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[FMI] Title Suggestion Prior to Publication

FMI Universitas Airlangga
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Jun 14, 2:57 PM

Dear authors,

Your manuscript "Correlation between Elevated Serum Transaminase (SGOT/SGPT) and Sepsis in Burn Patients in a Tertiary Hospital, Surabaya, Indonesia" has been accepted for publication in Folia Medica Indonesiana Vol. 58 No. 2 June 2022. As to improve the quality of your manuscript, we suggest you modify your manuscript title to "Elevated Serum Transaminase (SGOT/SGPT) and Sepsis in Burn Patients in a Tertiary Hospital, Surabaya, Indonesia".

If you are mind so, we would like to update the title of the manuscript in the OJS and the following manuscript file.

Best regards,
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[FMI] Editor Decision

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Dear Authors :

We have reached a decision regarding your submission to Folia Medica Indonesiana, "Elevated Serum Transaminase (SGOT/SGPT) and Sepsis in Burn Patients in a Tertiary Hospital, Surabaya, Indonesia"

Our Decision is to : **Publish Submission**

You can check your publication on https://e-journal.unair.ac.id/FMI/article/view/32865

Thank you.

Kuntaman Kuntaman
Department of Clinical Microbiology, Universitas Airlangga, Surabaya, Indonesia; PAMKI (Perhimpunan Dokter Spesialis Mikrobiologi Klinik Indonesia)
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FOLIA MEDICA INDONESIANA
pISSN 2353-8393, eISSN 2599-056X

Article Reg. Num. : 22006 | F5. 1

PEER REVIEW FORM

Title : Correlation Between Elevated of Serum Transaminases (SGOT/SGPT) with Sepsis in Burn Patients at Dr.Soetomo Hospital Surabaya		
Author(s) :		
NO.	**REVIEW POINTS***	**SUGGESTION**
1.	Is the article divided into Introduction, Materials and Methods, Results and Discussion (IMRAD) structure ?	The "Background" title can be revised into "Introduction"
2.	Is the article well-written (in English) including the grammar and structure ?	Not quite. There are minor misspellings, a few punctuation errors, and some preposition misuse.Correcting these grammatical issues will improve the quality of the article.
3.	Does the abstract provide the context or background for the study and state the study's purpose ?	Need sentence revision . The aim of the study is stated but not clear. In the abstract, the author wrote: "*The aim of this study was to determine the correlation between elevated serum transaminases. (SGOT/ SGPT) in burn patients*". The author didn't mention the relation with sepsis.
4.	Does the title represent the whole article content ?	yes
5.	Does the introduction clearly describe the problem, the scope and purpose of the study ?	Need revision.. Not clear enough. The author wrote too much about SGOT and SGPT but did not state the purpose of the study in the introduction section.

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6.	Is the stages of the study defined clearly and included statement(s) indicating that the study was approved by a responsible ethical review committee?	yes
7.	Are the statistical methods appropriate and sufficiently detailed in such a way that others with access to the data would be able to reproduce the results ?	Yes. The statistical tests were mentioned. Could mention the statistic program and the version.
8.	Are the results given appropiately (including in tables or figures) and well-explained in logical sequence in the text, tables, and figures, providing the main or most important findings. No repetition of the data in the tables or figures in the text.	Yes. Tables were provided and explained.
9.	Does the discussion show clear relationship between the results obtained and the basic concepts or hypothesis ? Emphasize new and important aspects of the study, statement of the study limitations, and explore the implications of the findings for future research and for clinical practice or policy.	Yes. The relationship between results and hypotheses was described. Study limitation and future implication were pointed out.
10.	Is the conclusion clear and brief, including the link between conclusions with the goals of the study.	The conclusion was unclear. The author didn't state the link between conclusion with the goal of the study.In the conclusion section, there was no need to repeat the result data. You need to summarize the result and state whether there was a significant correlation between SGOT/SGPT with sepsis or not.
11.	Does the author provide references to original research sources?	yes

Conclusion	Check (v)
• Can be published without correction	
• Can be published with correction	v
• Cannot be published	

