Prevalence of Frailty of Alzheimer's Disease Aged 60 or Older: A Systematic Review and Meta-Analysis

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Abstract

Objective: Frailty in elderly frailty can lead to a decline in cognitive function, making daily life more challenging for them. The importance of identifying the prevalence of frailty in the population Alzheimer's disease aged 60 and above lies in understanding the trends and distribution of frailty among older adults. This knowledge can drive efforts in the prevention, treatment, and management of frailty.This meta-analysis aims to evaluate the prevalence of frailty in individuals Alzheimer's disease aged 60 years and above. **Methods:** Relevant research articles on the prevalence of frailty in the elderly were systematically retrieved from databases such as Embase (Elsevier), Medline and PreMedline (OvidSP), PsycInfo (EbscoHost), SCOPUS, and the Cochrane Controlled Trials Register, covering the period to December 2022. Meta-analysis was performed using Revman 5.3 software. **Results:** A total of 11 articles, involving 35,453 participants, were included in the analysis. The included articles primarily consisted of randomized controlled trials (RCTs) or cross-sectional studies, which include that ≧60 years old: 4 articles ≧65 years old: 6 articles ≧70 years old: 1 article.The overall prevalence of frailty was found to be 9.23% (95% *CI*: 1.79~2.04). Subgroup analysis revealed that the prevalence of frailty was higher in elderly females (4.6%) compared to males (3.4%). With increasing age, the prevalence of Alzheimer's disease (AD) (2.7%) was higher than vascular frailty (VD) (0.8%). The prevalence of frailty was lower in illiterate individuals (6.6%) compared to literate individuals (7.2%). **Conclusion:** The prevalence of frailty is relatively high in individuals aged 60 years and above. Age, gender, education level, and marital status may influence the occurrence of frailty in the elderly.

Keywords: Frailty in the Elderly, Alzheimer's Disease, Prevalence, Meta-Analysis.

Introduction

Alzheimer's disease (AD), also referred to as senile frailty, is a neurodegenerative disorder that manifests with a gradual onset and gradual decline over a period of time.[1] Frailty in individuals aged 60 and beyond is frequently linked to disease progression and a deterioration in cognitive function in patients with Alzheimer's disease (AD).[2] Further investigation is warranted to explore several distinguishing attributes of frailty in individuals with Alzheimer's disease. Individuals diagnosed with Alzheimer's disease (AD) may encounter a deterioration in their physical capabilities, including diminished walking capacity, challenges with balance, and restrictions in doing daily tasks. Furthermore, individuals with Alzheimer's disease may experience muscle weakness, resulting in diminished strength in their limbs and limited ability to move.[3] Presently, there exist significant concerns regarding the systematic assessment of the occurrence of frailty in adults aged 60 and above who have been diagnosed with Alzheimer's disease (AD). The aforementioned concerns encompass deficiencies in the consistency and comparability of data collecting, limitations in sample size, absence of long-term tracking and longitudinal research, as well as insufficiencies in controlling biases and potential confounding variables. These aforementioned features possess the potential to offer insights into the frailty status of individuals diagnosed with Alzheimer's disease (AD) and might potentially exert

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a substantial influence on their overall health and quality of life.The user's text is missing, please provide the text so I can rewrite it in an At present, the primary research concerns pertaining to frailty encompass the absence of consensus in defining and establishing criteria for detecting frailty. Consequently, there is a pressing need for a standardised and unambiguous definition of frailty to facilitate comparative research endeavours.The comprehensive understanding of frailty remains incomplete, particularly regarding its intricate association with variables such as inflammation, metabolic problems, and neurological impairment. Additional investigation is required to thoroughly examine these systems. A wide range of assessment techniques exists for the evaluation of frailty, highlighting the necessity for the development of more precise and dependable procedures to enhance the accuracy and reliability of frailty screening and evaluation. The available intervention and management techniques for frailty are limited. Additional investigation and the formulation of efficacious intervention strategies are necessary in order to enhance the overall well-being and functioning capacity of fragile individuals.[4] Therefore, the notion of frailty was initially introduced. The global prevalence of frailty in the elderly varies between 4% and 59.1% depending on the operational concept of frailty used and the characteristics of the group being examined.[5] Based on a recent study, it was determined that the occurrence of frailty among older adults residing in the community, when categorised by the economic levels of their respective countries, was approximately 12.3% for middle-income countries. Additionally, a pre-frailty rate of 55.3% was observed. According to the cited source, the estimated prevalence of frailty in high-income nations was 8.2%, accompanied by a pre-frailty rate of 43.9%.[6] Research undertaken in several countries like Europe, the United States, Canada, and Australia has revealed a wide range of frailty rates, spanning from 4% to 60%.[7] There are multiple characteristics that exert an influence on an individual's tolerance to Alzheimer's disease (AD) pathology, and among these factors, frailty emerges as a significant determinant. According to recent research findings pertaining to frailty and Alzheimer's disease (AD), a strong association between these two conditions is widely acknowledged.

