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Meta-analysis

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Effects of Hypertension, Diabetes Mellitus, and Gender on Post Stroke Cognitive Impairment: Meta-Analysis

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ABSTRACT

Background: Post-stroke cognitive impairment is a serious problem that is often faced by individuals who have experienced a stroke. This study aims to determine and estimate the effects of hypertension, diabetes mellitus, and gender on post-stroke cognitive impairment through meta-analysis of primary research conducted by previous researchers.
Subjects and Method: This was a meta-analysis study using the PICO model which includes; P: post-stroke patients. I: hypertension, diabetes mellitus, and women. C: normotensive, without diabetes mellitus, and men. O: post-stroke cognitive impairment. A systematic search for primary studies was carried out in the PubMed database which was published from 2014 to 2023. The keywords used to search for primary studies were "Hypertension" AND "Diabetes Mellitus" AND "Post Stroke Cognitive Impairment". The inclusion criteria for the articles searched were primary studies with cross-sectional and cohort studies from 2014-2023 and reporting aOR values. Primary studies were selected using the PRISMA diagram and relevant primary studies were analyzed using Review Manager 5.3.
Results: There were 18 primary studies with cross-sectional and cohort study designs. The total sample obtained through a systematic review and meta-analysis was 9,103 post-stroke patients from France, China, Singapore, the Netherlands, Egypt, Ethiopia, and Uganda. The results of the analysis showed that hypertension increased the risk 1.56 times (aOR= 1.56; 95% CI= 1.11 to 2.19; p= 0.010) and diabetes mellitus increased the risk 1.58 times (aOR= 1.58; 95% CI= 1.23 to 2.05; p< 0.001) post-stroke cognitive impairment compared to people without hypertension and diabetes. Meanwhile, the female gender increases the risk of post-stroke cognitive impairment by 1.28 times (aOR= 1.28; 95% CI=1.16 to 1.42; p<0.001). The data is statistically significant.
Conclusion: hypertension, diabetes mellitus, and female gender increase the risk of post-stroke cognitive impairment.

Keywords: Hypertension, diabetes mellitus, women, post-stroke cognitive disorders.

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BACKGROUND

Stroke is a disease that many people suffer from. This disease can be experienced by someone starting from productive age (Monica et al., 2019). WHO defines stroke as a clinical sign that develops rapidly, due to focal or global disorders accompanied by symptoms that last for 24 hours or more, and can cause death without any clear cause. Around 80%-85% of strokes experienced by individuals fall into the ischemic stroke category. Ischemic stroke occurs due to obstruction or blood clots that occur in one or more large blood vessels in the cerebral circulation (Nopia and Huzaifah, 2020).

Stroke can cause damage and even death of brain cells, which can cause clinical abnormalities and result in disruption of mental activity processes or higher cortical functions, including cognitive function. Damage to brain cells after a stroke causes a decrease in cognitive, sensory, and motor functions, thereby hampering functional abilities ranging from movement activities, self-care, daily activities, and communication with people around normally (Pratiwi et al., 2019; Pudiastuti, 2011).

Many risk factors influence cognitive impairment after stroke, some of which are a history of hypertension, diabetes mellitus, and gender. Hypertension (BP >140 mmHg and BP > 90 mmHg) is a physiological risk factor for stroke (Zamzam et al., 2020). Stroke can cause functional brain disorders in the form of neurological deficits which are then referred to as cognitive dysfunction. The incidence of impaired cognitive function increases threefold after stroke and usually involves impaired visuospatial abilities, memory, orientation, language, attention, and executive function (Tumiwa et al., 2017).

Until now, gender is a factor that is still controversial. According to Nyenhuis and Gorelick (1998), men are more at risk of suffering from cognitive impairment after a stroke. However, other research such as that carried out by Pramudita and Pudjonarko (2016) found that there was no significant difference in gender differences in the risk of post-stroke cognitive impairment. Based on the description of this study, the aim is to determine and estimate the effects of hypertension, diabetes mellitus, and gender on post-stroke cognitive impairment through a meta-analysis of primary research conducted by previous researchers.

SUBJECTS AND METHOD

1. Study Design

This research was conducted using systematic review and meta-analysis methods using the PICO model. P: Post-stroke patients, I: hypertension, diabetes mellitus, and women, C: normotensive, without diabetes mellitus, and men, O: post-stroke cognitive impairment. A systematic search for primary studies was carried out in the PubMed database which was published from 2014 to 2023. The keywords used to search for primary studies were "Hypertension" AND "Diabetes Mellitus" AND "Post Stroke Cognitive Impairment".

2. Steps of Meta-Analysis

1) Create research questions using the PICO format, which involves defining the Population, Intervention, Comparison, and Outcome.
2) Search electronic and non-electronic databases such as PubMed for primary study articles.
3) Conduct a screening process to establish criteria for inclusion and exclusion, followed by a thorough critical assessment.
4) Gather data from the primary studies and compile effect estimates using the RevMan application.

5) Analyze the findings and formulate conclusions based on the interpreted results.

3. Inclusion Criteria

The primary study of this research is a full-text paper using a cross-sectional and cohort study design that analyzes the relationship between hypertension, diabetes mellitus, and women with post-stroke cognitive impairment. Analysis used multivariate with adjusted odds ratio (aOR) and 95% confidence interval. The research subjects were post-stroke patients.

