The Effect of 99 Percent Edible Bird's Nest (EBN) Extract Supplementation on Serum Interleukin-1 Beta (IL-1β) Levels in Health Workers Treating Covid-19 Cases in Dr. Soetomo General Hospital

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Abstract

EBN effectively inhibits the increase of proinflammatory cytokines (TNFα, IL-1β, and IL-6) due to lipopolysaccharide (LPS) administration in mice. Several reviews describe the positive immunomodulating effect of EBN on the respiratory tract and lungs against viral infections. There have been no in vivo studies in humans regarding the effects of EBN supplementation with 99% levels. This study was conducted to determine the effect of EBN supplementation on serum IL-1β levels of health workers at Dr Soetomo Hospital who handle COVID-19 cases. This can be preliminary research in efforts to prevent COVID-19 infection in medical personnel. The research was conducted pre-experimentally to health workers. All subjects were checked for initial serum IL-1β levels and were given 99% EBN supplementation for 14 days. All subjects were observed and checked for serum IL-1β levels after 14 days of EBN supplementation. Of the 50 research subjects, 58% were female, with a mean age of 37 years. The frequency of study subjects who experienced an increase, decrease, and no change in serum IL-1β levels after 14 days of 99% EBN supplementation were 22%, 72%, and 6%, respectively. The median serum IL-1β level of research subjects before 14 days of 99% EBN supplementation was 0.197 pg/ml (min – max: 0.097–1.107). The median after 14 days of EBN supplementation was 0.178 (min–max: 0.091–0.446) pg/ml. The results of the Wilcoxon difference test showed that there was a significant difference in IL-1β before and after 99% EBN supplementation with $p = 0.001$ ($p < 0.05$ was considered significant). In summary, there was a significant difference between serum IL-1β levels of research subjects before and after 14 days of 99% EBN supplementation ($p = 0.001$). EBN 99% has the effect of reducing serum IL-1β levels in healthcare workers who handle Covid-19 cases at RSUD Dr. Soetomo Surabaya.
Keywords: Healthcare workers, EBN, Interleukin-1β, COVID-19

1. Introduction

Corona virus Disease 2019 (COVID-19) is a disease caused by SARS-CoV-2 or Severe Acute Respiratory Syndrome Corona virus 2 (WHO, 2020). Health workers are a group that is very susceptible to infection because they are at the forefront of treatment (Mhango et al., 2020) and are increasingly under pressure due to increased workloads, health concerns for themselves and their families (Chen et al., 2020). In addition to wearing personal protective equipment (PPE) as part of an infection prevention and control strategy (Ministry of Health of the Republic of Indonesia, 2020), health workers need to maintain immune system homeostasis with adequate intake of macro and micro nutrients (Gombart et al., 2020; Jayawardena et al., 2020; Sumarmi, 2020). People with a good immune system are able to fight infection better so they avoid the transmission of infection (Ansori et al., 2020).

Swallow's nest or edible bird's nest (EBN) has traditionally been known as a food that can increase immunity (Norhayati et al., 2010). Sialic acid is the main bioactive component in EBN with a composition of about 10% and is dubbed "EBN acid" because it contains the highest EBN compared to other natural products (Dai et al., 2020). EBN can be able to inhibit influenza virus infection in human, avian and swine strains (Guo et al., 2006) as efficiently as commercial antivirals such as amantadine and oseltamivir (Haghani et al., 2017). EBN has been shown to reduce levels of IL-1, IL-6 and IL-8, where a significant decrease was found in IL-1 levels (Chua et al., 2013).

Interleukin-1 beta (IL-1β) is a key mediator of the inflammatory response. IL-1β is a proinflammatory cytokine produced by the innate immune system and is important for the body's defense response to infection and injury (Lopez-Castejon & Brough, 2011). Increased IL-1β has been shown to be associated with symptom severity in COVID-19 sufferers, so several therapeutic strategies have used IL-1 inhibition to avoid cytokine storms (Costela-ruiz et al., 2020; Ye et al., 2020). This research aims to determine the effect of EBN supplementation on serum IL-1β levels of health workers at Dr Soetomo Hospital as an effort to prevent COVID-19 infection and other infections.