A longitudinal study spanning seven years revealed a significant correlation between frailty and the presence of Alzheimer's disease. The utilisation of frailty indices has the potential to identify individuals who are at a heightened risk of acquiring senile frailty. This identification would enable the implementation of preventative methods that are both highly effective and specifically tailored to the needs of these individuals.[8] Nevertheless, there is considerable heterogeneity in the intervention outcomes regarding the prevalence of frailty among individuals aged 60 years and above, as indicated by several recent studies.[9,10] Furthermore, the quality of the most recent systematic reviews that assess these studies[11] is generally low, typically falling within grade C.In essence, addressing frailty in senior individuals with Alzheimer's disease has considerable importance in enhancing their overall quality of life, prolonging the advancement of the disease, mitigating the strain on carers, averting complications, and delivering comprehensive healthcare. By acknowledging the concept of frailty, a holistic strategy may be implemented to prioritise the physical and cognitive well-being of patients, so facilitating the preservation of their functionality and autonomy to the greatest degree achievable. This approach also serves to alleviate the strain experienced by both patients and their families.

Hence, the objective of this investigation is to perform a comprehensive analysis of the frequency of frailty among individuals aged 60 years and older who are diagnosed with Alzheimer's disease. This endeavour seeks to thoroughly examine the attributes of frailty within the elderly demographic, along with the resultant consequences for patients. The primary objective of this study is to examine the therapeutic significance of interventions aimed at preventing frailty in older adults.

Research Method

Literature search

A systematic review of the literature was conducted based on a protocol developed a priori by following the Preferred Reporting Items for Systematic Review and MetaAnalysis(PRISMA) statements.[12] The protocol was registered and is available at PROSPERO (CRD42023432682). A systematic literature search was performed in the following electronic databases: Pubmed and Embase and Elsevier, Medline and PreMedline (OvidSP), PsycInfo (EbscoHost), SCOPUS, and the Cochrane Controlled Trials Register, from the first available year to December 2022 The search strategy was developed for each electronic database using the combination of the following Medical Subject Heading (MeSH) and free-text terms:([weakness [MeSH]] AND [prevalence of weakness [MeSH]] OR [incidence rate of weakness [MeSH]] OR [epidemiology of weakness [MeSH]] OR [Alzheimer's disease [MeSH]] OR [senile frailty [MeSH]] OR [Post epidemiology[MeSH]] OR [vascular frailty [MeSH]] OR [incidence rate [MeSH]] OR [mortality rate of disease [MeSH]] OR [weak elderly individuals [MeSH]].

Literature inclusion and Exclusion Criteria

Inclusion criteria: (1) The cases included in the literature were collected from a specific region. (2) The studies conducted were based on sampling surveys rather than non-probability surveys. (3) The literature included studies on the elderly population aged 60 years and above including individuals aged 60 and above AD patients. Data from individuals below 60 years were excluded during data processing. (4) Case diagnosis required two steps: screening and confirmation. Trained personnel used the Mini-Mental State Examination (MMSE) and the Hasegawa frailty Scale (HDS) for screening. Positive cases were confirmed based on clinical diagnostic criteria for senile frailty and psychiatric diagnostic criteria.

Exclusion criteria: (1) Inaccurate study design and low reliability. (2) Lack of comprehensive and clear data or descriptive studies. (3)Inability to extract or convert original data from the literature. (4) Literature with ambiguous information or erroneous data calculations. (5) Duplicate publications, conference papers, or review articles. (6) Unclear study design.

(7) Inability to extract or convert original data from the literature. **Outcome criteria:** Case confirmation requires screening and diagnostic stages. In the first stage, trained researchers use the (Mine Mental State Examination, MMSE), Hasegawa frailty Scale (HFS), or (Blessed frailty Scale, BFS) and Composite International Diagnostic Interview (CIDI) to screen all sampled subjects.