4. Exclusion Criteria

Primary studies published other than in English, using measures of cognitive impairment other than the MoCA, and primary studies published before 2014.

5. Operational Definition of Variables

Cognitive disorders: are reception functions, memory, learning functions, thinking functions, and expressive functions.

Hypertension: a condition where the systolic blood pressure in a person's body is more than or equal to 140 mmHg and/or diastolic blood pressure is more than or equal to 90 mmHg.

Diabetes mellitus: is a chronic condition that occurs due to increased blood sugar levels in the body because the body cannot produce insulin.

A woman: a person (human) who has a vagina, can menstruate, get pregnant, give birth to children, and breastfeed.

6. Study Instruments

This study adopted the PRISMA flowchart diagram and quality assessment of primary studies using a critical assessment checklist from the cross-sectional and cohort study design.

7. Data Analysis

Data analysis was carried out using RevMan5.3. Forest plots and funnel plots were used to determine the size of the relationship and heterogeneity of the data. Fixed effect models were used for homogeneous data, while random effect models were used for heterogeneous data across studies.

RESULTS

Figure 1, shows the PRISMA flowchart results for primary studies relating to the relationship between hypertension, diabetes mellitus, and gender with post-stroke cognitive disorders. There are 18 primary studies in cross-sectional and cohort studies

Figure 2 shows a distribution map of primary studies on the effects of hypertension, diabetes mellitus, and gender on impaired cognitive function after stroke. There are 18 primary studies originating from 9 primary studies from China, 3 primary studies from Ethiopia, and 1 primary study each from Singapore, France, the Netherlands, Canada, Egypt, and Uganda.

Following an assessment of the studies' quality, a cumulative count of 18 articles with a cross-sectional and cohort study design. Table 1 shows the results of the primary study quality assessment for a cross-sectional study design of the effects of hypertension, diabetes mellitus, and gender on impairment after stroke and Table 2 shows the results of the primary study quality assessment for cohort study design of the effects of hypertension, diabetes mellitus, and gender on cognitive impairment after stroke.