2. Materials and Methods

2.1 Selection Criteria

The inclusion criteria for the research subjects were medical personnel in charge of handling COVID-19 at RSUD Dr. Soetomo Surabaya, over 18 years old, willing to participate in the study and sign the informed consent form, and willing to have blood drawn as evidenced by signing the consent form for medical treatment. Exclusion criteria for research subjects were having a history of allergy to EBN, having a history of allergy to high protein supplements, taking additional supplements other than EBN while being a research subject, being pregnant or breastfeeding, in a fever condition, and consuming or currently on steroid therapy.

2.2 Measurement of IL-1B Levels

Sampling in this study was done by consecutive sampling. Blood samples were taken twice, namely before and after consuming EBN with 99% levels for a period of 14 days. Five milliliters of blood from the vein was taken from the study sample and collected in a serum separator tube. Blood samples were processed for measurement of IL-1β levels in the laboratory. Serum IL-1β levels were measured from blood samples of research subjects using the Enzyme-linked Immunosorbent Assay (ELISA) method using the "BioRad 680 Micro plate Reader". Results are in pg/mL with a detection limit/standard range of 0.48-100 pg/mL. The value of changes in IL-1β levels was obtained based on the calculation of the average levels of IL-1β after supplementation (post test) compared to before supplementation (pre test).

2.3 Statistical Analysis

Data on the basic and clinical characteristics of the research subjects will be presented descriptively in the form of frequency and percentage for categorical data types, while for numerical data in the form of average and standard deviation. The data will be displayed in the form of tables or graphs. Statistical analysis used comparative numerical statistical test with two repeated measurements. The data used were IL-1β levels on the day before EBN 99% administration (day 0/ pre-test) and on day 15 after administration of 99% EBN (post-test). If a normal data distribution is obtained, a paired-t test will be used, whereas if the data is not normally distributed, a non-parametric Wilcoxon test (Wilcoxon Sign Rank Test) will be used. Data analysis will use SPSS for Windows version 23.0 for the process of collecting, recording, and calculating data.

3. Results

The total sample obtained was 50 subjects who were willing to participate in the study, and met the inclusion and exclusion criteria. Characteristics of research subjects are presented descriptively. General characteristics of research subjects including age, sex, height, weight, body mass index (BMI), race, history of allergies, and use of supplements can be seen in Table 1. The comorbid data can be seen in Table 2.

Table 1. General characteristics of research subjects

Characteristics	Results (n=50)
Sex	
Males	21 (42%)
Females	29 (58%)
Age (years)	
Mean ± standard deviation	37,34 ± 10,520
Median (range)	33,0 (26 – 73)
< 31	15 (30%)
31 – 40	22 (44%)
41 – 50	5 (10%)
> 50	8 (16%)
Height (cm)	
Mean ± standard deviation	161,20 ± 8,109
Median (range)	159,50 (147 – 178)
Weight (kg)	
Mean ± standard deviation	63,96 ± 13,910
Median (range)	62,40 (40 – 111)
Body Mass Index (kg/m^2)	
Mean ± standard deviation	24,52 ± 4,559
Median (range)	23,53 (17,09 – 36,24)
< 18,5	5 (10%)
18,5 – 24,9	24 (48%)
25 – 29,9	14 (28%)
≥ 30	7 (14%)
Ethnic Groups	

Javanese	45 (90%)
Other ethnics	5 (10%)
History of Allergy	
Yes	21 (42%)
No	29 (58%)
Dietary Supplement	
Yes	22 (44%)
No	28 (56%)

Tabel 2. Research Subject Comorbids

Comorbid	n (%)
Yes	15 (30%)
No	35 (70%)
Research Subject Comorbid	
Bronchial asthma	5 (33,3%)
Hypertension	3 (20,0%)
Anemia	2 (13,3%)
Chronic obstructive pulmonary disease	1 (6,7%)
Rhinitis allergy	1 (6,7%)
Hypertension and Diabetes Mellitus	2 (13,3%)
Hypertension, Diabetes Mellitus, and Bronchial asthma	1 (6,7%)

