

LOW TOTAL CHOLESTEROL SERUM LEVELS AS A POOR OUTCOME PREDICTOR FOR INTRA-CEREBRAL HEMORRHAGE STROKE

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ABSTRACT

Background: Stroke is affected by several factors, age, infection during treatment, obesity, and total cholesterol (TC) levels.

Objective: The study aimed to prove low TC serum levels as an unfortunate outcome predictor for intracerebral hemorrhage stroke.

Methods: This study is a prospective cohort design. The research did in the Stroke Unit of Sanglah Hospital, Denpasar, from July 1st, 2018 to January 31st, 2019. The study involved patients with hemorrhage strokes with low TC serum levels and aged 40-95 years. Depending on variable divided into two groups with low TC serum levels (<180 mg/dL) and normal TC serum levels (>180mg/dL). Independent variable is The National Institutes of Health Stroke Scale (NIHSS) as an outcome. The processing of data analysis using Mac for SPSS version 23.

Result: This study used 70 subjects. The age characteristics of the study subjects with a median value of 62 years in for low TC levels, and 57 years for normal TC levels, dominant in male (60%), working (71.5%), not obese (58.6%), stroke-related infections (51.4%), and mean arterial blood pressure (MABP) £130mmHg (90%). Subjects with low TC had a risk of 64 times experiencing adverse outcomes (RR = 64: CI 95% = 14.06-291.32: p <0.001). Multivariate analysis showed a low TC serum level as an independent variable.

Conclusion: Low TC serum levels as an independent predictor having a poor outcome in intracerebral hemorrhage stroke

Keywords: Intracerebral hemorrhage stroke, low total cholesterol, poor outcome.

Introduction

Stroke is a non-communicable chronic disease that often found in the community with old adulthood. Blood pressure, serum blood sugar levels, and controlled serum cholesterol levels play an essential role in determining post-stroke prognosis. TC serum levels significantly influence the mortality rate of stroke patients within three months after the onset of a bleeding stroke.¹

Nagasari Stroke Unit of Sanglah Hospital gained as much as 661 stroke patients consisted of 439 (66.4%) male patients and 222 (33.6%) female patients in the period from July 1st, 2018 to January 31st, 2019.² Aged < 40 years were 51 (7.7%) sufferers, aged 41-50 years were 140 (21.2%) patients, aged 51-60 years were 208 (31.5%) sufferers, and over the age of 60 in 262 (39.6%) sufferers. The number of patients with hemorrhagic strokes was 246 (37.2%) patients, and blockage strokes were 415 (62.8%) patients. Mortality among stroke patients with hemorrhagic is twice that of ischemic stroke.³ The average length of stay for a hemorrhagic stroke patient was 7.7 days with a stay cost of \$15,256 while the price of a stroke patient who survived was higher by \$17,442 with an average stay of 9.6 days.⁴

Methods

This research was observational analytic using a design study prospective cohort of pre- and post-test to see two groups of research subjects who had low and normal TC serum. The study did at Department of Neurology, Medical Faculty of Udayana University, Sanglah General Hospital Bali, Indonesia. The sample from a hemorrhagic stroke who underwent treatment at Sanglah Hospital in July, 1st 2018-January, 31st 2019 with criteria inclusion and exclusion. The inclusion criteria in this study were: (1) All supratentorial (2) Age 40-95 years, (3) Onset ≤ 48 hours, (4) Patients or families agree to participate in this study after being given approval after explanation (5) Volume <30 ml (6) Midline shift <4 mm. (7) TC level <180 mg/dL. (8) Hypertension. (9) Normal hemostasis (10) Composmentis. Exclusion criteria were: (1) Patients with traumatic brain injury, (2) Patients with history of statins, alcohol and drug use, (3) Patients without Computer Tomography (CT) examination of the head, (4) Patients with brain tumors (5) Impaired organ function: heart, lung, kidney and liver, (6) Diabetes Mellitus, (7) Patients with metabolic disorders: hypoalbumin, electrolyte imbalance (9) Patients on chemotherapy or radiotherapy, (10) Vegetarian. The instrument used in this

study consisted of a questionnaire. Questionnaires and data collection sheets were used to record basic data on patient characteristics, and the results of NIHSS examinations for the first and seventh day of treatment. A bad outcome is an increase in the NIHSS-2 score against a permanent NIHSS-1, □1, or death. Good outcomes found to decrease the NIHSS-2 score against NIHSS-1 by a difference of □2.5 Analisis the data with SPSS for Mac version 23.