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Article Reg. Num. : 22006

F5. 1

Japan, 30 March 2022

(BLINDED)

* according to ICJME Recommendations

Correlation Between Elevated Of Serum Transaminase (SGOT/SGPT) with Sepsis in Burn Patients at DR. SOETOMO HOSPITAL SURABAYA

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ABSTRACT

Introduction: Burns trigger hypermetabolic stress reaction that causes an inflammatory respose. When there is a sustained or increased hypermetabolic reaction, the inflammatory response can be life threatening such as sepsis and have a significant impact on hepatic metabolic function. After burns, varying degrees of liver injury are usually associated with burn severity. The aim of this study was to determine the correlation between elevated serum transaminases (SGOT/ SGPT) with sepsis in burn patients who were treated at RSUD Dr. Soetomo Surabaya period 1 January 2018-31 December 2020.

Method: This is a descriptive analytic study with retrospective cohort design. Data were taken from burn patient includes demografi, causes of burns, inhalation trauma, burn severity, increased serum transaminase (SGOT/SGPT), mortality and sepsis. The correlation between elevated serum transaminases (SGOT/SGPT) and sepsis was determined using the Spearman-Rho Rank statistic test.

Results: Burn patients with sepsis in RSUD Dr. Soetomo Surabaya period 1 January 2018-31 December 2020 was dominated by male patients (65.2%) and 26-55 years old (69.6%), flame was the highest cause of burns (80.4%), with burn area above 20% (91.3%), the highest severity of major burn (91.3%), and with no inhalation trauma (54.3%). In this study, there was an increase in SGOT of 69.6% and SGPT of 78.3%, with a mortality rate of 39.1%, with an average of 24 days inpatient.
Correlation test between elevated serum transaminase (SGOT) and sepsis showed an insignificant relationship ($P = 0.065$, $P > 0.05$) with a correlation coefficient of 0.200, and correlation between elevated serum transaminase (SGPT) and sepsis was found to be significant ($P=0.006$, $P<0.05$) with a correlation coefficient of 0.296.

Conclusion: There is no correlation between the increase of SGOT and sepsis but there is a significant correlation between the increase of SGPT and sepsis.

Ethic Number: 0536/LOE/301.4.2/VIII/2021

Keywords *Luka bakar, peningkatan SGOT/ SGPT, sepsis, SDGs.*

INTRODUCTION

Burns are body skin damage caused by heat trauma or cold trauma (*frost bite*). The causes are fire, hot water, electricity, chemicals, radiation and cold trauma (*frost bite*). This damage can include subcutaneous tissue. (Kemenkes RI, 2019)

The main cause of death in burn patients is multiple organ dysfunction syndrome (MODS), which is a direct response to sepsis. The same is true for all patients admitted to the intensive care unit and there has been little improvement in the survival of patients with sepsis over the last few decades. From these statistical data, various efforts have been made to increase the speed of diagnosis and shorten the treatment time for sepsis. (Greenhalg, 2017)

Previous studies have shown that burns produce a hypermetabolic stress reaction that causes an inflammatory response. When there is a sustained or increased hypermetabolic reaction, the inflammatory response can be life threatening and this has a significant impact on the metabolic function of the liver; after burns, the degree of liver injury varies with the severity of the burn. Research by Mosoumi *et al.*, 2017 found that there is a strong and positive correlation between liver enzymes and the degree of burn injury. The increase in liver enzymes immediately after burns may be due to the formation of hepatic edema, which leads to cell damage and release of liver enzymes.

Aminotransferases or transaminases are a group of enzymes that catalyze amino acids and oxoacids by the transfer of amino groups. Aspartate aminotransferase (AST), formerly called glutamate oxaloacetate transaminase (GOT), and alanine aminotransferase (ALT), formerly called glutamate pyruvate transaminase (GPT), are the two most clinically significant aminotransferases. The main clinical application of measurement of serum AST and ALT is the detection and diagnosis of the differential etiology of liver disease. Liver cell injury is manifested by increased serum transaminases activity before clinical signs and symptoms (such as jaundice) appear. Comparable elevations of AST and ALT are hallmarks of viral, toxic, or nonethanol-induced acute hepatitis. Similar serum transaminases levels under these conditions are thought to be due to the cellular release of only cytoplasmic enzymes associated with reversible liver cell damage. (vroon *et al*, 1990)

