

Shiraz E-Medical Journal
Vol. 10, No. 3, July 2009

<http://semj.sums.ac.ir/vol10/jul2009/88007.htm>

Abnormal Immunoglobulin Levels in Iranian Patients with Hematologic Malignancies.

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Received for Publication: May 10, 2009, Accepted for Publication: May 26, 2009.

Abstract:

Introduction: Hematologic malignancies can be associated with dysregulation of the immune system. There are some conflicting data regarding serum immunoglobulin levels in patients with such malignancies.

Material and method: In order to evaluate the humoral immunity of the patients with hematologic malignancies, 58 patients were enrolled in this study. 24 with acute lymphoblastic leukemia (ALL), 17 with acute myeloid leukemia (AML), eight with lymphoma, five with chronic lymphocytic leukemia, and four with multiple myeloma.

Results: There were six cases with decreased serum IgG level (5 AML and 1 ALL). Forty patients with elevated serum IgG levels (69%). 24 with elevated IgA and/or IgM level; 12 patients with elevation in all classes of immunoglobulin (8 ALL, 2 AML, and 2 lymphoma).

Conclusion: Serum immunoglobulin levels can be abnormal in the patients with hematologic malignancies. Abnormalities of IgG, especially elevated level, seem to be the most frequent finding encountered in these patients.

Keywords: Hematologic malignancies; Immunoglobulin; Leukemia; Lymphoma.

Introduction:

Hematologic malignancies and their treatment are among important causes of secondary immunodeficiency.^(1, 2) The majority of the affected patients do not have previous immunodeficiency.⁽¹⁾ However, development of malignancies such as leukemia could indicate a dysregulation in the immune system.⁽¹⁾

Different studies have evaluated quantitative and qualitative immunologic variables in malignancies. All have conflicting results.⁽³⁻¹²⁾ Serum immunoglobulin level is a parameter which seems to be abnormal in few patients with hematologic malignancies.⁽³⁻⁶⁾ There are reports which showed, that there was no significant difference in mean values of serum immunoglobulin's in patients with acute lymphoblastic leukemia (ALL), and age matched healthy subjects.⁽³⁻⁵⁾

The objective of this single center study is to evaluate the status of the humoral immunity in patients with hematologic malignancies.

Patients and Methods:

Fifty-eight patients with hematologic malignancies, which referred to Department of Oncology and Hematology of a referral hospital in the South-eastern Iran during 2005-2008, were enrolled in this study.

Characteristics of these patients were documented in a designed questionnaire. The concentrations of serum IgG, IgM, and IgA were determined by nephelometry (The Binding Site, UK). The values obtained from the patients were compared with normal values in Iran.⁽¹³⁾ The

serum reference intervals values were 636-1518 mg/dl for IgG, 39-283mg/dl for IgM, and 72-375 mg/dl for IgA; we also compared patient's serum immunoglobulin level with age and sex matched normal subjects.⁽¹³⁾ A level that fell outside the two standard deviations of the mean was considered elevated or depressed.

For statistical analysis, we used the computer program software SPSS, version 14. Quantitative variables were compared using the Student's t test. Results were considered significant, if the P-value was less than 0.05.

Results:

Characteristics of the Patients

A total of 58 patients (35 males and 23 females), with the age range of 7-79 years (mean 30.3 ± 17.5 years), entered in this study. The characteristics of the patients group were as follow; 24 with acute lymphoblastic leukemia (ALL), 17 with acute myeloid leukemia (AML), eight with lymphoma, five with chronic lymphocytic leukemia (CLL), and four with multiple myeloma (MM). (table 1)

Serum Immunoglobulin Levels

The mean serum immunoglobulin level at the time of diagnosis for IgG was 1650 mg/dl (300-2800 mg/dl), IgM was 308 mg/dl (range 24-580mg/dl), and 325 mg/dl (range 80-673) for IgA. There was no significant difference between patient's immunoglobulin levels with healthy controls.

Table 1, Characteristics of patients.

