IJSCIA
International Journal of Scientific Advances
ISSN: 2708-7972
Volume: 4 | Issue: 3 | May – Jun 2023 Available Online: www.ijscia.com
DOI: 10.51542/ijscia.v4i3.5

Correlation Between Hyperglycemia and Length of Stay in Severe Head Injury Patients at Prof. Dr. Igng Ngoerah Hospital

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ABSTRACT

Background: Head injury is one of the emergency cases in surgery that is often found in the emergency. From year to year, cases of head injuries have significantly increased. High blood glucose levels in head-injured patients are thought to correlate with the level of consciousness, especially in patients with severe head injuries. The severe head injury affects the various complications that occur, which affects the length of stay (LOS) in the hospital. ***Objectives:*** To determine the correlation between hyperglycemia and length of stay in patients with severe head injuries. ***Methods:*** This study is an analytical observational study with a prospective design. The research sample included patients with severe head injuries who came to the surgical emergency unit at Prof. Dr. IGNG Ngoerah Hospital and met the inclusion criteria in medical record data throughout November 2019 - April 2020, with 56 samples. ***Results:*** The mean random blood sugar measurement results were found to be higher in the LOS ≥7 days group (210.14±83.93 mg/dL) compared to the LOS group□7 days (165.88±92.44 mg/dL). Multivariate analysis using logistic regression found a significant relationship between mean hyperglycemia and LOS in patients with severe head injuries (OR 7.46; 95% CI [1.839-30.300]; P = 0.005) ***Conclusion:*** There is a significant correlation between mean hyperglycemia and the length of stay in patients with severe head injuries at Prof. Dr. IGNG Ngoerah Hospital.

Keywords: severe head injury; hyperglycemia; length of stay

INTRODUCTION

Data from the United States shows that there are 1,700,000 new cases of head injury, of which 275,000 patients are hospitalized, and 52,000 cases die.[1]. At Prof. Hospital Dr. IGNG Ngoerah Denpasar itselfThe incidence of head injury averages 2,000 cases per year, and 30% of them are patients with moderate and severe head injuries. The high morbidity and mortality rates in head injury cases indicate that this case requires special attention and comprehensive management.[2]

Generally, there are two types of damage caused by head injuries, including primary and secondary injuries. Immediate injuries occur due to direct trauma to the head, resulting in tissue damage and pathological changes in the brain. Tissue damage ranges from contusions, intracranial hemorrhage, or death of cells in the brain. Secondary injuries follow after the primary injury. Systemic complications can arise due to injuries in hypoxia, hypotension, hypertension, hyperglycemia, or hypoglycemia.[3]

Acute hyperglycemia will occur as a result of stress-induced release of catecholamine enzymes. High blood glucose levels in head-injured patients are thought to have a relationship with the level of consciousness of head-injured patients, especially in patients with severe head injuries. Research from Kafaki et al., 2016, stated that there was a significant relationship between the patient's blood sugar level and the severe head injury.[4]

The severe head injury affects the various complications, affecting the length of the patient's hospitalization. The longer the patient is treated, of course, will cause multiple problems for the patient, his family, and the hospital. Inflated treatment costs can be a thorny problem hospitals in the current Social Security Agency of Health era. Regarding patients, families must spend time, energy, and money to look after and care for patients in the hospital.

METHOD

This is an observational analytic study with a Prospective Study design to determine the correlation/relationship of hyperglycemia in severe head injury with a length of stay at Prof. Central General Hospital. Dr. IGNG Ngoerah Denpasar.

Secondary data collection through patient medical records from November 2019 – April 2020 or until the number of samples is fulfilled at the Prof. Central General Hospital. Dr. IGNG Ngoerah Denpasar. Implementation of research and data processing starts from May 2021 – August 2021. Inclusion criteria: Patients who are being treated and have been diagnosed with a severe head injury by the doctor in charge of the patient. Exclusion criteria: 1) Families of patients who refuse to be the study sample; 2) Patients who are forced home of their own free will; 3) Patients with a history of chronic diseases such as type II diabetic mellitus and stroke; 4) Multitrauma patient, with ISS Score > 16.