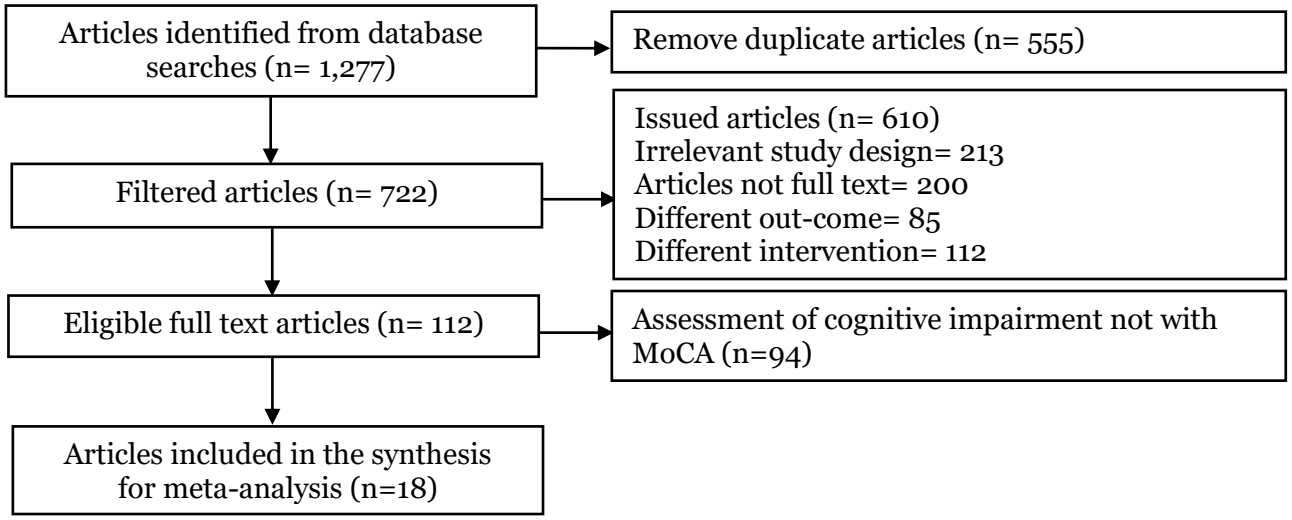

Figure 1. PRISMA flowchart

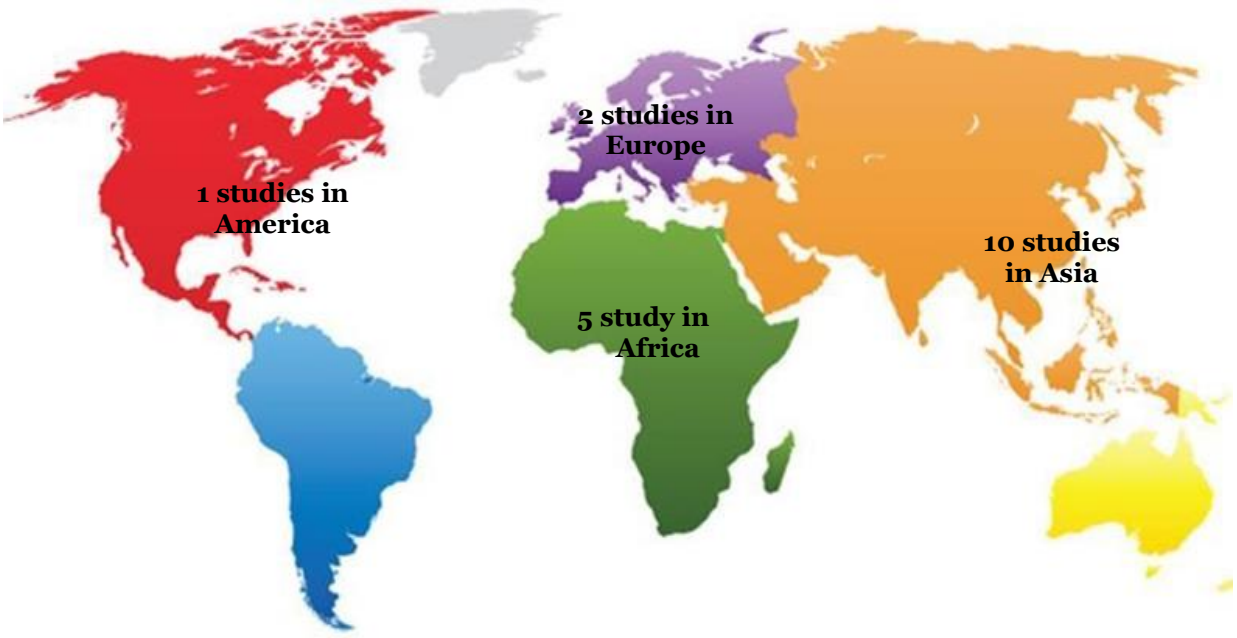

Figure 2. Map of the distribution of articles included in the meta-analysis

Table 1. Quality assessment of cross-sectional studies: the effects of hypertension, diabetes mellitus, gender on cognitive impairment after stroke

Primary Study	Questions													Total
	1a	1b	1c	1d	2a	2b	3a	3b	4	5	6a	6b	7	
Qu et al. (2015)	2	2	2	2	2	2	2	2	1	2	2	2	2	25
Li et al. (2016)	2	2	2	2	0	2	2	2	2	2	2	2	2	24
Chander et al. (2017)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Jiao et al. (2020)	2	2	2	2	2	1	2	2	1	2	2	2	2	24
Lin et al. (2020)	2	2	2	2	1	2	2	2	2	2	2	2	2	25
Esmael et al. (2021)	2	2	2	2	1	2	2	2	2	2	2	2	2	25
Yan et al. (2022)	2	2	2	2	1	2	2	2	1	2	2	2	2	24
Zou et al. (2022)	2	2	2	2	0	2	2	2	2	2	2	2	2	24
Cherkos et al. (2023)	2	2	2	2	2	2	2	2	2	2	2	2	2	26

Primary Study	Questions													Total
	1a	1b	1c	1d	2a	2b	3a	3b	4	5	6a	6b	7	
Li et al. (2023)	2	2	2	2	2	2	2	2	1	2	2	2	2	25
Kaddumukasa et al. (2023)	2	2	2	2	1	2	2	2	2	2	2	2	2	25
Zewde et al. (2023)	2	2	2	2	1	2	2	2	2	2	2	2	2	25

Description of the question criteria:

1a. Is the population in the primary study the same as the population in the PICO meta-analysis?

1b. Is the operational definition of the intervention, i.e. exposed status in the primary study the same as the definition intended in the meta-analysis?

1c. Is the comparison, i.e. unexposed status used by the primary study the same as the definition intended in the meta-analysis?

1d. Are the outcome variables studied in the primary study the same as the definitions intended in the meta-analysis?

2a. In analytical cross-sectional studies, did researchers randomly select samples from the population (random sampling)?

2b. Alternatively, if in an analytically cross-sectional study, the sample was not randomly selected, did researchers select the sample based on outcome status or based on intervention status?

3a. Were both exposure and outcome variables measured with the same instruments in all primary studies?

3b. If variables were measured on a categorical scale, were the cutoffs or categories used the same across primary studies?

4. If the sample was not randomly selected, had the researcher made efforts to prevent bias in choosing the study subject? For example, selecting subjects based on outcome status was not affected by exposure status (intervention), or in selecting subjects based on exposure status (intervention) was not affected by outcome status.

5. Whether the primary study researcher has made efforts to control for the influence of confusion (e.g., performing a multivariate analysis to control for the influence of several confounding factors)

6a. Did the researchers analyze the data in this primary study with multivariate analysis models (e.g., multiple linear regression analysis, multiple logistic regression analysis)

6b. Whether the primary study reports effect size or the association of the results of the multivariate analysis (e.g., adjusted OR, adjusted regression coefficient)

7. Is there no possibility of a conflict of interest with the research sponsor, which causes bias in concluding research results?

