Journal of Family Medicine

Open Access

Austin Publishing Group

Research Article

Etiological Evaluation in 766 Patients with Pancytopenia: A Single Center Experience

Erismis B[1]*, Gulcicek G[1], Sisman M[2], Yildirim B[1], Yilmaz D[1] and Demiriz I[3]

[1]Health Sciences University, Bakirkoy Dr. Sadi Konuk Education and Research Hospital, Internal Medicine Department, Turkey

[2]Batman State Hospital, Turkey

[3]Health Sciences University, Bakirkoy Dr. Sadi Konuk Education and Research Hospital, Hematology Department, Turkey

***Corresponding author:** Erismis B, Internal Medicine Department, Health Sciences University, Bakirkoy Dr. Sadi Konuk Education and Research Hospital, Istanbul, Turkey

Received: April 05, 2019; **Accepted:** May 10, 2019; **Published:** May 17, 2019

Abstract

Introduction: Pancytopenia is a clinical problem which is a common and wide differential diagnostic spectrum. and may occur with various mechanisms. In this study we aimed to determine the most common etiologic causes in patients with pancytopenia.

Materials and Methods: The records of patients aged 18 years and older, who applied to the Health Sciences University Bakirkoy Dr. Sadi Konuk Training and Research Hospital between 2012 and 2017 and who were diagnosed with pancytopenia according to WHO criteria were retrospectively reviewed.

Statistical Method: Mann-Whitney-U test was used for 2 groups and Kruskal-Wallis test was applied for 3 and more groups. Since no normal distribution was provided as a descriptive statistic, median and change interval values were given for continuous data.

Results: A total of 766 patients, 475 (62%) women and 291 (38%) men, were included in the study. In these patients, non-hematologic causes were found in 77.7% and hematologic causes in 22.3% of patients with pancytopenia. Hematological etiologies were 72.2% benign and 27.8% malignant. Non-hematological causes were divided into groups as renal diseases (6.1%), rheumatological diseases (2.4%), infective diseases (10.8%), endocrinological diseases (3.9), hypersplenism (14.5%), immunosuppressive drug use (17.5%), solid organ cancers (10.8%) and unidentified reasons (34.3%).

Conclusion: Pancytopenia should be evaluated carefully and the etiology should be detected quickly and corrected by appropriate treatment. It is an appropriate approach to exclude, first the non-hematological causes (especially immunosuppressive drug use, hypersplenism, infection and solid organ cancers, respectively) and the benign causes of hematological reasons.

Keywords: Pancytopenia; Anemia; Bisitopenia

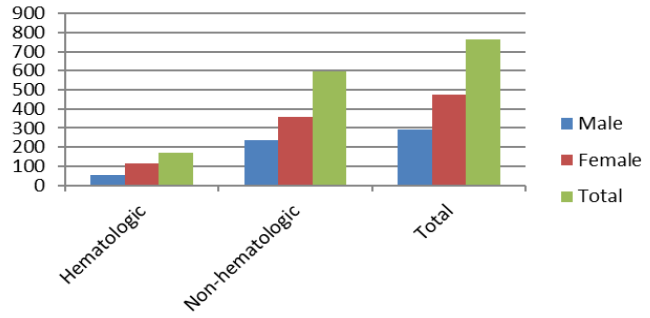
Introduction

The definition of pancytopenia adopted by the World Health Organization (WHO) includes the combination of all three parameters: Hemoglobin (Hb) - for non-pregnant women - <12g/dl and <13g/dl for men, absolute neutrophil count < 1800 /microl, platelet count <150000 /mm^3 [1]. In healthy adults, hematopoiesis occurs in the marrow where mature blood cells migrate to other regions with the circulatory system. The balance between blood cell production, distribution in other organs, and ongoing cellular destruction determines the levels of circulating blood cells [2-5]. Pancytopenia may occur with various mechanisms. The etiologic classification consists of bone marrow infiltration (hematological malignancies, metastatic cancers, myelofibrosis and infectious diseases, tuberculosis, fungal infections, etc.), bone marrow aplasia (vitamin B12 or folate deficiency, aplastic anemia, infectious diseases such as HIV, viral hepatitis, parvovirus B19 and drugs) and blood cell destruction or sequestration (disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, ineffective erythropoiesis - myelodysplastic syndrome, megaloblasitis disorders, hypersplenism). Although pancytopenia is a common clinical problem with a wide differential spectrum, there is not enough information about the incidence of causes except for a few studies [6-8]. In our study, the aim was to determine the most common etiologies in patients with pancytopenia and to contribute to the shortening of the transition period for appropriate treatment by making a rapid diagnosis.