The research sample was selected sequentially (consecutive) of all patients with severe head injuries who came for treatment at the IRD Surgery at Prof. Dr. IGNG Ngoerah Denpasar. Preparation for patient treatment is prepared according to standard operating procedures for head injuries at Prof. Dr. IGNG Ngoerah Denpasar. Statistics using descriptive analysis to describe the characteristics of the subjects and research variables. The hypothesis test aims to assess patients with severe head injuries with hyperglycemia and regular blood sugar for the patient's length of stay in the hospital. The mean difference is tested with an independent T-test if the data distribution is normal or with Mann-Withney if the data distribution is abnormal. The Multi-variable test will use the ANCOVA test to control confounding variables analytically. The whole process of analyzing the research data above uses the help of statistical software SPSS 24.0.

The research was carried out after being approved by the research ethics committee of the Faculty of Medicine of Udayana / RSUP Prof. Dr. IGNG Ngoerah with Research Permit Number: LB.02.01/XIV.2.2.1/28297/2021 and obtained Ethical Eligibility Statement No: 1842/UN14.2.2.VII.14/LT/2021. The researcher will bear all costs related to the research. The identity of the patient will be kept confidential.

RESULTS

Data from this study were taken from November 2019 to April 2020 at Prof. Central General Hospital. Dr. IGNG Ngoerah. The total samples collected were 56 samples. A more complete description of the essential characteristics of the sample can be seen in Table 1 and Table 2.

TABLE 1: Characteristics of respondents.

Variable	Frequency (%)
Gender	
Woman	15 (26.8%)
Man	41 (73.2%)
Age	
≥ 60 years	16 (28.6%)
< 60 years	40 (71.4%)
body mass index	
Obesity	23 (41.1%)
Normal	33 (58.9%)
Length of stay	
≥ 7 days	22 (39.3%)
< 7 days	34 (60.7%)
When blood sugar	
Hyperglycemia	26 (46.4%)
Normoglycemia	21 (37.5%)
hypoglycemia	9 (16.1%)
Exit state	
Die	29 (51.8%)
Life	27 (48.2%)

TABLE 2: Description of the average patient's basic characteristics.

Variable	Mean ± SD	95% CI	Median
Age (years)	43.25 ± 21.69	37.44 – 49.06	41.50
body weight (kg)	68.71 ± 13.05	65.22 – 72.21	68.00
Height(cm)	168.18 ± 8.21	165.98 – 170.38	170.00
BMI (kg/m2)	24.15 ± 3.51	23.21 – 25.09	24.18
LOS (days)	9.55 ± 11.06	6.59 – 12.52	7.00
random blood sugar level (mg/dL)	183.27 ± 91.06	158.88 – 207.66	188.50

Based on the normality test results that LOS was not normally distributed, we divided the patient's LOS by looking at the median value. So, we divided them into LOS ≥7 and LOS <7 categories. Following the cross-tabulation table, the samples were grouped based on the patient's LOS. After splitting the sample, it was found that the mean age in the LOS group <7 days was higher (45.12 ± 22.68 years) compared to the model in the LOS group ≥ 7 days (40.36 ± 20.24 years). The variables of weight, height, and BMI in the LOS <7 days group were similar (68.68 ± 14.12 kg; 167.74 ± 8.27 cm; 24.20 ± 3.59 kg/m2) compared to the LOS group ≥7 days (68.77 ± 11.51 kg; 168.86 ± 8.27 cm; 24.07±3.46 kg/m2).

The mean blood sugar check measurement results were found to be higher in the LOS ≥7 days group (210.14±83.93 mg/dL) compared to the LOS group ≥7 days (165.88±92.44 mg/dL). The data obtained was then carried out by bivariate analysis to determine whether a significant relationship existed between the variables examined and the patient's LOS. The study used is the independent sample T-test and Mann-Whitney. The bivariate analysis results showed no statistically significant difference in all variables between the two LOS groups (p≥0.05). Complete information can be seen in Table 3.

TABLE 3: Factors related to the length of stay (LOS) in patients with severe head injuries.