Description of Scoring:

Yes=2; Hesitate=1; No=0

Table 2. Results of primary study quality assessment for cohort study design of the effects of hypertension, diabetes mellitus, gender on cognitive impairment after stroke

Primary Study	Questions													Total
	1a	1b	1c	1d	2a	2b	3a	3b	4a	4b	5	6a	6b	7	
Jacquin et al. (2014)	2	2	2	2	2	2	2	2	1	2	2	2	2	2	27
Nijsse et al. (2017)	2	2	2	2	1	2	2	2	1	2	2	2	2	2	26
Swardfager et al. (2017)	2	2	2	2	1	2	2	2	2	2	2	2	2	2	27
Ding et al. (2019)	2	2	2	2	1	2	2	2	1	2	2	2	2	2	26
Ayehu et al. (2023)	2	2	2	2	2	2	2	2	1	2	2	2	2	2	27
Xu et al. (2023)	2	2	2	2	1	2	2	2	2	2	2	2	2	2	27

Description of the question criteria:

1a. Is the population in the primary study the same as the population in the PICO meta-analysis?

1b. Is the operational definition of the intervention, i.e. exposure status in the primary study, the same as the definition intended in the meta-analysis?

1c. Is the comparator, i.e. unexposed status used by the primary study the same as the definition intended in meta-analysis?
1d. Are the outcome variables examined in the primary studies the same as the definitions intended in the meta-analysis?
2a. At the start of the study, did the target population and reach population not experience the outcome being studied?
2b. Was there a distinction between exposed and unexposed groups at the start of the study?
3a. Are exposure and outcome variables measured with the same instruments in all primary studies?
3b. If the variable is measured on a categorical scale, are the cutoffs or categories used the same across primary studies?
4a. Is there no possibility of "Loss-to Follow-up Bias" in primary studies?
4b. Whether primary study investigators have made efforts to control the influence of confounding (e.g., selecting highly motivated subjects, subjects who are easy to follow, or providing incentives to subjects so they do not drop out)?
5. Whether the primary study researcher has made efforts to control the influence of confounding (for example, conducting a multivariate analysis to control the influence of a number of confounding factors, or performing matching)?
6a. Did the researcher analyze the data in this primary study with a multivariate analysis model (e.g., multiple linear regression analysis, multiple logistic regression analysis, Cox regression analysis)?
6b. Does the primary study report effect sizes or associations resulting from multivariate analysis (e.g. adjusted OR, adjusted regression coefficient)?
7. Is there no possibility of a conflict of interest with the research sponsor that could cause bias in concluding the research results?

Description of Scoring:

Yes=2; Hesitate=1; No=0

Table 3. Summary of primary studies with cross-sectional and cohort designs and their respective PICOs (N=9,103)

Author (year)	Country	Sampel	P	I	C	O
Jacquin et al. (2014)	France	Cohort	Stroke patients	DM	No DM	PSCI
Qu et al. (2015)	China	Cross Sectional	Stroke survivors	Urban recurrent stroke and hypertension	Rural first stroke and normotension	PSCI
Li et al. (2016)	China	Cross Sectional	Stroke patients	Hypertension and DM type 2	Normotension and non DM	PSCI
Chander et al. (2017)	Singapore	Cross Sectional	Stroke patients	hypertension and DM	Normotension and non DM	PSCI
Nijsse et al. (2017)	Netherland	Cohort	Stroke patients	Female	Male	PSCI
Swardfager et al. (2017)	Canada	Cohort	Stroke survivors	Hypertension and female	Hypertension and male	PSCI
Ding et al. (2019)	China	Cohort	Stroke patients	DM	No DM	PSCI
Jiao et al. (2020)	China	Cross Sectional	Stroke patients	DM	No DM	PSCI
Lin et al. (2023)	China	Cross Sectional	Stroke patients	Male, hyperglicemia, and hypertension	Female, no hyperglicemia and normotension	PSCI
Esmael et al. (2021)	Egypt	Cross Sectional	Stroke patients	Hypertension	Normotension	PSCI
Yan (Xu) et al. (2022)	China	Cross Sectional	Stroke patients	DM	No DM	PSCI
Zou et al. (2022)	China	Cross Sectional	Stroke patients	Female, hypertension, and DM	Male, normotension, and no DM	PSCI
Ayehu et al.	Ethiopia	Cohort	Stroke	Hypertension	Hypertension and	PSCI

Author (year)	Country	Sampel	P	I	C	O
(2023)			survivors	and female	male	
Cherkos et al. (2023)	Ethiopia	Cross Sectional	Stroke survivors	hypertension and DM	Normotension and non DM	PSCI
Li et al. (2023)	China	Cross Sectional	Stroke patients	Female	Male	PSCI
Kaddumukasa et al. (2023)	Uganda	Cross Sectional	after hospital admission for stroke	Hypertension	Normotension	PSCI
Xu et al. (2023)	China	Cohort	Stroke patients	Female, hyper-tension, and DM	Male, normotension, and no DM	PSCI
Zewde et al. (2023)	Ethiopia	Cross Sectional	Stroke survivors	Female	Male	PSCI

Table 4. Adjusted Odds Ratio (aOR) value on the effect of hypertension on post-stroke cognitive impairment

Primary Study	aOR	95%CI	
		Lower Limit	Upper Limit
Qu et al. (2015)	1.19	0.64	2.20
Li et al. (2016)	1.05	0.99	1.12
Chander et al. (2017)	1.34	0.73	2.47
Lin et al. (2020)	2.54	0.87	7.43
Esmael et al. (2021)	2.03	1.37	2.67
Zou et al. (2022)	1.32	1.01	1.73
Cherkos et al. (2023)	7.51	3.45	16.34
Kaddumukasa et al. (2023)	0.69	0.3	1.61

