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Meta-Analysis

Meta-Analysis: Depression as A Risk Factor for Dementia

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ABSTRACT

Background: Depression is a mental disorder which if not treated can cause other diseases, including the individual's physical condition. One of the risks that occur due to recurrent depression is dementia. Dementia can reduce a person's ability to survive due to decreased brain function. This study was aimed to determine the effect of depression (depression) as a risk factor for dementia (dementia).
Subjects and Method: This study was a meta-analysis, with a PICO covering Population= people with dementia. Intervention= depression. Comparison= without depression. Outcome= the risk of dementia. Research data was searched from several sources including: PubMed, Google Scholar, Springer Link, and Science Direct from 2011 until 2021 with the following keywords "dementia" AND "depression" OR "risk of dementia" AND “Hazard Ratio” AND "multivariate". The inclusion criteria used were full papers using English with a cohort study design from 2011-2021 by reporting the Adjusted Hazard Ratio (aHR) value. The selection of articles was carried out using the PRISMA flow diagram. Data processing using Review Manager software version 5.3 to determine the risk of depression variables on dementia.
Results: A total of 11 cohort studies were selected for a systematic review and meta-analysis. The data collected showed that depression can increase patients of dementia 1.38 times compared to without depression (aHR= 1.38; 95% CI= 1.38 to 1.70; p=0.003).
Conclusion: Depression increases the risk of developing dementia.

Keywords: depression, dementia, risk factor.

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BACKGROUND

The loss of cognitive abilities can reduce a person's quality of life, which can initially take care of himself to need to depend on others. Not only cognitive, mental abilities can be impaired in dementia patients. Dementia occurs because of a disorder in the brain that is chronic-progressive, where there is a disturbance of sublime functions in multiple cortical areas (multiple higher cortical function) resulting in a decrease in memory, thinking power, orientation, comprehension, numeracy, learning ability, language, and judgment. The decrease in these elements causes individuals to be unable to survive alone (Sopyanti et al., 2019).

Depression is a mental disorder that causes disruption of daily activities. This disorder is defined by the World Health Organization (WHO) as a global crisis and predicts that by 2020, it will become the number two contributor to a person's disability in life after cardiovascular disease.

Hundreds of people in the world have experienced depression, so WHO has set depression as one of the priorities to be handled (Kemenkes, 2014).

The incidence of depression may be 30% in vascular dementia and over 40% in Alzheimer's disease. The prevalence of depression in dementia has been reported to be 20–60%. The prevalence of major depression decreases as severity of dementia increases. Depressive symptoms have been estimated to occur in approximately 20-30% of people with dementia. (Kitching, 2015; Tsuno and Homma, 2009; Dementia Australia, 2020)

Depression that occurs in the elderly, often accompanied by organic pathologies, such as neurological disorders, abnormalities in brain structure and subcortical blood vessels, intima-media thickening of the carotid arteries which is a marker of atherosclerotic disease. Patients with vascular type depression show negative cognitive decline, are slower psychomotor, more apathetic, impaired executive function and respond to treatment worse. As a result, it can occur that reduces the individual's performance or ability to survive (Maramis, 2014). The aim of this study was to analyzed the relationship between depression and the risk of dementia.

SUBJECTS AND METHOD

1. Study Design

This research was a systematic review and meta-analysis. The articles used in this study were obtained from several data-bases, namely Google Scholar, PubMed, Springer Link and Science Direct between 2011 and 2021. The selection of articles was carried out using PRISMA flow diagrams. The keywords to search for articles are as follows "dementia" AND "depression" OR "risk of dementia" AND "Hazard Ratio" AND "multivariate".

2. Inclusion Criteria

The inclusion criteria for articles that can be reviewed are full-paper articles with cohort research methods, both prospective and retrospective. Selected articles are those that present the final results of the adjusted Hazard Ratio (aHR), articles that perform data analysis in multivariate form, articles that discuss depression and dementia.

3. Exclusion Criteria

Exclusion criteria for articles included research conducted in addition to the cohort study, articles published before 2011, articles featuring bivariate analysis so that the final results show only HR, percent, and mean differences.

4. Operational Definition of Variables

The search for articles was carried out by considering the eligibility criteria determined using the PICO model. The population in this study were patients diagnosed with depression.

