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Meta-Analysis
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Meta-Analysis the Effects of Hypertension, High Density Lipoprotein, and Diabetes Mellitus on the Risk of Stroke

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ABSTRACT

Background: Stroke is defined as an interruption of the blood supply to the brain which is usually caused by a blockage by a blood clot. This causes disruption of the supply of oxygen and nutrients to the brain resulting in damage to brain tissue. This study aims to analyze and estimate the effect of hypertension, high density lipoprotein, and diabetes mellitus on the risk of stroke.
Subjects and Method: This study is a systematic review and meta-analysis using the PRISMA flow chart and the PICO model. Population: adults. Intervention: hypertension, high density lipoprotein, and diabetes mellitus. Comparison: normal blood pressure, normal HDL, and normal blood sugar. Outcome: strokes. The databases used were PubMed, Google Scholar, Science Direct, and Proquest with keywords (hypertension OR "diabetes mellitus" OR "high density lipoprotein") AND stroke AND ("cross sectional" OR "case control") AND aOR. There were 9 case-control studies and 4 cross-sectional studies published in 2013-2023 that met the inclusion criteria. Analysis was performed with RevMan 5.3.
Results: 13 studies from Oman, Iran, Lebanon, Ghana, Finland, Nigeria, China, Japan and Saudi Arabia were selected for meta-analysis. Total sample was 71,037. Had history of hypertension (aOR= 5.48; 95% CI = 2.26 to 13.32; p= 0.002) and diabetes mellitus (aOR = 1.93 ; 95% CI= 1.45 to 2.57; p< 0.001) increased the risk of stroke. High HDL levels reduced the risk of stroke (aOR = 0.46; 95% CI = 0.27 to 0.79; p= 0.004).
Conclusion: History of hypertension and diabetes mellitus increase the risk of stroke. However, high HDL levels reduce the risk of stroke.

Keywords: hypertension, high density lipoprotein, diabetes mellitus, stroke.

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BACKGROUND

Stroke is defined as an interruption of the blood supply to the brain which is usually caused by a blockage by a blood clot. This causes disruption of the supply of oxygen and nutrients to the brain resulting in damage to brain tissue. Stroke is also said to be an acute disorder of nerve function caused by a sudden (within seconds) or quickly (within hours) cerebral circulation disorder, symptoms and signs appear that correspond to the disturbed focal area (Puspitasari, 2020).

According to WHO (World Health Organization), 15 million people suffer from stroke worldwide every year. Of these, 5 million people died and 5 million were permanently disabled (Susilawati & Nurhayati, 2018). According to the results of Riskesdas (2018) the prevalence of stroke in Indonesia rose from 7% in 2013 to 10.9% in 2018, if you look at current trends, it is expected to continue to increase to reach 23.3 million deaths in 2030 (Prayoga and Rasyid, 2022).

Stroke is a very dangerous event because it can cause disability and even death. To reduce the incidence of stroke which continues to increase, prevention efforts are needed regarding what are the risk factors that trigger its occurrence. There are two risk factors that trigger stroke, namely risk factors that can be controlled and those that cannot be controlled. The uncontrollable risk factor is gender. Risk factors that can be controlled include Body Mass Index (BMI), High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL), triglycerides, total cholesterol, blood pressure, and Blood Sugar Levels (KGD) (Astuti et al. , 2019).

Based on research by Ganguly et al. (2021), people with a history of hypertension have a risk of having a stroke 5.1 times compared to those without a history of hypertension. People with low HDL levels have a risk of having a stroke 3.3 times compared to normal HDL levels. Mohammad (2020) said that people with a history of diabetes mellitus have a risk of having a stroke 2.7 times compared to those without a history of diabetes mellitus.

Based on research conducted by Khodabandehlou et al. (2016) this research is supported by Kivioja et al. (2018) they concluded that low HDL levels affect the incidence of stroke. However, in contrast to the research conducted by Hu et al. (2023) which stated that low HDL levels had no effect on the incidence of stroke.

Based on several research findings on factors that influence the occurrence of stroke, it was found that there was a gap between the results of one study and another study, namely that there were differences in the adjusted odds ratio (aOR) and the p-value between the effects of hypertension, high density lipoprotein, and diabetes mellitus on the incidence of stroke. . Some of these studies were also conducted in different countries and in different years. Therefore, researchers are interested in conducting a study using a systematic review and meta-analysis of various results of previous primary studies.

The data obtained by the researchers will be analyzed using a meta-analytic study design, which is an epidemiological study that provides the strongest evidence in terms of causality by combining and statistically unifying the results of a number of independent primary studies that can be combined (Murti, 2018). This study aims to determine the effect of hypertension, high density lipoprotein, and diabetes mellitus on the incidence of stroke based on the results of similar previous studies.

SUBJECTS AND METHOD

1. Study Design

This research was conducted by systematic review and meta-analysis using primary data, namely data from similar previous research results. Article search using several databases, namely: PubMed, Google Scholar, Science Direct, and Proquest. The keywords used were (hypertension OR "diabetes mellitus" OR "high density lipoprotein") AND stroke AND ("cross sectional" OR "case control") AND aOR. There were 13 primary studies that met the inclusion criteria of this study.

2. Steps of Meta-Analysis

1) Formulate research questions through the PICO format (Population, Intervention, Comparison, Outcome).
2) Search for primary study research articles from several databases, namely: PubMed, Google Scholar, Science Direct, and Proquest Google Scholar.
3) Conducting article selection by determining inclusion and exclusion criteria and conducting critical assessments.
4) Extracting selected primary study data and synthesizing effect estimates using the RevMan 5.3 application.
5) Interpret the results and draw conclusions.

3. Inclusion Criteria

Full-text articles using a case-control or cross-sectional study design, the study subjects were adults, the study outcome was stroke, and the results of the analysis used were multivariate analysis with adjusted odds ratio (aOR) to measure the estimated effect.

4. Exclusion Criteria

Articles published in languages other than English, articles before 2013, and outcome measures in research are incomplete or do not clearly describe results.

5. Operational Definition

Stroke is a form of disease due to disruption of the blood supply to the brain, acute neurological dysfunction caused by a sudden and rapid disruption of blood vessels.

Hypertension is an increase in systolic blood pressure greater than 140 mmHg and diastolic greater than 90 mmHg on two measurements with an interval of 5 minutes in a state of sufficient rest (quiet).

High Density Lipoprotein is a high density lipoprotein and contains a lot of protein and little fat.

Diabetes Mellitus is a chronic metabolic disorder caused by the pancreas not producing enough insulin or the body not being able to use the insulin it produces effectively. The result is an increase in the concentration of glucose in the blood.

