SYSTEMATIC REVIEW: RISK FACTORS CONTRIBUTING TO ISCHEMIC STROKE IN YOUNG ADULTS

Keswini Gopalakrishnan¹, A.A Ngurah Subawa², Desak Gde Diah DharmaSanthi², Anak Agung Wiradewi Lestari²

¹Programme of Medicine and Health, Faculty of Medicine, Udayana University, Denpasar, Bali

²Department of Clinical Pathology RSUP Sanglah/ Faculty of Medicine, Udayana University, Denpasar, Bali

Email: keswini@yahoo.com

Abstract: Stroke is a neurological deficit due to acute focal injury of the Central Nervous System (CNS). However ischemic stroke is due to blockage in an artery that supplies blood to the brain. It is the most common type of stroke and there are several major and minor risk factors contributing to it such as hypertension, diabetes mellitus, consumption of alcohol, smoking, obesity and dyslipidemia. The minor risk factors are; gender, ethnicity, history of stroke in family,vascular disease, coronary disease, myocardial infaction, atrial fibrillation and heart failure. Through this study we aim to determine the risk factors contributing to ischemic stroke in young adults. Systematic review with inclusion and exclusion criteria through search engines obtained 338 journals that were reviewed. 8 journals were used as main reference in writing this review. The data obtained are in the form of descriptive analysis by narrating findings of scientific articles which are then arranged systematically and according to each topic discussed so that a conclusion is obtained that represents the entire content of the review. Based on the 8 journal that was reviewed I have observed that the risk factors of ischemic stroke in young adults can be divided into major and minor. The major risk factors are hypertension (87.5%), diabetes mellitus (87.5%) and dyslipidemia (87.5%). The minor risk factors are smoking (75%), high consumption of alcohol (50%) and obesity (25%). The major risk factor contributing to ischemic stroke in young adults are dominantly hypertension, diabetes mellitus and dyslipidemia. The minor risk factors are obesity, high consumption of alcohol and smoking.

Keywords: ischemic stroke, risk factor, young adult.

1. INTRODUCTION

Stroke is characterised as a neurological deficit credited to an acute focal injury of the central nervous system (CNS) due to vascular reason such as cerebral infarction, intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH). Stroke can be further broken down into 2 types which are ischemic and hemorrhagic. Ischemic stroke has known to be the most comon type of stroke that occurs and this is due to blockage of blood vessel in the neck or the brain. Blockage of such is caused by "the formation of a clot within a blood vessel in he brain or neck, called thrombosis; the movement of the clot from another part of the body such as the heart to the brain which is known as embolism; or a severe narrowing of an artery in or leading to he brain, known as stenosis".²

By refereing to the journal Ischaemic stroke in young aduts: a global perspective, age can be categorised into young adults which are ages between 18 to 50 of years, while older adults are above 51 years of age. Therefore in my journal, I have based my research on said journal and written about young adults with the age range of 18 to 50 years of age. Ischemic stroke in young adults is undeniably more uncommon than that among more older adults, yet the underlying pathogeneses furthermore, risk factors are more different. Around 10% to 15% of all strokes happen in adults around the age of 18 to 50 years. To some degree, because of the lower percentage of occurance, the analysis of stroke in younger adults can be hard to separate from stroke emulates and to distinguish the reason or the fundamental pathogenesis. 4

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Ischemic stroke can be further broken down into 3 major subtypes such as thrombotic cerebral infarction, embolic cerebral infarctionand lacunar cerebral infarction.⁵ The system of categorizing stroke was developed in the multicenter Trial of ORG 10172 in Acute Stroke Treatment which involved the division of stroke into different subtypes according to neurological signs, cerebral imaging and ancillary diagnostic test results.⁶

According to the Clinical Profile of Patients with Cerebrovascular Disease at Stroke Unit, Sanglah General Hospital, Denpasar, Bali journal stroke is an increasing cause of morbidity and mortality in Indonesia. The percentage of younger generation being affected is 19.5% which are mostly younger than 45 years of age. More cases were recorded by men compared to women and the most common type encountered was Ischemic stroke which was 53.7%. Globally the incident of stroke in young adults ranges from 5 to 15 per 100 000 person-years in European studies however in most Northern-American, Australian and Asian studies its been recorded around 20 to 100 000 person-years whereas in some African countries and Iran its 40 to 100 000 person-years. However, the exact global stroke incident is still questionable as the prevelance data is still lacking from many African and Asian countries.³

Risk factors for ischemic stroke in younger adults are not unique to younger adults and overlap considerably with those of older adults but do vary in terms of the percent contribution to ischemic stroke subtypes. The overall risk factors are gender, ethnicity, history of stroke in family, active smoker, alcohol consumption, obesity, hypertension, vascular disease, coronary disease, myocardial infaction, atrial fibrillation, heart failure, diabetes mellitus and dyslipidemia. From the listed risk factors above the major risk factors that causes ischemic stroke in young adults are; hypertension, diabetes mellitus, obesity, alcohol consumption, dyslipidemia and smoking.