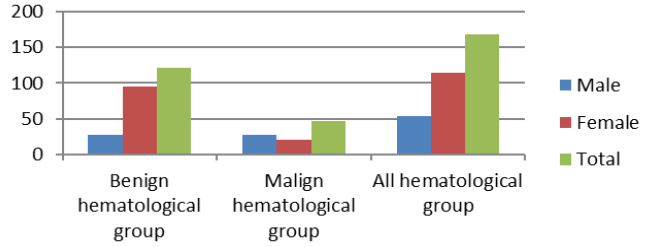
Materials and Methods

The records of patients 18 years and older, who applied to the Health Sciences University Bakırkoy Dr. Sadi Konuk Training and Research Hospital Internal Medicine outpatient clinics from, 2012 to 2017 and who were diagnosed with pancytopenia according to WHO criteria were retrospectively analyzed. Gender, age, Hemoglobine (Hb), hematocrit (Hct), white blood cell count, platelet count, mean corpuscular volume (MCV), reticulocyte count, lactate dehydrogenase (LDH), vitamin B12, folic acid, serum iron, ferritin levels, TSH, fT4, fT3, drug (immunosuppressive) use, presence of hepatomegaly and/or splenomegaly, bone marrow aspiration and biopsy results and diagnoses leading to pancytopenia after the analyzes were recorded. The patients were divided into 2 groups according to hematological and non-hematological etiologies, which primarily led to pancytopenia. Hematologic etiology group was further divided into two groups as benign and malignant causes.

Citation: Erismis B, Gulcicek G, Sisman M, Yildirim B, Yilmaz D and Demiriz I. Etiological Evaluation in 766 Patients with Pancytopenia: A Single Center Experience. J Fam Med. 2019; 6(5): 1177.



Graphic 1: Gender distribution among groups.



Graphic 2: Gender distribution between hematological subgroups.

The non-hematologic etiological group was further divided into subgroups as; infectious, rheumatologic, endocrinological, renal diseases, hypersplenism, immunosuppressive drug use, solid organ cancers and others (undetectable).

Statistical method

The normality tests were performed for each variable in the study and Kolaporov-Smirnov and Shapiro-Wilk tests were performed. Since the variables were not normally distributed due to $p < 0.05$, non-parametric methods were preferred in the analyzes. Mann-Whitney-U test was used for 2 groups and Kruskal-Wallis test was applied for 3 and more groups. Since no normal distribution was provided as a descriptive statistic, median and change interval (max-min) values were given for continuous data. Frequency (frequency) distribution tables for categorical data were interpreted. Data are presented as percentage and number. The analyzes were performed with SPSS 22.0 statistical analysis program and significance level was considered as $p < 0.05$.

Results

A total of 766 patients, 475 (62%) women and 291 (38%) men, were included. The mean age of men was 60.6 years, the mean age of women was 55.5 years, and the average age of all patients was 57.5 years. Non-hematological causes were found in 77.7% and hematological causes in 22.3% of patients with pancytopenia. Gender distribution among both groups is shown in Graphic 1. Hematological etiologies were 72.2% benign and 27.8% malignant. Gender distribution in hematological subgroups is shown in Graphic 2. Non-hematological causes were divided into groups as renal diseases (6.1%), rheumatological diseases (2.4%), infective diseases (10.8%), endocrinological diseases (3.9), hypersplenism (14.5%), immunosuppressive drug use (17.5%), solid organ cancers (10.8%) and unidentified reasons (34.3%). Gender and etiology distribution of non-hematological group is shown in Table 1. Differences between the hematological and non-hematological groups (Table 2) and benign and malignant groups from the hematological subgroups (Table 3) were shown in the tables below. Age (p=0.024), LDH (p=0.000), serum iron (p=0.032), ferritin (p=0.000) and vitamin B12 (p=0.000) levels were significantly higher in the non-hematological group. According to the comparison between hematological groups; Hb (p=0.000), Hct (p=0.000), white blood cell count (p=0.000) and platelet count (p=0.002) were significantly higher in benign hematological group. Serum iron (p=0.001), ferritin (p=0.000) and vitamin B12 (p=0.004) levels were significantly higher in the malignant hematological group.

Table 1: Nonhematological group sex - etiology distribution.

Etiology	Male	Female	Total / %
Infectious causes	22	42	64 / 10,7
Rheumatological	0	14	14 / 2,3
Hypersplenism	33	53	86 / 14,4
Endocrinological causes	5	18	23 / 3,8
Immunosuppressive drug use	49	55	104 / 17,4
Renal causes	18	18	36 / 6,05
Solid organ cancers	38	26	64 / 10,7
Other reasons	71	133	204 / 34,2
Total	**236**	**359**	**595 / 100**

Fifty-five (17.2%) out of 319 patients with abdominal ultrasonography had hepatomegaly and 92 (28.8%) had splenomegaly. Bone marrow aspiration and biopsy was performed in only 33 (4.3%) of all patients. Because in other patients there was a non-haematological cause and no need to performe bone marrow biopsy.

