



CORRELATION BETWEEN SGOT AND SGPT LEVELS WITH POSITIVE HBSAG LEVELS

KORELASI ANTARA SGOT DAN SGPT DENGAN KADAR HBSAG POSITIF

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ABSTRACT

Background: Serum Glutamic Oxaloacetate Transaminase (SGOT) and Serum Glutamic Pyruvic Transaminase (SGPT) are transaminase enzymes used to determine liver damage. The increase in both enzymes can indicate the level of liver cell damage. Hepatitis B surface antigen (HBsAg) is an antigen that can indicate an acute infection or a chronic carrier. **Purpose:** This study aims to determine the correlation between SGOT and SGPT levels with positive HBsAg levels.

Method: It is a cross-sectional study using medical records from patients with positive HBsAg who performed SGOT and SGPT examinations at the Haji Public Hospital, East Java Province, in 2021. The correlation analysis used in this study is Kendall's tau correlation because the data contains outliers and is not normally distributed. **Result:** Based on the results, it is known that there is no significant correlation between SGOT and SGPT levels with positive HBsAg levels. The correlation coefficient for each is 0.110 and 0.144. **Conclusion:** It can happen because HBsAg levels vary between the disease's different phases, the patient's characteristics, and the levels of SGOT and SGPT.

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ABSTRAK

Latar belakang: Serum Glutamic Oxaloacetate Transaminase (SGOT) dan Serum Glutamic Pyruvic Transaminase (SGPT) merupakan enzim transaminase yang digunakan untuk mengetahui kerusakan hati. Peningkatan kedua enzim tersebut dapat menunjukkan tingkat kerusakan sel hati. Antigen permukaan hepatitis B (HBsAg) adalah antigen yang dapat menunjukkan infeksi akut atau pembawa kronis. **Tujuan:** Penelitian ini bertujuan untuk mengetahui hubungan antara kadar SGOT dan SGPT dengan kadar HBsAg positif.

Metode: Penelitian *cross-sectional* menggunakan rekam medis dari pasien dengan HBsAg positif yang menjalani pemeriksaan SGOT dan SGPT di RSUD Haji Provinsi Jawa Timur tahun 2021. Analisis korelasi yang digunakan dalam penelitian ini adalah korelasi *Kendall's tau* karena data mengandung *outlier* dan tidak berdistribusi normal. **Hasil:** Berdasarkan hasil tersebut diketahui bahwa tidak terdapat hubungan yang bermakna antara kadar SGOT dan SGPT dengan kadar HBsAg positif. Koefisien korelasi masing-masing adalah 0,110 dan 0,144. **Kesimpulan:** Hal ini dapat terjadi karena kadar HBsAg bervariasi antara fase penyakit yang berbeda, karakteristik pasien, dan kadar SGOT dan SGPT.

Kata kunci:
HBsAg, Hepatitis B, SGOT, SGPT



INTRODUCTION

Hepatitis B is a viral infection caused by the hepatitis B virus and attacks the liver, which can be an acute or chronic infection of the hepatitis B virus (Bagus Eka Utama Wija, 2020; Ditjen Bina Kefarmasian & Alat Kesehatan, 2005; Gan *et al.*, 2022). Most hepatitis B infections progress to cirrhosis and hepatocellular carcinoma. In 2019, it was estimated that 296 million people worldwide were infected with the hepatitis B virus, which caused the death of 820.000 people, with 1.5 million new infections yearly (Ditjen Bina Kefarmasian & Alat Kesehatan, 2005; Esmaeelzadeh *et al.*, 2017; Nafi'ah Rahma Maulidia *et al.*, 2020; WHO, 2022). The primary screening for hepatitis B virus infection is HBsAg, which aims to detect the presence of the hepatitis B virus in the blood (Ditjen Bina Kefarmasian & Alat Kesehatan, 2005; Gan *et al.*, 2022; Jaroszewicz *et al.*, 2010; Juspar, 2017). *Hepatitis B Surface Antigen* (HBsAg) is one of the serological markers detected positively since the hepatitis B virus entered within 2 - 6 weeks and will be detected within a few weeks to months in acute hepatitis B (Gan *et al.*, 2022; Hilman *et al.*, 2002; Jaroszewicz *et al.*, 2010). According to Baig (2009), Dooley *et al.* (2011), Ruggieri *et al.* (2018), HBsAg is closely related to pre-cancerous dysplasia. Hence, it is possible that the higher the HBsAg, the more severe the liver damage.