Therefore from the data obtained from the journals, I will like to find out which are the main risk factors contributing to ischmeic stroke in young adults based on all the risk factors.

2. METHODS

Protocol and Registration

A comprehensive summary in the form of a systematic review regarding the Risk factors contributing to ischemic stroke in young adults. The protocols used in this study are The Center for Review and Dissemination and The Joanna Briggs Institute Guideline as a guide in evaluating the quality of the collected studies. Systematic review assessment uses the PRISMA checklist to determine the completion of studies that have been found and adjusted to the objectives set.⁸

Eligibility Criteria

The strategy used in finding articles is the PICOS framework which consists of:

- 1. Population is the population or problem that will be analyzed based on this systematic review topic.
- 2. Intervention is an action in the form of therapy given to cases in accordance with this systematic review topic.
- 3. Comparation is another action or intervention that is used as a comparison. If none of these are applicable, the control group in the selected study is used.
- 4. Outcome is the result or outcome obtained in previous studies in accordance with the topic of this systematic review.
- 5. Study design is a research design used by selected articles for further review.

Further description of the PICOS framework used in this systematic review can be seen in table 1.

Table 1. PICOS framework criteria for systematic review the risk factors contributing to ischemic stroke in young adults.

PICOs framework	Inclusion Criteria	Exclusion Criteria				
Population	A study using a population of	A study using a population above				
	young adults aged 18 to 50	50 years of age and without				
	years with ischemic stroke	history of ischemic stroke				
Intervention	Studies evaluating treatment	There were no exclusion criteria				
	interventions in the form of IV					
	injection of recombinant tissue					
	plasminogen activator (tPA)					
Comparison	The comparison intervention	There were no exclusion criteria				

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	groups used Were between younger adults and older adults					
Outcome	Studies that describe the risk	Studies that do not address the risk				
	factors of ischemic stroke in	factors of ischemic stroke in young				
	young adults	adults				
Study design	Randomized control trial,	Case control, animal studies,				
	original research	literature review				

In addition, the eligibility criteria are also used through the publication year of the articles used, namely 2010-2020 as inclusion criteria with national and international journals.

Information Sources

Literature searches conducted during December 2020 to March 2021 against literature obtained from previous researchers or secondary data in the form of national and international journals using the database such as PubMed, Science Direct, and Google Scholar.

Literature Tracing Strategy

Literature search is carried out by keywords and using filters in the form of MeSH (Medical Subject Headings) and text words so that it can make it easier to find the literature to be used. The filters used were: ischemic stroke, risk factor, young adult.

Study Selection

Based on the results of a literature search through the database that was previously mentioned using keywords and filters, 338 articles were obtained. Furthermore, a selection was carried out in the form of screening based on the title and abstract so that there were 33 articles. A total of 33 articles were then analyzed thoroughly using inclusion and exclusion criteria so that there were 8 articles that could be used in this systematic review.

Data Collection Process

The checklist sheet obtained from PRISMA was used by researchers to evaluate the literature used and extract data from articles which were then typed according to the thesis guide. Furthermore, the data collection process carried out is as follows:

- 1. Use of guides in the form of The Center for Review and Dissemination and the Joanna Briggs Institute and the PRISMA Checklist.
- 2. Use of keywords and filters in the form of MeSH to find literature in the database
- 3. Determination of the database used in this study is PubMed and Google Scholar
- 4. The determination of the eligibility criteria is carried out using the PICOS framework and criteria in the form of inclusion and exclusion.
- 5. The study selection process was carried out by reading the entire article according to the PRISMA flow.
- 6. Taking into account the possibility of bias results with the JBI Critical appraisal, then the appropriate article will be analyzed and synthesized in this systematic review.

Types of Data and Variables

Based on the topics used in this systematic review, it should have data on several variables as follows:

- 1. Research characteristics data in the form of the type of study used, location, research year, number of patients, type of stroke, age, risk factors of stroke.
- 2. The type of intervention used as therapy.
- 3. Limitations faced by researchers in conducting analysis or research processes.

