

Association between Dementia and Diabetes Mellitus: A Systematic Review

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ABSTRACT

Background: The association between diabetes mellitus and dementia is not well-established such that found between diabetes mellitus and vascular diseases. This article aimed at reviewing the longitudinal prospective studies which evaluated the association between diabetes mellitus and incidence of dementia among different age groups of patients.

Methods: An electronic search was performed by Google Scholar, PubMed, and Sciencedirect to identify all relevant articles. The number of eligible articles based on titles and abstracts were 21 eligible articles. After that, the irrelevant, duplicated and other reviews studies were excluded based on, which resulted in the exclusion of 13 irrelevant articles. Finally, 7 articles were included in this review. The data collected about mean age of the population, type and duration of diabetes, the strength of association and the statistical significance.

Results: The strength of association between dementia and diabetes mellitus varied in the included studies, the reported ratios varied from a relative risk of 1.2 to a 4.77. Regarding the statistical significance of these associations, all the studied articles revealed significant associations with P values less than 0.05.

Conclusion: This review supported the evidence of the association between diabetes mellitus and occurrence of dementia depending on the findings of the recent epidemiological studies.

Keywords: Dementia; Diabetes Mellitus; Alzheimer; Cognitive.

INTRODUCTION

Diabetes mellitus is a metabolic disease that associated with an absolute or relative shortage in insulin secretion ⁽¹⁾. It is a growing public health problem with recent projections of an increase in international prevalence from 2.8% in 2000 to 4.4% in 2030 ⁽²⁾. Dementia is the severe deterioration of cognitive functions which is usually associated with old age when about a third of people above 85 years old could be affected ⁽³⁾. Similarly, the occurrence of diabetes mellitus increases with age to reach 15% prevalence among people above 80 years old ⁽³⁾.

The vascular diseases have been found responsible for adverse health effects such as cognitive impairment and dementia. However, diabetes mellitus has not similar well-established associations. Many studies, after adjustment of age effect, found that diabetes mellitus is an independent predictor for the incidence of dementia and impairment of cognitive functions ⁽⁴⁻⁶⁾. However, these studies used cross-sectional designs that characterized by an absence of the temporal relationship which should be initiated between the risk factor (diabetes mellitus) and outcome (dementia).

The longitudinal approaches are more appropriate to study the presence and magnitude of such association ⁽⁷⁾. In a longitudinal study conducted by Whitmer *et al.* ⁽⁸⁾. Patients with a history of major hypoglycemic shocks were at a

higher risk of dementia. Another longitudinal study reported a strong relationship between diabetes mellitus and dementia related to the incidence of stroke with lower risk in Whites than in Blacks ⁽⁹⁾. A study reported twofold elevated risk of dementia among patients with diabetes mellitus ⁽¹⁰⁾. The reported cognitive decrements including verbal, memory, and information processing ability.

However, the limited psychometric screening and inaccurate cognitive function tests reduced the confidence on the findings of these studies. This article aimed at reviewing the longitudinal prospective studies which evaluated the association between diabetes mellitus and incidence of dementia among different age groups of patients.

METHODS

Keywords and search strategy

The keywords and search strategy used in this review were showed in the summary of search findings (table 1). All steps of the systematic review (identification, screening, eligibility, inclusion) were conducted in this review.

Eligibility Criteria

All articles published in English language and published in the last decade (since 2006) were

eligible to be included in this review. The number of eligible articles based on titles and abstracts was 21 eligible articles. After that, the irrelevant, duplicated and other reviews studies were excluded based on, which resulted in the exclusion of 13 irrelevant articles. Finally, 7 articles were included in this review.

Data Sources

An electronic search was performed by Google Scholar, PubMed, and Science direct search engines using Boolean operators. The search strategy used here was demonstrated in the table (1).

Data Extraction

To ensure that, the extraction of all required information in regard to the association between diabetes mellitus and dementia was done, two reviewers conducted the searching and screening of the eligible articles.

The data were collected in data extraction form shown in table (2), including the following:

- Study design
- Sample size
- Age group of the patients
- Type of diabetes mellitus
- The duration of diabetes mellitus
- Type of psychomotor screening tests
- Type of cognitive function tests
- The odds ratio and relative risk of the associations
- The statistical significance of the association

The study was done after approval of ethical board of Jazan university.

RESULTS

The search of the literature, after exclusion of irrelevant, duplicated and review studies revealed 7 studies which met the inclusion criteria. Included studies aimed at comparing the Association between dementia and diabetes mellitus.

The sample size of included studies ranged from 104 cases in a study conducted by **Plastino *et al.***⁽¹¹⁾ to more than two million persons representing people registered in Danish psychiatric registration⁽¹²⁾. The mean age

Association between dementia and diabetes mellitus of participants ranged from 64.2 years in the study conducted by **Lin *et al.***⁽¹³⁾ to 85 years in a study conducted by **Ahtiluoto *et al.***⁽¹⁴⁾.

In relation to the type of diabetes, the following studies reported include type I & type II diabetes among their participants^(15, 13). Three studies reported only type II diabetes among their participants^(11,16,17). Regarding the type of psychomotor screening tests, only one study conducted by⁽¹²⁾ reported using data from the Danish Psychiatric Central Research Register.

Concerning the type of cognitive function tests used, four studies reported positively, the Diagnostic and Statistical Manual of Mental Disorders criteria (DSM) was used as a tool in research study⁽¹⁵⁾ which reported using the 3rd or 4th edition. **Lin *et al.***⁽¹³⁾ reported inpatient and outpatient databases relied on the ICD-9-CM (International Classification of Diseases, Ninth Revision, and Clinical Modification).