Diagnosis	Number of Patients		Age (years)		Sex	
	Frequency	Percent	Median	Range	Male	Female
ALL	24	41	19.5	7-63	11	13
AML	17	29	35	20-71	11	6
Lymphoma	8	14	16.5	8-48	7	1
CLL	5	9	39	14-71	3	2
MM	4	7	49	38-79	3	1
Total	58	100	24.5	7-79	35	23

ALL: acute lymphoblastic leukemia, AML: acute myeloid leukemia, CLL: chronic lymphocytic leukemia, MM: multiple myeloma.

Table 2, Patients with high serum levels of immunoglobulins.

Diagnosis	Total		Patients with elevated IgG	
	Frequency	Percent	Frequency	Percent
ALL	24	41	18	45
AML	27	29	11	28
Lymphoma	8	14	6	15
CLL	5	9	3	8
MM	4	7	2	5
Total	58	100	40	100

ALL: acute lymphoblastic leukemia, AML: acute myeloid leukemia, CLL: chronic lymphocytic leukemia, MM: multiple myeloma.

Serum Immunoglobulin by Disease

Different types of hematologic malignancies were found to have differences in their serum immunoglobulin level. However there was no significant difference between immunoglobulin levels and diagnostic groups. (Figure 1)

Patients with Normal Immunoglobulin Levels

Four patients (3 male and 1 female), had all serum immunoglobulin level in normal range (6.9%), Two had lymphoma, one CLL and one ALL.

Patients with Low Immunoglobulin Levels

Six patients (4 male and 2 female) had decreased serum IgG level (10.3%). (Five had AML and one with ALL). Out of these six patients, four had IgA and/or IgM levels elevated and two with both IgA and IgM elevation. There was no patient with reduced serum IgA or IgM level.

Patients with High Immunoglobulin Levels

Forty patients (23 male and 17 female) had elevated levels of IgG (69%). (Table 2) IgA and IgM levels showed to be correlated with each other (P-value= 0.07). (Figure 2) in these group. No correlation was found between serum IgG and other two immunoglobulin classes.

In 24 patients with elevated IgG levels, IgA and/or IgM were also elevated. Only 12 patients had IgG levels within normal range, five had increased IgA and three increased IgM. (five had ALL, one with AML, two with lymphoma, two with CLL and two with multiple myeloma)

Discussion:

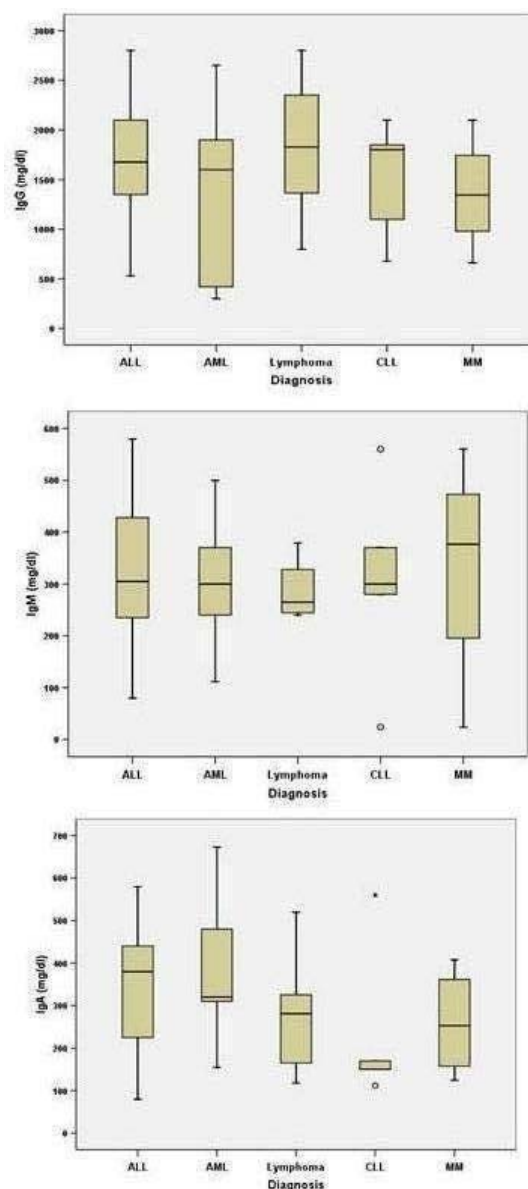
There are conflicting data regarding abnormalities in the serum immunoglobulin level in patients with leukemia.⁽³⁻⁶⁾ In this study, approximately 90% of our cases exhibited abnormality in at least one serum immunoglobulin level. This rate is relatively higher than previous reports.