Risk Assessment of Bias in Individual Studies

The risk assessment can be carried out using the JBI Critical Appraisal in analyzing the methodology used by the study that will be used in the preparation of this systematic review. A critical appraisal (CA) was conducted to assess a study as

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8 having a score of at least 50% meeting the CA criteria. The risk of bias in this systematic review uses an evaluation of research methods in each study consisting of:

- 1. Theory: the explanation in the form of a theory presented is inappropriate, out of date, and lacks credibility.
- 2. Design and research instruments: designs that do not fit the research objectives and instruments that are invalid or reliable.
- 3. Variables: unsuitable research that do not address the characteristic to be Observed.
- 4. Analysis: use of the type of analysis that is not in accordance with the standards of analysis.

Summary Measures

The intervention given regarding the risk factors contributing to ischemic stroke in young adults was the main variable evaluated in this systematic review. The results of the literature search used were based on JBI CA and PRISMA which were then presented in the form of characteristics, type of stroke, age, and number of risk factors obtained based on the study.

Synthesis of Results

The result synthesis used in this systematic review is a descriptive method, namely an explanation in the form of a narrative description in describing the results obtained. The narrative explanation used aims to gather evidence about the Risk factors contributing to ischemic stroke in young adults and develop a coherent and systematic textual narrative. The data were evaluated by review questions namely background, theoretical framework, research objectives, research content, research design, sample size, sampling method, sample description, validity and reliability, instruments used, statistical analysis, and analysis of results.

Additional Analysis

The analysis used in this systematic review is descriptive analysis by narrating the findings of scientific articles. This study did not use any other additional analysis techniques, the researcher only summarized the results in the literature then analyzed descriptively with a description in the form of a narrative explanation.

3. RESULTS

Literature Selection

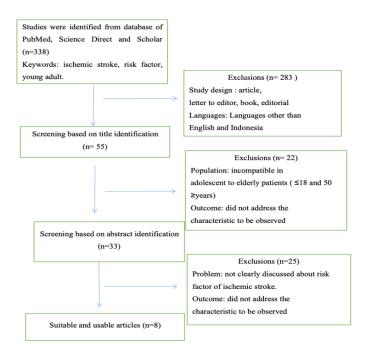


Figure 1. Literature Search Flow Diagram Characteristics Of Risk Factors Contributing to Ischemic Stroke in Young Adults.

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Study Characteristic

The characteristics of the articles used are 8 study articles (table 2) consist of case control study (2), prospective cohort (1), and retrospective cohort (5) taken from published period 2010 to 2020. The population in the study of the articles used in this systematic review is a population originating from 18 countries. Patient mean ages ranged from 18 years to 50 years (younger adults).

Table 2. Characteristics of the Study Used

Study	Type of Study	Location	Year Research	Total Patient	Age Mean±SD/ Median(min- max) Years
Mitchell et al., 2015	Case control study	Washington, DC	1992-2008	2291	40.8 ±7.1
Aigner <i>et al.</i> , 2017	Case control study	Germany	2007-2010	10625	44.8±4.2
Putaala <i>et al.</i> , 2012	Retrospective cohort	Finland, Norway, Austria, Belgium, France, Germany, Hungary, The Netherlands, Switzerland, Greece, Italy, Turkey	1988-2010	3944	43(36-46)
Van Alebeek et al., 2018	Prospective cohort	Netherlands	1980-2010	656	40.07±7.7
111 21 (11. /311.)	Retrospective cohort	Northeast United States	2005-2010	215	37.5±7
	Retrospective cohort	Turkey	2003-2009	192	40.2±5.7
Moond et al., 2020	Retrospective cohort	India	2014-2018	160	36.2
Renna et al., 2014	Prospective cohort	Italy	2005-2013	150	41±8

Table 3. Risk Factor Frequency of Ischemic Stroke in Young Adults

Characteristics	Total Studies	Number of Patients with	Number of Patients		
Characteristics	Total Studies	Characteristics	Checked		
Gender					
Females	8	3653	18018		
Males	8	4665	16016		
Ethnicity					
Black	2	569			
White	2	775	2506		
Others	1	81			
History of stroke in family					
Yes	4	610	4446		
No]	14049	7770		
Active smoker					
Yes	7	3528	17577		
No]	14049			
Alcohol intake					
Yes	4	664	11127		
No	7	10463			
Obesity (BMI)					
<25	2	1157	12916		
25-30		1145	12710		

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>30		10614		
Hypertension				
Yes	7	3065	17577	
No	7	14512	1/3//	
Valvular disease				
Yes	4	50	1223	
No] 4	1173	1223	
Coronary disease				
Yes	4	332	14944	
No	7 4	14612	14944	
Myocardial infarction				
Yes	2	15	848	
No		833	040	
Atrial fibrilation				
Yes	4	173	4975	
No	4	4802	4373	
Heart Failure				
Yes	3	114	4309	
No	3	4195	4307	
Diabetes mellitus				
Yes		807	17557	
No	7	16750	17557	
Dislipidemia			_	
Yes	7	2403	15733	
No	,	13330	13733	

Based on the table above, the gender of the patient as stated in 8 articles shows that the patient is predominantly male. There are 2 articles that include data in the form of patient race with predominantly white skin tone (race). The majority found no history of stroke in the family and also did not consume alcohol reported in 4 articles. Almost all articles (7) identified curret smoke as a risk factor. Hypertension, diabetes mellitus and dyslipidemia were reported as risk factors in 7 studies. In contrast to coronary disease, valvular disease, and atrial fibrillation which were only reported in 4 studies. Only 2 studies identified myocardial infarction as a risk factor.

