

# Elderly Immunity Improvement after Getting Synbiotic and Zinc Combinations

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## ABSTRACT

Elderly is one group of people who have a risk of changing immune function. Changes in immune function in the elderly, especially in the immune system mediated by cells. In accordance with the increase in age, the elderly immune system decreases the immune response against infectious and non-infectious diseases. Based on this, it is easy for the elderly to develop diseases such as infectious diseases, hypertension, coronary heart disease, cancer, autoimmune diseases, and other chronic diseases. The increasing number of elderly people is one indicator of the success of development as well as a challenge in development. The purpose of this study was to analyze the improvement of elderly immunity after getting synbiotics and zinc. The type of this research was an experimental study in which volunteers were given zinc + synbiotic combination supplements. Further measurements of IL-2, IFN- $\gamma$  and IL-10 were carried out. Furthermore, the measurement results were compared to find out the differences in elderly immune expression. Analysis of normality and homogeneity to determine parametric or non-parametric statistical tests with the Shapiro-Wilk test if it meets parametric requirements then the analysis used in this study was t-test to evaluate the effect of supplementation (pre-post test). The results showed that synbiotic + zinc combination supplementation could potentially increase IL-2 profile ( $p = 0.000$ ), IFN- $\gamma$  ( $p = 0.019$ ), and IL-10 ( $p = 0.010$ ) significantly in the elderly. Based on the results, it could be concluded that synbiotic + zinc combination supplementation has the potential to increase IL-2, IFN- $\gamma$ , and IL-10 profiles in the elderly.

**Keywords:** Zinc and synbiotic combination, Immune, IL-2, IFN- $\gamma$ , IL-10

## INTRODUCTION

There has been a major population explosion at this time, according to the statistics center, namely in 2004 of 16,522,311 and while in 2020 it was predicted that the number of elderly would increase by 28 million. This is a very large amount so that if no efforts are made to increase elderly welfare since now it will cause problems and could be a big problem in the future. The tendency of this problem to occur is also marked by the figure of elderly dependence according to the 2008 BPS Susenas

of 13.72%. The population dependency rate will be high and felt by the population of productive age if it is coupled with the dependency of the population aged less than 15 years, where currently the population is less than 15 years of 29.13% <sup>(1)</sup>

According to the results of the Basic Health Research in 2007 showed that urban elderly showed morbidity rates of 27.42, rural elderly at 33.35 and urban and rural morbidity rates of 31.11. These data shows the tendency of morbidity in the elderly has increased from year to year. The most common elderly sufferers are joint disorders followed by hypertension, cataracts, stroke, mental emotional disorders, heart disease and diabetes mellitus. Besides that, the cause of death at the age of 65 years and over in men is stroke (20.6%), chronic lower respiratory tract disease (10.5%), pulmonary

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tuberculosis (TB) (8.9%), hypertension (7.7%), NEC (7.0%), ischemic heart disease (6.9%), other heart disease (5.9%), diabetes mellitus (4.9%), liver disease (4.4%) and pneumonia (3.8%). While for women the most cause of death was stroke (24.4%), hypertension (11.2%), NEC (9.6%), chronic lower respiratory tract disease (6.6%), diabetes mellitus (6.0%), ischemic heart disease (6.0%), other heart diseases (5.9%), TB (5.6%), pneumonia (3.0%) and liver disease (2.2%)<sup>(2)</sup>. This condition certainly must get the attention of various parties. Aging people who are sick will become a burden for families, communities and even the government, so that it will become a burden in development<sup>(3)</sup>.

A number of studies have shown that the prevalence of malnutrition in the elderly is very high and is often only realized when the elderly must be hospitalized<sup>(4)</sup>. A study in Jakarta showed that about two-thirds of elderly people suffer from thiamine deficiency<sup>(5)</sup>. Immune function also decreases with age, resulting in increased incidence of infectious and malignant (cancer) diseases. Research on immune function in the elderly introduces a thought that the immune system in the elderly has specific characteristics, the immune system will not only decrease with increasing age, but immune system regulation disorders will be more progressive throughout its life<sup>(6)</sup>. Initial changes occur in the cellular immune system compared to humoral, immune system evolution associated with decreased thymus function. Nutritional factors play an important role in the immune response in a healthy elderly, one of which is zinc.

Food substrates reach the large intestine can affect the composition and activity of bacteria present through fermentation of capacity in the elderly. Metabolic products from intestinal bacteria can affect the immune system. Modulation of intestinal microflora by diet is the basis for the concept of probiotics<sup>(8)</sup> and prebiotics<sup>(7)</sup>.