Aspartate transaminase or a spartate aminotransferase (AST) catalyzes the reversible transfer of amino groups between aspartate and glutamate and, as such, is an important enzyme in amino acid metabolism. AST is found in the liver, heart, skeletal muscle, kidneys, brain, and red blood cells. Serum AST levels, serum ALT (alanine transaminase) levels, and their ratio (AST/ALT ratio) are commonly measured clinically as biomarkers for liver health (Giannini, 2005)

The purpose of this study was to determine the correlation between elevated serum transaminase (SGOT/SGPT) with sepsis in burn patients.

METHOD

This study was an observational analytic study for both descriptive and analytic purposes with a retrospective cohort design. The source of data in this study was the medical record of Dr. Hospital. Soetomo Surabaya for the period 1 January 2018 to 31 December 2020 which met the inclusion criteria of all burn patients who were treated with sepsis and had complete medical records with exclusion criteria patients with electrical burns, history of comorbidities in the liver and patients who did not have complete medical record. Sampling in this study using the total sampling method. Data collection from the patient's medical record has been approved by the Health Research Ethics Committee of Dr. RSUD. Soetomo Surabaya.

The data taken in this study included patient characteristics (gender and age of the patient), degree of burn severity, burn area, causes of burns, inhalation trauma, increase in

serum transaminase (SGOT/SGPT) average long stay and mortality in injured patients. burn. Data on the increase in serum transaminase SGOT and SGPT will be tested for correlation with sepsis using the above variables. The correlation with sepsis will be determined using the Rhank Spearman-Rho statistical test. All data obtained are presented in tabular form.

RESULTS

Obtained 276 patients and 86 (31.2%) patients entered the inclusion criteria with 46 patients with sepsis (*American burn association sepsis* criteria, 2007) and 40 patients not experiencing sepsis. Data were processed statistically with *SPSS 25 Version* and displayed in tabular form.

Table 1. The sex distribution of burn patients with infection and being treated at RSUD Dr. Soetomo Surabaya Period 1 January 2018 – December 2020.

Sex	N=46	Persentase (%)
Male	**30**	**65,2**
Female	16	34,8

It was found that the number of male patients who experienced sepsis in burn patients was higher as shown in table 1, male 30 people (65.2%), while the number of female patients was only 16 people (34.8%).

Table 2. Age distribution of burn patients with infection and being treated at RSUD Dr. Soetomo Surabaya Period 1 January 2018 – December 2020.

Age (Tahun)	N=46	Persentase (%)
0-5	1	2,2
6-11	2	4,3
12-16	3	6,5
17-25	9	19,5
26-35	11	23,9
36-45	**12**	**26,1**
46-55	4	8,7
56-65	1	2,2
>65	1	2,2

As shown in table 2, the age group with the most burns was in early adulthood, ranging from 36-45 years as many as 12 patients (26.1%), while the least group with 1 patient each (2.2%) was the group. 0-5 years old, 55-65 years old >65 years old.

Table 3. Distribution of etiology / causes of burns in patients treated at RSUD Dr. Soetomo Surabaya Period 1 January 2018 – December 2020.

Etiologi	N=46	Persentase (%)
Scald	8	17,4
Fire	**37**	**80,4**
Thermal contact	1	2,2

The causes of burns in burn patients with sepsis include fire in 37 patients (80.4%), scald in 8 patients (17.4%) and thermal contact in 1 patient (2.2%).

Table 4. Classification of the severity of burns in patients treated at RSUD Dr. Soetomo Surabaya Period 1 January 2018 – December 2020.

Severity of burn	N=42	Persentase (%)
Minor	0	0
Moderate	4	8,7
Major	**42**	**91,3**

The severity of burn patients according to the American burn association in 2007 was divided into 3 and found 4 patients (8.7%) moderate and 42 patients (91.3%) major as shown in the table above.

Table 5. Classification of burn area in patients treated at RSUD Dr. Soetomo Surabaya Period 1 January 2018 – December 2020.