Acute hepatitis B consists of 4 phases: incubation, prodromal, icterus, and healing. The incubation phase ranges from 1 - 6 months, from the time of virus transmission to the onset of symptoms. The prodromal phase is between the onset of the first symptoms and symptoms of jaundice. The icterus phase lasts 1 - 6 weeks and is characterized by the yellowing of the eye's sclera. The healing phase is the disappearance of the symptoms of jaundice and other complaints. Chronic hepatitis B persists for more than six months from the onset of symptoms. It consists of 3 phases: immunotolerance, immunoactive, and residual. The immunotolerance phase is a replicative phase with a high HBsAg level. The immunoactive phase is a necroinflammatory process characterized by an increase in SGPT. The residual phase occurs when the body destroys the virus, causing the rupture of infected liver cells (Chen *et al.*, 2019; Rustanti, 2018).

People with hepatitis B will generally also perform laboratory tests related to *Serum Glutamic Oxaloacetate Transaminase* (SGOT) and *Serum Glutamic Pyruvic Transaminase* (SGPT), which is an indication of a disturbance in the liver cells. Both are transaminase enzymes used to determine liver damage (Astiti *et al.*, 2016; Gan *et al.*, 2022; Maulidia, 2019; Oktaviani, 2012; Rahayu *et al.*, 2018; Vaillant, 2021). The higher the increase in SGOT and SGPT enzymes, the more severe liver cell damage (Gan *et al.*, 2022; Pane and Khairunnisa, 2016; Rahayu *et al.*, 2018). The SGOT enzyme is found in

the cytoplasm and mitochondria of hepatocyte cells. Hence, this enzyme is less specific for determining the level of liver cell damage when compared to the SGPT enzyme, which is only located in the cytoplasm of hepatocyte cells (Pradnyawati, 2018; Rahayu *et al.*, 2018). Increased SGOT and SGPT can be caused by liver cell damage, hepatitis, metastatic carcinoma, heart failure, and granulomatous caused by alcohol consumption (Fanani, 2017; Nafi'ah Rahma Maulidia *et al.*, 2020). The SGPT enzyme increases significantly when liver disease occurs. Thus, it can be used to monitor the course of hepatitis and cirrhosis. SGOT highly affects organ damage such as heart, liver, muscle, skeletal, and kidney. Although the increase in SGOT is not specific to liver disease, SGOT may be elevated in cirrhosis, hepatitis, and liver cancer (Difa, 2020; Esmaeelzadeh *et al.*, 2017; Gan *et al.*, 2022; Nafi'ah Rahma Maulidia *et al.*, 2020; Oktaviani, 2012; Rahayu *et al.*, 2018). The increase in SGOT and SGPT in acute hepatitis B occurs at the beginning of the icteric phase, up to ten times the normal value, and one hundred times in severe conditions. There was a decrease of 50% in the second week since the icteric phase, but in the healing phase, the transaminase values were not normal and would be normal 2 - 3 months after infection (Wahyudi and Saturti, 2017).

According to Difa (2020), Esmaeelzadeh *et al.* (2017), Maulidia (2019), Oktaviani (2012), Rahayu *et al.* (2018), HBsAg-positive patients tend to have SGOT and SGPT levels above normal (Dwi Indah V., 2011; Esmaeelzadeh *et al.*, 2017; Gan *et al.*, 2022). Also, there was a relationship between increased SGPT levels and HBsAg levels in hepatitis B patients. Hence, this study aims to determine the correlation between SGOT and SGPT levels with positive HBsAg levels.