Before receiving 99% EBN supplementation for 14 days, the study subjects underwent initial examination. The results of the initial serum IL-1β levels can be seen in Table 3. Initial serum IL-1β levels in the subjects of this study had a mean standard deviation of 0.024 0.178 pg/ml and a median of 0.197 pg/ml with a range of 0.097 pg/ml to 1.107 pg/ml. Data distribution test of initial serum IL-1β levels based on the characteristics of research subjects can be seen in Table 4.

Table 3. Initial Serum IL-1β Levels of Research Subjects

Variable	n	Mean ± standard deviation	Median (min – max)
Initial Serum IL-1β Level	50	0,024 ± 0,178	0,197 (0,097 – 1,107)

Table 4. Data Distribution of Initial Serum IL-1β Levels Based on the Characteristics of Research Subjects

Characteristics	n	p value
Sex		
Males	21	< 0,001
Females	29	0,417
Age (years)		
< 31	15	< 0,001
31 – 40	22	< 0,001
41 – 50	5	0,422
> 50	8	0,499
Body Mass Index		
< 18,5	5	0,429
18,5 – 24,9	24	< 0,001
25 – 29,9	14	0,151
≥ 30	7	< 0,001
Comorbid		
Yes	15	<0,001
No	35	< 0,001
Ethnic Groups		
Javanese	45	< 0,001
Other ethnics	5	< 0,001
History of Allergy		

Yes	21	< 0,001
No	29	< 0,001
Dietary Supplement		
Yes	22	0,239
No	28	< 0,001

*) p <0,05 = significant

The results of the Shapiro-Wilk normality test showed that the initial serum IL-1β data was not normally distributed. Differences in initial serum IL-1β based on the characteristics of research subjects were then analyzed further using the Mann-Whitney test (for 2 sample groups) and Kruskal-Wallis (for 3 sample groups) with the results shown in Table 5. Further test results with Mann-Whitney for each BMI group can be seen in Table 6.

Table 5. Differences in Initial Serum IL-1β Levels Based on Characteristics of Research Subjects

Characteristics	n	Median (min – max)	p value
Initial IL-1β	50	0,197 (0,097 – 1,107)	
Sex			
Males	21	0,197 (0,128 – 1,107)	0,172*
Females	29	0,197 (0,097 – 0,299)	
Age (years)			
< 31 th	15	0,185 (0,111 – 0,950)	
31 – 40 th	22	0,195 (0,097 – 1,107)	0,837**
41 – 50 th	5	0,192 (0,151 – 0,275)	
> 50 th	8	0,230 (0,155 – 0,295)	
Body Mass Index			
< 18,5	5	0,146 (0,116 – 0,243)	
18,5 – 24,9	24	0,214 (0,111 – 0,950)	0,024**
25 – 29,9	14	0,180 (0,097 – 0,351)	
≥ 30	7	0,252 (0,199 – 1,107)	
Comorbid			
Yes	15	0,230 (0,125 – 1,107)	0,079*
No	35	0,179 (0,097 – 0,950)	
Ethnic Groups			
Javanese	45	0,199 (0,097 – 0,950)	0,201*
Other ethnics	5	0,150 (0,128 – 1,107)	
History of Allergy			
Yes	21	0,209 (0,097 – 1,107)	0,549*
No	29	0,185 (0,111 – 0,950)	
Dietary Supplement			
Yes	22	0,186 (0,097 – 0,351)	0,241*
No	28	0,205 (0,125 – 1,107)	