Discussion

Pancytopenia can be fatal if it cannot be diagnosed early [9]. Therefore, rapid detection of the underlying cause is extremely important in terms of coping with the disease and prognosis. It is important to investigate the the most common pancytopenia etiologies and which may be less frequent but more serious, in the differential diagnosis. Gayathri BN et al. reported a mean age of 41 years and male gender as a dominant in a prospective study of 104 pancytopenia patients aged between 2 and 80 years in India. Also, splenomegaly was more common than hepatomegaly in their study [10]. M. Premkumar et al. found that the mean age was 32.8 / year and male gender was dominant in their study which evaluating the hematological etiology with 140 pancytopenia patients. As the etiological frequency; Megaloblastic anemia (60.7%), infectious causes (16.4%), aplastic anemia (7.8%) and leukemia (9.2%) were detected [11]. In a study conducted by Imbert et al. with 213 adult pancytopenia patients in France, it was observed that malign hematological causes were more frequent that was not compatible with our study. According to this study, malignant myeloid disorders (acute myeloid leukemia, MDS and myelofibrosis) 42% and malignant lymphoid disorders 18% accounted for 60% of all hematological etiologies. The group containing the benign etiologies such as megaloblastic anemia was found to be 17% [8]. It was thought that this difference could be related with adequate nutrition and socio-cultural level of the patient population. Dr. Atif Sitwat Hayat et al. Found that 72.94% of the patients were male and 27.05% were female.

Table 2: Differences between hematological and non-hematological groups of variables, Mann-Whitney-U test results.

	Group	N	Average row	Mann-Whitney-U statistics	p
Age	hematologic	171	352.41	45556	**0.024***
	non-hematologic	595	**392.44**		
	Total	766			
Hb	hematologic	171	373.93	49236	0.521
	non-hematologic	595	386.25		
	Total	766			
Hct	hematologic	171	389.82	49791	0.671
	non-hematologic	595	381.68		
	Total	766			
White Blood Cell Count	hematologic	171	372.79	49040	0.472
	non-hematologic	595	386.58		
	Total	766			
Platelet Count	hematologic	171	384.25	50745	0.96
	non-hematologic	595	383.29		
	Total	766			
LDH	hematologic	171	302.59	37036	**0.000***
	non-hematologic	595	**406.75**		
	Total	766			
MCV	hematologic	171	369.5	48478	0.346
	non-hematologic	595	387.52		
	Total	766			
TSH	hematologic	171	144.42	8183.5	0.319
	non-hematologic	595	155.95		
	Total	766			
Ft4	hematologic	171	124.73	5179.5	0.975
	non-hematologic	595	125.07		
	Total	766			
Serum iron	hematologic	171	155.59	10917.5	**0.032***
	non-hematologic	595	**176.03**		
	Total	766			
Ferritin	hematologic	171	137.38	9006.4	**0.000***
	non-hematologic	595	**181.61**		
	Total	766			
Folate	hematologic	171	119.68	5863.5	0.853
	non-hematologic	595	117.97		
	Total	766			
Vitamin B12	hematologic	171	140.6	9447.1	**0.000***
	non-hematologic	595	**194.14**		
	Total	766			

In the etiological evaluation, they found that non-cancerous causes were more frequent with a rate of 63.52% [12]. Bhagwan Singh Yadav et al., found the mean age of 35.15 ± 12.6 years and an equal female / male ratio in gender distribution, in their study with 58 pancytopenia patients above the age of 18 [13]. In the study of T. N. Dubey et al., which included 70 patients over 13 years of age, the male / female ratio was 1.4/1. In the etiological evaluation, megaloblastic anemia was in the first place with a rate of 41.4%. Aplastic anemia with the ratio of 22.9%, hypersplenism 15.7% and leukemic diseases 14.2% were also found in the etiology [14].

In our study, the mean age was 57.5 year and different from the

Table 3: Differences between benign and malign hematological groups, Mann-Whitney-U test results.