Variable	LOS ≥7 days (n=22)				LOS <7 days (n=34)		p-value
	Mean ± SD	Mean ± SD	95% CI	Median	95% CI	Median	
Age (years)	40.36±20.24	45.12±22.68	37.20-53.03	42.00	31.39-49.34	41.50	0.294b
body weight (kg)	68.77±11.51	68.68±14.12	63.75-73.60	68.50	63.67-73.88	68.00	0.979a
Height (cm)	168.86±8.27	167.74±8.27	164.85-170.62	170.00	165.19-172.53	172.00	0.415b
BMI (kg/m2)	24.07±3.46	24.20±3.59	22.94-25.45	24.28	22.54-25.61	23.59	0.899a
random blood sugar levels (mg/dL)	210.14±83.93	165.88±92.44	133.63-198.14	172.50	172.92-247.35	221.00	0.075a

*significant p-value < 0.05; an analysis using an independent sample T-test; b analysis using Mann-Whitney.

The categorical variable cross-tabulation table also grouped samples based on the patient's LOS. The data were then subjected to bivariate analysis to determine whether there was a significant relationship between the variables examined and the patient's LOS. The study used is Pearson Chi-Square.

From the analysis results, it was found that there was a statistically significant difference in the random blood sugar levels variable between the two LOS groups (p<0.05). Meanwhile, for other variables, there was no difference between the two LOS groups (p≥0.05). Complete information can be seen in Table 4.

TABLE 4: Factors related to the length of stay (LOS) in patients with severe head injuries.

Variable		Length of Stay		p-value
		<7 days (n=34) n (%)	>7 days (n=22) n (%)	
Gender	Woman	10 (66.7)	5 (33.3)	0.581
	Man	24 (58.4)	17 41.5)	
Age	>60 years	12 (75.0)	4 (25.0)	0.166
	< 60 years	22 (55.0)	18 (45.0)	
BMI	Obesity	15 (65.2)	8 (34.8)	0.565
	Normal	19 (67.6)	14 (42.4)	
Random blood sugar level	Hyperglycemia	10 (38.5)	16 (61.5)	0.006*
	Normoglycemia	17 (81.0)	4 (19.0)	
	hypoglycemia	7 (77.8)	2 (22.2)	
exit state patient	Die	20 (69.0)	9 (31.0)	0.190
	Life	14 (51.9)	13 (48.1)	

Ket. Chi squeare test, *significant p value <0.05.

Biobased on the bivariate test results above, we found a significant relationship between random blood sugar levels and LOS in severe head injury patients. We then performed a multivariate analysis to determine which variables in the random blood sugar levels (Hyperglycemia, Normoglycemia, and Hypoglycemia) were most related to the patient's LOS. The multivariate analysis used is logistic regression analysis.

Based on the study results shown in Table 5, hyperglycemia offers a value of p = 0.005, where the importance of p <0.05 so that Ho is rejected, which means there is a relationship between hyperglycemia and LOS in severe head injury patients. In addition, it was found that the incidence of hyperglycemia has a risk of 7.46 times in patients with severe head injuries to experience LOS ≥7 days.

TABLE 5: Relationship between blood glucose and length of stay (LOS) in patients with severe head injuries.

Variable independent	p-value	Adjusted Odds ratio	95%CI
Current blood sugar (random blood sugar) level			
Normoglycemia		1	
Hyperglycemia	0.005	7,46	1,839-30,300
hypoglycemia	0.986	0.98	0.141-6.846

Ket. Logistic Regression Test, significant p-value 0.05; Length of stay (long patient care in days).

DISCUSSION

There were 56 respondents from patients with severe head injuries at Prof. Dr. IGNG Ngoerah Denpasar who joined in this research. Based on the findings of this study, most of the patients were male (73.2%), and the rest were female (26.8%). This finding aligns with research conducted by Siahaya et al. (2020), which states that patients with severe head injuries are generally male.[5] Several factors cause this. Namely, men usually do outdoor activities and have physical activities and jobs that are riskier than women, for example, construction workers and motorbike riders. In addition, the high prevalence of male patients with head injuries compared to female patients is also caused by male deviant behavior, such as violating traffic rules or driving at high speed.[6].