Results

Table.1 Characteristics of Research Subjects

Characteristics	Total Cholesterol		Subject n (%)
	Low n (%)	Normal n (%)	
Age (year), Median (min-maxs)	62 (49-93)	57 (50-76)	
> 55 years old	29 (58)	21 (42)	50 (71.5)
≤55 years old	6 (30)	14 (70)	20 (28.5)
Sex			
Male	23 (54.8)	19 (45.2)	42 (60)
Female	12 (42.9)	16 (57.1)	28 (40)
Occupation			
Working	22 (44)	28 (56)	48 (71.5)
Unworking	13 (65)	7 (35)	20 (28.5)
Infection during stroke			
Yes	20 (55.6)	16 (44.4)	36 (51.4)
No	15 (44.1)	19 (55.9)	34 (48.6)
Obesity			
Yes	10 (34.5)	19 (65.5)	29 (41.4)
No	25 (61)	16 (39)	41 (58.6)
MABP			
> 130mmHg	3 (42.9)	4 (57.1)	7 (10)
≤130mmHg	32 (50.8)	31 (49.2)	63 (90)
Poor Outcome	32 (86.4)	5 (13.6)	37 (52)
Good Outcome	3 (9)	30 (91)	33 (48)
Cholesterol Total	156,5	195	
Median (min-maks)	(117-179)	(180-200)	

Table 2. Bivariate analysis

Characteristics	Outcome		RR (CI=95%)	P
	Poor n (%)	Good n (%)		
TC Levels	32 (91.4)	3 (8.6)	64 (14.06-291.32)	<0.001
Low	5 (14.3)	30 (85.75)		
Normal				

Discussion

The group of subjects with hemorrhagic stroke with poor outcomes was found more in the group of low TC serum levels of 32 people (91.4%) compared to the normal TC serum levels of 5 people (14.1%). In contrast, the group of stroke patients with good outcomes was found more in the whole TC serum group of 30 people (85.7%) compared to the low TC serum level of 3 people (8.6%).

Inthe *Chi-Square* test with *continuity correction* get a significant relationship (RR = 64: CI 95% = 14.06-291.32: p <0.001). Patients with hemorrhagic strokes with low serum TC levels are 64 times more likely to experience bad outcomes than normal serum TC levels. Neuroradiology researcher found multifocal hypointense lesions in *T2-weighted Magnitude Resonance Imaging* (MRI) as a marker of small bleeding associated with low TC serum levels. The profile of low TC serum levels is associated with the risk of

death in stroke patients as evidenced by the presence of multifocal lesions on MRI images with p <0.05.⁶

Research Roquer et al. (2005) obtained different results from researchers. This difference occurs due to differences in research methods, sample size, inclusion and exclusion criteria, and dependent variables. Researchers used a prospective cohort design with a sample size of 70 subjects divided into groups of low and normal TC serum levels with a *cut* value of 180mg/dL, the difference between NIHSS-1 and NIHSS-2 outcomes as the dependent variable. In the study of Roquer, et al. (2005), using a retrospective cohort study design, with a sample size of 184 subjects divided into groups of serum TC levels *cut* values of 166 mg / dL, with death outcomes as the dependent variable.⁷ Serum TC levels are low as independent variables, and mortality outcomes are a dependent variable. Statistical analysis found that the group of low TC serum levels (<166 mg / dL) might have a risk of death 3 times greater than the group of TC levels (> 166 mg / dL) with a value of p = 0.002 (HR = 3.13; 95% CI = 0 , 83-11.08). Decrease in low serum TC levels within 24 hours of a hemorrhagic stroke to date is unclear.⁷

Research Ramírez *et al.* (2009) shows that low serum TC levels are closely related to increased mortality in ICH strokes, and are increasing at the age of 70-89 years. Setianto *et al.* (2015), high C-Reactive Protein (CRP) is also poor outcome in ICH Stroke.⁸ Raisa *et al.* (2018), there were no influences between Glial Fibrillary Acidic Protein (GFAP) and ICH Stroke outcome.⁹ In prospective studies in Japan, morbidity and mortality increased in patients with serum TC levels <160 mg / dL or LDL-C levels <80 mg / dL.¹⁰