This study analyzed the effect of synbiotic supplementation, zinc and synbiotic and zinc combinations on immune responses with IL-2, IFN- $\gamma$  and IL-10 markers in the elderly<sup>(9)</sup>. The role of the

immune system in the elderly is the importance of increasing IL-2 levels as cytokines for T lymphocyte proliferation, IFN- $\gamma$  is a proinflammatory cytokine and IL-10 as an antiinflammatory cytokine against immune response, then this study will focus on "Enhancing Elderly Immunity After Getting Synbiotic and Zinc combination".

## MATERIALS AND METHOD

This study aimed to find facts about the function of synbiotic supplementation and zinc on the immune response at the same time can be implemented in a national program for enhancing immunity for guests. This research was conducted in 2016 in the Mangasa Health Center working area of Health Office of Makassar City, South Sulawesi Province, Indonesia. The main sources needed in this study were: 1) serum, obtained from blood, 2) ELISA<sup>(10)</sup> to measure levels of IL-2, IFN- $\gamma$  and IL-10 which was carried out in the Laboratory of the Hasanuddin University Hospital of Education, Makassar, Indonesia, 3) research subjects were > 60 years old, Makassar tribe, having no history of infectious and degenerative diseases based on doctor's recommendations, so the sample size of 36 people was divided into 3 groups.

This effective method was proven by implementing several steps: 1) measuring instrument validation (ELISA test) by comparing the results of laboratory tests to measure and the accuracy of the measuring instrument to be used, 2) measuring blood serum using the ELISA test before and after getting synbiotics and zinc for 3 months, 3) measured levels of IL-2, IFN- $\gamma$  and IL-10 by taking  $\pm 5$  cc of blood, 4) comparing measurement results before and after synbiotic supplements and zinc to determine elevated levels of IL-2, IFN- $\gamma$  and IL-10.

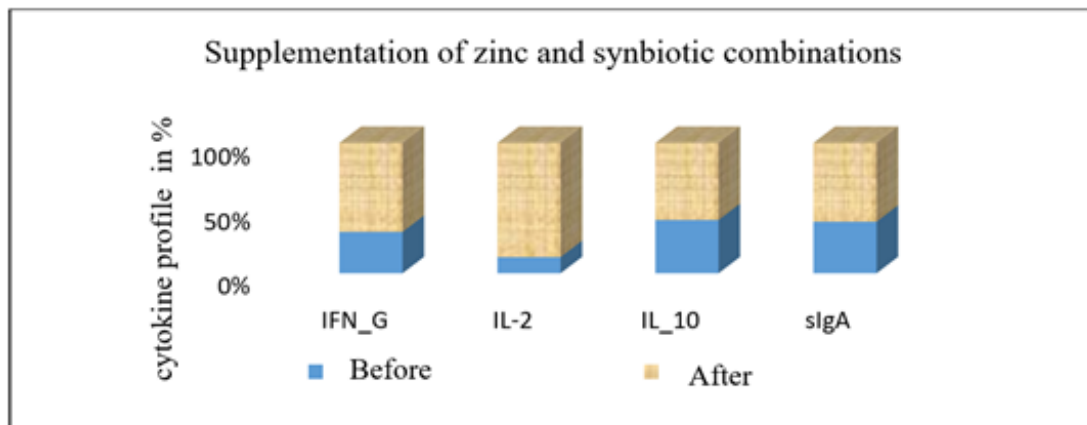
## FINDINGS

Effect of Zinc - Synbiotic combination supplementation on the variables of IFN- $\gamma$ , IL-2, and IL-10 in the elderly

**Table 1. Different Test Results between Variable Zinc + Sinbiotic Supplementation Groups IFN- $\gamma$ , IL-2, and IL-10**

Variable	Zinc-Sinbiotic Combination Supplementation					P-value of T-Test
	Min	Max	Mean	Standard Deviation	Median	
IFN- $\gamma$	50.11	519.85	179.05	116.23	154.65	0.019
IL-2	412.63	1036.35	734.64	205.21	708.98	0.000
IL-10	72.95	232.12	146.29	50.76	133.63	0.010

Table 1 shows that there was a significant effect of zinc-synbiotic combination supplementation on all four cytokine profiles ( $p < 0.05$ ).



**Figure 1. Average of Cytokine Profile in Supplementation of Zinc + Sinbiotic Group**

Figure 1 shows that in the zinc + sinbiotic supplementation group the highest increase in IL-2 profile before and after zinc + synbiotic supplementation was given. Non-varying increases in IL-10 profiles.

The effects of synbiotic and zinc combination supplementation found scientific evidence that the immune response in the elderly for all variables had been increased previously and after the provision of synbiotic and zinc supplements. This synbiotic and zinc supplementation can be implemented and useful in a national program for enhancing immunity for the elderly

## DISCUSSION

The results of the study on elderly after zinc + sinbiotic treatment showed that there was a significant increase in IFN- $\gamma$ , IL-2, IL-10 and sIgA, this meant that there was a balance / homeostasis between Th1 and Th2. This is because zinc has one function for IFN- $\gamma$  expression in T cells<sup>(11)</sup>. Therefore the mechanism of action of the synbiotic will be corrected by the presence of zinc in the IFN- $\gamma$  expression in T cells.