*) p <0,05 = significant

Table 6. Differences in Initial Serum IL-1β Levels Based on BMI Group

Body Mass Index	n	Median (min – max)	p value*
< 18,5	5	0,146 (0,116 – 0,243)	0,094
18,5 – 24,9	24	0,214 (0,111 – 0,950)	
< 18,5	5	0,146 (0,116 – 0,243)	0,266
25 – 29,9	14	0,180 (0,097 – 0,351)	
< 18,5	5	0,146 (0,116 – 0,243)	0,019
≥ 30	7	0,252 (0,199 – 1,107)	
18,5 – 24,9	24	0,214 (0,111 – 0,950)	0,188
25 – 29,9	14	0,180 (0,097 – 0,351)	
18,5 – 24,9	24	0,214 (0,111 – 0,950)	0,137
≥ 30	7	0,252 (0,199 – 1,107)	

25 – 29,9	14	0,180 (0,097 – 0,351)	0,006
≥ 30	7	0,252 (0,199 – 1,107)	

*) p <0,05 = significant

Changes in IL-1β levels were obtained based on the calculation of the average levels of IL-1β after supplementation (posttest) compared to before supplementation (pretest). The results of the Shapiro-Wilk normality test on data on changes in serum IL-1β levels can be seen in Table 7. Differences in serum IL-1β levels between observations were then analyzed using the Wilcoxon signed rank test with the results shown in Table 8. The median serum IL-1β level of study subjects before 14 days of EBN supplementation was 0.197 pg/ml and the median after 14 days of EBN supplementation was 0.178 pg/ml. The lowest serum IL-1β level at baseline was 0.097 pg/ml and the highest was 1.107 pg/ml. Meanwhile, after 14 days of EBN supplementation, the lowest serum IL-1β level was 0.091 pg/ml and the highest was 0.446 pg/ml. The results of the Wilcoxon difference test showed that there was a significant difference ($p < 0.05$) in IL-1β before and after EBN supplementation ($p = 0.001$).

Table 7. Data Distribution of Changes in Serum IL-1β Levels

IL-1β Serum	Median (min – max)	n	p value*
Posttest - Pretest	-0,024 (-0,89 – 0,19)	50	< 0,001

*) p <0,05 = significant

Table 8. Differences in Serum IL-1β Levels Before and After EBN Supplementation

IL-1β	n	Median (min – max)	Difference Median (min – maks)	p value*
Before	50	0,197 (0,097 – 1,107)	-0,024 (-0,89 – 0,19)	0,001
After	50	0,178 (0,091 – 0,446)		

*) p <0,05 = significant

After 14 days of EBN supplementation, there were differences in serum IL-1β levels which can be seen in Figure 1. Median serum IL-1β levels before EBN supplementation were higher (0.197 pg/ml) than after (0.178 pg/ml). The median difference in IL-1β was -0.024 pg/ml. Differences in changes in serum IL-1β levels based on the characteristics of the research subjects were then sub-analyzed using the Mann-Whitney and Kruskal-Wallis test which can be seen in Table 9. Differences in initial serum IL-1β levels based on the category of change (decreasing, constant or increasing) were then tested for the Shapiro-Wilk distribution which can be seen in Table 10. Differences in initial IL-1β levels based on the change category were then analyzed using the Kruskal-Wallis test and the results can be seen in Table 11.

