The Role of Immune Response in Immunocompromised Conditions

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ABSTRACT

A patient is said to be immuno-compromised (IC) if one or more of his or her natural and adaptive defense mechanisms are unable to function normally. Thus, immunocompromised patients are easily susceptible to infection. Aim of study: to determine the immune response in immunocompromised patients that makes them easily susceptible to infection. Method: the study was designed as a cross-sectional analytic observational study using multi-variant statistical tests. The samples were classified into the IC and Non-IC groups, consisting of 14 people, 10 men, and 4 women, who were examined for the following immunological variables: IL–10, IFN-γ, TNF-α, IL-Iβ, IgG, C3, and C4. The results demonstrated a significant difference in the immune response of subjects from the IC and NIC groups ($p<0.05$), with a significantly higher TNF-α, IL–10 and IgG levels, and a lower C3 level in the IC group. Conclusion: during IC conditions, there is a disorder in the natural as well as adaptive C3 natural immune system, making patients more susceptible to infection.

Keywords: *Immune Response, Immunocompromised, Non–Immunocompromisee, Infection*

INTRODUCTION

Immunocompromised (IC) patients suffer from a malfunction of the natural and adaptive defense mechanisms of the body, making them more susceptible to infection and making infection more dangerous to their survival.[1]

Imbalance of the immune system may also play a role in the development of infection. Such imbalance may occur during the following conditions:

1. Humoral immune system defect: complement and antibody deficiency that disturbs the ability to opsonize and kill bacteria.
2. Defect in the cellular immune system: disturbed phagocytic system (neutrophils and macrophages) and the specific cellular immune system.
3. Basic immune status: a difference in the natural ability to produce TNF (high and low response).
4. Administration of immunosuppressant agents.
5. Autoimmune disease, cancer, liver cirrhosis, chronic renal failure.[2]

To establish the conditions in a patient, we could evaluate the patient's immune response. Usually, patients who are immunocompromised (IC) have a malfunctioning or lower immune response.

According to Dale, patients with diabetes mellitus, liver cirrhosis, chronic renal failure, and old age belong to the IC group, and are thus more susceptible to infection. IC patients who suffer from infection often suffer from severe complications such as sepsis and septic shock, ending in death.[1,3,4]

The most common IC cases in the Department of Internal Medicine are those with diabetes mellitus, liver cirrhosis, and chronic renal failure. These three conditions often cause patients to suffer from infection as a complication, and infections often result in sepsis and death.

This study tries to answer the question on what part of the immune response of immunocompromised (IC) patients makes them more susceptible to disease.

STUDY METHOD

The study was designed as an analytic observational study of immunocompromised (IC) and Non-Immunocompromised (NIC) patients.

We chose a cross-sectional analytic observational study since observation and data collection could be conducted simultaneously, while each study subject only has to be observed once.

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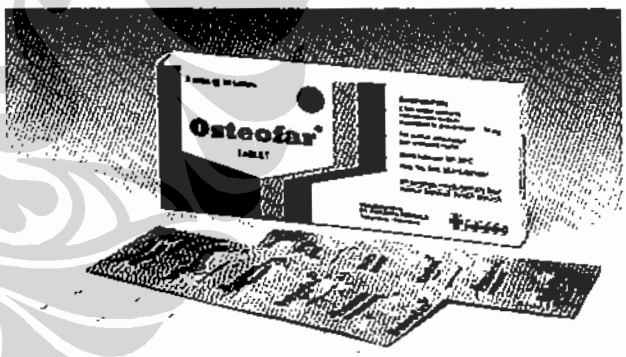

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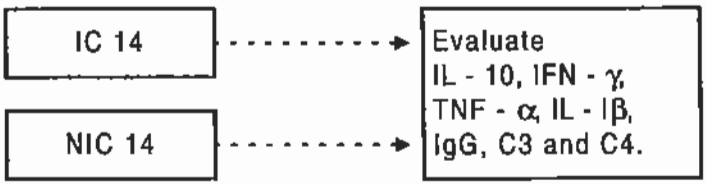
Table 1. Different Types of Immunocompromised Conditions