MATERIAL AND METHOD

This study used data obtained from the medical records of patients with positive HBsAg who performed SGOT and SGPT examinations simultaneously at the Haji Hospital in Surabaya, East Java Province in 2021. This hospital had approved a permission letter for data collection (070/728/102.10/2022). The data analysis used in this study is *Kendall's tau* correlation

Kendall's tau correlation

Kendall's tau correlation is a nonparametric correlation method that is more robust against outliers than *Spearman* correlation. This correlation requires that the data type used is at least ordinal. *Kendall's tau* correlation coefficient can be calculated by Formula 1 (Wozniak, 1991).

$$\tau = \frac{P - Q}{n - (n-1)/2} \dots\dots\dots (1)$$

In (1) is the coefficient of correlation, P is the number of concordant pairs, and Q is the number of discordant pairs. The correlation coefficient has a value between -1 to +1. The closer to zero, the weaker the relationship between the two variables, and the closer to -1 or +1, the stronger the relationship. A positive correlation coefficient indicates a directly proportional relationship between the two variables, while a negative one indicates an inverse relationship between the two variables (Johnson and Bhattacharyya, 2009).

RESULT

The data of HBsAg-positive patients with SGOT and SGPT levels at the Haji Hospital in Surabaya, East Java Province, in 2021 are shown in Table 1. The results showed that the highest number of HBsAg-positive patients was in the age range of 51 - 60 years old (31 people, 26.50%), while the lowest number in the age range of 71 - 80 and 81 - 90 years old was one person. This study's lowest and highest ages were 18 and 85, respectively. Based on gender, males were more dominant (60 people, 51.30%) than females (57 people, 48.70%). SGOT examination with normal level was 91 people (77.78%), and above normal was about 26 people (22.22%). On the SGPT examination, there were 92 people with normal levels (80.34%) and 25 people above normal (19.66%). Before conducting a correlation analysis, first, a descriptive analysis was conducted to determine the characteristics of the data.

Based on Figure 1, it is known that the distribution of HBsAg levels in patients with normal and above normal SGOT levels is not much different, although there is a high difference in the median value. The median HBsAg level in patients with normal SGOT levels (<40 U/L) is 3876, while in patients with above normal SGOT levels (>40 U/L) is 5539. Conversely, the distribution of HBsAg levels in patients with normal and above-normal SGPT levels is also the same. However, the distribution of HBsAg levels in patients with above-normal SGPT levels (>41 U/L) is more centered on HBsAg levels, which are higher than in patients with normal SGPT levels (<41 U/L). The median HBsAg level in patients with SGPT levels above normal is 6235, while in patients with crude SGPT, it is normal at 3656.

Based on Figure 2, it can also be seen that the plot between SGOT and SGPT levels and HBsAg levels does not show a relationship pattern because, at normal SGOT and SGPT levels, HBsAg levels tend to be evenly distributed. Furthermore, to determine the relationship between the two variables, a correlation analysis was conducted with *Kendall's tau* correlation with the results, as shown in Table 2.

Table 2 shows that HBsAg levels have a positive correlation coefficient with SGOT and SGPT levels, which are 0.110 and 0.144, respectively. It means that SGOT and SGPT levels also tend to increase when HBsAg levels increase, and vice versa. However, based on statistical tests, HBsAg levels did not significantly correlate with SGOT and SGPT levels. The *p-value* indicates this for both correlation coefficients more than a (0.05).