Depression: Respondents who have symptoms of depression or are diagnosed with a depressive disorder by experts. Depression can be diagnosed with ICD-10 criteria.

Dementia: Respondents who are diagnosed with a dementia disorder by experts.

5. Study Instruments

The stages of this study follow the PRISMA Flow diagram and the assessment of the quality of research articles using Critical Appraisal Checklist for Cohort Study by The Joanna Briggs Institute (JBI).

6. Data Analysis

After these criteria were met, the researchers processed the data using the Review Manager software version 5.3 to determine the correlation between the variables of depression (depression) and dementia (dementia). The data in the study were analyzed using the Review Manager application (RevMan 5.3). Forest plots and funnel plots were used to determine the size

of the relationship and heterogeneity of the data. The fixed effect model is used for homogeneous data, while the random effect model is used for heterogeneous data across studies.

The article search process was carried out using the PRISMA flow chart which can be seen in Figure 1. The total articles obtained were 11 articles consisting of 4 from Asia, 2 America 5 from Eropa. Figure 2 shows the area of the article taken and according to the inclusion criteria.

RESULTS

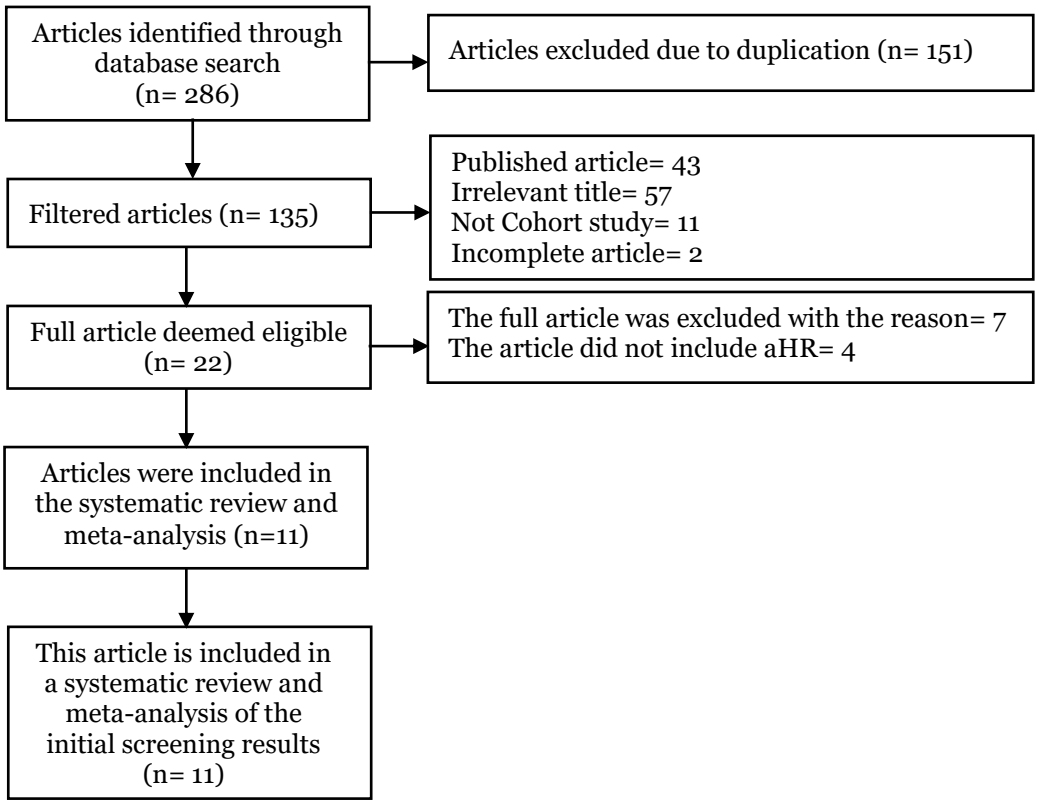

Figure 1. PRISMA Flow Diagram

Table 1. Assessment of study quality

No	Indicators	Publication (Author, Year)					
		Carr et al. (2021)	Gilsanz et al. (2018)	Lee et. (2021)	Fang et al. (2020)	Peakman et al. (2020)	Ouk et al. (2020)
1.	Were the two groups similar and recruited from the same population?	1	1	1	1	1	1
2.	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	1	1	1	1	1	1
3.	Was the exposure measured in a valid and reliable way?	1	1	1	1	1	0
4.	Were confounding factors identified?	1	1	1	1	1	1
5.	Were strategies to deal with confounding factors stated?	1	1	1	1	1	1
6.	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	1	1	1	1	1	1
7.	Were the outcomes measured in a valid and reliable way?	1	1	1	1	1	1
8.	Was the follow up time reported and sufficient to be long enough for outcomes to occur?	1	1	1	1	1	1
9.	Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	1	1	1	1	1	1
10.	Were strategies to address incomplete follow up utilized?	1	1	1	1	1	1
11.	Was appropriate statistical analysis used?	1	1	1	1	1	1
Total		**11**	**11**	**11**	**11**	**11**	**10**

Note: 1: Yes; 0: No

Table 1. Cont.

No	Indicators	Publication (Author, Year)				
		Lewis et al. (2018)	Oh et al. (2020)	Perna et al. (2019)	Lin et al. (2016)	Heser et al. (2020)
1.	Were the two groups similar and recruited from the same population?	1	1	1	1	1
2.	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	1	1	1	1	1