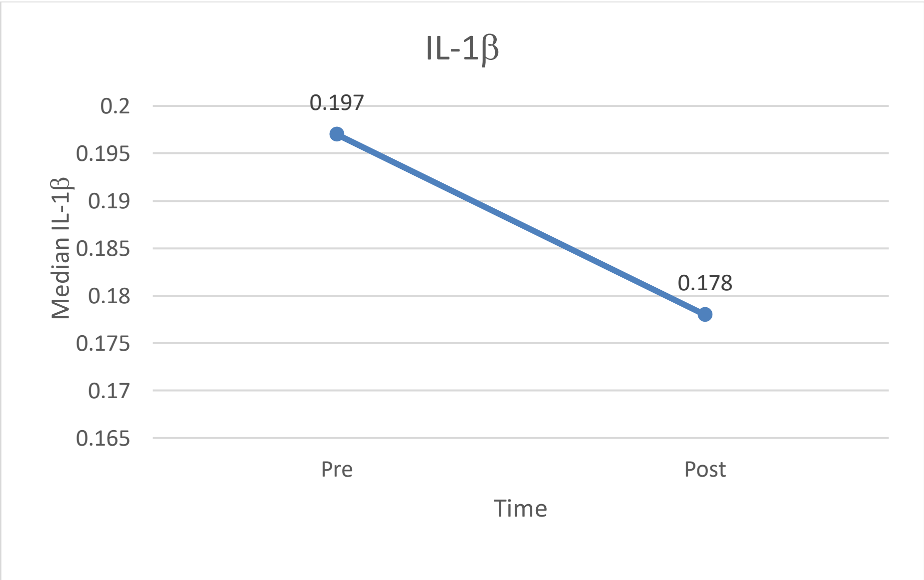

Figure 1. Median Differences in Serum IL-1β Levels Based on Observation Time

Table 9. Differences in Changes in Serum IL-1β Levels Based on the Characteristics of Research Subjects

Characteristics	n	Decrease	Constant	Increase	p value
IL-1β Post - Pre	50	36 (72%)	3 (6%)	11 (22%)	-

Sex					
Males	21	15 (71,4%)	2 (9,5%)	4 (19%)	0,960*
Females	29	21 (72,4%)	1 (3,4%)	7 (24,1%)	
Age (years)					
< 31 th	15	11 (73,3%)	0 (0%)	4 (26,7%)	0,309**
31 – 40 th	22	18 (81,8%)	2 (9,1%)	2 (9,1%)	
41 – 50 th	5	3 (60%)	0 (0%)	2 (40%)	
> 50 th	8	4 (50%)	1 (12,5%)	3 (37,5%)	
Body Mass Index					
< 18,5	5	4 (80%)	0 (0%)	1 (20%)	0,490**
18,5 – 24,9	24	18 (75%)	2 (8,3%)	4 (16,7%)	
25 – 29,9	14	8 (57,1%)	1 (7,1%)	5 (35,7%)	
≥ 30	7	6 (85,7%)	0 (0%)	1 (14,3%)	
Comorbid					
Yes	15	12 (80%)	1 (6,7%)	2 (13,3%)	0,381*
No	35	24 (68,6%)	2 (5,7%)	9 (25,7%)	
Ethnic Groups					
Javanese	45	34 (75,6%)	2 (4,4%)	9 (20%)	0,122*
Other ethnic	5	2 (40%)	1 (20%)	2 (40%)	
History of Allergy					
Yes	21	17 (81%)	0 (0%)	4 (19%)	0,305*
No	29	19 (65,5%)	3 (10,3%)	7 (24,1%)	
Dietary Supplement					
Yes	22	16 (72,7%)	0 (0%)	6 (27,3%)	0,901*
No	28	20 (71,4%)	3 (10,7%)	5 (17,9%)	

*) p <0,05 = significant

Table 10. Test for Normal Distribution of Initial IL-1β Level Data Based on Change Category

Serum IL-1β	n	p value*
Decrease	36	< 0,001
Constant	3	0,788
Increase	11	0,162

*) p <0,05 = significant

Tabel 11. Differences in Initial IL-1β Levels Based on Change Category

Serum IL-1β	n	Median (min – max)	p value*
Decrease	36	0,224 (0,097 – 1,107)	0,006
Constant	3	0,179 (0,131 – 0,250)	
Increase	11	0,155 (0,111 – 0,261)	

*) p <0,05 = significant

The results of the Kruskal-Wallis test showed that there was a significant difference in the initial IL-1β levels between the groups of IL-1β changes ($p < 0.05$). Then, a further sub-analysis was carried out for the differences in initial IL-1β levels between groups of changes using the Mann-Whitney test which can be seen in Table 12. The results of the follow-up test using the Mann-Whitney difference test showed a significant difference ($p < 0.05$) between the groups that experienced a decrease and an increase in serum IL-1β levels ($p = 0.002$).