Table 1. Characteristics of HBsAg-positive patients with *Serum Glutamic Oxaloacetate Transaminase* (SGOT) and *Serum Glutamic Pyruvic Transaminase* (SGPT) levels at the Haji Hospital in Surabaya

Characteristic	HBsAg-positive patients (%)	SGOT level		SGPT level	
		Normal (%)	Above normal (%)	Normal (%)	Above normal (%)
Sex					
Female	57 (48.70)	46 (80.70)	11 (19.30)	49 (85.96)	8 (14.04)
Male	60 (51.30)	45 (75.00)	15 (25.00)	43 (71.67)	17 (28.33)
Age (years)					
10 - 20	2 (1.71)	2 (100.00)	-	1 (50.00)	1 (50.00)
21 - 30	17 (14.53)	16 (94.12)	1 (5.88)	13 (76.47)	4 (23.53)
31 - 40	24 (20.51)	20 (83.33)	4 (16.67)	19 (79.17)	5 (20.83)
41 - 50	16 (13.68)	9 (56.25)	7 (43.75)	11 (68.75)	5 (31.25)
51 - 60	31 (26.50)	24 (77.42)	7 (22.58)	28 (90.32)	3 (9.68)
61 - 70	25 (21.37)	18 (72.00)	7 (28.00)	18 (72.00)	7 (28.00)
71 - 80	1 (0.85)	1 (100.00)	-	1 (100.00)	-
81 - 90	1 (0.85)	1 (100.00)	-	1 (100.00)	-

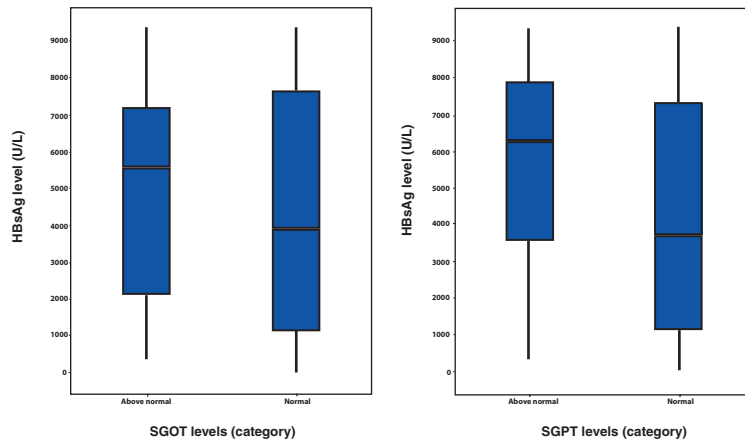


Figure 1. Boxplot Hepatitis B surface antigen (HBsAg) levels by Serum Glutamic Oxaloacetate Transaminase (SGOT) and Serum Glutamic Pyruvic Transaminase (SGPT) levels

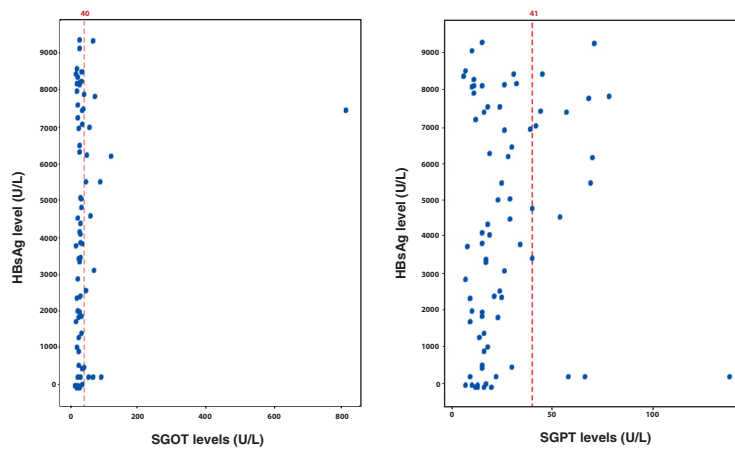


Figure 2. Scatterplot between Serum Glutamic Oxaloacetate Transaminase (SGOT) and Serum Glutamic Pyruvic Transaminase (SGPT) level with Hepatitis B surface antigen (HBsAg) level

Table 2. Kendall's tau correlation

Variable 1	Variable 2	Correlation	
HBsAg level	SGOT level	τ	0.110
		<i>p-value</i>	0.161
	SGPT level	τ	0.144
		<i>p-value</i>	0.066

DISCUSSION

This study used 117 data on SGOT and SGPT levels in HBsAg-positive patients at the Haji Hospital in Surabaya, East Java Province in 2021. Patient characteristics data were grouped by sex and age, as shown in Table 1. The highest number of HBsAg-positive patients were in the age 51 - 60 years old (26.50%) and male (51.30%). The results of this study showed that the largest HBsAg-positive (in the age of 51 - 60 years old) was the productive age of growing old, susceptible to hepatitis B infection due to too much activity outside. The male gender is more dominant than the female in HBsAg-positive. It might be related to drug use through used syringes and tattooing with unsterile needles.