3.	Was the exposure measured in a valid and reliable way?	1	1	0	1	1
4.	Were confounding factors identified?	1	1	1	1	1
5.	Were strategies to deal with confounding factors stated?	1	1	1	1	1
6.	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	1	1	1	1	1
7.	Were the outcomes measured in a valid and reliable way?	1	1	1	1	1
8.	Was the follow up time reported and sufficient to be long enough for outcomes to occur?	1	1	1	1	1
9.	Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	1	1	1	1	1
10.	Were strategies to address incomplete follow up utilized?	1	1	1	1	1
11.	Was appropriate statistical analysis used?	1	1	1	1	1
	Total	**11**	**11**	**10**	**11**	**11**

Note: 1: Yes; 0: No

Table 2. Main descriptions of studies on the association of depression with the risk of developing dementia

Author, Year	Country	Study Design	Sample Size	Population	Intervention	Comparison	Outcome	aHR (95%CI)
Carr et al. (2021)	Scotland	Prospective Cohort	1,064	People with Dementia	Depression	Without Depression	The risk of dementia in patients with type II diabetes mellitus	2.37 (1.37 to 4.10)
Gilsanz et al. (2018)	California	Retrospective Cohort	3,742	People with Dementia	Depression	Without Depression	The risk of dementia in patients with type I diabetes mellitus	1.72 (1.12 to 2.65)
Lee et al. (2021)	Hong Kong	Retrospective Cohort	16,608	People with Dementia	Depression	Without Depression	The risk of developing dementia in geriatrics	1.13 (1.05 to 1.21)
Fang et al. (2020)	Taiwan	Retrospective Cohort	6,065	People with Dementia	Depression	Without Depression	The risk of developing dementia	1.55 (1.06 to 2.25)
Peakman et al. (2020)	London	Retrospective Cohort	806	People with Dementia	Depression	Without Depression	The risk of developing dementia	0.65 (0.55 to 0.77)
Ouk et al. (2020)	Ontario, Canada	Retrospective Cohort	23,579	People with Dementia	Depression	Without Depression	The risk of dementia in patients with acute ischemic stroke	1.27 (1.08 to 1.49)
Lewis et al. (2018)	London	Retrospective Cohort	3,374	People with Dementia	Depression	Without Depression	The risk of developing dementia	0.94 (0.71 to 1.24)
Oh et al. (2020)	South Korea	Prospective Cohort	4,456	People with Dementia	Depression	Without Depression	The risk of developing dementia in geriatrics	3.02 (1.56 to 5.85)
Perna et al. (2019)	German	Retrospective Cohort	6,114	People with Dementia	Depression	Without Depression	The risk of developing dementia	1.13 (0.88 to 1.43)
Lin et al. (2016)	Taiwan	Retrospective Cohort	49,955	People with Dementia	Depression	Without Depression	The risk of developing dementia	3.10 (2.13 to 4.52)
Heser et al. (2020)	German	Prospective Cohorts	4,255	People with Dementia	Depression	Without Depression	The risk of developing dementia	1.31 (1.07 to 1.62)