	Group	N	Average row	Mann-Whitney-U statistics	p
Age	benign	122	79.88	2242.5	**0.023***
	malign	47	**98.29**		
	Total	169			
Hb	benign	122	**93.73**	1802	**0.000***
	malign	47	62.34		
	Total	169			
Hct	benign	122	**93.43**	1839	**0.000***
	malign	47	63.13		
	Total	169			
White Blood Cell Count	benign	122	**93.23**	1862.5	**0.000***
	malign	47	63.63		
	Total	169			
Platelet Count	benign	122	**92.3**	1977	**0.002***
	malign	47	66.06		
	Total	169			
LDH	benign	122	81.65	2458.5	0.151
	malign	47	93.69		
	Total	169			
MCV	benign	122	81.36	2422.5	0.113
	malign	47	94.46		
	Total	169			
TSH	benign	122	39.47	1567.8	0.584
	malign	47	36.52		
	Total	169			
Ft4	benign	122	24.29	1254.9	0.304
	malign	47	28.65		
	Total	169			
Serum iron	benign	122	46.73	1796.3	**0.001***
	malign	47	**68.47**		
	Total	169			
Ferritin	benign	122	46.7	1952.2	**0.000***
	malign	47	**72.23**		
	Total	169			
Folate	benign	122	34.58	1162.1	0.378
	malign	47	39.38		
	Total	169			
Vitamin B12	benign	122	50.52	1836.3	**0.004***
	malign	47	**70.15**		
	Total	169			

literature the female gender was dominant. The difference in mean age was considered to be related only to the inclusion of the adult population in our study. We also showed that non hematological causes more common than hematological ones and similar to literature, we showed that benign causes (72.8%) were more frequently in the hematological etiology.

Conclusion

Pancytopenia should be evaluated carefully and the etiology should be detected quickly and corrected by appropriate treatment. In studies conducted, gender dominance is different for each study, so it is not true to say that pancytopenia is more common in male or female

sex. According to our study, it is an appropriate approach to exclude, first the non-hematological causes (especially immunosuppressive drug use, hypersplenism, infection and solid organ cancers, respectively) and the benign causes of hematological reasons. When family physicians encounter patient with pancytopenia, they should be calm and after diagnosis treat the benign causes. If there is no benign cause than they should refer the patients to advanced center immediately.

References

1. Valent P. Low blood counts: immune mediated, idiopathic, or myelodysplasia. Hematology Am Soc Hematol Educ Program. 2012; 2012: 485.
2. Young NS, Abkowitz JL, Luzzatto L. New Insights into the Pathophysiology of Acquired Cytopenias. Hematology Am Soc Hematol Educ Program. 2000: 18-38.
3. Pascutti MF, Erkelens MN, Nolte MA. Impact of Viral Infections on Hematopoiesis: From Beneficial to Detrimental Effects on Bone Marrow Output. Front Immunol. 2016; 7: 364.
4. Marks PW. Hematologic manifestations of liver disease. Semin Hematol. 2013; 50: 216-221.
5. Risitano AM, Maciejewski JP, Selleri C, Rotoli B. Function and malfunction of hematopoietic stem cells in primary bone marrow failure syndromes. Curr Stem Cell Res Ther. 2007; 2: 39.
6. Savage DG, Allen RH, Gangaidzo IT, et al. Pancytopenia in Zimbabwe. Am J Med Sci. 1999; 317: 22-32.
7. Tilak V, Jain R. Pancytopenia-a Clinico-Hematologic Analysis of 77 Cases. Indian J Pathol Microbiol. 1999; 42: 399-404.
8. Imbert M, Scoazec J-Y, Mary J-Y, Jouzult H, Rochant H, Sultan C. Adult Patients Presenting with Pancytopenia: A Reappraisal of Underlying Pathology and Diagnostic Procedures in 213 Cases. Hematologic Pathology. 1989; 3: 159-167.
9. Khodke K, Marwah S, Buxi G, Yadav RB, Chaturvedi NK. Bone marrow examination in cases of pancytopenia. J Indian Acad Clin Med. 2001; 2: 55–59.
10. Gayathri B N, Rao KS. Pancytopenia: A clinico hematological study. J Lab Physicians. 2011; 3: 15-20.
11. M Premkumar. Cobalamin and Folic Acid Status in Relation to the Etiopathogenesis of Pancytopenia in Adults at a Tertiary Care Centre in North India. Anemia. 2012: 707402.
12. Atif Sitwat Hayat. Pancytopenıa; Study For Clınıcal Features And Etıologıcal Pattern At Tertıary Care Settıngs In Abbottabad 1 2 3 4 Dr. The Professional Medical Journal.
13. Bhagwan Singh Yadav, Amit Varma and Priyanka Kiyawat. Clinical profile of pancytopenıa: a tertıary care experıence. International Journal of Bioassays ISSN: 2278-778X CODEN: IJBNHY.
14. TN Dubey. The Common Causes Leading to Pancytopenia in Patients Presenting in Hospital of Central India. International Journal of Contemporary Medical Research. 2016; 3.

Citation: Erismis B, Gulcicek G, Sisman M, Yildirim B, Yilmaz D and Demiriz I. Etiological Evaluation in 766 Patients with Pancytopenia: A Single Center Experience. J Fam Med. 2019; 6(5): 1177.