Besides that, most males start sleeping late, while the liver detoxification process occurs in the range of 11 p.m. to 1 a.m., where this process will take place during a person's periods of sleep. The increase in SGOT and SGPT levels in males is higher than in females due to several factors, such as lifestyle, including smoking and consuming alcohol.

Figure 1 indicates that patients with above-normal SGOT and SGPT levels tend to have higher HBsAg levels than patients with normal SGOT and SGPT levels. The results is aligned with a study conducted by Dwi Indah V. (2011), Esmaelzadeh *et al.* (2017), Gan *et al.*, (2022), which showed that there was a relationship between increased SGPT levels and HBsAg levels in hepatitis B patients. However, statistically, there will be

no difference in HBsAg levels in patients with normal or above normal SGOT and SGPT levels because the distribution of the data intersects with each other.

The relationship between two variables can be known graphically or statistically. The relationship between the two variables can be seen through a scatterplot, as shown in Figure 2. Figure 2 shows that there are levels of SGOT and SGPT that differ from levels of other SGOT and SGPT, indicating that there are outliers in the data. In addition, based on the normal category (<40 U/L for SGOT levels and <41 U/L for SGPT levels) and above normal, it was seen that more HBsAg-positive patients had normal SGOT and SGPT levels than patients with higher SGOT and SGPT levels. Increased levels of SGOT and SGPT occur in patients with acute hepatitis B because the immune response is strong, so T cells will fight the virus and damage liver cells where the virus replicates. Liver cells are destroyed, and enzymes in the initial intracellular liver cells are released into the bloodstream. Meanwhile, in inactive hepatitis B carriers, the levels of SGOT and SGPT are normal because the virus cannot replicate or is inactive (Difa, 2020; Esmaeelzadeh *et al.*, 2017; Nafi'ah Rahma Maulidia *et al.*, 2020; Oktaviani, 2012; Rahayu *et al.*, 2018). The data may have more carrier inactive patients than acute hepatitis B patients, so there are more patients with normal SGOT and SGPT levels.

According to Chevaliez (2013), Gan *et al.* (2022), Jaroszewicz *et al.* (2010), HBsAg levels can vary according to the disease's phase and the patient's characteristics. It was noted that HBsAg levels decreased slowly in most patients who achieved a virological response. HBsAg levels vary during the natural course of infection. HBsAg is at its highest level in the early immune tolerance phase. An immune clearance phase follows the immune tolerance phase. During this phase, HBsAg levels decrease slowly and progressively. The lowest HBsAg level was found during the inactive carrier phase (Chevaliez, 2013; Gan *et al.*, 2022; Jaroszewicz *et al.*, 2010).

CONCLUSION

Based on the results, it is known that there is no significant correlation between SGOT and SGPT levels with positive HBsAg levels. Higher HBsAg levels do not necessarily indicate more severe liver damage based on SGOT and SGPT levels. HBsAg levels vary according to the phase of the disease and the patient's characteristics, as well as the levels of SGOT and SGPT. Nevertheless, this study has limitations because it is an observational study, and data on characteristics and medical records is limited, which hinders a thorough examination of the association between HBsAg, SGOT, and SGPT. Furthermore, many other factors can affect or indicate the severity of liver damage that can be

analyzed more comprehensively and used in future studies-consideration of other variables that may affect the requirement of more data in further research.