The findings of patients with severe head injuries at Prof. Dr. IGNG Ngoerah Denpasar were 1-81 years old. There were 40 patients (71.4%) aged less than 60 years and 16 other patients (28.6%) aged 60 years and over. Similar results were obtained by Hsu et al. (2018) in Taiwan, where there were more patients under the age of 65 (73.5%) compared to patients aged 65 years or older (26.5%). [7] Motor vehicle accidents are the most common cause of trauma in patients under 65.[8] This is due to using private motorized vehicles, which is common in the country. The prevalence of accidents is also high, with conditions similar to those in Indonesia, especially in Bali. On the other hand, falls are the most common cause of head trauma. [8,9]

The high mortality rate in severe head injury patients was also found in this study, which was 51.8%. The high mortality rate in severe head injury patients depends on several factors, such as mean arterial pressure (map), presence of respiratory distress or not, pupil reactivity, age >60 years, low blood pressure, hypoxemia, and hypernatremia. [10,11]. Apart from these factors, Prabhakaran et al. (2017) also found that the high mortality rate of severe head injury patients was also influenced by the condition of whether the patient was sent directly to and entered the trauma center (direct transfer) or not (non-direct transfer).[12].

Hyperglycemia is one of the most common secondary complications of severe head injury and is often associated with poor clinical outcomes. In this study, 26 patients (46.4%) had hyperglycemia, 21 patients (75%) were still normoglycemic, and 9 other patients (16.1%) had hypoglycemia. One of the causes of increased blood sugar levels is stress response due to brain trauma or stress-induced hyperglycemia (SIH).

Activation of the hypothalamus-pituitary-adrenal axis and the sympathetic nervous system due to brain trauma increases neuro-hormonal levels and performance and induces insulin resistance. This process causes an increase in catecholamine hormones, cortisol, glucagon, and growth hormone. These hormones increase metabolic processes and glycogenolysis, which causes excessive intravascular glucose production.[13] In addition, brain injuries that damage the pituitary gland and hypothalamus and underlying medical conditions such as diabetes mellitus can also cause hyperglycemia. [14,15]

This study's average body mass index (BMI) in head-injured patients was 24.15 kg/m2. Based on previous research, BMI does not have a significant relationship with the type and severity of head injury or the prognosis or outcome of head injury. [16,17] In this study, BMI was also not associated with LOS from severe head injury patients.

The length of stay (LOS) data we obtained showed that patients with severe head injury were treated the longest for 56 days and the fastest to be treated for less than one day because the patient died while being treated. Several factors affect the patient's LOS in the hospital, namely hospital support facilities, presence of accompanying organ injuries, extracranial complications, patient's GCS scale, ventilator use, age, gender, and of course, the severity of the damage. These factors have been identified as significant risk factors for prolonged LOS.[18]. In-line research by Da Silva et al. at the Irmandade da Santa Casa Hospital de Misericórdia de São Paulo, Brazil, showed that patients with severe head injuries had the most LOS of more than 30 days, compared to patients with mild and moderate head injuries.[19]

Patients with normoglycemia had LOS for approximately 6 days (6.29 ± 8.48 days). This finding differs from that of Lazaridis et al. (2015) previously stated that patients with severe head injuries had ICU LOS for approximately 19 days.[20]Kafaki et al. also found that LOS patients with blood sugar <200 mg/dL had LOS in the hospital for about 24 days.[21]This difference can be caused by differences in the number of samples where both studies used a sample size of more than 200 so that the LOS obtained was similar, which also caused the difference with this study which only used 56 samples. In addition, differences in hospital service facilities also affect differences in LOS in normoglycemic patients.

This study's LOS findings in hypoglycemia patients lasted approximately 3 days.

This study's common finding of LOS in hypoglycemia patients is related to the possible dangers of low blood sugar. The systematic review and meta-analysis by Hermanides et al. (2018) stated a strong dependency relationship between low blood sugar levels and death in patients with severe head injuries [22].

They were based on the results of this study, obtaining a longer length of stay in patients with hyperglycemia compared to normoglycemia or hypoglycemia. Researchers found patients with hyperglycemia experienced a length of stay of approximately 14 days. Based on the 2016 National Health Statistics Report, the average length of stay of patients with head injuries with hyperglycemia in care is 7.3 days, while intensive care is 1.2 days. In patients with head injuries without indications for intensive care, the average length of stay was around 3.2 days. Regarding gender, the length of stay of male patients was longer than that of female patients, namely 6.5 days for men and 5.0 days for women. In terms of age group, head injury patients aged 35-44 years have a longer length of stay than other age groups, which is around 8.2 days. Research by Kafaki et al. stated that the average length of hospital stay in head-injured patients with hyperglycemia was around 9.23 days. The average length of ICU stay was around 7.45 days.[4]