Risk of Study Bias

The study quality of each article that was determined as the source of systematic review was determined based on the quality analysis of The JBI Critical Appraisal Tools Case Control Studies and The JBI Critical Appraisal Tools Cohort Studies, so that 8 articles were obtained according to the systematic review. The literature results that have been analyzed and determined in a systematic review are as follows

Table 4. Study Assessment Results Using The JBI Critical Appraisal Tools

Reference		The JBI Critical Appraisal Tools									Result	
Reference	1	2	3	4	5	6	7	8	9	10	11	Kesuit
Mitchell et al., 2015	V	V	V	v	V	V	V	V		v		9/10 (90%)
Aigner et al., 2017	v		v			v	V	V		V		6/10 (60%)
Putaala <i>et al.</i> , 2012	v	v	v	v			v	V	v		v	8/11 (72%)
Van Alebeek et al., 2018	v		v	v	V	v	V	V	V		v	9/11 (81%)
Ji <i>et al.</i> , 2013	v	v	v	v			v	V	v		v	8/11 (72%)
Balci <i>et al.</i> , 2011	v	v	V	v	v	v	v				v	8/11 (72%)
Moond et al., 2020	v	V	V	v		v	v				v	7/11 (63%)
Renna et al., 2014	v	V	V	v	V	V	V	V	v	V	v	11/11 (100%)

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When using the JBI Critical Appraisal Tools Cohort Studies, There are 11 questions to guide the appraisal of systematic reviews or meta-analyses. Each question should be answered as "yes", "no", or "unclear". (1) Is the review question clearly & explicity stated? (2) Were the inclusion criteria appropriate for the review question? (3) Was the search strategy appropriate? (4)Were the sources and resources used to search for studies adequate? (5)Were the criteria for appraising studies appropriate? (6) Was critical appraisal conducted by two or more reviewers independently? (7) Were there methods to minimize errors in data extraction? (8) Were the methods used to combine studies appropriate? (9)Was the likelihood of publication bias assessed? (10)Were recommendations for policy and/or practice supported by the reported data? (11)Were the specific directives for new research appropriate?

Of the 8 studies that met the criteria for this systematic review (Table 4), the results obtained are 2 articles of case control study and 6 articles of cohort (1 prospective and 5 retrospective). After performing critical appraisal using The JBI critical appraisal tools, case control studies are given a quality score of six to nine while cohort studies are given a total quality score of seven to eleven on the checklist. Based on the overall study summarized, all research on average contains variable characteristics that are ready to be observed. The assessment bias in the study shows that the results of articles that are assigned to systematic reviews are at risk of selection bias because the determination of sample size in some articles is by non-probability techniques, resulting in a lack of random selection procedures in the study samples.

Risk of Bias from Entire Study

The risk of bias from the review results on several research articles can occur so it is necessary to identify it so that there is no cross-study bias. In the articles that were selected for analysis, most of the studies were cohorts, some articles found the risk of bias such as some characteristics, for example, the risk factors found were not completely proven as it was still in trial. In addition, other confounding variables are also not well paid attention to, and the solutions for these confounding variables are not explained so that they will participate and influence the research results such as genetics and obstructive sleep apnea.

4. DISCUSSION

Summary of Evidence

This systematic review is a summary of the risk factors contributing to ischemic stroke in young adults. In addition, the results of data collected from several studies indicate that the most common risk factors includes hypertension, diabetes, obesity, high consumption of alcohol and smoking.

Stroke is characterised as a neurological deficit credited to an acute focal injury of the central nervous system (CNS) due to vascular reason such as cerebral infarction, intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH). Stroke can be further broken down into 2 types which are ischemic and hemorrhagic. Ischemic stroke has known to be the most comon type of stroke that occurs and this is due to blockage of blood vessel in the neck or the brain. Blockage of such is caused by "the formation of a clot within a blood vessel in he brain or neck, called thrombosis; the movement of the clot from another part of the body such as the heart to the brain which is known as embolism; or a severe narrowing of an artery in or leading to he brain, known as stenosis".