In the study of Iribarren, *et al.* (1995) by comparing two groups of low TC serum (<180 mg / dL) with normal serum TC groups (180-239 mg / dL). Outcomes of death obtained by a hemorrhagic stroke with low TC serum levels had a risk 2.41 times more likely to die than the normal serum TC group (95% CI = 1.45-4.00; p <0.001).^{11,12} TC serum needed for the continuation of intracellular chemical processes. The combination of low TC serum and triglyceride levels has an important role in maintaining the integrity of cellular membranes. Erythrocyte membrane damage (*fragility*), decreased platelet aggregation function in vivo and in vitro due to low TC levels play a role in poor treatment outcomes.¹³ Low serum total cholesterol levels also cause reduced endothelial adhesion power in arteries, loss of communication, and weak inter-cell linkages, and increased the length of time needed for the regeneration of blood vessel walls.¹⁴ A chronic weakness of the artery walls, which can trigger the emergence of microaneurysms.¹⁵

Research Chen *et al.* (2017) found groups with serum TC levels of 160 mg / dL had almost twice the risk of having a bad outcome with an NIHSS > 15, and three times more deaths in the three months after a stroke than the TC group > 200mg/dL.¹ In the study of Chen *et al.* (2017) using a retrospective cohort method, the chronology of death three months after stroke derived from family information. *The Taiwan Stroke Registry* data consists of 39 Government Hospitals with a stroke unit service. The total sample recorded as stroke sufferers from the period May 1, 2006 - April 30, 2009, was 4000 patients. Inclusion criteria that a head injury did not cause all stroke patients with hemorrhagic. Stroke patients with post-stroke blockage excluded so that only 2444 stroke patients met the inclusion

criteria. The independent variable used serum TC levels <160 mmHg and >200mmHg. NIHSS treatment outcomes with a *cut value of* > 14, and *Modified Rankin Scale* (MRS) with a *cut value of* > 2, and mortality three months post-stroke. Chen *et al.* (2017) research results differ from researchers due to differences in study designs.¹ Chen *et al.* (2017) used a retrospective cohort method, while researchers used a prospective cohort. Samples used by researchers according to inclusion criteria, serum TC levels in researchers used a *cut value of* <180mg / dL as a treatment group and 180-200mg/dL as a control group. Research Chen, *et al* (2017) with a *cut value of* <160mg/dL in the treatment group and >200mg/dL as a control group. Sample size, researchers used 70 hemorrhagic stroke patients, while Chen *et al.* (2017) 2444 patients (1). Stroke outcomes in researchers used the NIHSS instrument on the first and seventh day of treatment. The difference in points between NIHSS-1 and NIHSS-2 according to the operational definition categorized as a dependent variable on a nominal scale in both good and bad outcomes. Chen *et al.* (2017), using three instruments as a bad outcome. NIHSS with a *cut value of* > 14 as a bad outcome assessed only on the first day of treatment, MRS with a *cut of* > 2 experiencing disability disruption, and three months of death post-stroke. The difference in the use of NIHSS care scores, the difference in the *cut of* NIHSS scores, causes the results of the study to differ from those of Chen *et al.* (2017). Researchers get a group of TC serum levels <180mg / dL possibility of risk 64 times more likely to have worse outcomes than the group TC serum 180-200mg /dL. Research Chen *et al.*, (2017) found a group with low serum TC levels <160 mg /dL have a risk of death two times greater than the group of serum TC levels >200 mg / dL.¹ Munir *et al.* (2015) NIHSS and random blood sugar have been not a relationship for stroke outcome.¹⁶

NIHSS as a predictor of death 30 days after a stroke obtained on the first day of treatment with a *cut value of* > 20 (0-20 vs.> 20). NIHSS has a sensitivity of 81% and a specificity of 90%.¹⁷ In this study using NIHSS as the first and seventh day hemorrhagic stroke output instruments with different NIHSS-1 and NIHSS-2 scores according to the operational definition and not using a *cut of* > 20 as an adverse outcome.

Based on multivariate analysis, low TC serum found as an independent risk factor for treatment outcomes. Hemorrhagic stroke sufferers are likely to have a 64 times greater risk of experiencing an adverse outcome compared to patients with normal TC TC levels (RR = 64; 95% CI = 14.01-291.3; p <0.001).

Conclusion

Low TC serum levels as an independent predictor having a poor outcome in intracerebral hemorrhage stroke

Conflict of Interests

There were no financial supports or relationships between authors and any organizations or professional bodies that could pose any conflict of interest.

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