Figure 2. Map of the study area

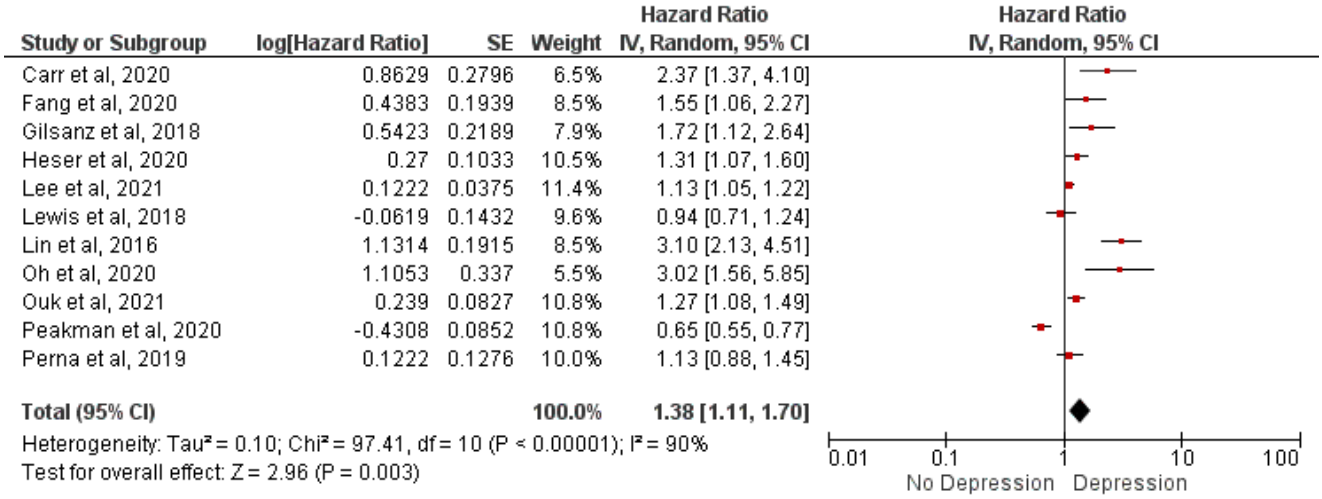

Figure 3. Forest plot of depression and incidence of dementia

The interpretation of the results of the meta-analysis of depression as a risk factor for dementia can be seen in the Forest Plot image. Based on the results of the analysis on the figure, it can be seen that 9 out of 11 articles reported that depression can affect the occurrence of dementia. The heterogeneity was high between the primary studies (I^2= 90%; p< 0.001). So, a random effects model is used. In the analysis of the data in the Forest plot, depression increased the risk of developing dementia by 1.38 compared with non-depressed respondents, and was statistically significant (aHR= 1.38; 95% CI= 1.11 to 1.70; p= 0.003).