Ischemic stroke can be further broken down into 3 major subtypes such as thrombotic cerebral infarction, embolic cerebral infarctionand lacunar cerebral infarction. The system of categorizing stroke was developed in the multicenter Trial of ORG 10172 in Acute Stroke Treatment which involved the division of stroke into different subtypes according to neurological signs, cerebral imaging and ancillary diagnostic test results which are.

Thrombotic cerebral infarction results from the artherosclerotic obstruction of enormous cervical and cerebral arteries with ischemia in every region of the obstructed artery. This is due to the obstruction at site of the principle artherosclerotic lesion or to embolism from this site to a more distal cerebral arteries.⁹

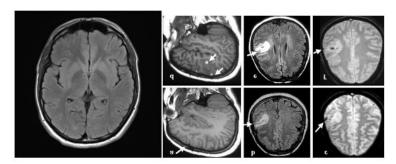


Figure 4.1: Normal brain MRI vs MRI of brain with Thrombolitic Cerebral Infarction. 10

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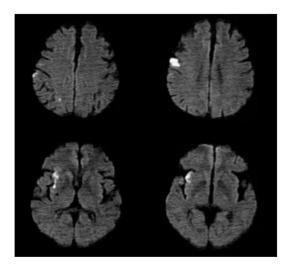


Figure 4.2: Identification of Embolic Stroke Patterns by Diffusion-Weighted MRI.¹¹

Embolic cerebral infarction is due to embolism of coagulation in the cerebral arteries coming from different parts of th arterial framework for instance from the cardial lesions, either at the site of the valves or at the cardial cavities or due to unstable rhythm with statis of the blood which allows clotting within the heart similar to atrial fibrillation.¹²

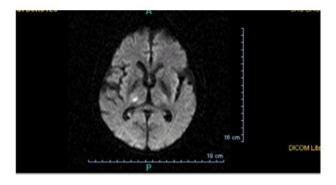


Figure 4.3: Lacunar infarct on brain MRI (diffusion-weighted).¹²

Lacunar cerebral infarction are small deep infarcts in the territory of small penetrating arteries as seen in the MRi picture due to local diseease of these vessels, mainly related to chronic hypertension. ¹³

According to the Clinical Profile of Patients with Cerebrovascular Disease at Stroke Unit , Sanglah General Hospital, Denpasar , Bali journal stroke is an increasing cause of morbidity and mortality in Indonesia. The percentage of younger generation being affected is 19.5% which are mostly younger than 45 years of age. More cases were recorded by men compared to women and the most common type encountered was Ischemic stroke which was 53.7%.

Ischemic stroke in younger adults are far less common than that of older adults yet the underlying pathogenesis and risk factors are more diverse. ¹⁴ Recent studies, both in the United States and Europe, have suggested that ischemic stroke in younger adults is increasing and have demonstrated increases in traditional stroke risk factors that are typically common among older adults (hypertension, dyslipidemia, diabetes mellitus, tobacco use, and obesity) to also be common among younger acute stroke patients. ¹⁵ Risk factors for ischemic stroke in younger adults are not unique to younger adults and overlap considerably with those of older adults but do vary in terms of the percent contribution to ischemic stroke subtypes. The following risk factors and comorbodities were identified, the major risk factors based on the journals observed are: hypertension, diabetes, dyslipidemia. The minor risk factors from the journals observed are: obesity, alcohol consumption, smoking and this is because most of the journals obtained have discussed less about said risk factors.

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It has been well established that hypertension is the main risk factor for stroke as hypertension can cause stroke through numerous mechanism. A high intraluminal pressing factor will prompt extensive alteration in endothelium and smooth muscle functions in intracerebral courses. The excessive stress on the endothelium can build porousness over the bloodbrain barrier and local or multifocal brain oedema. Endothelial obstruction and altered blood cell- endothelium interaction can prompt formation of local thrombi and ischaemic lesions. Fibrinoid necrosis can cause lacunar infarcts through central stenosis and occlusions. Degenerative changes in smooth muscle cells and endothelium inclines for intracerebral hemorrhages. Besides, hypertension quickens the arteriosclerotic interaction, consequently improving the probability for cerebrallesions related to stenosis and embolism originating from huge extracranial vessels, the aortic arch and from the heart. Hypertension was characterised as a systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥ 90 mmHg. High prevalence of hypertension among younger patients was related to obesity, smoking, and hyperlipidemia similar to other developed countries of Asia. Roughly 35% of youthful ischaemic stroke patients were determined to have hypertension. In the Global Burden Study, the PAR for hypertension was most recorded in Southeast Asia (54.8%) and most minimal in Eastern and focal Europe and the Middle East (40.7%).

