to age group (<20 years) in ethic groups

Causes	Afghan	Pushtoon	Bloch	Punjabi	Hazara	Total	%
Malaria	3	1	2	1	2	9	5.00
AA	1	1	1	0	1	4	2.22
TB	3	0	0	0	3	6	3.33
LK	2	2	0	1	0	5	2.78
Hepatitis	1	2	0	0	0	3	1.67
IDA	3	1	0	0	0	4	2.22
OD	1	0	0	1	2	4	2.22
Total	14	7	3	3	8	35	19.44

Table-7: Causes of pancytopenia according to age group (21–40 years) in ethic groups

Causes	Afghan	Pushtoon	Bloch	Punjabi	Hazara	Total	%
Malaria	4	3	4	2	5	18	10.00
AA	2	1	2	2	2	9	5.00
TB	1	3	4	1	1	10	5.56
LK	5	1	2	2	0	10	5.56
Hepatitis	0	3	0	0	0	3	1.67
IDA	0	0	0	0	1	1	0.56
OD	0	1	3	0	0	4	2.22
Total	12	12	15	7	9	55	30.56

Table-8: Causes of pancytopenia according to age group (>40 year) in ethic groups

Causes	Afghan	Pushtoon	Bloch	Punjabi	Hazara	Total	%
Malaria	7	5	6	5	3	26	14.44
AA	3	2	2	2	2	11	6.11
TB	5	5	2	1	0	13	7.22
LK	8	3	2	2	2	17	9.44
Hepatitis	1	6	4	3	2	16	8.89
IDA	0	0	0	1	1	2	1.11
OD	0	0	2	2	1	5	2.78
Total	24	21	18	16	11	90	50

Table-9: Clinical manifestations according to the causes of pancytopenia

Clinical manifestation	Malaria	AA	TB	LK	HP	IDA	OD	Total	%
No. of patient	53	24	40	21	22	7	13	180	
Fever	52	16	21	15	17	2	5	128	71.11
Fatigue	23	8	10	10	7	5	6	69	38.33
Dizziness	12	7	9	0	9	4	5	46	25.56
Weight loss	6	5	7	13	12	3	1	47	26.11
Anorexia	6	4	7	5	5	2	3	32	17.78
Night sweat	25	1	7	0	3	1	2	39	21.67
Pallor	21	10	13	11	10	4	7	76	42.22
Dyspnoea	20	4	16	0	0	3	2	36	20.00
Pleurisy	6	0	15	5	6	1	5	38	21.11
Splenomegaly	5	12	3	3	4	0	5	32	17.78
Bleeding	4	6	4	3	6	1	5	29	16.11
Hepatomegaly	4	6	1	1	0	2	2	16	8.89
LP	7	3	1	4	2	4	1	22	12.22

HP: Hepatitis; LP: Lymph adenopathy

Table-10: Haematological parameters in pancytopenic patients (Mean)

	Means							
Diagnosis	Hb (g/dl)	RBC (million/mm^3)	TLC (µl)	PCV (%)	MCH (ρg)	MCV (fl)	MCHC (g/dl)	Platelets (per mm^3)
Malaria	3.4	2.6	1,100	9.5	30.0	84.9	35.7	63,000
AA	7.0	1.3	1,925	18.8	25.6	89.1	30.0	42,000
LK	5.9	1.2	1,850	29.5	17.2	60.8	28.2	38,600
TB	9.1	2.7	2,400	15.5	27.0	74.0	32.9	55,000
HP	9.5	2.3	2,750	21.2	28.5	71.0	36.4	130,000
IDA	2.5	1.5	3,000	13.5	23.6	65.5	28.0	135,000
OD	6.5	2.7	2,200	22.5	23.5	62.5	24.5	90,000
Normal Values	14–18	4–6	4,000–11,000	40–45	28–32	76–96	32–36	150,000–400,000

Hb[1]=Haemoglobin; ESR[2]=Erythrocyte sedimentation rate; RBC[3]=Red blood cells; TLC[4]= Total leukocyte count; PCV[5]=packed cell volume; MCH[6]=mean corpuscular haemoglobin; MCV[7]=mean corpuscular volume; MCHC[8]=mean corpuscular haemoglobin concentration

DISCUSSION

Pancytopenia has several causes and the diagnosis is dependent on the cause (disease). The frequency of these causes has been reported in a limited number of studies.[1,5,10] Malaria was considered the most common cause of pancytopenia in this study. Malaria corresponded to the fourth and second most frequent cause in pancytopenic patient's respectively.[11,5] Malaria due to Plasmodium falciparum has been implicated as a cause of pancytopenia. The high incidence of malaria was observed in low income group with lack of hygiene (sanitation) in the home or area. Eliminate places around home where mosquitoes breed and hide, spraying insecticides on home's premises to kill adult mosquitoes those come inside are critical. Taking anti-malaria medications for malaria prophylaxis is good strategy to prevent malaria.[12,13]

The second commonest cause of pancytopenia observed in both ethnic groups in the present study was leukaemia (17.22%). There are noticeable evidences that after a few months of nuclear explosions on Hiroshima and Nagasaki, Japan, leukaemia began to appear among the survivors at an abnormally high rate. Some leukaemia victims were foetuses within their mothers' wombs when exposed to radiation[3], same kind of problem was observed after Chernobyl explosions, French nuclear tests in Algeria[6] and USA military activities in Iraq (1991) have bombarded huge amounts of uranium contamination over large areas of Algeria and Iraq.[7] As a result the people, animals, and environments in these areas have been and will continue to be irradiated by ionizing radiation for long periods of time.[8] These all incidences make strong argument that higher cases of leukaemia in Afghan ethnic group are also suffering of war since long time and due to

bombing use of chemical and toxic material water and soil is contaminated that lead to leukaemia.