Quality Assessment of Literature

Two researchers independently conducted a literature quality evaluation, and the results were compared and discussed. When no consensus was reached, the third researcher participated in the discussion and made the final decision. The Newcastle-Ottawa Quality Assessment Scale (NOS) is a tool that evaluates research study quality and bias risk. It assesses three key components: study group selection, group comparability, and exposure/outcome determination. Studies receive points for meeting each criterion, and the total score indicates overall methodological quality and bias risk, with higher scores indicating better quality

Statistical method

RevMan 5.3 (Cochrane Collaboration, Copenhagen, Denmark) was used for meta-analysis. Relative risk (RR) and standardized mean difference (SMD) were used for statistical analysis within a 95% confidence interval (CI). SMD within a 95%. Before combining the study results, I-square statistics and heterogeneity chi-square tests were used to evaluate statistical heterogeneity among the included studies. I^2>50% or P<0.10 were considered to indicate significant heterogeneity among the studies. The total RR or SMD score was calculated with a 95%. I using a random-effects model when heterogeneity was present, and a fixed-effects model was used when heterogeneity was absent. The outcome evaluation indicators in this study were binary variable, represented by mean square deviation or weighted mean square deviation, and presented with a 95%.

Result

Search results

A total of 732 relevant articles were initially identified. Using Endnote software and manual cross-referencing, duplicate articles were removed. After reviewing the titles and abstracts, 45 articles were obtained in the initial screening. Further reading of the full texts resulted in 15 articles for final screening. Nineteen articles that did not meet the inclusion criteria were excluded. Ultimately, 11 English articles were included for meta-analysis. The flowchart of the literature selection process is shown in Figure 1.