Predisposing Factor	Effect on The Immune System	Type of Infection
Drugs or X-ray in immunosuppressed patients, allograft recipients (kidney, bone marrow, heart transplant), and cancer treatment	Reduced cellular and humoral immunity	Pulmonary infection, bacteremia, fungal infection, urinary tract infection
Immunosuppressant viruses (rubella, herpes, virus EB, hepatitis virus, HIV)	Viral replication within the lymphoid cell, thus disrupting its function	Secondary bacterial infection (as well as fungal and protozoa infection in AIDS)
Tumor	Immune system cell replacement	Bacteremia, pneumonia, urinary tract infection
Malnutrition	Lymphoid hypoplasia, reduced lymphocyte count in the bloodstream, reduced phagocytosis ability	Measles, tuberculosis, respiratory and gastrointestinal tract infections
Smoking, inhalation of particles (silica, spores, fungi)	Pulmonary inflammation, immune complex deposition for spores and fungi	Respiratory tract infection, allergic response
Chronic endocrine disorders (diabetes)	Reduced phagocytosis ability	Staphylococcal infection, tuberculosis, upper respiratory tract infection, bacteremia, etc.
Primary immuno deficiency	Reduced cellular and humoral immunity	

(Quoted from reference No. 5)

Cross-Sectional Study Design in IC and NIC Patients



Schematic Illustration of a Cross-Sectional Study

When we find an IC patient, we find a NIC patient as a control. We match the age and sex of the subjects in the IC and NIC groups. Then we take blood samples to evaluate the immune response according to the aim of the study.

Sampling Criteria

Sampling for this study was performed by choosing the study subjects from IC patients that come for medical assistance at the out-patient unit of the Functional Unit of Internal Medicine of Dr. Moewardi Public Local Hospital. When we encounter an IC patient, we immediately take blood samples without consideration of the time, the time span, or the degree of illness. We then find an NIC match that has the same sex and age. Blood samples were taken by the author himself, or other trained professionals.

Study Variables

Establishment of IC condition in this study uses the clinical criteria in patients easily susceptible to disease, including diabetes mellitus, liver cirrhosis, and chronic liver failure. The immunological variables used are IL–10, IFN-γ, TNF-α, IL-Iβ, IgG, C3, and C4.

Variable Evaluation Method

We evaluated the study variables with the following methods: C3 and IgG with the nephelometric method; C4 with the immunoturbidimetric method; IL-10 and IL-1β with the imunochemiluninesence method; TNF-α and IFN-γ with the elisa sandwich method.

STUDY RESULTS

The results of the analytic observational study on the 14 IC and 14 NIC patients in this cross-sectional study were as follows:

1. Basic Data

To prove that the sample group was homogenous, we performed a homogenicity test on the characteristics of the sample groups, and a normality test on the variables to be analyzed.

In the IC group, the 14 samples had an average age of 50.3 ± 8.6 years, while in the NIC group, the 14 samples had an average age of 47.9 ± 11.8 years.

The samples for each group consisted of 10 men and 4 women. The data was analyzed using a homogenicity test of the sample groups, which demonstrated that the two groups were homogenous. Seven variables (IL–10, IFN-γ, TNF-α, IL-Iβ, IgG, C3 and C4) were evaluated to illustrate the patient's immune response, with a variable normality test demonstrating a normal distribution (with the IIDN test).

2. Group Variability Test of Immune Response Data

A multivariate analysis was performed to distinguish the immune response of the IC group and the NIC group (14 samples respectively) based on 7 immune response variables (IL–10, IFN-γ, TNF-α, IL-Iβ, IgG, C3 and C4).

In order to determine the difference in the immune response of IC and NIC countries, 2 types of samples from the IC and NIC groups were compared. Multivariate analysis demonstrated a significant difference ($p<0.05$), where the IL–10, TNF-α, and IgG levels of IC patients were higher than in NIC patients, while C3 levels of IC patients were lower than that of NIC patients.