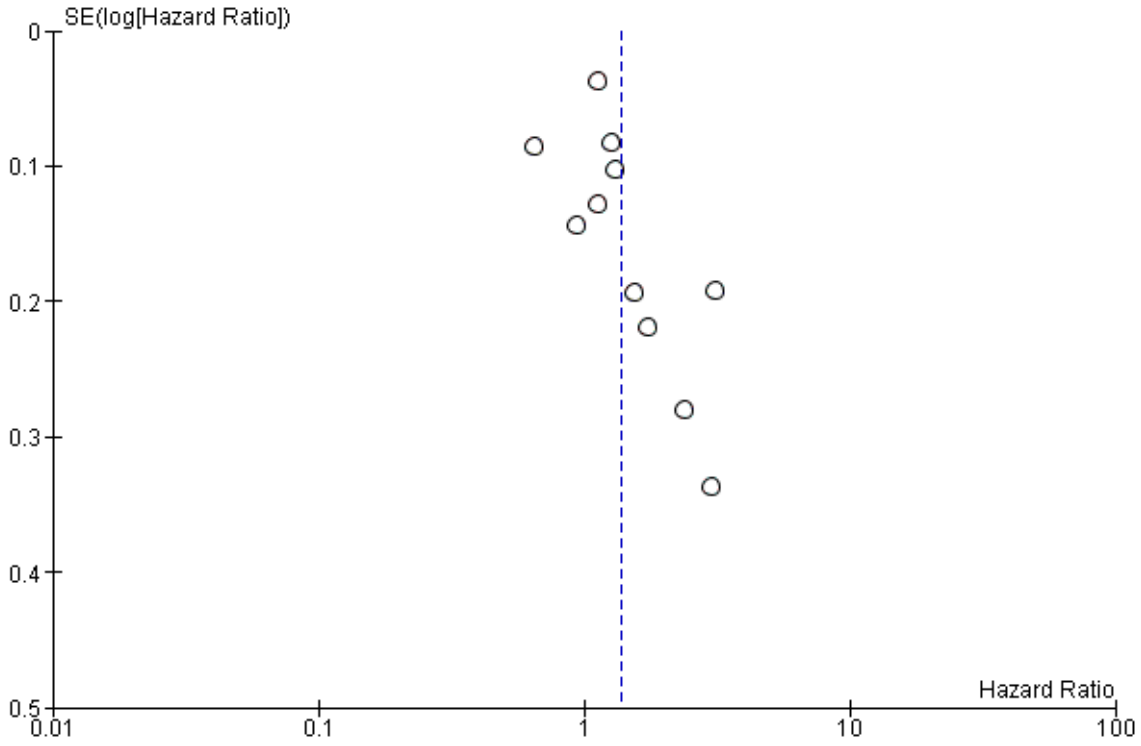

Figure 4. Funnel plot of depression and incidence of dementia

From the Figure 4, it shows that there is a publication bias where the plot distance between right and left looks asymmetrical, then the number of right and left plots is not same, there are 3 plots on the left and 5 plots on the right, where there are 2 plots that touch the line between the right and left plot sections.

DISCUSSION

From this study, it can be seen that depression is a risk factor for the incidence of dementia, with a sufficient value (aHR= 1.38) or respondents with depression are 1.38 times more likely to have dementia than respondents who do not experience depression. These results are in line with the research from Ou et al., 2019 in Taiwan which took samples of respondents with urinary tract infections who experienced depression and had a 1.32 times higher likelihood of developing dementia than those who did not have lower urinary tract infections.

In addition, this study is also in accordance with research from Almeida et al., 2017 in Western Australia which states that depression is a modifiable factor to reduce the risk of developing dementia. In this study, depression was divided into mild-to-moderate and severe with results showing that severe depressive symptoms may induce dementia in taller patients. Although the same study also explains that the use of antidepressants does not reduce the incidence of dementia.

Furthermore, Johansson et al., 2019 research in Latin America also supports the results of this study where respondents with depression can experience dementia 1.63 times than those without, and 1.28 times in respondents with symptoms of subsyndrome depression. Depression in this study used the ICD-10 criteria.

According to Wu et al., 2020 who conducted a study in European societies (from the Survey of Health, Aging, and Retirement in Europe), found that respondents aged over 80 years with depression experienced 1.52 times the risk of dementia than those without depression. The study also suggests that interventions targeting depressed patients aged 60-79 years and those with major depression can be an effective strategy to prevent dementia.

Like the research of Ou et al. in 2019, Brewster et al. (2021) also conducted a similar study but in patients with age-related Hearing Loss (HL), where patients treated with HL had lower rates of depression and a 1.29 times reduced risk of developing dementia than patients not treated with HL. These results indicate that the triggering factors for depression can vary so that depression is one of the modifiable risk factors for dementia.

Furthermore, according to WHO's understanding that health does not only include physical health, but mental health also needs to be considered. Other factors such as economy, environment, culture can also affect a person's mental which results in his physical health as well. The limitations of this study were using only English journals, the number of journals was not much, and critical appraisal is only done by one person.

AUTHOR CONTRIBUTION

Hesthi Krisnawati is the researcher who selects the topic, searches for and collects research data, analyzes the data and reviews research documents.

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CONFLICT OF INTEREST

The researcher stated that there was no conflict of interest in this research.

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