

# Hypogammaglobulinemia in patients with lymphoma and its impact on infectious complications

Hyo-jin Ahn<sup>1</sup>, Su-Mi Choi<sup>1</sup>, Yeong-woo Jeon<sup>2</sup>

<sup>1</sup>Division of Infectious Diseases, Department of Internal Medicine, The Catholic University of Korea, Seoul, Korea

<sup>2</sup>Division of Hematology, Department of Internal Medicine, The Catholic University of Korea, Seoul, Korea



## Background

Hypogammaglobulinemia is associated with lymphoma due to disease itself or related therapy and is known to cause infections especially by encapsulated bacteria.

## Aim

The aim of this study was to investigate the frequency and patterns of hypogammaglobulinemia and its impact on infectious complications in patient with lymphoma.

## Methods

We reviewed medical records of adult patients with lymphoma, who underwent immunoglobulin G (IgG) test from Jan 1, 2019 to Feb 29, 2020. Analysis was done with first IgG test results of each patients. We analyzed the frequency of hypogammaglobulinemia, infectious complications and outcome during follow-up period. Patients were grouped by number of repeated chemotherapy. Patients who had 1-3 times of chemotherapy were defined as group 1 and 4-6 times as group 2. Group 3 was defined as patients with over 7 times of chemotherapy or salvage chemotherapy and group 4 as patients with palliative care without chemotherapy. Hypogammaglobulinemia was defined as a serum IgG level below 600 mg/dL.

Table 1. Demographic characteristics of the patients (N = 102)

Characteristics	No. (%)
Sex (M:F)	54:48 (52.9:47.1)
Median age, y (range)	
Lymphoma classification	
Hodgkin's disease	5 (4.9)
Non-Hodgkin's disease	93 (91.2)
Chronic lymphocytic leukemia	3 (2.9)
Mixed type	1 (1.0)
Histologic subtype	
Diffuse large B cell lymphoma	39 (41.9)
Follicular lymphoma	14 (15.1)
MALT lymphoma	4 (4.3)
Mature T cell lymphoma	22 (23.7)
Mantle cell lymphoma	5 (5.4)
Other subtypes	10 (10.8)
Underlying disease	
Pulmonary disease	2 (2.0)
Kidney disease	2 (2.0)
Hepatobiliary disease	5 (4.9)
Endocrinologic disease	29 (28.4)
Autoimmune disease	3 (2.9)
Cardiologic disease	30 (29.4)
Cancer (except lymphoma)	2 (2.0)
Others	9 (8.8)

## Results

A total of 102 patients were enrolled and data analysis was done with 101 patients excluding 1 MALT lymphoma patient resolved after H. pylori eradication therapy. None of the patients had surgical or medical asplenia. Among 101 patients, 12 (11.9%) patients had hypogammaglobulinemia. No patients had hypogammaglobulinemia before chemotherapy. There was no difference in the frequency of hypogammaglobulinemia between lymphoma subtypes. Mean IgG level had decreasing tendency by number of chemotherapy and had statistic significance ( $p < 0.05$ ). Although it was not statistically significant, neutropenic fever occurred more frequently in patients with hypogammaglobulinemia (41.7% vs. 21.3%,  $p > 0.05$ ). Also, infectious complications was more frequently observed in patients with hypogammaglobulinemia (33.3% vs. 20.2%,  $p > 0.05$ ). There was no case with encapsulated bacterial infection (*S. pneumoniae*, *H. influenzae*, *N. meningitidis*). The frequency of hypogammaglobulinemia was not higher in the group patients who received more repetitive chemotherapy.

Table 2. Frequency of hypogammaglobulinemia by number of chemotherapy

	Total N=101*	HD N=5	NHD N=93*	CLL N=3	Mixed type N=1
Pre-treatment	0/17 (0)	0/0 (0)	0/17 (0)	0/0 (0)	0/0 (0)
Chemotherapy group					
Group 1 (chemo 1-3 times)	4/26 (15.4)	1/3 (33.3)	3/22 (13.0)	0/1 (0)	0/0 (0)
Group 2 (chemo 4-6 times)	3/24 (12.5)	0/1 (0)	2/21 (9.5)	0/2 (0)	0/0 (0)
Group 3 (chemo over 7 times or salvage)	2/30 (6.6)	0/1 (0)	2/29 (6.9)	0/0 (0)	0/0 (0)
Group 4 (palliative care)	3/4 (75.0)	0/0 (0)	3/3 (100.0) <sup>†</sup>	0/0 (0)	0/1 (0)

\* 1 MALT lymphoma patient resolved after H. pylori eradication therapy was excluded

<sup>†</sup> group 4 patients with non-Hodgkin's disease had significant hypogammaglobulinemia compared to other groups ( $P < 0.05$ ).

Table 3. Frequency of hypogammaglobulinemia in non-Hodgkin's disease patients by number of chemotherapy

	DLBCL N=39	Follicular N=13	MALT N=4	Mature T N=22	Mantle N=5	Others N=10	Total N=93
Pre-treatment	0/8 (0)	0/1 (0)	0/2 (0)	0/5 (0)	0/0 (0)	0/1 (0)	0/17 (0)
Chemotherapy group							
Group 1 (chemo 1-3 times)	0/5 (0)	0/3 (0)	0/0 (0)	2/9 (22.2)	1/1 (100.0)	0/4 (0)	3/22 (13.6)
Group 2 (chemo 4-6 times)	1/10 (10.0)	1/4 (25.0)	0/0 (0)	0/3 (0)	0/1 (0)	0/3 (0)	2/21 (9.5)
Group 3 (chemo over 7 times or salvage)	1/15 (6.7)	1/5 (20.0)	0/1 (0)	0/4 (0)	0/2 (0)	0/2 (0)	2/29 (6.9)
Group 4 (palliative care)	1/1 (100.0)	0/1 (0)	0/0 (0)	1/1 (100.0)	1/1 (100.0)	0/0 (0)	3/3 (100.0)

Table 4. Mean IgG level of pre-treatment and chemotherapy group

	Pre-treatment	Group 1	Group 2	Group 3	Group 4	P value
Mean IgG level	1368.2	948.1	936.9	804.0	427	< 0.05

Table 5. Frequency of neutropenic fever and infection complications

	Total N=101	Patients with Hypogammaglobulinemia N=12	Patients without Hypogammaglobulinemia N=89	P value
Neutropenic fever	24/101 (23.8)	5/12 (41.7)	19/89 (21.3)	.12
Infection complications	23/101 (22.8)	4/12 (33.3)	18/89 (20.2)	.30

## Conclusions

Neutropenic fever, infectious complications and infection related death were higher in patients with hypogammaglobulinemia, though it had no statistical significance. But it is a limitation of retrospective study that patients with neutropenic fever and infectious complications done more IgG study than the others. Further analysis with the results of consecutive IgG tests, which was repeatedly performed more than two times, is in progress.

## References

1. Infections in patients with cancer, Robert W. Finberg. Harrison's Principles of Internal Medicine, 20th ed. 2015. McGraw-Hill Education
2. Barmettler S, Ong MS, Farmer JR, Choi H, Walter J. Association of Immunoglobulin Levels, Infectious Risk, and Mortality With Rituximab and Hypogammaglobulinemia. JAMA Netw Open. 2018;1(7):e184169