Burn area	N=46	Persentase (%)
< 20%	4	8,7
> 20%	**42**	**91,3**

In this study, there were 4 patients (8.7%) with burn area <20% and 42 patients (91.3%) with burns above 20%, as shown in table 5, and divided according to ANZBA 2016

Table 6. Burn patients who experienced inhalation trauma in patients treated at RSUD Dr. Soetomo Surabaya Period 1 January 2018 – December 2020.

Inhalation Trauma	N=46	Persentase (%)
Yes	21	45,7
No	**25**	**54,3**

In this study, 21 patients (45.7%) and 25 patients (54.3%) did not experience inhalation trauma

Table 7. Burn patients who experienced an increase in SGOT in patients treated at RSUD Dr. Soetomo Surabaya Period 1 January 2018 – December 2020.

Increase SGOT	N=46	Persentase (%)
Yes	**32**	**69,6**
No	14	30,4

In this study, there were 32 patients (69.6%) with elevated SGOT and 14 patients (30.4%) with non-increased SGOT, as shown in table 7.

Table 8. Burn patients who experienced an increase in SGPT in patients treated at RSUD Dr. Soetomo Surabaya Period 1 January 2018 – December 2020.

Increase SGPT	N=46	Persentase (%)
Yes	**36**	**78,3**
No	10	21,7

It was found that 36 patients (78.3%) SGPT increased and 10 patients (21.7%) SGPT did not increase, described in table 8

Table 9. The mortality rate in burn patients with sepsis who was treated at the Dr. Soetomo Surabaya Period 1 January 2018 – December 2020.

Mortality	N=46	Persentase (%)
Yes	18	39,1
No	**14**	**60,9**

And the mortality rate of patients with sepsis, 18 patients (39.1%) who died and 28 patients (60.9%) who did not die are depicted in table 9.

Relationship between increased serum transaminase (SGOT and SGPT) with the incidence of sepsis

Table 10. Spearman-Rho SGOT Rank Correlation Test Results

Correlations				
			Sepsis	SGOT
Spearman's rho	Sepsis	Correlation Coefficient	1.000	.200
		Sig. (2-tailed)	.	.065
		N	86	86
	SGOT	Correlation Coefficient	.200	1.000
		Sig. (2-tailed)	.065	.
		N	86	86

Table 11. Spearman-Rho SGPT Rank Correlation Test Results

Correlations				
			Sepsis	SGPT
Spearman's rho	Sepsis	Correlation Coefficient	1.000	.296
		Sig. (2-tailed)	.	.006
		N	86	86
	SGPT	Correlation Coefficient	.296	1.000
		Sig. (2-tailed)	.006	.
		N	86	86

The analysis was carried out using the Spearman-Rho Rank test. The test is stated to have a significant relationship if the p value <0.05. The test results are presented in the following table.

Analysis of the results of statistical tests of the relationship between increased serum transaminase (SGOT) and sepsis using Rank Spearman-Rho got a sig / P value of 0.065 and the relationship between increased serum transaminase (SGPT) and sepsis using Rank Spearman-Rho got a sig / P value of 0.006 as shown in table 10 and table 11.

DISCUSSION

This study was conducted to determine the relationship between increased serum transaminase (SGOT/SGPT) on the incidence of sepsis in burn patients who were treated at RSUD Dr. Soetomo Surabaya period 1 January 2018-31 December 2020. There were 276 patients with 86 patients (31.2%) included in the inclusion criteria and 190 patients (68.8%) entering the exclusion criteria (electrical injury, patients with liver disorders/diseases, data on incomplete patients), where 46 patients (53.4%) were septic and 40 patients (46.6%) were not septic, Gomez R., *et al*, conducted an autopsy study of the causes of death in burn patients in 2009 stating 60% deaths were caused by infectious complications and MODS.

The percentage of burn patients who experienced sepsis was dominated by male patients, namely 65.2%. A study states that estrogen in women has the effect of increasing immune function (Angele *et al*, 2014). This is one of the factors that causes infection in burn patients more in male patients than female patients.