Tabel 12. Differences in Initial IL-1β Levels by Change Group

Serum IL-1β	n	Median (min – max)	p value *
Decrease	36	0,224 (0,097 – 1,107)	0,268
Constant	3	0,179 (0,131 – 0,250)	
Decrease	36	0,224 (0,097 – 1,107)	0,002
Increase	11	0,155 (0,111 – 0,261)	

Constant	3	0,179 (0,131 – 0,250)	0,350
Increase	11	0,155 (0,111 – 0,261)	

*) p <0,05 = significant

4. Discussion

Initial serum IL-1β levels in the subjects of this study had a mean standard deviation of 0.024 0.178 pg/ml and a median of 0.197 pg/ml with a range of 0.097 pg/ml to 1.107 pg/ml. This result appears to be different from a study in the general population in Florence, Italy which reported a mean serum IL-1β level in healthy subjects of 0.31 0.05 pg/ml (Di Iorio et al., 2003). Research on laboratory staff as healthy subjects in Heidelberg, Germany also reported that the normal value of serum IL-1β levels in healthy men was 1.0 ± 2.8 pg/ml and healthy women was 0.5 ± 0.7 pg/ ml (Sadeghi et al., 2005). Research in Trieste, Italy reported that serum IL-1β levels in young adult research subjects were below the lower limit of levels that could still be detected by the equipment used, namely 3.2 pg/ml (Kleiner et al., 2013). The difference in the results in this study could be caused by differences in the characteristics of the subjects, the time of taking and various things that affect the levels of cytokines.

This study showed the median initial serum IL-1β level of research subjects was 0.197 pg/ml and the median after 14 days of EBN supplementation was 0.178 pg/ml. The lowest serum IL-1β level at baseline was 0.097 pg/ml and the highest was 1.107 pg/ml. Meanwhile, after 14 days of EBN supplementation, the lowest serum IL-1β level was 0.091 pg/ml and the highest was 0.446 pg/ml. The median difference in IL-1 β at baseline was -0.024 pg/ml with a range of -0.89 – 0.19 pg/ml and a statistically significant difference in serum IL-1β levels before and after EBN supplementation (p = 0.001). These results are consistent with in vitro studies on Madin-Darby canine kidney (MDCK) cells and in vivo in mice showing that administration of EBN extract increased IL-1β (and IL2, IL6 and TNFα) in the study subject group without infection and the group that had been treated with influenza virus infection on the first day (early phase). But on the third day (resolution phase), EBN decreased IL-1β which was accompanied by an increase in anti-inflammatory cytokine levels so as to prevent damage due to excessive cytokine production (Haghani et al., 2016). This is in accordance with the theory that sialic acid in EBN has an immunomodulating effect on IL-1β levels. Sialic acid can be bound to immune cells by interaction with siglec which is expressed by immune cells. In the initial phase of infection, sialic acid binding and activating siglec will activate signaling pathways for IL-1β production by monocytes or macrophages. Meanwhile, in conditions of excessive inflammation or resolution of infection, sialic acid will interact with inhibitory siglec which will inhibit the production of IL-1β and other pro-inflammatory cytokines, and activate signaling pathways for the production of anti-inflammatory cytokines. This mechanism is the mechanism of the human immune system to achieve a homeostasis (Lübbers, et al., 2018). Health workers have an increased risk of exposure to SARS-COV-2 because of the clinical procedures they perform on COVID-19 patients and the high rate of exposure to the COVID-19 virus among health workers in care centers (Ashinyo et al., 2020). Exposure to COVID-19 infection can lead to the release of pro-inflammatory cytokines, including interleukin IL-1β and IL-6 (Theobald et al., 2020).