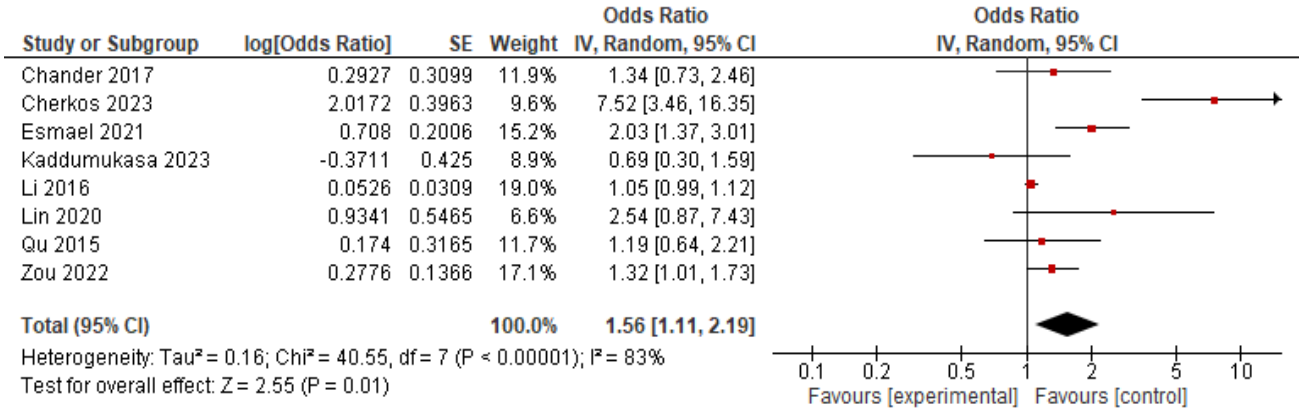

Figure 3. Forest Plot of the effect of hypertension on the risk of post-stroke cognitive impairment

Figure 3 shows the forest plot that post-stroke patients with hypertension are 1.56 times more likely to experience cognitive impairment compared to post-stroke patients who do not suffer from hypertension and this is statistically significant (aOR= 1.56; 95% CI=1.11 to 2.19; p=0.010). Heterogeneity of research data shows I^2= 83% (random effect model).

Figure 4 show the funnel plot that the distribution of effect estimates from the primary studies of this meta-analysis lies more to the left of the vertical line of mean estimates than to the right, indicating public-

cation bias. Because the publication bias tends to be to the left of the average vertical line which is in a different direction from the location of the diamond shape in the forest plot, the publication bias tends to reduce the effect of true hypertension on cognitive impairment in post-stroke patients (underestimate).

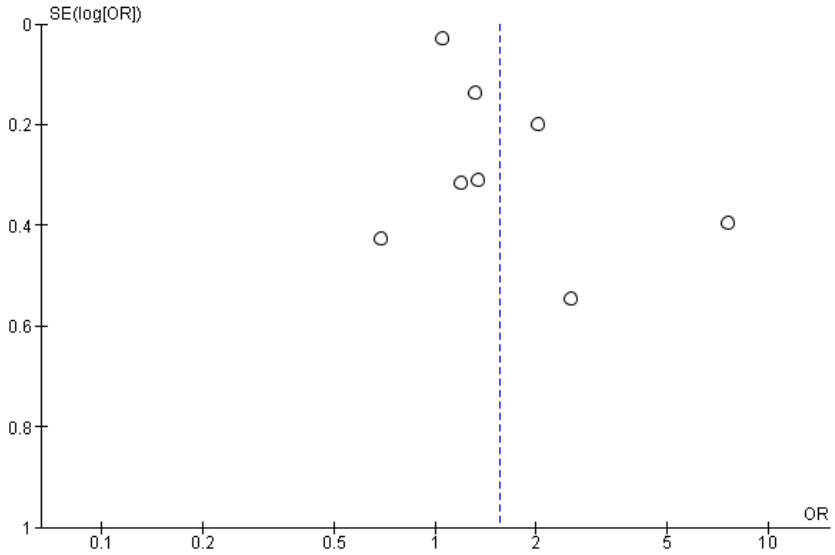

Figure 4. Funnel Plot of the effect of hypertension on the risk of post-stroke cognitive impairment

Table 5. Adjusted Odds Ratio (aOR) values on the effect of diabetes mellitus on post-stroke cognitive impairment

Primary Study	aOR	95%CI	
		Lower Limit	Upper Limit
Jacquin et al. (2014)	3.48	1.03	11.73
Li et al. (2016)	2.24	1.63	3.08
Chander et al. (2017)	1.32	0.81	2.16
Ding et al. (2019)	5.82	2.06	16.41
Jiao et al. (2020)	1.24	0.85	1.80
Yan et al. (2022)	1.64	0.92	2.82
Zou et al. (2022)	1.28	0.96	1.70
Cherkos et al. (2023)	0.80	0.28	2.30
Xu et al. (2023)	1.34	0.87	2.08

Figure 5 shows the results of subgroup analysis in the cohort study showed that post-stroke patients with diabetes mellitus were 2.73 times more likely to experience cognitive impairment compared to post-stroke patients who did not suffer from diabetes mellitus but this was not statistically significant (aOR=2.73; 95% CI=1.00 to 7.44; p=0.050). Heterogeneity of research data shows I^2= 75% (random effect model). The results of subgroup analysis in a cross-sectional study showed that post-stroke patients with diabetes mellitus had a 1.46 times risk of experiencing cognitive impairment compared to post-stroke patients who did not suffer from diabetes mellitus and this was statistically significant (aOR=1.46; 95% CI=1.14 to 1.88; p =0.003). Heterogeneity of research data shows I^2= 50% (random effect model). The overall results show that post-stroke patients with diabetes mellitus are 1.58 times more likely to experience cognitive impairment compared to post-stroke patients who do not suffer from diabetes

mellitus and this is statistically significant (aOR=1.58; 95% CI=1.23 to 2.05; p<0.001). Heterogeneity of research data shows I^2= 57% (random effect model).