Based on the researchers' findings, the incidence of hyperglycemia is the main factor that has a significant relationship to the length of stay of severe head injury patients. Previous research by Kafaki et al. reported in a study that hyperglycemia had a substantial relationship to the mortality and morbidity of patients with severe head injuries. Kafaki et al. also mentioned that hyperglycemia in head injuries causes patients more extended stays than those without hyperglycemia.[4]Based Ha et al. also reported a significant relationship between hyperglycemia and increased morbidity of severe head injury patients while in hospital, which tended to worsen compared to patients with average glucose[23] The findings of Shi et al. also found that only about 7.8% of severe head injury patients with hyperglycemia survived with a hospital stay of around 21 days.[13]In addition, research by Rau et al. reported that decreased GCS was associated with increased blood glucose levels; in this study, hyperglycemia occurred in 63.6% of severe head injury patients, and based on Kongwad et al., 54.9% of patients with intracerebral hemorrhage.[24,25] Research by Yuksel et al. showed a relationship between the incidence of hyperglycemia in patients with severe head injuries. However, there is no significant relationship between the incidence of hyperglycemia in head-injured patients with a length of stay in hospital > 5 days.[26] In addition, several other factors, such as age, gender, and body mass index, that we analyzed did not have a significant relationship with the length of stay of patients with severe head injuries.

Many pathophysiological theories are thought to have a close relationship as the main cause of increased glucose in the blood. In cases of head injury, the occurrence of hyperglycemia is thought to be caused by the stress response due to brain trauma. In a study involving 184 patients with severe head injuries with hyperglycemia, 82.6% were found to be caused by a stress response or stress-induced hyperglycemia (SIH). When the brain is traumatized, the hypothalamus-pituitary-adrenal axis and the sympathetic nervous system are activated, causing the effect of increasing neuro-hormonal levels and performance and inducing insulin resistance. This process causes an increase in catecholamine hormones, cortisol, glucagon, and growth hormone. These hormones encourage an increase in metabolic processes (become hypermetabolism) and glycogenolysis, which causes excessive intravascular glucose production. Catecholamine hormones also inhibit the binding of insulin to glucose which causes insulin resistance with hyperinsulinemia and stimulates excessive production of the hormone cortisol, thereby increasing the process of gluconeogenesis, which causes an increase in the amount of glucose produced by the body. [4,13,23]

Conditions of hyperglycemia exacerbate head injury through various pathways. Hyperglycemia reduces the metabolic response of the Krebs cycle, which causes a decrease in ATP production and an increase in anaerobic glycolysis, leading to lactate accumulation. Excessive lactate production will cause a reduction in body PH and decreased function of brain cells. Hyperglycemia also stimulates the formation of reactive oxidants / ROS, which are free radicals. Hyperglycemia increases intracerebral blood viscosity, which causes decreased transport of oxygen into brain cells, exacerbating ischemia and increasing the degree of edema of brain tissue. [4,13]

This research certainly has limitations. One of the limitations of this study is the difference in facilities from the existing health services at Prof. Hospital. Dr. IGNG Ngoerah Denpasar compared to other hospitals with more complete or lower facilities. This factor causes the results of this study to be generalized to only some severe head injury cases in Indonesia.

CONCLUSION

Based on the results and discussion above, the conclusions of this study are as follows.

- There is a significant relationship between hyperglycemia and the length of stay in patients with severe head injuries. There is no significant relationship between normoglycemia and hypoglycemia on the length of stay in Prof. General Hospital. Dr. IGNG Ngoerah Denpasar.
- The average length of stay of patients with severe head injuries who experience hyperglycemia at Prof. Dr. IGNG Ngoerah Denpasar, namely 14.19 ± 12.82 days.
- The mean length of stay of patients with severe head injuries who experience normoglycemia at Prof. Dr. IGNG Ngoerah Denpasar, namely 6.29 ± 8.48 days.
- The mean length of stay of patients with severe head injuries who experience hypoglycemia at Prof. Dr. IGNG Ngoerah Denpasar, namely 3.78 ± 3.38 days.

ACKNOWLEDGMENTS

The authors would like to thank the Department of Surgery, Prof. Dr. IGNG Ngoerah Hospital, for the support authors in this work.

DECLARATIONS

- Funding: No funding sources
- Conflict of interest: None declared
- Ethical approval: The study was approved by the institutional ethics committee

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