The synbiotic role in modulating the immune response of the elderly by influencing the maturation of dendritic cells. APC in this case is a dendritic

cell which is a determinant of Th1 / Th2 balance and development of tolerance. Several types of dendritic cells that can direct the immune response according to the activation environment or kinetic activation<sup>(12)</sup>. Inhibition of maturation of dendritic cells in turn leads to a reduction in pro-inflammatory cytokines of interferon gamma (IFN $\gamma$ ), IL-4 and IL-5 from T cells. IL-10 also inhibits the production of other inflammatory mediators such as IL-1 and tumor necrosis alpha factor (TNF) by macrophages. In naive CD4 + T cells, IL-10 inhibits CD28 signaling rendering these cells can properly activate. IL-10 is not always inhibitory, it can also promote B cell activation and stimulate NK cell proliferation. When IL-10 is produced and secreted, acts specifically on IL-10 receptors, a structure consisting of two subunits; IL-10 receptor 1 and IL-10 receptor 2. After binding to cytokines, the receptor subunit is associated with signal transduction molecules in the cytoplasm of cells expressing receptors, encouraging signals that primarily inhibit the activity of some of the

genes needed to produce an immune response, but can also promote activation of some specific target cells as mentioned above.

### CONCLUSION

Based on the results of the study it can be concluded that both synbiotic and zinc supplementation are even symbiotic and zinc combinations to increase the profile of IL-2, IL-10 IFN-  $\gamma$ . Therefore it is recommended to use zinc supplements as immunomodulators on things that cause Th1 and Th2 immunity in the elderly to stay healthy and do the same research but check serum zinc levels in the elderly (sample).

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**Ethical Clearance :** Research ethics was obtained after the researcher made a presentation in front of the Ethics Committee of Faculty of Public Health, Airlangga University and had received a certificate with the number 525-KEPK.

### REFERENCES

1. Martono H. Elderly and Systemic Impacts in the Life Cycle (Lanjut Usia dan Dampak Sistemik dalam Siklus Kehidupan) [Internet]. Komnas Lansia. 2010 [cited 2013 Nov 19]. Available from: <http://www.komnaslansia.go.id>
2. Kemenkes RI. Basic Health Research 2007 (Riset Kesehatan Dasar 2007). Jakarta: Badan Penelitian dan Pengembangan Kesehatan Kementerian Kesehatan Republik Indonesia; 2007.
3. BKKBN. The State Comes to Realize Elderly Welfare (Negara Hadir Wujudkan Kesejahteraan Lansia) [Internet]. Badan Koordinasi Keluarga Berencana Nasional. 2015 [cited 2015 Nov 12]. Available from: <http://www.bkkbn.go.id>
4. Maryam RS, Ekasari MF. Get to Know the Elderly and Care (Mengenal Usia Lanjut dan Perawatannya). Jakarta: Salemba Medika; 2008.
5. Gross, Schultink. Micronutrient Deficiency in Urban Indonesia [Internet]. Research Gate. 1997 [cited 2015 Nov 12]. [https://www.researchgate.net/publication/13626277\\_Micronutrient\\_deficiency\\_in\\_urban\\_Indonesia](https://www.researchgate.net/publication/13626277_Micronutrient_deficiency_in_urban_Indonesia).
6. Lesourd B, Mazari L. Nutrition and Immunity in The Elderly. Pubmed. Gov. NCBI. 1999.
7. Gibson GR, Probert HM, Loo JV, Rastall RA, Roberfroid MB, 2004. Dietary Modulation of the Human Colonic Microbiota: Updating the Concept of Prebiotics. Pubmed. Gov. NCBI. 1999.
8. Fuller R. Probiotics in Man and Animals. J Appl Bacteriol. Pubmed.Gov. NCBI. 1989.
9. Hartono R, Wirjatmadi B, Dachlan YP. Effect of Zinc and Sinbiotic Supplement on Cytokine Profiles in the Elderly (Pengaruh Suplementasi Seng dan Sinbiotik terhadap Profil Sitokin Lanjut Usia). Dissertation. Surabaya: Universitas Airlangga, Surabaya Indonesia; 2017.
10. Lequin RM. Enzyme Immunoassay (EIA)/Enzyme-Linked Immunosorbent Assay (ELISA)". Clinical Chemistry. 2005;51(12):2415–8. doi:10.1373/clinchem.2005.051532. PMID 16179424.
11. Haase H, Lothar R. The Immune System and the Impact of Zinc during Aging. Immun Ageing. 2009;6:9. Biomed Central
12. Moser M, Murphy KM. Dendritic Cell Regulation of TH1-TH2 Development 2000. Nat Immunol. 1(3):199-205 Pubmed.gov