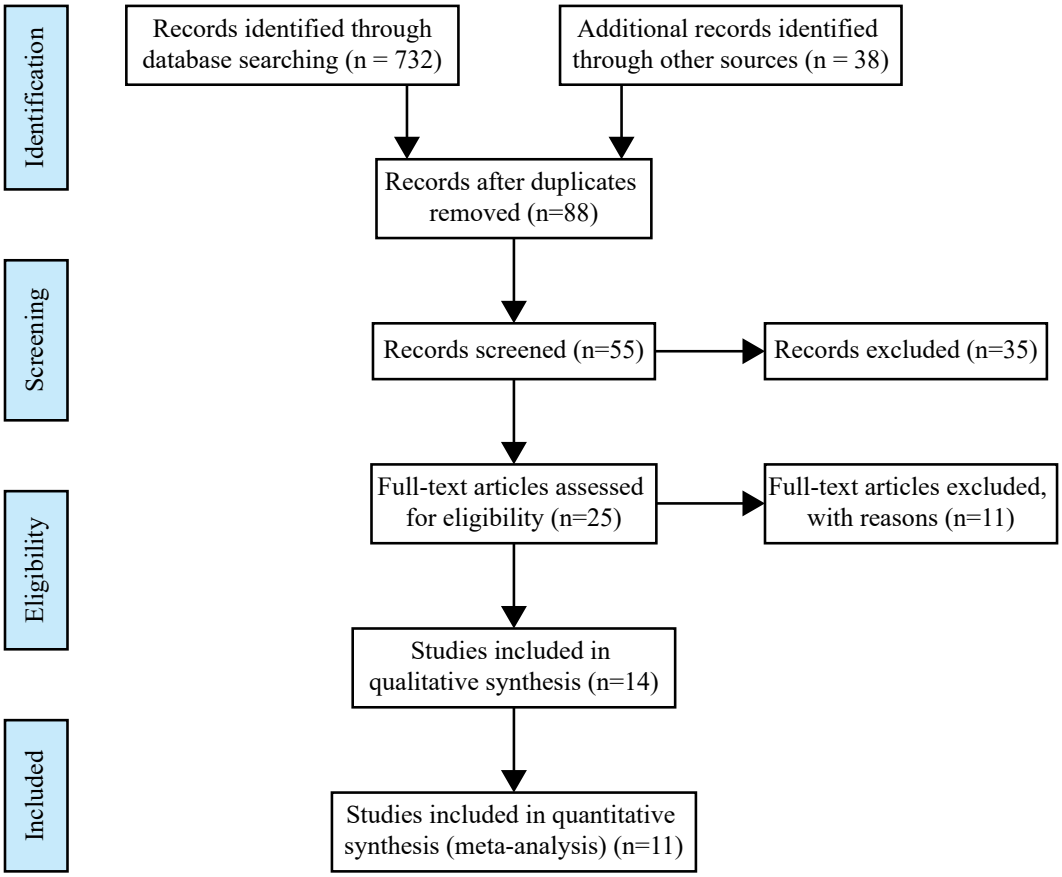

Figure1. PRISMA flowchart detailing the study selection process

Quality assessment of included studies

Among the 11 papers included in this study, 4 papers had a high methodological quality rating of 7 points and above., 5 papers had a medium quality rating of , 6 points and

below, and 2 papers had a low quality rating of 3 points and below. Three papers described specific methods, 1 papers reported concealed allocation methods, and 5 papers had comparable outcome indicators, of which 8 were randomized controlled trials.

Basic characteristics of included studies

A total of 11 cross-sectional study, with a total of 35453 participants. The articles included consisted of normal individuals and patients diagnosed elderly frailty aged 60 and above. Among them, 3 studies used DSM-IV and CCMD-3 as the main diagnostic criteria, while 10 studies used DSM-IV and CCMD-3 as the primary diagnostic tools. The duration of illness was 3 months, and the minimum follow-up time was 3 weeks. The primary outcome measure for efficacy assessment was based on DSM-IV[13,14] and CCMD-3[15-19], and the Mini-Mental State Examination (MMSE)[11] was used as a secondary outcome measure. In addition to DSM-IV[20,21], the Composite International Diagnostic Interview (CIDI)[7] was also utilized.

Table 1: characteristics of included studies

References	year	location	Sample size (female/ male)	Age	Time	Outcome	frailty rate (%)	Alzheimer's disease prevalence rate (%)	Quality score
Borges M K[14]	2019	America	3213/3212	≧65	2000-2015	①②③⑧	1.32	4.21	7
Cezar N O C[15]	2017	Netherlands	1232/1434	≧60	1994-2015	①②⑥	5.65	6.32	7
Fougère B[16]	2017	France	867/965	≧65	2000-2015	①②⑥⑧	4.87	6.32	2
Furtado G E[17]	2018	Germany	2656/22867	≧70	1998-2016	①②⑤⑥	2.34	8.65	6
Gifford K A[18]	2019	America	2312/2121	≧65	1995-2015	①②⑤	4.65	3.87	5
Jia L[19]	2020	China	1645/1867	≧60	1999-2012	⑦⑧	3.21	5.21	3
Kojima G[20]	2016	United Kingdom	2131/2432	60-80	2000-2010	②⑤	12.32	3.65	6
Panza F.[21]	2018	United Kingdom	3153/3432	≧65	2000-2009	①②⑥	9.43	4.98	7
Shimada H[22]	2013	America	3124/3123	60-90	2000-2005	①②③	2.32	3.98	7
Tsutsumimoto K[23]	2019	America	2231/2432	≧60	2000-2017	①②⑦⑧	3.12	2.12	5
Wang C[24]	2017	China	2123/2765	≧65	2000-2016	①②④⑦	3.32	4.16	6

Note: ①CCMD-3; ②ICD-10; ③DSM-IV; ④CCMD-3. ⑤DSM-IV; ⑥Mini-Mental State Examination (MMSE); ⑦Mini-Mental State Examination (MMSE); ⑧Composite International Diagnostic Interview (CIDI).

Analysis of frailty Prevalence

The data analysis included 11 selected references[14-24]. The results of the heterogeneity test showed significant heterogeneity among the studies (P<0.05, I^2=47%). Therefore, a fixed-effect model was used for the meta-analysis. The results showed that the overall prevalence of frailty in mainland China was 9.23% (95% *CI*: 1.79-2.04).