Figure 6 shows the funnel plot of the cohort studies shows that the distribution of effect estimates from the primary studies of this meta-analysis lies more to the left of the vertical line of mean estimates than to the right, indicating publication bias. Because the publication bias tends to be to the left of the average vertical line which is in a different direction from the location of the diamond shape in the forest plot, the publication bias tends to reduce the actual effect of diabetes mellitus on cognitive impairment in post-stroke patients (underestimate).

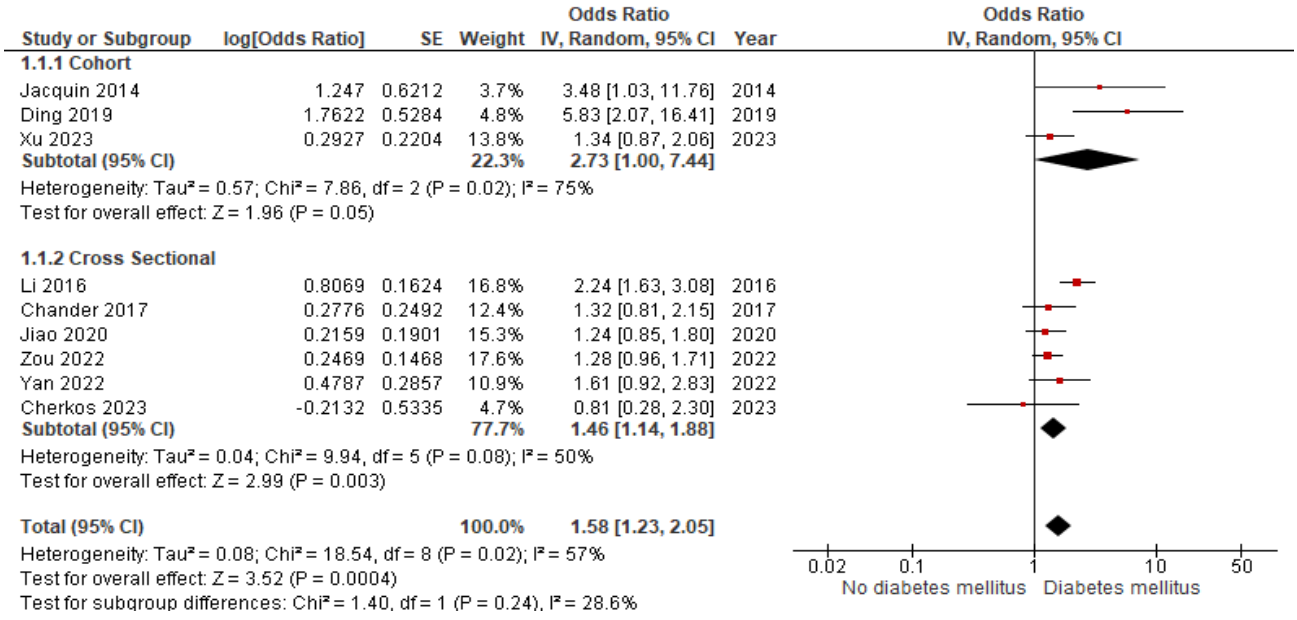

Figure 5. Forest plot of the effect of diabetes mellitus on the risk of cognitive impairment after stroke

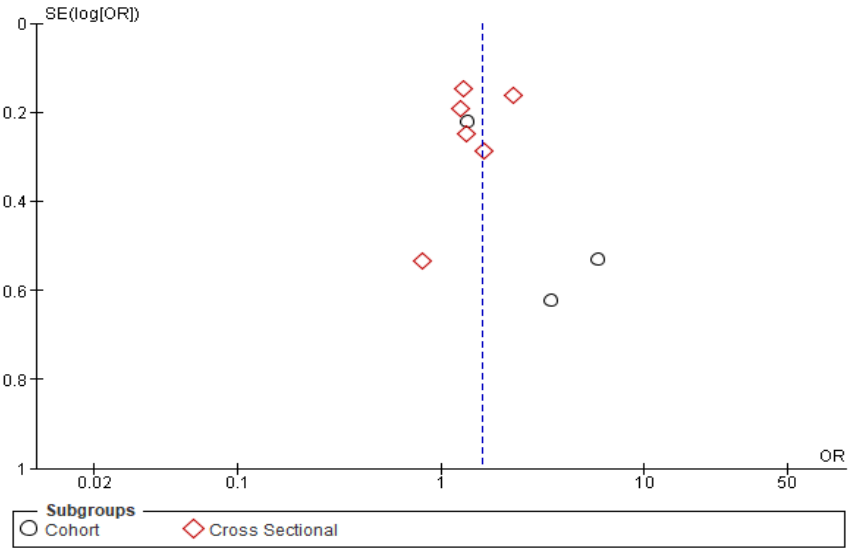

Figure 6. Funnel plot of the effect of diabetes mellitus on the risk of cognitive impairment after stroke

Funnel plots of cross-sectional studies show that the distribution of effect estimates from the primary studies of this meta-analysis lies more to the right of the vertical line of mean estimates than to the left, indicating publication bias. Because the publication bias tends to be to the right of the average vertical line which is in the same direction as the diamond shape in the forest plot, the publication bias tends to increase the actual effect of diabetes mellitus on cognitive impairment in post-stroke patients (overestimate).