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REFERENCE

- Astuti, M.Y.D., Herawati, S., Subawa, A.A.N., 2016. Umur dan Jenis Kelamin sebagai Faktor Risiko Peningkatan Kadar Serum Glutamik-Piruvic Transaminase (SGPT) pada Pasien Diabetes Melitus Tipe 2 di Rumah Sakit Umum Pusat Sanglah. *J. Med. Udayana* Vol.10(9), Pp. 78-81.
- Bagus Eka Utama Wija, I., 2020. Hepatitis B pada Anak. *J. Kedokt. Univeristas Palangkaraya*. Vol. 8(2), Pp. 985-997.
- Baig, S., 2009. Gender Disparity in Infections of Hepatitis B Virus. *J. Coll. Physicians Surg.--Pak. JCPSP* Vol. 19(9), Pp. 598-600.
- Chen, L., Shi, J., Lu, Z., Ye, Y., Zhou, X., Tan, Y., 2019. Baseline HBsAg Levels Associated with HBsAg Loss in HBeAg-Negative Chronic Hepatitis B Infection with Persistently Normal Alanine Aminotransferase. *Clin. Res. Hepatol. Gastroenterol*. Pp. 310-316.
- Chevaliez, S., 2013. Is HBsAg Quantification Ready, for Prime Time? *Clin. Res. Hepatol. Gastroenterol*. Vol. 37(6), Pp. 559-563.
- Difa, Z.S., 2020. Korelasi Kadar SGOT dan SGPT terhadap Kadar Bilirubin Total Pada Pasien dengan HBsAg Positif di Rumah Sakit Umum Haji Surabaya Periode Bulan Januari 2017 sampai dengan Februari 2020 (Thesis (Tugas Akhir D3)). Universitas Airlangga, Fakultas Vokasi, Departemen Kesehatan.
- Ditjen Bina Kefarmasian & Alat Kesehatan, 2005. Pharmaceutical Care untuk Penyakit Diabetes Mellitus. Direktorat Bina Farmasi Komunitas Klinik, Direktorat Jenderal Bina Farmasi & Alkes, Departemen Kesehatan RI, Jakarta.
- Dooley, J.S., Lok, A., Burroughs, A., Heathcote, J., 2011. *Sherlock's Diseases of the Liver and Biliary System*. Clin. Med. 11.
- Dwi Indah V., A., 2011. Hubungan Peningkatan SGPT dengan Hasil HBsAg pada Pasien Hepatitis B di Rumah Sakit Marsudi Waluyo pada Tahun 2011. *SDH* Vol. 2(1), Pp. 1-12.