6. Instrument

The quality assessment of the main articles in this study used the Primary Study Quality Assessment for Case-Control and Cross-Sectional Observational Study Designs.

7. Data Analysis

The articles in this study were collected using the PRISMA diagram and analyzed using the Review Manager 5.3 application (RevMan 5.3) by calculating the effect size and heterogeneity (I2) to determine the combined research model and form the final results of the meta-analysis. The results of data analysis are presented in the form of forest plots and funnel plots.

RESULTS

The process of searching for primary articles related to the effect of hypertension, high density lipoprotein, and diabetes mellitus on the incidence of stroke in this meta-analysis study was carried out in several databases and the results obtained were 13 articles which can be seen in Figure 1 PRISMA Flow Diagram. The total number of articles in the initial search process was 3,081 articles. After the process of deleting published articles, 1,244 articles were found, with 154 of them meeting the requirements for a full text review. Furthermore, as many as 13 articles that met the quality assessment were included in the quantitative synthesis using meta-analysis.

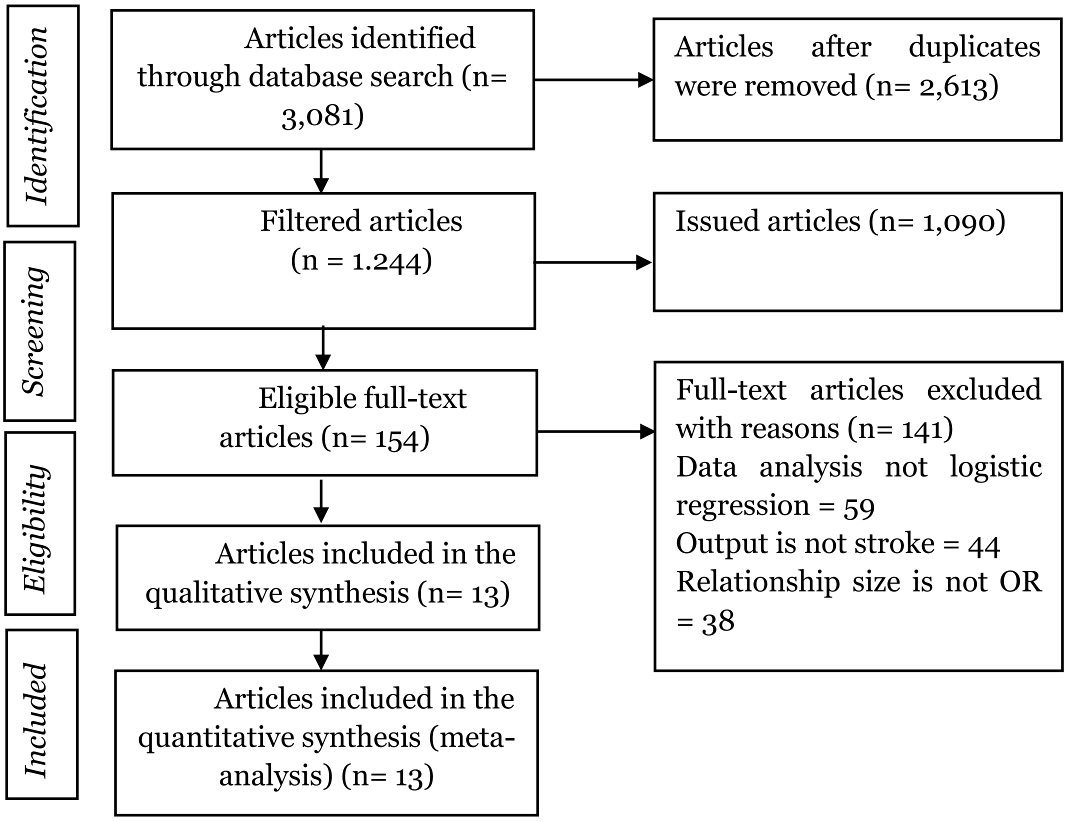

Figure 1. PRISMA flow diagram

Figure 2 shows the distribution area of the 13 primary articles used in this study, namely from the continents of Asia, Africa and Europe. There are 10 research articles from the continent of Asia, 2 research articles from the continent of Africa, and 1 article from the continent of Europe. The research locations are from Finland, Nigeria, Ghana, Oman, Iran, Lebanon, Saudi Arabia, China, and Japan.

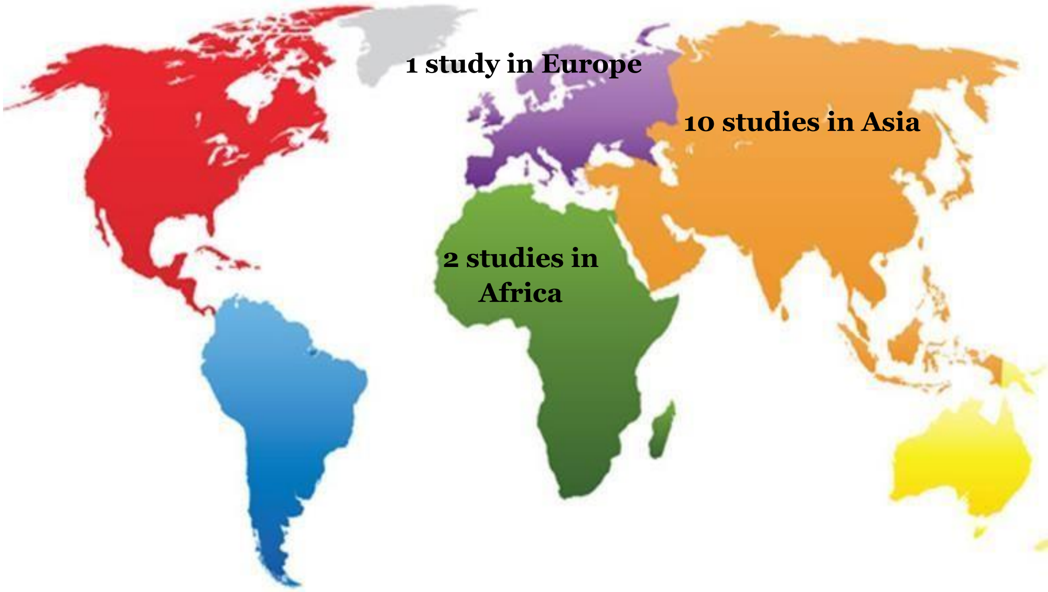

Figure 2. Map of the research area on the effect of hypertension, high density lipoprotein, and diabetes mellitus on the incidence of stroke

Table 1 shows the results of the primary research quality assessment used for this study. The assessment of the quality of the primary studies in this study was carried out using the Primary Study Quality Assessment for Case-Control and Cross-Sectional Observational Study Designs in Meta-Analytic Research sourced from the Master's Program in Public Health, Post-graduate School, Universitas Sebelas Maret.