The fourth common cause of pancytopenia between ethnic both group was aplastic anaemia (13.33%). Similar findings with aplastic anaemia were reported.[14,3] In contrast a higher incidence of aplastic anaemia (54%) was reported in the Philippines[16] and in Nepal (29.5%).[17] In the present study, males were affected with aplastic anaemia much more frequently than females, which might be a result of a higher incidence of occupational exposure to chemicals and of pesticide exposure as a common etiological agent for aplastic anaemia.

The most common clinical manifestation was fever (71.11%) which was universal in all patients, followed by progressive pallor (42.22%), which is more often observed in malaria and aplastic anaemia. Other non-specific features were also observed, such as easy fatigability (38.33%), dizziness (25.56%), and weight loss (26.11%), in patients. These symptoms were observed more in, malaria, aplastic anaemia, and leukaemia patients. Correlation between pancytopenia and fever, pallor and easy fatigability was noticed; this is in accordance with other studies.[10,11,3] The results of haematological parameters (Hb, TLC, Platelets and MCV) of the patients are in agreement with the findings of many researchers.[2,3,10] The most important aspect of management of pancytopenia that anaemic patients may be corrected by transfusion of packed red cells to maintain haemoglobin level above 12–14 gm/dl and provide platelets count >150,000/mm^3.

CONCLUSIONS

Malaria, aplastic anaemia, tuberculosis, leukaemia, hepatitis, iron deficiency anaemia and other infectious diseases are considered the leading reasons of pancytopenia in both ethnic groups. The most common clinical manifestation was progressive fever, fatigability, dizziness, pallor, weight loss and splenomegaly. Leukaemia and aplastic anaemia were found to be the most serious causes of pancytopenia in Afghan ethnic groups. Severe pancytopenia has important relation with the clinical conclusion and can be used as a prognostic marker.

REFERENCES

1. Firkin F, Chesterman C, Pennigton D, Rush B. De Gruchy's Clinical Hematology in Medical Practice. (5th Eds.) Oxford: Blackwell;1989.
2. Jha A, Sayami G, Adhikari RC, Panta AD, Jha R. Bone Marrow Examination in Cases of Pancytopenia, J Nepal Med Assoc 2008;47(169):12–7.
3. Gamal AH, Safa AR. Patterns of pancytopenia in Yemen. Turk J Hematol 2008;25:71–4.
4. Savage DG, Allen RH, Gangaidzo IT, Levy LM, Gwanzura C, Moyo A, Mudenge, B. Pancytopenia In Zimbabwe. American J Med Sci 1999;317(1):22–32.
5. RERFe (Radiation Effects Research Foundation). 2007. Introduction to the Radiation Effects Research Foundation. www.rerf.or.jp/shared/introd/introRERFe.
6. Al-Aboudi AK, Jarabii R. French Criminal Nuclear Tests in South Algeria, Oran University, College of Science, Faculty of Biology, Dar Al Gharb, Oran, Algeria, 2000. Available at: www.uraniumweaponsconference.de/speakers/khadum_du.pdf
7. Aalem AH, 1998, Effects of Depleted Uranium on Human Health in Basrah, International Scientific Symposium on The Use of DU and its Impact on Man and Environment in Iraq, Baghdad, 2–3 Dec 1998. Available at: www.uraniumweaponsconference.de/speakers/khadum_du.pdf
8. Shaafi R, Lieb WR. Cation movement in the high sodium erythrocyte of the cat. J Gen Physiol 1967;50:1746–51.
9. Iqbal W, Hassan K, Ikram N, Nur S. Aetiological breakup of 208 cases pancytopenia. J Rawal Med Coll 2001;5(1):7–9.
10. Osama I, Haider ZB, Anwer F, Nisar H. Patterns of pancytopenia patients in a general medical ward and a proposed diagnostic approach. J Ayub Med Coll Abbottabad 2004;16:8–13.
11. Shishir KB, Jagdish C, Shashi N, Sunita S, Varinder S, Ashok KD. Pancytopenia in children: etiological profile. J Trop Pediat 2005;51:236–9.
12. Arya TV, Prasad RN. Fatal pancytopenia in falciparum malaria. J Assoc Physicians India 1989;37:469–70.
13. Hemmer R. Airport malaria in Luxembourg. Euro Surveillance Weekly 1999;3:790–819.
14. Kishor K, Marwah S, Buxi G, Yadav RB, Chaturvedi NK. Bone marrow examination in cases of pancytopenia. J Ind Acad Clin Med 2001;2:55–9.
15. Lyn B, Irene RC, Marina DS. Clinico-hematologic and pathologic profile of adult Filipino pancytopenic patients. Turk J Hematol 2005;22 Suppl:Abstract:809;Poster:716.
16. Ratna MG. Study of clinical profile, causes, modalities of treatment and final outcomes of pancytopenia in Nepalese adult population. Thesis of Doctor of Medicine of Tribhuvan University, Kathmandu, Nepal.2004:83–96.
17. Mussarrat N, Fazl R. The incidence of underlying pathology in pancytopenia -an experience of 89 cases. J Postgrad Instit 2004;18:76–9.

Address for Corresponding:

Dr. Mohammad Masood Tariq, Centre for Advanced Studies in Vaccinology and Biotechnology, University of Baluchistan, Brewery Road Quetta, Pakistan. **Tel:** (Off): +92-81-2853843, **Cell:** +92-300-3867178.
Email: tariqkianiraja@hotmail.com