This study showed that there was no significant difference in changes in IL-1β based on the characteristics of the research subjects (p > 0.05). Research subjects who experienced a decrease in serum IL-1β levels after EBN supplementation were almost the same in the male (71.4%) and female (72.4%). The decrease in IL-1β in this study after EBN supplementation by ethnicity was experienced by the Javanese (75.6%). The decrease in serum IL-1β levels based on age was mostly experienced by the group 31-40 years (81.8%) which is also the age range of the majority of the subjects of this study. The decrease in IL-1β after EBN supplementation based on BMI category was most experienced by the 30 group (85.7%). The decrease in IL-1β after EBN supplementation based on comorbidity was most experienced by the comorbid group (80%). The decrease in IL-1β in this study after EBN supplementation based on allergy history category was experienced by those with allergies (81%).

The decrease in IL-1β in this study after EBN supplementation based on supplement consumption was experienced by the group taking supplements (72.7%) almost as much as those not taking supplements (71.7%). The PLifeCOVID-19 study revealed that during the COVID-19 outbreak in March 2020 there was an increase in public interest and consumption of immune-related compounds and foods. Interest in immune-related nutrients, bioactive compounds, and foods such as vitamins C and D, zinc, selenium, garlic, ginger, turmeric, honey, echinacea, elderberry, Nigella sativa, Glycyrrhiza glabra reaches its peak during the first or second wave of COVID-19. Vitamin D, vitamin C, zinc, probiotics, curcumin, quercetin have been extensively studied in SARS-CoV-2 infection. Preliminary surveys have found these substances have anti-SARS-CoV-2 effects and can provide prophylactic and adjuvant therapy against the effects of COVID-19. Other studies have linked zinc, selenium, or vitamin C deficiency to a worse COVID-19 outcome. Adequate serum vitamin D and C levels may reduce the incidence of COVID-19-associated cytokine storms which are further correlated with lung injury and poor COVID-19 prognosis. (Hamulka et al., 2021).

The sub-analysis in this study showed that there was a significant difference in initial serum IL-1β levels based on the type of post-supplementation IL-1β change (decreasing, constant or increasing) with p = 0.006. Further test results showed that there was a difference in baseline IL-1 between the group with decreased and increased serum IL-1β levels (p = 0.002). These results are consistent with the previous theory that EBN supplementation can increase or decrease serum IL-1β levels. The difference in these results could be due to the exact status of infection and inflammation of each subject in this study is not known and distinguished. In contrast to the study of Haghani et al. which divided the treatment of research subjects into 3, namely subjects without infection, subjects with infection in the early phase, and subjects with infection in the resolution phase (Haghani et al., 2016). EBN supplementation has a pro-inflammatory or anti-inflammatory effect depending on the infection status and/or inflammatory status of the person taking it. In conditions of low levels of pro-inflammatory cytokines, sialic acid binding to EBN with activating siglec on immune cells will stimulate increased production of pro-inflammatory cytokines to fight infection. Meanwhile, in conditions where the levels of pro-inflammatory cytokines are high (usually occurs in the infection phase towards resolution), sialic acid will bind to inhibitory siglec on immune cells, which will suppress the production of pro-inflammatory cytokines and stimulate the production of anti-inflammatory cytokines with the aim of preventing the occurrence of a cytokine storm that causes inflammation. It can damage body tissues (Lübbers, et al., 2018).

The difference in immune response in this study was seen from variations in post-supplementation serum IL-1 levels (decreasing, constant or increasing) was not influenced by each variable characteristic of the research subjects but was more influenced by initial serum IL-1β levels and various other factors that affecting serum IL-1β levels which could not be fully controlled in this study such as variations in stress exposure and infectious or inflammatory conditions during 14 days of EBN supplementation. In addition, differences in serum IL-1β levels are also thought to be due to differences in host factors (eg siglec polymorphism, or other genetic and non-genetic factors), environment, and gut microbiome in each human (Ter Horst et al., 2016).

5. Conclusion

In conclusion, this study showed a significant difference between serum IL-1β levels of research subjects before and after 14 days of 99 percent EBN supplementation ($p < 0.001$). Edible Bird's Nest (EBN) 99% has the effect of reducing serum IL-1β levels in health workers who handle Covid-19 cases at RSUD Dr. Soetomo Surabaya based on initial serum IL-1β levels.

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