Based on the assessment of the quality of the studies, a total score of 14 answers was obtained, indicating that each study was of good quality, so it deserved to be included in the meta-analysis.

Table 1. Results of the quality assessment of case-control studies on the effect of hypertension, high density lipoprotein, and diabetes mellitus on the incidence of stroke

Author (Year)	Criteria of Questions							Total
	1	2	3	4	5	6	7	
Ganguly *et al.* (2020)	2	2	2	2	2	2	2	14
Khodabandehlou *et al. (*2016)	2	2	2	2	2	2	2	14
El-Hajj *et al.* (2019)	2	2	2	2	2	2	2	14
Sarfo *et al.* (2022)	2	2	2	2	2	2	2	14
Kivioja *et al.* (2018)	2	2	2	2	2	2	2	14
Owolabi *et al.* (2018)	2	2	2	2	2	2	2	14
Mohammad (2020)	2	2	2	2	2	2	2	14
Zhang *et al.* (2021	2	2	2	2	2	2	2	14
Chei *et al.* (2013)	2	2	2	2	2	2	2	14

Description of the question criteria:

1. Formulation of research questions in the acronym PICO

a. Was the population in the primary study the same as the population in the PICO meta-analysis?

b. Is the operational definition of exposure/ intervention in the primary study the same as the definition intended in the meta-analysis?

c. Was the comparison used in the primary study the same as that planned for the meta-analysis?

d. Were the outcome variables studied in the primary study the same as those planned in the meta-analysis?

2. Methods for selecting research subjects

a. Does the accessible population represent the target population?

b. Were the case and control groups selected at the beginning of the study?

3. Methods for measuring comparisons (intervention) and outcome variables

a. Were exposure/intervention and outcome variables measured by the same instrument (measuring instrument) in all primary studies?

b. If variables are measured on a categorical scale, are the cutoffs or categories used the same between the primary studies?

4. Design-related bias

a. Is there a possibility of "Recall Bias"?

b. What have the primary studies done to prevent or address this bias?

5. Methods to control confounding

a. Was there any confusion in the results/ conclusions of the primary study?

b. Did the primary study investigator use appropriate methods to control for the effects of ambiguity?

6. Methods of statistical analysis

a. In case-control studies, was a multivariate analysis performed? Multivariate analysis includes multiple linear regression analysis, multiple logistic regression analysis, Cox regression analysis.
b. Whether the primary study reports effect sizes or relationships on multivariate analysis (eg, adjusted OR, adjusted regression coefficient)

7. Conflict of interest

Is there a conflict of interest with the research sponsor?

If there is a conflict of interest, give a value of "0".

If there is no conflict of interest, give a value of "2".

If in doubt, rate it "1".

Table 2 Results of quality assessment of cross-sectional studies on the effect of hypertension, high density lipoprotein, and diabetes mellitus on the incidence of stroke

Author (Year)	Criteria of Questions							Total
	1	2	3	4	5	6	7	
Zhang et al. (2017)	2	2	2	2	2	2	2	14
Xing et al. (2019)	2	2	2	2	2	2	2	14
Yi et al. (2020)	2	2	2	2	2	2	2	14
Li et al. (2022)	2	2	2	2	2	2	2	14

Description of the question criteria:

1. Formulation of research questions in the acronym PICO

a. Was the population in the primary study the same as the population in the PICO meta-analysis?
b. Is the operational definition of exposure/ intervention in the primary study the same as the definition intended in the meta-analysis?
c. Was the comparison used in the primary study the same as that planned for the meta-analysis?
d. Were the outcome variables studied in the primary study the same as those planned in the meta-analysis?

2. Methods for selecting research subjects

a. Descriptive cross-sectional (prevalence) study: Was the sample randomly selected?
b. Analytic cross-sectional study: Was the sample chosen randomly or purposively?

3. Methods for measuring comparisons (intervention) and outcome variables

a. Were exposure/intervention and outcome variables measured by the same instrument (measuring instrument) in all primary studies?
b. If variables are measured on a categorical scale, are the cutoffs or categories used the same between the primary studies?

4. Design-related bias

a. What is the Response Rate?
b. Is non-response related to outcome?

5. Methods to control confounding

a. Was there any confusion in the results/ conclusions of the primary study?
b. Did the primary study investigator use appropriate methods to control for the effects of ambiguity?

6. Methods of statistical analysis

a. In which cross-sectional study was a multivariate analysis performed?

Multivariate analysis includes multiple linear regression analysis, multiple logistic regression analysis, Cox regression analysis.

b. Does the primary study report effect sizes or relationships on multivariate analysis? (eg, adjusted OR, adjusted regression coefficient).

7. Conflict of Interest

Is there a conflict of interest with the research sponsor?

If there is a conflict of interest, give a value of "0".

If there is no conflict of interest, give a value of "2".

If in doubt, rate it “1”.

Effect of Hypertension on Stroke Incidence

Table 2 presents a description of the 7 observational case-control study articles as a source for a meta-analysis of the effect of hypertension on stroke events.

Table 2. Description of the primary hypertension studies included in the meta-analysis

Author (Year)	Country	Sample	P	I	C	O
Ganguly *et al.* (2020)	Oman	510	>18 years	Hypertension	Normotension	Stroke
Khodabandehlou *et al.* (2016)	Iran	144	>40 years	Hypertension	Normotension	Stroke
El-Hajj *et al.* (2019)	Lebanon	300	>15 years	Hypertension	Normotension	Stroke
Sarfo *et al.* (2022)	Ghana	2,431	>18 years	Hypertension	Normotension	Stroke
Kivioja *et al.* (2018)	Finlandia	2,364	25-49 years	Hypertension	Normotension	Stroke
Owolabi *et al.* (2018)	Nigeria	4,236	>18 years	Hypertension	Normotension	Stroke
Mohammad (2020)	Saudi Arabia	194	>40 years	Hypertension	Normotension	Stroke

Based on table 2, the description of primary research on the effect of hypertension on the incidence of stroke was conducted through a meta-analysis of 7 articles. The research locations varied, namely Oman, Iran, Lebanon, Ghana, Finland, and Nigeria. In this study, similarities were found, namely the study design used case-control, the research subjects were adults, the intervention given was hypertension with normal blood pressure as a comparison. In this study, there were differences in the number of samples used, namely the smallest was 144 and the largest sample was 4,236. The total number of samples included in the meta-analysis of the effect of hypertension on the incidence of stroke was 10.179 respondents.