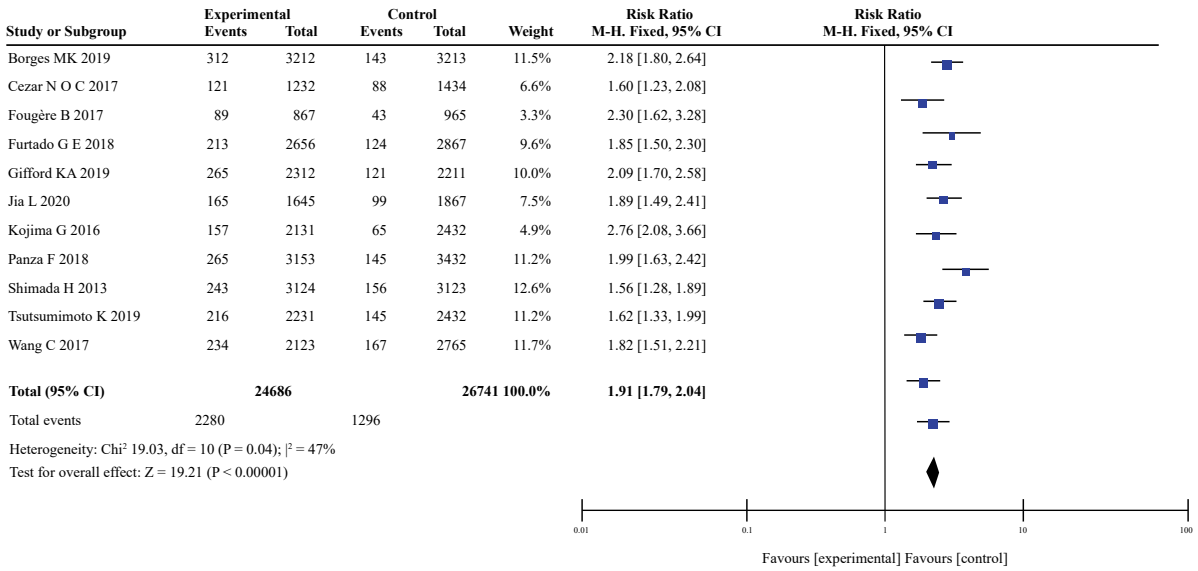

Figure 3. Random Forest Analysis Results of frailty Prevalence

Analysis of frailty Prevalence in Different Subgroups of Older Adults

An analysis was conducted on the prevalence of frailty in different subgroups based on gender, age groups, frailty subtypes, and marital status. During the model testing process, heterogeneity analysis was performed, and the I^2 values were all less than 50%, indicating no substantial heterogeneity. The results are shown in Table 2.

The subgroup analysis results revealed that the prevalence of frailty in elderly females (4.6%) was higher than that in males (3.4%). As age increased, the prevalence of frailty also increased, and it multiplied significantly when the age was ≥75 years. The prevalence of Alzheimer's disease (AD) (2.7%) was higher than vascular frailty (VD) (0.8%). The prevalence of frailty in illiterate individuals (6.6%) was lower than that in literate individuals (7.2%). Among the marital status subgroups, the prevalence of frailty in non-married individuals (including widowed, living alone, divorced, etc.) (7.3%) was higher than that in married individuals (3.1%).

Table 2: Prevalence of frailty in Different Subgroups of Older Adults

Groups	Reference	Disease prevalence (%)	95%CI (value)	Heterogeneity test		
				I^2 (value)	*Q* value	*P* value
			Gender			
Male	8	3.4	0.10~0.21	45.7	0.877	0.000
Female	8	4.6	0.32~0.43	48.9	0.988	0.000
			Years			
60~	5	0.4	1.89~2.32	43.1	0.887	0.000
65~	6	2.4	1.12~2.43	46.2	0.987	0.000
70~	2	4.5	1.21~2.12	21.6	0.865	0.000
75~	2	7.5	0.21~0.97	46.8	0.994	0.000
80~	2	23.5	3.21~4.54	44.7	0.887	0.000
			Subgroup			
AD	4	2.7	1.21~1.98	48.5	0.994	0.000
VD	5	0.8	1.32~2.03	32	0.991	0.000
			Literacy level			
Illiterate	6	6.6	3.32~4.21	49.7	0.975	0.001
Non-illiterate	6	7.2	2.43~3.12	49.7	0.965	0.000
			Marital status			
Married	7	3.1	1.10~2.01	43.2	0.991	0.000
Unmarried	7	7.3	1.10~2.01	50.1	0.993	0.000

Publication Bias Analysis

Funnel plot analysis revealed potential publication bias in the included studies, but the Egger's test (Q=1.21, *P*=0.07) suggested no significant publication bias. Sensitivity analysis indicated good stability of the meta-analysis results (Figure 4).