- Esmaeelzadeh, A., Saadatnia, H., Memar, B., Mokhtari Amirmajdi, E., Ganji, A., Goshayeshi, L., Meshkat, Z., Pasdar, A., Vosoughinia, H., Farzanehfar, M., Tehranian, S., Ghaffarzadehgan, K., Rajabzadeh, F., Ahadi, M., 2017b. Evaluation of Serum HBV Viral Load, Transaminases and Histological Features in Chronic HBeAg-Negative Hepatitis B Patients. *Gastroenterol. Hepatol. Bed Bench* Vol. 10(1), Pp. 39-43.
- Fanani, D.N., 2017. Gambaran Enzim SGOT dan SGPT Pada Pasien Hepatitis B di Laboratorium Klinika Surabaya Periode 2017. Univ. Airlangga.
- Gan, Qinyi, Huang, Y., Zhu, C., Zhao, S., Fu, H., Cai, M., Wang, J., Zhang, C., Guo, S., Cao, Z., Xie, Q., 2022. qHBsAg for the Identification of Liver Histological Abnormalities in HBeAg-Negative Chronic Hepatitis B Patients with Normal and Mildly Elevated ALT Levels. *Can. J. Gastroenterol. Hepatol.* Vol. 2022, Pp. 8695196.
- Hilman, K., Djajadiredja, S.H., Prasetya, E., Meilianau, 2002. Penatalaksanaan Hepatitis B Kronik. *Maranatha J. Med. Health* Pp. 1-8.
- Jaroszewicz, J., Calle Serrano, B., Wursthorn, K., Deterding, K., Schlue, J., Raupach, R., Flisiak, R., Bock, C.-T., Manns, M.P., Wedemeyer, H., Cornberg, M., 2010. Hepatitis B Surface Antigen (HBsAg) Levels in The Natural History of Hepatitis B Virus (HBV)-Infection: A European Perspective. *J. Hepatol.* Vol. 52(4), Pp. 514-522.
- Johnson, R.A., Bhattacharyya, G.K., 2009. *Statistics: Principles and Methods*, 6 th. ed. Wiley Global Education.
- Juspar, E., 2017. Tes Hepatitis B Virus Deoxyribo Nucleic Acid (HBV DNA) Pada Ibu Hamil Hepatitis B Surface Antigen (HBsAg) Non Reaktif di Rumah Sakit Khusus Ibu dan Anak Pertiwi Makassar. Univ. Hasanuddin Makassar.
- Maulidia, V.N.R., 2019. Kadar SGOT, SGPT, dan Albumin pada Pasien dengan Hepatitis B Kronis di RSUD Dr. Soetomo Surabaya (Penelitian Analitik Cross-Sectional). Univ. Airlangga.
- Nafi'ah Rahma Maulidia, V., Wardhani, P., Setyoboedi, B., 2020. AST, ALT, and Albumin Level in Chronic Hepatitis B Patients with and without Complications of Cirrhosis and Hepatocellular Carcinoma. *Indones. J. Clin. Pathol. Med. Lab.* Vol. 26(3), Pp. 250-349.
- Oktaviani, I., 2012. *Aspek Farmakokinetika Klinik Obat-Obat yang digunakan pada Pasien Sirosis Hati Di Bangsal Interne RSUP Dr. M.Djamil Padang Periode Oktober 2011-Januari 2012*. Sebastopol, CA : Universitas Andalas.
- Pane, R.A., Khairunnisa, 2016. *Pemeriksaan SGOT dan SGPT pada Pasien di Balai Laboratorium Kesehatan Daerah Sumatera Utara (Thesis)*. Universitas Sumatera Utara.
- Pradnyawati, N.W., 2018. Analisis Kadar Albumin Serum terhadap Aspartate Transaminase (AST), Alanin Transaminase (ALT) dan Rasio De Ritis pada Pasien Hepatitis B di RSUP Sanglah, Denpasar. *E-J. Med. Udayana* Vol. 7(6), Pp. 1-8.
- Rahayu, S.E., Sukeksi, A., Nuroini, F., 2018. Hubungan Kadar SGOT-SGPT pada Pasien TB Pengobatan Fase Awal di Puskesmas Pati. Univ. Muhammadiyah Semarang.
- Ruggieri, A., Gagliardi, M.C., Anticoli, S., 2018. Sex-Dependent Outcome of Hepatitis B and C Viruses Infections: Synergy of Sex Hormones and Immune Responses? *Front. Immunol.* Vol. 9, Pp. 1-7.
- Rustanti, R.A., 2018. *Profil Imunitas terhadap Hepatitis B Pada Pendorong Darah Reguler di Unit Donor Darah PMI Kota Semarang (Thesis)*. Universitas Diponegoro, Program Studi Kedokteran, Fakultas Kedokteran.
- Vaillant, A., 2021. *Transaminase Elevations during Treatment of Chronic Hepatitis B Infection: Safety Considerations and Role in Achieving Functional Cure*. *Viruses* Vol. 13(5), Pp. 745.
- Wahyudi, H., Saturti, T.I.A., 2017. *Hepatitis*. Fakultas Kedokteran Universitas Udayana/RSUP Sanglah, SMF Ilmu Penyakit Dalam.
- WHO, 2022. *Hepatitis B*. URL <https://www.who.int/news-room/fact-sheets/detail/hepatitis-b>
- Wozniak, P.J., 1991. *Applied Nonparametric Statistics (2nd ed.)*. *Technometrics* Vol. 33(3), Pp. 364-365.