Table 3 lists the results of a statistical summary of the estimated effect with the highest aOR value of 14.24 and the lowest aOR value of 1.43. CI 95% with the largest range of 4.02 to 50.44, while the smallest range is 1.17 to 1.75.

Table 3. Data of adjusted odds ratio (aOR) and 95% confidence interval (95% CI) on the effect of hypertension on the incidence of stroke

Author	Year	aOR	95% CI	
			Lower Limit	Upper Limit
El-Hajj	2019	14.24	4.02	50.44
Ganguly	2020	5.17	2.92	9.15
Khodabandehlou	2016	6.92	2.12	22.59
Kivioja	2018	1.43	1.17	1.75
Mohammad	2020	2.10	1.02	4.32
Owolabi	2018	11.93	7.09	20.07
Sarfo	2022	10.34	6.91	15.47

The forest plot in Figure 3 shows that hypertension increases the likelihood of stroke. People with a history of hypertension have a risk of having a stroke 5.48 times compared to those without a history of hypertension and the results of the relationship are statistically significant (aOR= 5.48; 95% CI= 2.26 to 13.32; p= 0.002). The effect estimates between studies showed high heterogeneity (I^2= 95%; p <0.001), with the calculation of the average effect estimation using the Random Effect Model (REM) approach.

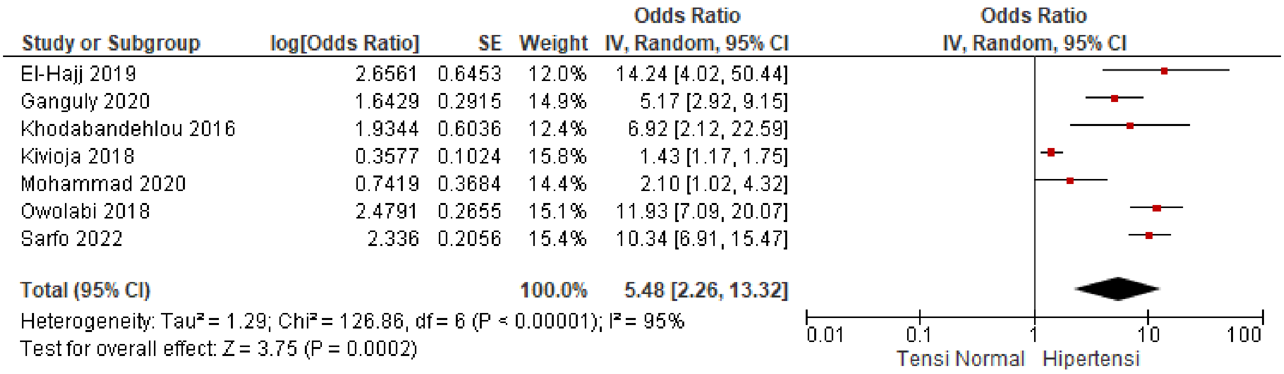

Figure 3. Forest plot of the effect of hypertension on the incidence of stroke

The funnel plot in Figure 4 shows the distribution of effect estimates slightly more to the right than to the left of the mean vertical line for the primary study with a small sample, indicating a slight publication bias. Because the estimated effect on the funnel plot is more on the right side of the same as the diamond shape on the forest plot which is located to the right of the vertical line of hypothesis 0, the publication bias tends to overestimate the true effect (overestimate).

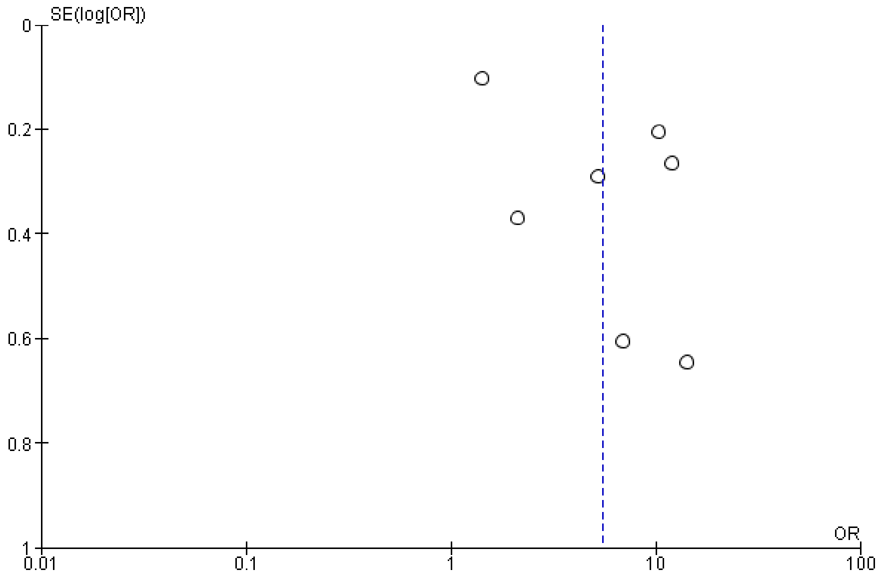

Figure 4. Funnel plot of the effect of hypertension on the incidence of stroke

Effect of High Density Lipoprotein on Stroke Incidence

Table 4 presents descriptions of 5 observational cross-sectional study articles as a source of meta-analysis of the effect of high density lipoprotein on stroke events.

Table 4 presents descriptions of 5 observational cross-sectional study articles as a source of meta-analysis of the effect of high density lipoprotein on stroke events

Author (Year)	Country	Sample	P	I	C	O
Ganguly et al. (2020)	Oman	510	>18 years	High HDL	Normal HDL	Stroke
Khodabandehlou *et al.* (2016)	Iran	144	>40 years	High HDL	Normal HDL	Stroke
Zhang *et al.* (2021)	China	4,926	>35 years	High HDL	Normal HDL	Stroke
Chei *et al.* (2013)	Jepang	13,314	40-85 years	High HDL	Normal HDL	Stroke
Kivioja *et al.* (2018)	Finlandia	2,364	25-49 years	High HDL	Normal HDL	Stroke

Based on table 4 description of primary research on the effect of high density lipoprotein on the incidence of stroke, a meta-analysis of 5 articles was carried out. The research locations varied, namely Oman, Iran, China, Japan, and Finland. In this study, similarities were found, namely the study design used case-control, the research subjects were adults, the intervention given was high HDL compared to normal HDL. In this study there were differences in the number of samples used, namely the smallest numbered 144 and the largest sample numbered 13,314.

Table 5 lists the results of a statistical summary of the estimated effect with the highest aOR value of 0.93 and the lowest aOR value of 0.14.