Table 6. Adjusted Odds Ratio (aOR) values for the effect of gender on post-stroke cognitive impairment

Primary Study	aOR	95%CI	
		Lower Limit	Upper Limit
Nijsse et al. (2017)	1.18	0.64	2.17
Swardfager et al. (2017)	1.72	1.05	2.80
Zou et al. (2022)	0.89	0.67	2.17
Ayehu et al. (2023)	1.39	1.22	2.69
Li et al. (2023)	1.59	1.07	2.37
Xu et al. (2023)	1.05	0.74	1.49
Zewde et al. (2023)	0.74	0.26	2.16

Figure 7 shows the results of subgroup analysis in cross-sectional studies showed that female post-stroke patients had a 1.06 times risk of experiencing cognitive impairment compared to male post-stroke patients but this was not statistically significant (aOR=1.06; 95% CI=0.86 to 1.31; p=0.560). Heterogeneity of research data shows I^2= 50% (fixed effect model).

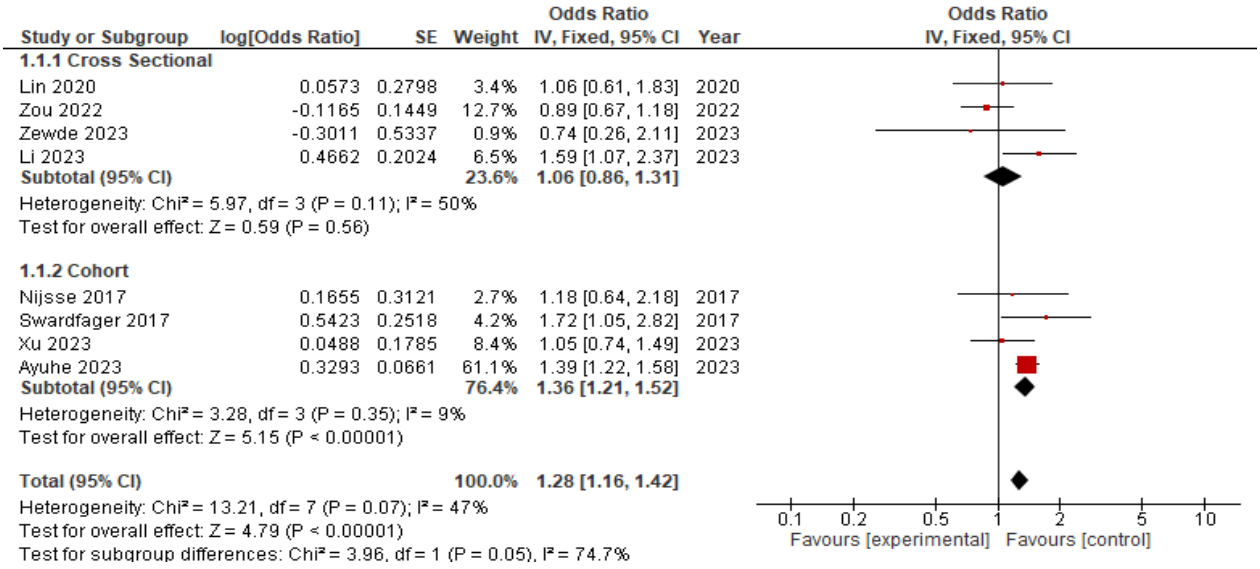

Figure 7. Forest Plot of the effect of female gender on cognitive impairment after stroke

The results of subgroup analysis in the cohort study showed that female post-stroke patients were 1.36 times more likely to experience cognitive impairment compared to male post-stroke patients and this was statistically significant (aOR=1.36; 95% CI=

1.21 to 1.52; p< 0.001). Heterogeneity of research data shows I^2= 9% (fixed effect model). The overall results show that female post-stroke patients are 1.28 times more likely to experience cognitive impairment compared to male post-stroke patients and this is statistically significant (aOR= 1.28; 95% CI=1.16 to 1.42; p<0.001). Heterogeneity of research data shows I^2= 47% (fixed effect model).