In this study where the highest incidence was at the age of 26-55 years as many as 32 patients who were early adulthood to late elderly who were of productive age.

The causes of burns in sepsis patients in the most studies included fire as many as 37 patients (80.4%), scald as many as 8 patients (17.4%) and thermal contact as many as 1 patient (2.2%). The most burning data from the Ministry of Health of patients treated at RSCM for the period 2012-2016 were fire as much as 53.1% then hot water/scald 19.1%, electricity 14%, thermal contact 5% and chemical contact 3%. The gender of burn patients was found to be male as much as 62.8% (58 patients), female 37.2% (32 patients), this is in accordance with data released by the American Burn Association in 2017 where 67% of burn patients were male and 33% women, where the highest incidence is at the age of 26-55 years as many as 32 patients who are early adulthood to late elderly who are of productive age.

The results of this study indicate that the highest percentage of severity of burns accompanied by sepsis is in the degree of major burn 41 patients (91.3%) with the highest burn area > 20% with a total of 41 (91.3%) patients. The study of Justin *et al*, 2021 stated that patients with burn area greater than 20% have a high risk of sepsis and death where extensive burns cause substantial damage to the skin which inhibits the ability of the skin as a major barrier to infection.

In this study, from 23 patients with inhalation trauma, 21 patients (91.3%) had sepsis with a mortality rate of 30.4% for patients with inhalation injury. Inhalation trauma increases 10% to 20% of morbidity and mortality in burn patients and inhalation trauma has also been found to be an independent predictor of mortality in burn patients. Inhalation trauma also causes increased bronchial blood flow delivering activated polymorphonuclear leukocytes and cytokines to the lungs, which potentiates the inflammatory response. The loss of bronchial epithelium and the effects of ROS (*Reactive Oxygen Species*) result in the loss of plasma proteins and fluids from the intravascular space into the alveoli and bronchioles. Transvascular protein shift causes exudate and blockage formation within the airways, leading to alveolar collapse or complete occlusion of the airways, increased blood flow to the injured lung segment, decreased ventilation of the collapsed segment, contributing to ventilation-perfusion mismatch as the main mechanism of hypoxemia after trauma. inhalation. Atelectasis, immune system dysfunction, and mechanical ventilation predispose to pneumonia as a common complication of inhalation injury. (Patrick F. Walker *et al*, 2015)

The average length of stay of burn patients with sepsis who were treated in 2018 that entered the inclusion criteria was 25 days, the average length of stay of burn patients with

sepsis who were treated in 2019 who entered the inclusion criteria was 23 days and the average length of stay of patients Burns treated with sepsis in 2020 that entered the inclusion criteria were 30 days, with the average length of stay for sepsis patients in 2020 was 21 days, so it can be concluded that the average length of stay of burn patients treated at RSUD Dr Soetomo Surabaya period 1 January 2018 to December 31, 2020, those who experience sepsis are 24 days

Relationship between increased serum transaminase (SGOT and SGPT) with the incidence of sepsis

The increase in SGOT with sepsis does not have a significant relationship where the pValue value is 0.065 (pValue > 0.05) and there is a significant relationship between the increase in SGPT and the pValue value is 0.006 (pValue < 0.05) with a correlation coefficient of 0.296 which is positive, both the above aminotransferases in the liver. However, SGOT is also obtained differently in heart, skeletal muscle, kidney, brain and red blood cells, and SGPT has low concentrations in skeletal muscle and kidney, therefore, elevated serum levels of SGPT are more specific for liver damage. In the liver, SGPT is only localized in the cellular, whereas SGOT is found in the cytosol (20%) and mitochondria (80%). (Eduardo G et al, 2005). In this study, data on SGOT and SGPT in the second week was due to the observation that serum SGOT, SGPT, and ALKP peaked during the first week post-burn and approached the normal range of 3-5 weeks post-burn. If the damage persists or sepsis occurs, the enzymes increase or increase again. (Jeschke et al., 2007) Where this indicates continued damage and most of the burns treated at RSUD dr Soetomo Surabaya for the period January 1, 2018 to December 31, 2020 were diagnosed with sepsis in the second week and the magnitude of SGOT and SGPT increased slightly < 5 times the value normal where an increase in SGOT in 46 septic patients was found to be a mild increase (<5 times the normal value) in 31 patients and a mild increase in SGPT value (<5 times the normal value) in septic patients was found in 32 patients. To distinguish whether the increase in serum transaminases is caused by sepsis or other diseases, it is necessary to carry out various kinds of investigations,