Table 5. Data of adjusted odds ratio (aOR) and 95% confidence interval (95% CI) effect of high density lipoprotein on the incidence of stroke

Author	Year	aOR	Lower Limit	Upper Limit
Chei	2013	0.47	0.20	1.10
Ganguly	2020	0.29	0.17	0.49
Khodabandehlou	2016	0.14	0.04	0.49
Kivioja	2018	0.55	0.41	0.74
Zhang	2021	0.93	0.77	1.12

The forest plot in Figure 5 shows that high density lipoprotein reduces the likelihood of stroke. People with high HDL levels had a risk of having a stroke by 0.46 times compared to normal HDL levels and the results of the relationship were statistically significant (aOR= 0.46; 95% CI= 0.27 to 0.79; p<0.004). Effect estimates between studies show high heterogeneity (I2 = 86%; p= 0.001), with the calculation of the average effect estimation using the Random Effect Model (REM) approach.

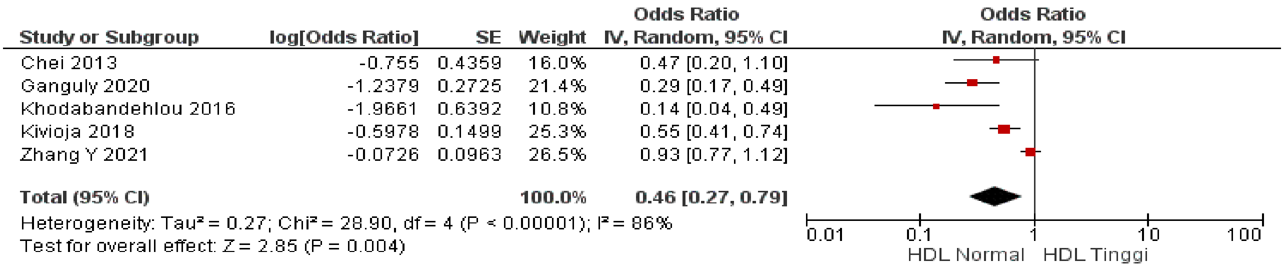

Figure 5. Forest plot of the effect of high density lipoprotein on the incidence of stroke

The funnel plot in Figure 6 shows that the distribution of effect estimates is slightly more to the left than to the right of the mean vertical line for primary studies with small samples. Figure 6 shows that there is a publication bias (overestimate).

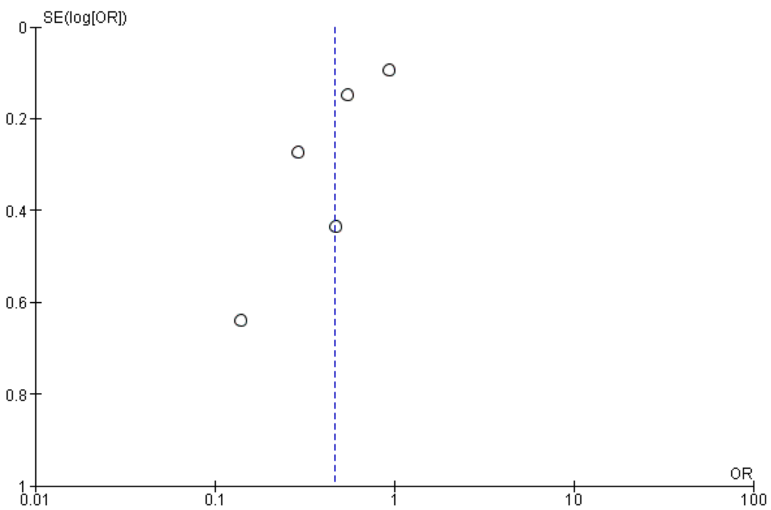

Figure 6. Funnel plot of the effect of high density lipoprotein on the incidence of stroke

Effect of Diabetes Mellitus on Stroke

Table 6 presents descriptions of 8 observational case-control and cross-sectional study articles as a source of meta-analysis of the effect of diabetes mellitus on stroke events. Based on table 6 description of primary research on the effect of diabetes mellitus on the incidence of stroke, a meta-analysis of 4 articles was carried out. The research locations varied, namely Iran, Lebanon, and Saudia Arabia. In this study, similarities were found, namely the study design used case-control, the research subjects were adults, the intervention provided was diabetes mellitus with normal blood sugar in comparison. In this study there was a difference in the number of samples used, namely the smallest was 144 and the largest sample was 2,431.

Table 6. Description of primary diabetes mellitus case-control studies included in the meta-analysis

Author (Year)	Country	Sample	P	I	C	O
Khodabandehlou *et al.* 2016	Iran	144	>40 years	Diabetes melitus	Normal blood sugar	Stroke
El-Hajj et al. (2019)	Lebanon	300	>15 years	Diabetes melitus	Normal blood sugar	Stroke
Mohammad (2020)	Saudi Arabia	194	>40 years	Diabetes Melitus	Normal blood sugar	Stroke
Sarfo *et al.* (2022)	Ghana	2,431	>18 years	Diabetes Melitus	Normal blood sugar	Stroke

Based on table 7, the description of primary research on the effect of diabetes mellitus on the incidence of stroke was conducted through a meta-analysis of 4 articles. Research location in China. In this study, similarities were found, namely the study design used cross-sectional, the research subjects were adults, the intervention provided was diabetes mellitus with normal blood sugar in comparison. In this study there were differences in the number of samples used, namely the smallest was 4,100 and the largest sample was 16,829.

Table 7. Description of the primary cross-sectional studies of diabetes mellitus included in the meta-analysis

Author (Year)	Country	Sample	P	I	C	O
Zhang *et al.* (2017)	China	4,100	>40 years	DM	Normal blood sugar	Stroke
Xing *et al.* (2019)	China	10,926	>40 years	DM	Normal blood sugar	Stroke
Yi *et al.* (2020)	China	16,892	>40 years	DM	Normal blood sugar	Stroke
Li *et al.* (2022)	China	10,700	>40 years	DM	Normal blood sugar	Stroke

Table 8. Data adjusted odds ratio (aOR) and 95% confidence interval (CI 95%) case-control study of the effect of diabetes mellitus on the incidence of stroke

Author	Year	aOR	95% CI	
			Lower Limit	Upper Limit
Li et al.	2022	1.32	0.92	1.89
Xing et al.	2019	1.37	1.12	1.68
Yi et al.	2020	1.65	1.31	2.08
Zhang et al.	2017	1.38	0.94	2.03

Table 9. Data of adjusted odds ratio (aOR) and 95% confidence interval (95% CI) cross-sectional study of the effect of diabetes mellitus on the incidence of stroke

Author	Year	aOR	95% CI	
			Lower Limit	Upper Limit
El-Hajj	2019	1.51	0.38	6.00
Mohammad	2020	2.72	1.94	3.81
Owolabi	2018	2.70	1.96	3.72
Sarfo	2022	3.44	2.60	4.55

The forest plot in Figure 7 shows that diabetes mellitus increases the likelihood of stroke. People with a history of diabetes mellitus had a risk of having a stroke 1.93 times compared to those without a history of diabetes mellitus and the results of this relationship were statistically significant (aOR= 1.93; 95% CI= 1.45 to 2.57; p < 0.001). The effect estimates between studies showed high heterogeneity (I^2= 84%; p= 0.01), with the calculation of the average effect estimation using the Random Effect Model (REM) approach.