Diabetes is a well-established risk factor for stroke. It causes pathological chanages in blood vessels at different areas and can prompt stroke if cerebral vessels are directly affected. ¹⁹ It affects the body's ability to create insulin. Since it plays an important role maneuvering glucose into cells from the bloodstream as it fails to do so the patient is left with high glucose level in their blood. Overtime, the excess glucose causes buildup of clots or fats deposit inside vessels that supply blood to the neck and brain, known as atherosclerosis. Increase of deposit causes the blood vessel to narrow or to be blocked, this hinders blood flow to the brain causing sroke to occur. ²⁰ Diabetes mellitus has been identified up to 10% of young stroke patients ²¹ The main three nations with the most elevated predominance incorporate India, China and the USA. The PAR for diabetes mellitus was most recorded in Southeast Asia (28.6%) and least in Western Europe, North-America and Australia (3.5%). ¹⁹

Obesity increases the risk of ischemic stroke due to inflammation caused by excessive fatty tissue. This causes difficulty in blood flow and increases risk of blockage or clotting which results in stroke²² Obesity can be detected by other than body mass index (BMI), such as waist to hip ratio which has shown stronger association with stroke risk.²³ Waist circumference is used as a risk predictor to developing metabolic syndrome, associated with increased risk of cardiovascular disease and diabetes mellitus type 2.²⁴ Higher prevelance is detected in the USA which is 61.1%, Europe 54.8% and East Mediterranean 46% compared with Africa 26.9%, Western Pacific 25.4% and Southeast Asia 13.7%.³

Dyslipidemia contributes to ischemic stroke due to high level of cholestrol or lipids in the body. This causes trouble in blood stream and expands hazard of blockage or thickening which causes stroke.²³ Dyslipedemia is more often found in patients with extracranial or intracranial large artery atherosclerosis and cerebral small vessel disease (CVSD).²² About 50% to 60% of young adult patient with stroke have dyslipidemia which is more common in men compared to women. The general global prevalence of dyslipidaemia was highest in Europe (54%), followed by the North-America (48%), Southeast Asia (29%) and Africa (22.6%).³

High consumption of alcohol has also been associated with increase of risk towards ischemic. Heavy alcohol use which is more than two drinks per day and binge drinking that is more than four drinks in one sitting may increase the risk of recurrent stroke. This is because alcohol contributes to many medical conditions that are risk factors for stroke such as high blood pressure, diabetes, being overweight, atrial fibrillation and liver damage. Heavy episodic alcohol consumption is associated with an increased risk of stroke in young adults (PAR 17.3; 95%CI 14.2 to 20.5 and OR=2.2; 95%CI 1.9 to 2.5) in European countries. Various examinations discovered regional contrasts in the relationship between alcohol comsumption and stroke or other cardiovascular disease, clarified by contrasts in drinking example and sort of liquor. The prevelance is higher in major league salary nations contrasted and low-pay nations. Moreover, episodic heavy alcohol comsumption is higher among men contrasted and women.

Tobacco usage and smoking also increases risk of ischemic stroke about two times more and is associated with ischemic stroke and higher risk of hemorrhagic stroke.²⁹ Conceivable components by which primary and environmental tobacco smoke exposure can increase risk of stroke and cardiovascular disease are various and incorporates carboxyhemoglobinemia, expanded platelet aggregability, high fibrinogen level, low HDL-Cholestrol and toxic effects of compounds such as 1.3-butadiene, a fume stage constituent of ecological tobacco smoke that has been appeared to quicken atherosclerosis.³¹ In stroke patients of all ages, the highest prevalence is reported in Europe (28.7%) and in Southeast Asia (24.8%), whereas the lowest prevalence was reported in Africa (13.9%). The risk of stroke ranges with a PAR of 4.5% in Africa to a PAR of 18.0% in Western Europe, North-America and Australia.²⁸

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The main factor when it comes to administrating treatment for ischemic stroke patients is to ensure that blood flow to the brain is quickly restored. This can be achieved by administrating emergency IV injection in the form of alteplase which is a recombinant tissue plasminogen activator (tPA). The injection is usually administered intravenously in the arm within the first 3 hours. Sometimes tPA can also be given up to 4.5 hours since initial occurance of stroke symptoms. Alteplase functions to restore blood flow by dissolving the blood clot that causing the ischemic stroke. This is achieved by converting plasminogen to the proteolytic enzyme plasmin, which lyses fibrin as well as fibrinigen. Alteplase is administered intravenously at a concentration of 1 mg/mL for the treatment of acute ischemic stroke. Recommended dosage is 0.9mg/kg. The dosage ought not to surpass

90mg . 10% of total dosage gets directed as an intravenous (IV) bolus for more than 1 minute while the infusion of the rest occurs for over 60 minutes.³³

Limitation

Based on the research, the dominant cross sectional study has limitations on the limited research sample. This was followed by a prospective cohort study which had limited follow-up and follow-up to assess definite characteristics. This systematic review found the risk of bias as a limitation of various studies. The biases found from this study include selection bias and information bias. In addition, the risk of bias can also be found from the literature search due to the risk factors found were not completely proven as some were still in trial or was not researched till the full extend such as consumption of alcohol and smoking or high intake of tobacco.