Eduardo G *et al*, 2005 stated that minimal or mild increase in serum aminotransferase is the most common biochemical change encountered in daily clinical practice and additional investigations need to be carried out to determine the cause of the increase in serum transaminase whether the cause is extrahepatic or intrahepatic. Alcohol abuse and to a lesser extent drug-induced liver injury are frequently associated with mild aminotransferase abnormalities, and causality should be ruled out clinically. In the western world, chronic viral hepatitis, autoimmune hepatitis and hereditary hemochromatosis are the most common causes of mild aminotransferase changes, and investigations to rule out the above patient causes need to be performed (HBsAg, anti-HCV, ANA test) and if none of the above diseases is found, attention should be paid. whether the patient suffers from *Nonalcoholic Fatty Liver Disease* (NAFLD) or steatohepatitis which is also frequently encountered in clinical practice. In acute liver damage, the patient's pharmacological history is very important. All drugs that have been given are considered again and the risks and benefits of administration are considered. Suspicion of NAFLD is raised in the presence of conditions associated with the metabolic syndrome and insulin resistance (elevated body mass index, diabetes, hyperlipemia, hypertension), although this disease can occur in patients without associated factors. (Eduardo G *et al*, 2005).

Research Limitations

This study has several limitations that can indirectly affect the results of the study, such as the use of secondary data (medical records)

CONCLUSION

There is no correlation between the increase of SGOT and sepsis (P = 0.065, P> 0.05), but the increase of SGPT and sepsis have significant correlation, pValue is 0.006 (pValue < 0.05) with a correlation coefficient of 0.296.

In future research, it is expected to conduct research with different titles and comorbidities so that they can add insight and minimize the effects of existing comorbidities and research is carried out regularly.