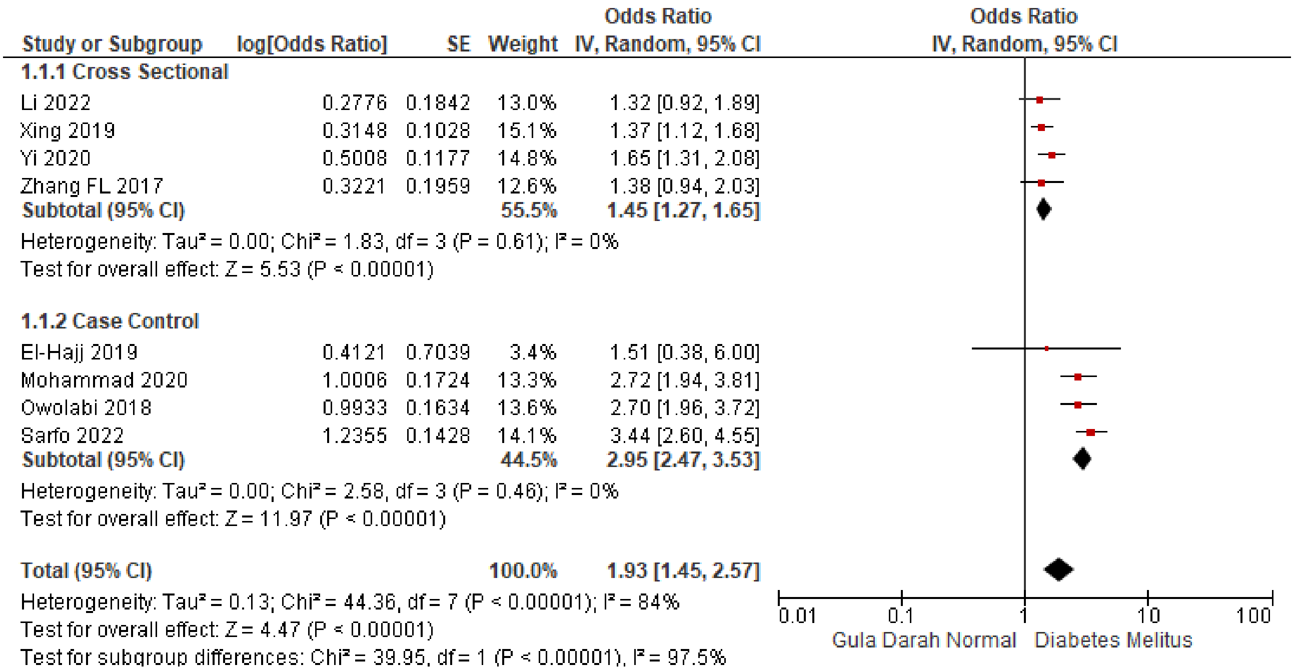

Figure 7. Forest plot of the effect of diabetes mellitus on the incidence of stroke

The funnel plot in Figure 8 shows that the distribution of effect estimates is slightly more to the left than to the right of the mean vertical line for primary studies with small samples. Figure 8 shows that there is publication bias (underestimate).

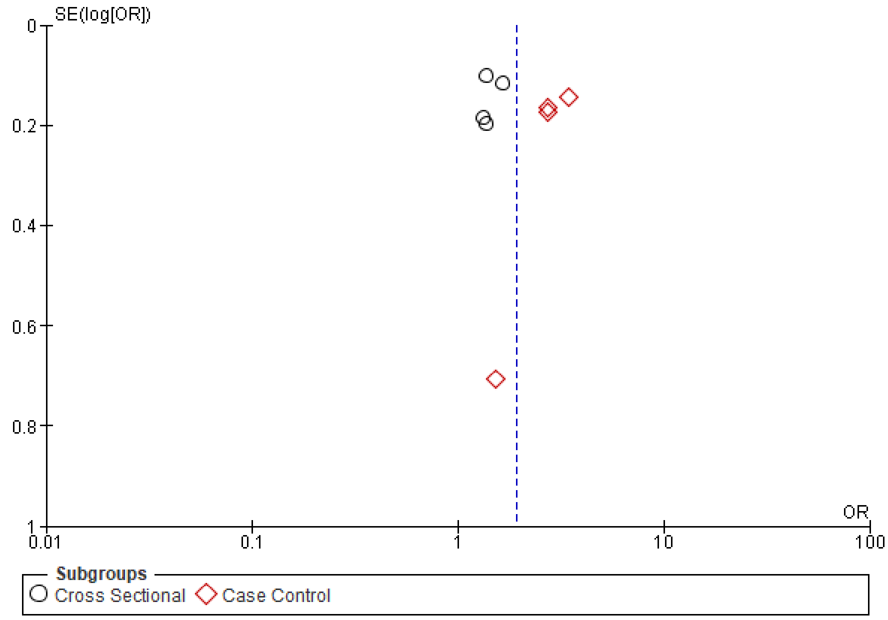

Figure 8. Funnel plot of the influence of diabetes mellitus on the incidence of stroke

DISCUSSION

1. Effect of Hypertension on Stroke

Hypertension can trigger a stroke. This is because hypertension gives blood pressure a high range and pushes the sides of the arteries consistently. In addition, hypertension places an additional workload on the heart, damaging arteries and organs over time. Therefore, people diagnosed with hypertension are more likely to have a stroke. A study also shows about 87% of strokes are caused by narrowing of blood vessels in the brain. This narrowing blocks blood flow to brain cells, thereby increasing the number of blood clots in the artery walls. In addition, around 13% of blood vessels rupture near the brain which causes a stroke (Puspitasari, 2020).

A total of 7 case-control observational research articles as a source of meta-analysis of the effect of hypertension on the incidence of stroke. This study shows that hypertension increases the likelihood of stroke. People with a history of hypertension have a risk of having a stroke 5.48 times compared to those without a history of hypertension. In line with research that has been conducted to determine the effect of hypertension on the incidence of stroke, including by El-hajj et al., (2019) which shows that people who suffer from hypertension will be at risk 12.5 times compared to those who do not suffer from hypertension. Musung et al., (2022) also said that people who have a history of hypertension will be at risk of having a stroke by 8.1 times higher than those who are not hypertensive.