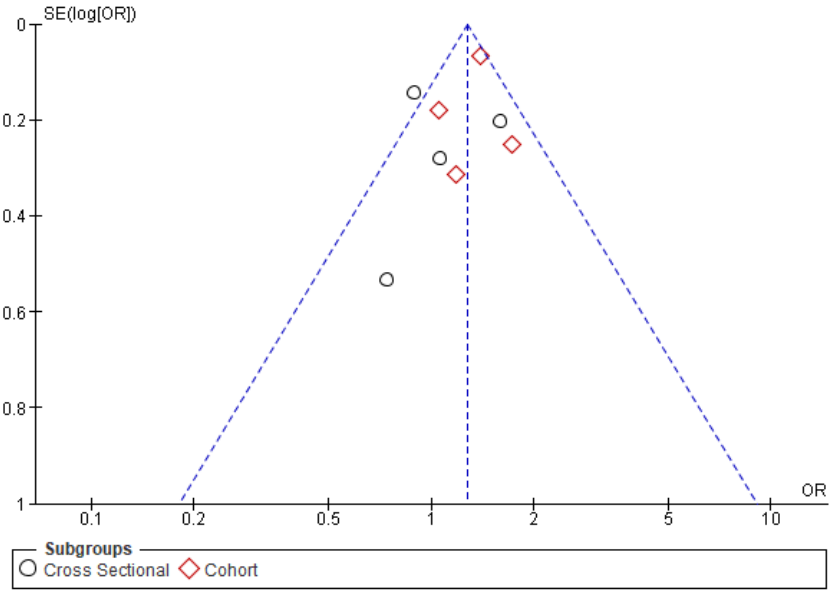

Figure 8. Funnel plot of the effect of female gender on cognitive impairment after stroke

Figure 8 shows the funnel plot of the cohort studies shows that the distribution of effect estimates from the primary studies of this meta-analysis is symmetrical between the right and left of the vertical line of mean estimates, indicating no publication bias.

Funnel plots of cross-sectional studies show that the distribution of effect estimates from the primary studies of this meta-analysis lies more to the left of the vertical line of mean estimates than to the right, indicating publication bias. Because the publiccation bias tends to be to the left of the average vertical line which is in a different direction from the location of the diamond shape in the forest plot, the publication bias tends to increase the effect of actual gender on cognitive impairment in post-stroke patients (underestimate).

RESULTS

Based on the results of analysis from 18 primary studies, it shows that hypertension has a 1.56 times risk of experiencing cognitive impairment compared to post-stroke patients who do not suffer from hypertension and this is statistically significant (aOR= 1.56; 95% CI=1.11 to 2.19; p=0.010). These results are in line with research conducted by Tzuorio (2007) that hypertension is directly related to the occurrence of stroke. Stroke itself can cause disturbances in cognitive function. Hypertension can cause brain blood vessels to burst and narrow so that blood flow to the brain will be disrupted, and brain cells will die. Risk factors for hypertension such as obesity, smoking habits, excessive sodium consumption, and excessive alcohol consumption can trigger the appearance of plaque deposits

(atherosclerotic/atherothrombosis) in large blood vessels which causes the blood vessels to narrow. Atherosclerosis that forms in blood vessels easily ruptures and falls off, so if it breaks off it will cause blockage of the smaller brain blood vessels, and if it occurs in the brain it will cause symptoms of stroke. If a stroke patient is treated late for reperfusion therapy, tissue or parts of the brain that do not receive blood flow cannot be saved, causing a decline in post-stroke cognitive function.

Research by Saedi et al. (2016) said that there is a relationship between diabetes mellitus which can cause complications in the form of mild cognitive impairment (MCI) such as dementia. This research is in line with the results of this meta-analysis which shows that post-stroke patients with diabetes mellitus are 1.58 times more likely to experience cognitive impairment compared to post-stroke patients who do not suffer from diabetes mellitus and this is statistically significant (aOR= 1.58; 95%CI= 1.23 to 2.05 ; p<0.001) In patients with type 1 diabetes mellitus, cognitive impairment, visual perception, decreased psychomotor speed and decreased attention were found. Patients with type 2 diabetes mellitus also have an increased risk of developing dementia, where in patients with type 2 diabetes mellitus seen from MRI, brain atrophy occurs, where global brain atrophy will occur 3 times faster than the normal aging process.

Hyperglycemia and insulin resistance can result in chronic complications in patients on long-term treatment, such as macrovascular, microvascular complications and neuropathy complications, which can cause impaired cognitive function. Diabetes mellitus patients will experience an increase in HbA1c, where HbA1c will undergo several reaction stages to become irreversible products, namely AGEs (Advanced Glycosylation End Products). High blood glucose levels cause the accumulation of AGEs in various tissues, where AGEs are the main source of free radicals, one of which is the brain. This triggers pro-inflammatory mechanisms and tissue damage, including brain tissue, which can cause impaired cognitive function.

The third variable used in this meta-analysis was the effect of gender on post-stroke cognitive impairment. The results of this study show that female post-stroke patients are 1.28 times more likely to experience cognitive impairment compared to male post-stroke patients and this is statistically significant (aOR=1.28; 95% CI=1.16 to 1.42; p<0.001). This research is in line with research from Kalaria (2016) which states that women are more at risk of experiencing cognitive impairment after experiencing a stroke. This is related to the neuroprotective role of adiponectin. The decrease in serum adiponectin levels associated with the aging process was found more in women than men. Risk factors that can increase the occurrence of cognitive impairment after stroke include hypertension, diabetes mellitus, and female gender.

AUTHOR CONTRIBUTION

Sukandriani Utami, Emirza Nur Wicaksono, and Amalia Choirunnisa are the authors who chose the topic, searched, collected primary studies and analyzed. Nindita Arum Veibiyani and Bhisma Murti reviewed the documents.

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CONFLICT OF INTEREST

There is no conflict of interest in this study.

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