Ethic Number:
0536/LOE/301.4.2/VIII/2021

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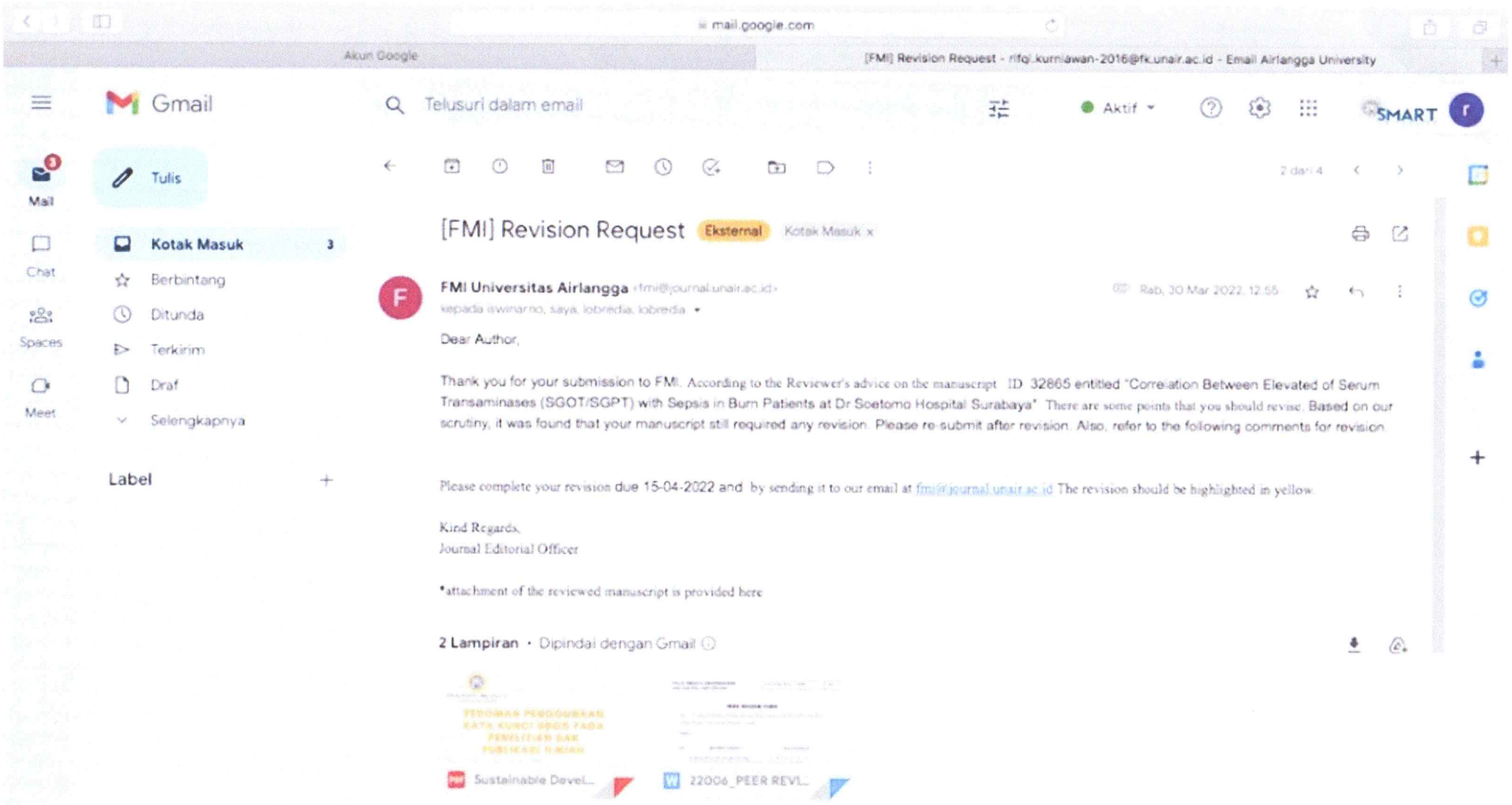
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Rab, 30 Mar 2022, 12.55
Dear Author,
Thank you for your submission to FMI. According to the Reviewer's advice on the manuscript ID: 32865 entitled "Correlation Between Elevated of Serum Transaminases (SGOT/SGPT) with Sepsis in Burn Patients at Dr Soetomo Hospital Surabaya" There are some points that you should revise. Based on our scrutiny, it was found that your manuscript still required any revision. Please re-submit after revision. Also, refer to the following comments for revision
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Jl. Mayjen Prof. Dr. Moestopo No. 6-8, Telp. 031-5501071-5501073, Fax. 031-5501164
SURABAYA 60286

SURAT EXEMPTION

(" LETTER OF EXEMPTION ")

Ref. No. : 0536/LOE/301.4.2/VIII/2021

Judul Protokol Penelitian	:	Korelasi antara peningkatan serum transaminase (SGOT/SGPT) terhadap kejadian sepsis pada pasien luka bakar di RS DR. Soetomo Surabaya periode 1 Januari 2018 - 31 Desember 2020
Dokumen yang disetujui	:	0559/108/4/II/2021 (versi: 8)
Tanggal terbit	:	5 Agustus 2021
Berlaku sampai	:	5 Agustus 2022
Peneliti Utama	:	Dr. Iswinarno Doso Saputro, dr., Sp.BP-RE (K)
Peneliti Lain	:	1. Lobredia Zarasade, dr., Sp.BP-RE (K) 2. Rifqi Kurniawan, dr
Instalasi/Tempat Penelitian	:	RSUD Dr. Soetomo

Komite Etik Penelitian Kesehatan RSUD Dr Soetomo menyatakan bahwa dokumen diatas sesuai dengan The Office for Human Research Protections (OHRP) dibawah persyaratan the U.S. Department of Health and Human Services (HHS) Regulasi 45 CFR bagian 46 untuk **exempt review**.

Dr. Dominicus Husada dr., SpA(K)
Ketua Panel 4

Dr. Evelyn Komaratih dr., SpM(K)
Sekretaris Panel 4