Table 2. The Sex and The Average Age of The Study Subjects

No.	Group	Total	Male	Female	Age
1.	IC	14	10	4	50.3 ± 8.6
2.	NIC	14	10	4	47.9 ± 11.8

DISCUSSION

Based on this study, the TNF-α level is higher in IC patients than in NIC patients ($p<0.05$), which means that there is an increase in plasma TNF-α levels. TNF-α is a cytokine expressed in minute (virtually nothing) amounts by macrophages under normal conditions, and is a protective cellular immune response. Increased TNF-α causes depression of bone marrow activity, lymphopenia, increased coagulation system, and influences the procoagulant balance and the anti-coagulant balance, as well as causes muscle proteolysis, causing cachexia that results in immunodeficiency.[6,7,8] Increased TNF-α levels in IC patients demonstrate that their immune response was no longer physiological.

The IL-10 levels of IC patients were increased than that of NIC patients ($p<0.05$), which demonstrates disrupted Th2 lymhocyte function, demonstrating that the immune response was no longer physiological. IL-10 is an anti-inflammatory cytokine produced by lymphocyte Th2 after stimulation from Antigen Presenting Cells (APC). It is a humoral immune response. During inflammation, its concentration increases rapidly and remains high in the blood, and then gradually falls in line with the inflammation stimuli, making it very possible to find IL-10 in the blood of IC patients. Such condition can demonstrate a disorder of the adaptive immune system of the IC patients.[3,9,10,11]

Table 3. Multivariate Analysis of The IC and NIC Subjects

	IC	NIC	
Variable	**Mean ± Sd**	**Mean ± Sd**	**p value**
IL – 10	10.515 ± 3.438	7.321 ± 1.754	0.005
INF - γ	12.944 ± 16. 940	5.225 ± 1.433	Ns
TNF - α	24.179 ± 8.378	16.771 ± 6.148	0.013
IL - Iβ	2.014 ± 0.370	2.371 ± 0.671	Ns
IgG	16.186 ± 2.817	13.876 ± 2.775	0.038
C3	1.050 ± 0.351	1.449 ± 0.462	0.016
C4	24.286 ± 9.738	27.929 ± 8.235	Ns

(p < 0,05);
Ns: Not Significant
n = 28

Increased IgG indicates a disruption in the system stimulation (humoral immune response). In IC patients, increased IgG levels may demonstrate that endothelial cell damage more easily occurs in IC patients. IgG is the main component of serum immunoglobuline. IgG is a humoral immune response with an effective opsonin characteristics, since phagocytes, monocytes, macrophages, and killer cells (K cells) have Fc IgG receptor. However, if IgG is greatly or excessively increased, a reverse effect occurs, where target cells (endothelial cells) are destroyed.[5,12,13]

In IC patients, the plasma C3 concentration is reduced. C3 is a molecule from the non-specific immune system that dissolves in the plasma when inactive, but can be activated any time by substances such as antigens, toxins, and immune complex. Activated complements rapidly increase in levels. The activation results in a biologically active mediator.[5,14]

C3 is a component needed for opsonization, chemotaxis, and elimination of antigen-antibody complex, causing lysis of bacterial cell walls. Reduced plasma C3 levels in IC patient causes a reduced defense mechanism towards bacteria, making the body more susceptible to infection.[2,5]

Based on the discussion above, we could find increased IL-10 cytokine, TNF-α, and IgG levels in IC patients compared to NIC patients, while C3 levels were lower in IC patients. This demonstrates that the cellular and humoral immune response of IC patients were no longer physiological, and the adaptive immune system has been disturbed, or is no longer normal. The results of the discussion above was in line with the definition of IC by Sneller, that states that in IC, there is a defect/abnormality in the adaptive and natural immune system function, allowing infection to be fatal.

CONCLUSION

Based on the analysis of this study, we could conclude that in IC patients, there is a defect in the body's immune system, or an absence of homeostasis. There is an increase in cellular immune response, in the form of TNF-α, increased IGG and IL-10 humoral immune response, and reduced natural immune system (C3). C3 is the first immune system component to react to foreign immunogens (microorganisms). Thus, reduced C3 levels increase susceptibility to infection.

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