Increased IgG level was the most common abnormality observed in our patients (70%). This was followed by increased IgA and IgM level seen in 59% and 36% of the patients, respectively. However, the mean serum immunoglobulin level did not differ significantly in our patients, compared to age-matched normal subjects. This was in concordance with most previous studies^(3-6, 8), although one study reported an increased serum IgG level compared to control group.⁽⁷⁾ Even though the mean IgG level was higher than other immunoglobulin classes in our study, it was still in the normal range.

In previous studies, large numbers of patients groups showed decreased in one or more immunoglobulin's level.^(9, 14, and 15) It is suggested that the reduced immunoglobulin levels observed in these patients are due to decreased normal immunoglobulin-producing lympho-

cytes.⁽⁹⁾ Moreover this reduction in immunoglobulin's could be primarily related to the leukemic process.^(16, 17) In our study, there was large number of patients with reduced IgG levels, which suggests that this immunoglobulin class could be more susceptible to the leukemic process.

Figure 1, Serum immunoglobulin levels of diseases.



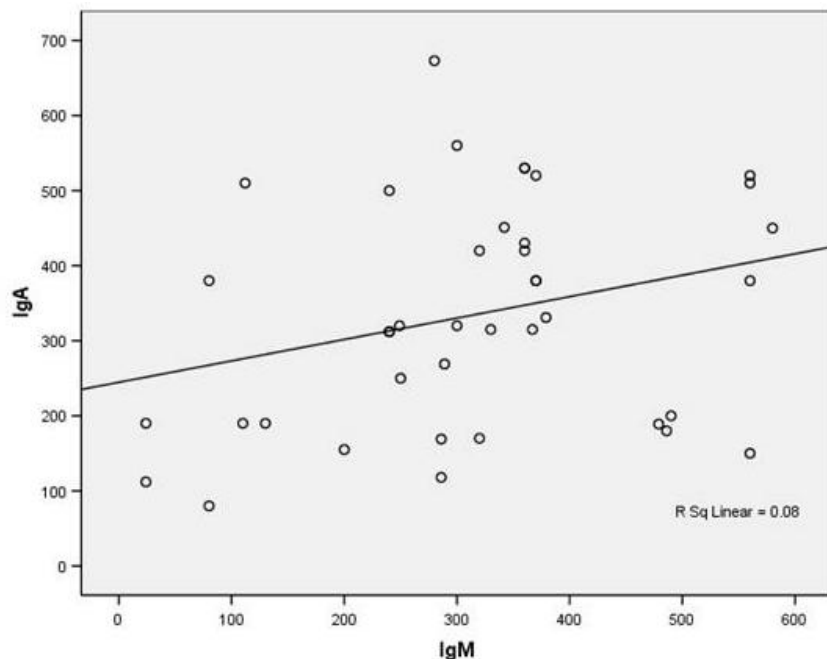


Figure 2, Association of serum levels of IgA and IgM (mg/dl) in the patients with increased serum levels of IgG.

There are several studies which investigated immunoglobulin levels in patients with hematologic malignancies mainly with ALL.^(3, 5-9) However, abnormal serum immunoglobulins in other hematologic malignancies, which is also seen in our study needs to be fully investigated.

There are a number of studies which investigate the role of IgG as a prognostic factor.^(3, 7, 10-12) It has been found that patients with low IgG levels at diagnosis have an increased mortality rate^(3, 9, and 18), others reported that patients with high IgG levels have a lower survival.⁽⁷⁾ Although we did not perform long-term study on this group of patients, we do recommend a cohort study.

In conclusion, serum immunoglobulin levels can be abnormal in patients with hematologic malignancies at the time of

diagnosis. Abnormalities of IgG, especially elevated levels, seem to be the most frequent finding encountered in these patients.

Acknowledgements:

The Respectable officials of Immunology and Hematology Oncology wards who facilitate performance of this research are hereby appreciated.

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