2. Effect of High Density Lipoprotein on Stroke

Low levels of HDL will result in the formation of atherosclerotic plaques which can result in a stroke in someone (Hasan et al., 2022). A total of 5 case-control observational research articles as a source of meta-analysis of the effect of high density lipoprotein on the incidence of stroke. This study shows that high density lipoprotein reduces the possibility of stroke. People with high HDL levels had a risk of having a stroke by 0.46 times compared to normal HDL levels and the results of the relationship were statistically significant (aOR= 0.46; 95% CI= 0.27 to 0.79; p<0.004).

The following research was conducted to determine the effect of HDL on the incidence of stroke, including by Khodabandehlou et al., (2016) showed that people who have low HDL levels will be at risk of having a stroke by 6.8 times higher than those who do not have low HDL levels. According to Ganguly et al., (2021) people who have low HDL levels will be at risk 3.3 times compared to those who do not have low HDL levels.

3. Effect of Diabetes Mellitus on Stroke

Diabetes increases the risk of stroke because excess glucose in the blood causes vasculopathy, making it more likely to develop hypertension and atherosclerosis. In addition, diabetes increases the risk of blood clots, which can cause heart attacks and strokes. Excess sugar in the blood has a direct effect on the walls of blood vessels, binding to and changing the structure of the proteins and molecules that line blood vessels, making vessels thicker, less elastic, and more likely to trigger thrombosis. Thicker and less elastic blood vessels mean that blood has a harder time flowing through the narrower openings, and must do so at a higher pressure. These changes cause tissue damage which is called end organ damage. The smaller space for blood to flow means a greater chance that a clot can completely block a blood vessel, causing a stroke or heart attack.

A total of 8 cross-sectional and case-control observational research articles as a source of meta-analysis of the effect of diabetes mellitus on the incidence of stroke using subgroup analysis showed that diabetes mellitus increases the likelihood of stroke. People with a history of diabetes mellitus had a risk of having a stroke 1.93 times compared to those without a history of diabetes mellitus and the results of this relationship were statistically significant (aOR= 1.93; 95% CI= 1.45 to 2.57; p < 0.001).

This research is in line with Benjamin et al., (2016) which states that there is an effect of diabetes mellitus on the incidence of stroke. People who have a history of diabetes mellitus have a 3.4 times higher risk of having a stroke compared to people who do not have a history of diabetes mellitus. Mohammad, (2020) also said that people who have a history of diabetes mellitus will be at risk 2.7 times compared to those who do not have a history of diabetes mellitus.

AUTHORS CONTRIBUTION

Najlah Amalia as a researcher who selects topics, searches for and collects research data. Vitri Widyaningsih and Burhannudin Ichsan analyzed the data and reviewed research documents.

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CONFLICT OF INTEREST

There is no conflict of interest in this study.

REFERENCE

Astuti AT, Subanti S, Susanti Y (2019). Regresi logistik biner untuk mengetahui faktor risiko yang mempegaruhi stroke non-hemoragik pada usia produktif (Binary logistic regression to determine the risk factors that affect non-hemorrhagic stroke in productive age).

Benjamin LA, Corbett EL, Connor MD, Mzinganjira H, Kampondeni S, Choko A, Hopkins M, et al. (2016). HIV, antiretroviral treatment, hypertension, and stroke in Malawian adults a case-control study. Neurology, 86.

Boehme A K, Esenwa C, & Elkind M S V. (2017). Stroke risk factors, genetics , and prevention. Circ. Res., 472–495. https://doi.org/10.1161/CIRCRESAHA.116.308398

CEBMa. (2014). Critical appraisal for case-control study. Center for Evidence Based Management.https://www.cebma.org/wp-content/uploads/Critical-Appraisal-Questions-for-a-Case-Control-Study.pdf

Chei C, Yamagishi K, Kitamura A, Kiyama M, Imano H, Ohira T, Cui R, et al. (2013). High-density lipoprotein subclasses and risk of stroke and its subtypes in Japanese population. Stroke, 327–333. https://doi.org/10.1161/STROKEAHA.112.674812

Chen R, Ovbiagele B, & Feng W. (2017). Diabetes and stroke: epidemiology, pathophysiology, pharmaceuticals and outcomes. Am J Med Sci., 351(4): 380–386. https://doi.org/10.1016/j.amjms.2016.01.011.Diabetes

Cochrane. (2014). RevMan 5.3 user guide. Cochrane Library.

Daneshfard B, Izadi S, Shariat A, Toudaji M A, Beyzavi Z, Niknam L (2015). Epidemiology of stroke in Shiraz, Iran. Iran. J. Neurol., 14(3): 158–163.

Dinata C A, Syafrita Y, & Sastri S. (2013). Gambaran faktor risiko dan tipe stroke pada pasien rawat inap di bagian penyakit dalam RSUD Kabupaten Solok Selatan periode 1 Januari 2010 - 31 Juni 2012 (Overview of risk factors and types of stroke in inpatients in the internal medicine department of Solok Selatan District General Hospital for the period 1 January 2010 - 31 June 2012). Jurnal Kesehatan Andalas, 2(2): 57–61.

El-hajj M, Salameh P, Rachidi S, Al-hajje A, & Hosseini H. (2019). Cigarette and waterpipe smoking are associated with the risk of stroke in Lebanon. J Epidemiol Glob Health., 9(1): 62–70.

Ganguly S S, Gujjar A R, Harthi H Al, Hashmi A Al, Jaju S, Al-Mahrezi A, & Al-Asmi A R. (2021). Risk factors for ischaemic stroke in an Omani Community. Sultan Qaboos Univ. Med. J., 21(4): 585–590.

Harahap HS, Hunaifi I, Sahidu MG, Gunawan E, Putri SA, Susilawati NN A, Kholida BH (2021). Hipertensi sebagai determinan utama untuk peningkatan risiko stroke pada populasi penduduk di daerah Pesisir (Hypertension as the main determinant for increased risk of stroke in the population in the Coastal area). Jurnal Kedokteran Unram, 10(3): 789–795.

Hasan A M, Rahmayani F, Rudiyanto W (2022). Pengaruh kadar LDL dan HDL pada stroke. Jurnal Penelitian Perawat Profesional (The Effect of LDL and HDL levels on stroke. Journal of Professional Nurse Research), 4(4): 1245–1252.

Hill MD (2014). Stroke and diabetes mellitus. Handbook of clinical neurology. Elsevier, 126: 167–174. https://doi.org/10.1016/B978-0-444-53480-4.0-0012-6

Hu Y, Song M, Wu D, Zhang Y, Li G, & Luo H. (2023). The association between HDL-C and stroke in the middle-aged and elderly : a cross-sectional study. Brain Behav., 1–8. https://doi.org/-

10.1002/brb3.2901

Kementrian Kesehatan RI (2014). Profil kesehatan Indonesia 2014.