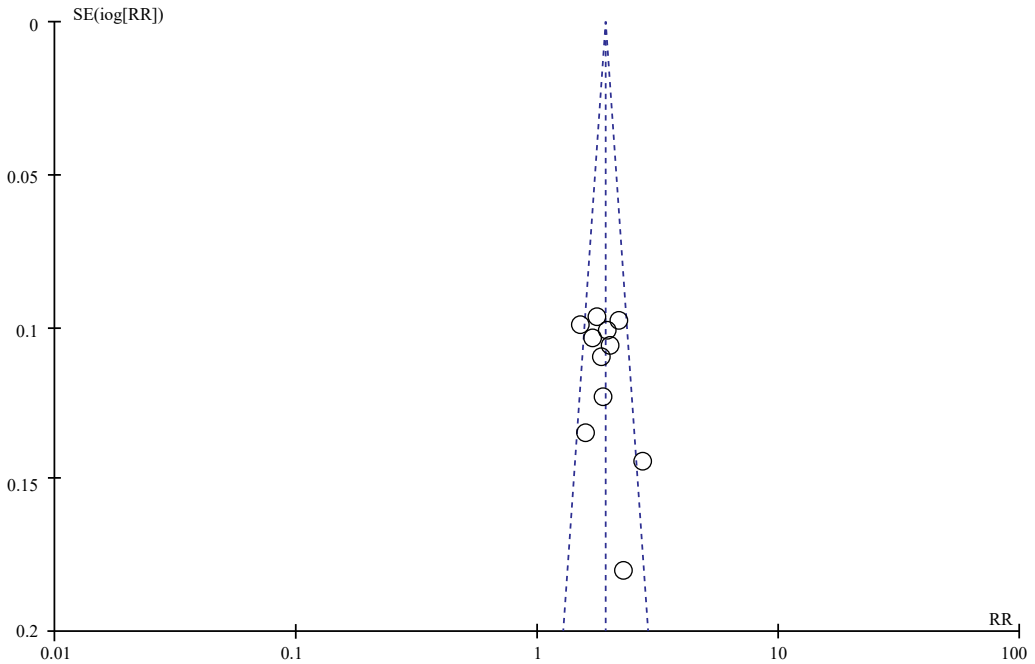

Figure 4. Funnel plot analysis results of the included studies

Discussion

Alzheimer's disease (AD) is a neurodegenerative disorder frequently characterised by the presence of frailty symptoms. The examination of frailty within the population affected

by Alzheimer's disease contributes to the advancement of our comprehension regarding the impact of frailty on the progression of the disease. Additionally, it establishes a foundation for the timely identification and proficient treatment of individuals with Alzheimer's disease.[3] The investigation of frailty in population A holds significant significance for clinical diagnosis and management, prediction and prevention, the formulation of intervention strategies, and the attainment of a full understanding of the underlying pathogenic mechanisms. This research endeavours to enhance the quality of life for those diagnosed with Alzheimer's disease (AD) and alleviate the societal and individual burdens associated with the condition.The present study conducted a comprehensive review and examination of a total of 11 pertinent scholarly articles, encompassing epidemiological surveys conducted in 9 different provinces. The research revealed that the incidence of frailty among adults aged 60 years and older was 9.23%, a figure that aligns with the percentages documented in European and American nations. Alzheimer's disease (AD) and vascular frailty (VD) continue to be the primary forms of frailty observed in the senior population, with corresponding prevalence rates of 2.7% and 0.8%. The observed rates in this study exhibit an increase compared to the research data collected before to 2004, with a more notable distinction between the rates of AD and VD. The pre-2004 ratio of AD to VD was 2.2:1, a finding that aligns with contemporary domestic research. The incidence of Alzheimer's disease (AD) surpasses that of vascular dementia (VD), and further investigation is required to validate the long-term patterns of these two ratios through longitudinal research.[22] Hence, it can be inferred that there has been a rise in the prevalence of Alzheimer's disease (AD) among the senior demographic in recent times, and it poses a greater likelihood of manifestation when compared to vascular dementia (VD). Nevertheless, the validity of this tendency necessitates the conduction of extensive longitudinal research in order to provide additional substantiation.The observed I2 value of 47% in the study may be ascribed to methodological and design variations, which could have contributed to the occurrence of heterogeneity. The observed diversity in study results may be attributed to factors such as disparities in the selection criteria of the study population, variations in data collection procedures, and discrepancies in statistical analysis approaches employed across the articles.