5. CONCLUSION AND SUGGESTIONS

Conclusion

Based on the journals reviewed for the purpose of this systematic review which is to find out the risk factors contributing to ischemic stroke in young adults, it can be concluded that there are major and minor risk factors. The major risk factor consists of hypertension (70%), diabetes mellitus(70%) and dyslipidemia (70%) wherease the minor risk factor consists of obesity (25%), high consumption of alcohol (50%) and smoking (75%). It has also been concluded that younger adults around the age 18 to 50 years old are just as susceptible towards ischemic stroke as the older adults.

Suggestions

For other researchers, it is hoped that they will be able to carry out a follow up analysis about the outcome of the intervention and the prognosis of the risk factors contributing to ischemic stroke in young adults so that it can provide a more informative and complete description of a systematic review.

REFERENCES

- [1] Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A, Elkind MS, George MG, Hamdan AD, Higashida RT, Hoh BL. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2013 Jul;44(7):2064-89.
- [2] Randolph SA. Ischemic stroke workplace Health Saf 64: 444.
- [3] Boot E, Ekker MS, Putaala J, Kittner S, De Leeuw FE, Tuladhar AM. Ischaemic stroke in young adults: a global perspective. Journal of Neurology, Neurosurgery & Psychiatry. 2020 Apr 1;91(4):411-7.
- [4] George MG. Risk factors for ischemic stroke in younger adults: a focused update. Stroke. 2020 Mar;51(3):729-35.
- [5] Krishnamurthi RV, Barker-Collo S, Parag V, Parmar P, Witt E, Jones A, Mahon S, Anderson CS, Barber PA, Feigin VL. Stroke incidence by major pathological type and ischemic subtypes in the Auckland regional community stroke studies: changes between 2002 and 2011. Stroke. 2018 Jan;49(1):3-10.
- [6] Wei W, Li S, San F, Zhang S, Shen Q, Guo J, Zhang L. Retrospective analysis of prognosis and risk factors of patients with stroke by TOAST. Medicine. 2018 Apr;97(15).
- [7] Tini K, Samatra ID, Wiryadana KA, Supadmanaba IG. Clinical profile of patients with cerebrovascular disease at Stroke Unit, Sanglah General Hospital, Denpasar, Bali. Cross Mark. 2020.