Khodabandehlou M, Mansournia MA, Mehrpour M, Holakouie-Naieni K (2016). Risk factors asociated with ischemic stroke: a case-control study. Journal of Biostatistics and Epidemiology, 2(3): 111–117.

Kivioja R, Martinez-majander N, Gordin D, Havulinna A S, Aarnio K, Curtze S, Rodr J, Surakka I, et al. (2018). Risk factors for early-onset ischemic stroke: a case-control study. J. Am. Heart Assoc., 1–9. https://doi.org/-10.1161/JAHA.118.009774

Li Z, Hu Q, Ji W, Fan Q (2022). Prevalence of stroke and associated risk factors : a population-based cross-sectional study from the Qinghai-Tibet Plateau of China. BMJ Open, 12, 1–10. https:-//doi.org/10.1136/bmjopen-2022-065605

Lindgren A. (2014). Risc factors. In: NORVING, B. (ed.) Oxford textbook of stroke and cerebrovascular disorder. Oxford University Press.

Mabruri MA, Retnowati L, Lingling (2019). Faktor risiko yang mempengaruhi kejadian stroke pada pasien usia pertengahan (45-60 tahun) di ruang krissan RSUD Bangil Kabupaten Pasuruan (Risk factors that influence the incidence of stroke in middle-aged patients (45-60 years) in the chrysanthemum room at Bangil Hospital, Pasuruan Regency). Jurnal Keperawatan Terapan, 5(02): 172–183.

Mandala AS, Esfandiari F (2020). Hubungan tekanan darah terkontrol dan tidak terkontrol terhadap kadar high density lipoprotein pasien hipertensi (Relationship between controlled and uncontrolled blood pressure on high density lipoprotein levels in hypertensive patients). Jurnal Ilmiah Kesehatan Sandi Husada, 11(1): 379–386. https://doi.org/10.35816/jiskh.v10i2-.296

Meschia JF, Bushnell C, Boden-albala B, Braun LT, Bravata D M, Chaturvedi S, Creager M A, et al. (2014). Guidelines for the primary prevention of stroke. https://doi.org/10.1161/STR.000000 0000000046

Moenadjat R, Kekalih A, Friska D, Widyahening IS, Lalisang TJM (2020). Penelitian bedah seri 1 (Series 1 surgical research): penelitian berbasis bukti. Universitas Indonesia Publishing.

Mohammad Y. (2020). Siesta and risk for ischemic stroke: results from a case-control study. Medicina, 56(222): 1–8.

Murti B. (2018). Prinsip dan metode riset epidemiologi (5th ed.) (Epidemiological research principles and methods (5th ed.)). Program Studi Ilmu Kesehatan Masyarakat.

Musung J M, Kakoma P K, Bugeme M, Banze J P M, Mukeng C K, Muyumba O N, Kamalo B M, et al. (2022). Risk factors for hemorrhagic stroke among adults in the democratic republic of the Congo : a hospital-based study in a limited resource setting. Stroke Res. Treat., 1–7.

Nikolakopoulou A, Chaimani A, Veroniki AA, Vasiliadis HS, Schmid CH, Salanti G (2014). Characteristics of networks of interventions : a description of a database of 186 published networks. Plos One, 9(1): 1–10. https://doi.org/-10.1371/journal.pone.0086754

Nopia D, Huzaifah Z (2020). Hubungan antara klasifikasi stroke dengan gangguan fungsi kognitif pada pasien stroke (Relationship between stroke classification and impaired cognitive function in stroke patients). Journal of Nursing Invention, 1(1): 16–22.

Owolabi M O, Sarfo F, Akinyemi R, Gebregziabher M, Akpa O, Akpalu A, Wahab K, et al. (2018). Dominant modifiable risk factors for stroke in Ghana and Nigeria (SIREN): a case-control study. J. Am. Heart Assoc., 1–9. https://doi.org/10.1016/S2214-109X(18)-30002-0

Prayoga A, Rasyid Z (2022). Determinan kejadian stroke iskemik pasien rawat inap di RSUD Petala Bumi Provinsi Riau Tahun 2019 (Determinants of the incidence of ischemic stroke inpatients at Petala Bumi Hospital, Riau Province in 2019). Jurnal Kesehatan Komunitas, 8(1): 52–58.

Puspitasari PN (2020). Hubungan hipertensi terhadap kejadian stroke (The relationship of hypertension to the incidence of stroke). Jurnal Ilmiah Kesehatan Sandi Husada, 12(2): 922–926. https://doi.org/10.35816/jiskh.-v10i2.435.

Retnawati H, Apino E, Kartianom, Djidu H, Anazifa RD (2018). Pengantar analisis meta (Introduction to meta analysis). Parama Publishing.

Sarfo F S, Ovbiagele B, Akpa O, Akpalu A, Wahab K, Obiako R, Komolafe M, et al. (2022). Risk factor characterization of ischemic stroke subtypes among west africans. Stroke, 52, 134–144. https://doi.org/10.1161/STROKEAHA.120.032072

Sedgwick PML (2015). How to read a funnel plot in a meta-analisis. The BMJ. 351. doi: https://doi.org/10.1136/bmj.h4718.

Susilawati F, Nurhayati (2018). Faktor resiko kejadian stroke di rumah sakit (Risk factors for stroke in hospital). Jurnal Keperawatan, XIV(1): 41–48.

Tugasworo D, Retnaningsih (2018). Stroke A-Z. UNDIP PRESS Semarang.

Wang H, Wu M, Tu Q, & Li M. (2022). Risk factors for stroke in a population of central China. Medicine, 101(46): 1–6.

Xing L, Jing L, Tian Y, Liu S, Lin M, Du Z, Ren G. (2019). High prevalence of stroke and uncontrolled associated risk factors are major public health challenges in rural northeast China : A population-based study. Int J Stroke. 0(0), 1–13. https://doi.org/10.1177/-1747493019851280

Yi X, Luo H, Zhou J, Yu M, Chen X, Tan L, Wei W, et al. (2020). Prevalence of stroke and stroke related risk factors : a population based cross sectional survey in southwestern China. BMC Neurology, 20(5): 1–10.

Zhang Y, Li J, Liu C, Yu H, Chen C, Bi C, Fang C, et al. (2021). High-density lipoprotein cholesterol and the risk of first ischemic stroke in a chinese hypertensive population. Clin Interv Aging. 16, 801–810. https://doi.org/-10.2147/CIA.S295252.