Furthermore, the presence of heterogeneity might be attributed to discrepancies in the demographic features of the sampled populations, including factors such as age, gender, and disease severity.In comparison to other studies or nations, it is evident that the prevalence of frailty associated with Alzheimer's disease (AD) is relatively elevated. This observation can be attributable to various variables, including population structure and lifestyle choices. Frailty associated with Alzheimer's disease (AD) within a population may manifest age-related attributes. As individuals progress in age, there is a potential for an elevated susceptibility to frailty in patients diagnosed with Alzheimer's disease. This underscores the necessity for focused consideration towards older individuals with Alzheimer's disease (AD) in healthcare settings, as well as the implementation of appropriate therapies and management strategies. In therapeutic settings, it is advisable to offer gender-specific intervention recommendations as a means of effectively managing and enhancing frailty symptoms in individuals diagnosed with Alzheimer's disease (AD). The incidence of frailty may be increased in persons with Alzheimer's disease who experience rapid disease progression or have severe symptoms. This statement underscores the significance of disease evaluation and staging in individuals with Alzheimer's disease (AD) in order to facilitate prompt detection and focused therapies for frailty.

The present study's analysis provides further confirmation that gender and age are significant risk factors for frailty among the elderly population. The prevalence rate exhibits a progressive increase as individuals age, with females demonstrating a much greater prevalence rate compared to males. Frailty has a prevalence of 12.7% among adults aged 70 and above. Given the accelerated ageing of the population, there will be a rise in the proportion of elderly individuals, resulting in a corresponding increase in the absolute number of instances of frailty.[23] The incidence of AD-related frailty is notably higher in women compared to males, which can be attributed to several variables. One such factor is the fall in oestrogen levels that women experience following menopause, which may influence the development of AD-related frailty. The presence of oestrogen has been observed to have a beneficial impact on neuroprotection and cognitive function, resulting in an increased vulnerability of women to frailty symptoms following a decrease in oestrogen levels. Females typically exhibit a higher life expectancy in comparison to males, so affording them increased prospects for the development of Alzheimer's disease (AD) and associated frailty.A lower degree of education is identified as a risk factor for frailty in older adults, exhibiting a notably reduced prevalence rate among those who are illiterate as opposed to those who are literate. Moreover, the marital status of individuals plays a significant role in determining the prevalence rate of frailty among the senior population. Specifically, being widowed and residing in solitary conditions are identified as risk factors associated with the development of frailty in later life. This underscores the significance of marital and familial connections for the older population.[24] The existence of heterogeneity can potentially be influenced by the inclusion of unpublished study findings, as these may exhibit discrepancies when compared to published findings. Heterogeneity can also arise from inherent disparities among research, including divergences in study design, sample characteristics, and intervention measures. These variations may be attributed to factors such as the distinct objectives, contexts, and methodological decisions made in various research investigations.

The research employed the technique of meta-analysis to examine the gathered data. Despite the limited sample

size employed in the study, the samples were acquired by sampling surveys, and the cases examined in the literature were carefully screened and diagnosed, hence establishing the credibility of the findings.[25]

Limitation

However, this study has the following limitations: i) the number of outcome indicators included in the literature makes less literature available for combined analysis; ii) there is variability in the research methods of the included literature, and the overall outcome analysis differs to some extent; iii) the small size of the included literature has low power and possible publication bias, which will affect the feasibility and accuracy of the study results; iv) there is still a need for more participants Some characteristics are not clear enough, such as subgroups for conducting CCMD-3/ ICD-10/DSM-IV/CCMD-3, which may affect the accuracy and feasibility of subgroup analysis, as well as such as racial and regional differences, age and disease status step to improve the rationality of study design, in addition to age, sample size also have an impact to some extent, and some subgroups have a small sample size.

Conclusion

The research results show that the prevalence rate of frailty in the age group of 60 and above AD patients and above is 9.23%. As age increases, the prevalence rate of frailty in the elderly also rises. This may be related to world currently being in a peak period of population aging. Frailty is commonly observed among individuals aged 60 years and above AD patients, with a relatively high prevalence. The occurrence of frailty in the elderly can be influenced by various factors, including age, gender, education level, and marital status.

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