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- [8] Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Jama. 2000 Apr 19;283(15):2008-12.
- [9] Moond V, Bansal K, Jain R. Risk Factors and Subtyping of Ischemic Stroke in Young Adults in the Indian Population. Cureus. 2020 Nov;12(11).
- [10] Yao Q, Zhang L, Zhou J, Li M, Jing W, Li X, Han J, He L, Zhang Y. Imaging Diagnosis of Transient Ischemic Attack in Clinic and Traditional Chinese Medicine. BioMed research international. 2019 Feb 17;2019.
- [11] Wessels T, Röttger C, Jauss M, Kaps M, Traupe H, Stolz E. Identification of embolic stroke patterns by diffusion-weighted MRI in clinically defined lacunar stroke syndromes. Stroke. 2005 Apr 1;36(4):757-61.
- [12] Arboix A, Alió J. Acute cardioembolic cerebral infarction: answers to clinical questions. Current cardiology reviews. 2012 Feb 1;8(1):54-67.
- [13] Regenhardt RW, Das AS, Ohtomo R, Lo EH, Ayata C, Gurol ME. Pathophysiology of lacunar stroke: history's mysteries and modern interpretations. Journal of Stroke and Cerebrovascular Diseases. 2019 Aug 1;28(8):2079-97.
- [14] Solcà M, Ronchi R, Bello-Ruiz J, Schmidlin T, Herbelin B, Luthi F, Konzelmann M, Beaulieu JY, Delaquaize F, Schnider A, Guggisberg AG. Heartbeat-enhanced immersive virtual reality to treat complex regional pain syndrome. Neurology. 2018 Jul 31;91(5):e479-89.
- [15] Ji R, Schwamm LH, Pervez MA, Singhal AB. Ischemic stroke and transient ischemic attack in young adults: risk factors, diagnostic yield, neuroimaging, and thrombolysis. JAMA neurology. 2013 Jan 1;70(1):51-7.
- [16] Harris S, Al Rasyid MK, Mesiano T, Hidayat R. Association of high blood homocysteine and risk of increased severity of ischemic stroke events. The International journal of angiology: official publication of the International College of Angiology, Inc. 2019 Mar;28(1):34.
- [17] Chen YM, Lin YJ, Po HL. Comparison of the risk factor profile, stroke subtypes, and outcomes between stroke patients aged 65 years or younger and elderly stroke patients: A hospital-based study. International Journal of Gerontology. 2013 Dec 1;7(4):205-8.
- [18] Wajngarten M, Silva GS. Hypertension and stroke: update on treatment. European Cardiology Review. 2019 Jul;14(2):111.
- [19] Feigin VL, Roth GA, Naghavi M, Parmar P, Krishnamurthi R, Chugh S, Mensah GA, Norrving B, Shiue I, Ng M, Estep K. Global burden of stroke and risk factors in 188 countries, during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. The Lancet Neurology. 2016 Aug 1;15(9):913-24.
- [20] Chen R, Ovbiagele B, Feng W. Diabetes and stroke: epidemiology, pathophysiology, pharmaceuticals and outcomes. The American journal of the medical sciences. 2016 Apr 1;351(4):380-6.
- [21] Tun NN, Arunagirinathan G, Munshi SK, Pappachan JM. Diabetes mellitus and stroke: a clinical update. World journal of diabetes. 2017 Jun 15;8(6):235.
- [22] Aigner A, Grittner U, Rolfs A, Norrving B, Siegerink B, Busch MA. Contribution of established stroke risk factors to the burden of stroke in young adults. Stroke. 2017 Jul;48(7):1744-51.
- [23] Kernan WN, Inzucchi SE, Sawan C, Macko RF, Furie KL. Obesity: a stubbornly obvious target for stroke prevention. Stroke. 2013 Jan;44(1):278-86.
- [24] Mitchell AB, Cole JW, McArdle PF, Cheng YC, Ryan KA, Sparks MJ, Mitchell BD, Kittner SJ. Obesity increases risk of ischemic stroke in young adults. Stroke. 2015 Jun;46(6):1690-2.
- [25] Bener A, Yousafzai MT, Darwish S, Al-Hamaq AO, Nasralla EA, Abdul-Ghani M. Obesity index that better predict metabolic syndrome: body mass index, waist circumference, waist hip ratio, or waist height ratio. Journal of obesity. 2013 Aug 13;2013.
- [26] Djoussé L, Ellison RC, Beiser A, Scaramucci A, D'Agostino RB, Wolf PA. Alcohol consumption and risk of ischemic stroke: the Framingham Study. Stroke. 2002 Apr 1;33(4):907-12.

Vol. 9, Issue 1, pp: (14-25), Month: April 2021 - September 2021, Available at: www.researchpublish.com

- [27] Oza R, Rundell K, Garcellano M. Recurrent ischemic stroke: strategies for prevention. American family physician. 2017 Oct 1;96(7):436-40.
- [28] Reynolds K, Lewis LB. Nolen. et al. Alcohol Consumption and Risk of Stroke: A Meta-analysis. J Am Med Assoc. 2003;289:579-88.
- [29] O'Donnell MJ, Chin SL, Rangarajan S, Xavier D, Liu L, Zhang H, Rao-Melacini P, Zhang X, Pais P, Agapay S, Lopez-Jaramillo P. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. The lancet. 2016 Aug 20;388(10046):761-75.
- [30] Nordahl H, Osler M, Frederiksen BL, Andersen I, Prescott E, Overvad K, Diderichsen F, Rod NH. Combined effects of socioeconomic position, smoking, and hypertension on risk of ischemic and hemorrhagic stroke. Stroke. 2014 Sep;45(9):2582-7.
- [31] Shah RS, Cole JW. Smoking and stroke: the more you smoke the more you stroke. Expert review of cardiovascular therapy. 2010 Jul 1;8(7):917-32.
- [32] Ford GA, Ahmed N, Azevedo E, Grond M, Larrue V, Lindsberg PJ, Toni D, Wahlgren N. Intravenous alteplase for stroke in those older than 80 years old. Stroke. 2010 Nov 1;41(11):2568-74.
- [33] Reed, M., Kerndt, C. C., & Nicolas, D. (2020). Alteplase. Retrieved March 3, 2021, from https://www.ncbi.nlm. nih.gov/books/NBK499977/#:~:text=Mechanismof Action,-Alteplase is a&text=Alteplase converts plasminogen to the,half- life of 72 minutes.