Plastino *et al.*⁽¹¹⁾ utilized the Mini Mental State Examination (MMSE), while the Clinician's Global Impression (CGI), were utilized by another study conducted by **Ahtiluoto *et al.***⁽¹⁴⁾ where assessment based on data obtained from interviews, health examinations, previous health and social work records, and tests of cognitive functions and functional capacity.

The strength of association between dementia and diabetes mellitus varied in 7 studies, where the reported ratios varied from a relative risk of 1.2 in the study carried out by **Katon *et al.***⁽¹²⁾ to a 4.77 in a study conducted by **Akomolafe *et al.***⁽¹⁵⁾

Regarding the statistical significance of these associations, all studies found significant associations with P values were less than 0.05⁽¹¹⁻¹⁸⁾. Other important outcomes were only noted in a study carried out by **Chatterjee *et al.***⁽¹⁷⁾ stating that women with diabetes had a 19% greater risk for the development of vascular dementia than men.

Table (1): Summary of search results

Search Engine	Search Terms	Papers	Titles of the eligible articles based on the title and abstracts	Excluded	Included
Google Scholar	Dementia and diabetes mellitus (2007-2017)	34000	9 eligible studies	3 reviews + 2 irrelevant study + 2 duplicated	2 studies included
PubMed	Dementia and diabetes mellitus (2007-2017) (human studies)	1641	10 eligible studies	4 duplicated + 3 reviews	3 included
Science Direct	Dementia and diabetes mellitus (2007-2017) (Only journals)	7515	2 eligible studies	-	2 studies included
Total		43156	21 eligible studies	14 excluded studies	7 included studies

Table (2): Summary of the findings

Study citation (Author-Year)	Study design	Sample size	Mean age group of the patients	Type of diabetes mellitus	Mean duration of diabetes mellitus	Type of psychomotor screening tests	Type of cognitive function tests	The measures of the association between dementia and D.M.	The statistical significance of the association
[14]	a population-based neuropathologic study	553 individuals	85	Not reported	Not reported	Not reported	interviews, health examinations, previous health and social work records, and tests of cognitive function and functional capacity	1.77 (1.14–2.74)	At baseline= 0.074 At death= 0.381
[19]	prospective cohort study	3075 community dwelling older adults of white and black race/ethnicity	74.0 years;	Not reported	Not reported	Not reported	determined by the date of the first available record of a dementia diagnosis	2.2; 95% CI, 1.1-4.6)	P < .03
[12]	a national population-based cohort study	of 2 454 532 adults	65 years old	Not reported	Not reported	using data from the Danish Psychiatric Central Research Register	using data from the Danish National Patient Register	1.20 (95% CI, 1.17-1.23)	(P < .001) for those younger than 65 years. (P = .001) for those 65 years or older.
[11]	prospective, open-label, observational study	104 patients	76.2±16.4 years	diabetes Mellitus type-2	Not reported	Not reported	mini Mental State Examination (MMSE) and the Clinician's	there is an association between dementia	(P=.001). For both (MMSE) AND (CGI)

							Global Impression (CGI),	and DM	
[16]	a cross-sectional	8213 subjects Among all of these, 1,109 subjects with T2DM	65 years	type 2 diabetes mellitus	Not reported	Not reported	DSM-IV criteria	there is an association between dementia and DM	P < 0.05
[15]	a prospective community-based cohort study	2210 persons	70 years	both type 1 DM and type 2 DM	Not reported	Not reported	diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria	4.77	P=.02
[13]	7-year follow-up study	a total of 15 404 diabetic subjects	64.2 years	both	Not reported	Not reported	inpatient and outpatient databases based on ICD-9-CM diagnostic codes	DM with hypoglycemic attacks 2.76 (95% CI 2.06–3.70). DM Without Hypoglycaemic attacks 1.60 (95% CI 1.19–2.14, P = 0.003),	P < 0.001

DISCUSSION

In this review, the association between dementia and diabetes mellitus was examined. The results showed that the factors in consideration being the patients' age and type of diabetes mellitus. Both types of diabetes mellitus were associated with the decrement of cognitive function but the association was most consistent for type 2 diabetes and older patients. This included studies with higher means of age showed a tendency to report a higher association between dementia and diabetes mellitus in patients^(14, 15, 19).

The majority of included studies were prospective epidemiological studies^(11-13, 15, 19), while the remaining two studies were large-scale population-based surveys^(14, 16).

The most important findings among all included studies were the reporting of significant associations between dementia and diabetes mellitus in different age groups and different populations. They differed only in the strength of these associations, assessed by odds ratio and relative risks. The strength of this association varied from a 1.2 in the study (12) carried out by **Katon *et al.***⁽¹²⁾ to a 4.8 in another study conducted **Akomolafe *et al.***⁽¹⁵⁾.

Evidence gathered from the included studies revealed that diabetes mellitus is an important risk factor for incidence of dementia, which is usually associated with a progressive deterioration of cognitive skills⁽²⁰⁾. In another hand, the decline in cognitive skills can result in inadequate self-control of blood glucose, which leads to more complications accompanied with episodes of hyper- and hypoglycemia⁽²¹⁾. The study of Lin and Shen showed that the patients suffered more frequently to hypoglycemic episodes are linked to stronger association with dementia than those without. The included studies showed that the association between dementia and diabetes mellitus seems to be more related to the occurrence of hypoglycemic episodes rather than to the type of diabetes mellitus.

The relationship linked dementia to diabetes mellitus act as a positive feedback cycle where uncontrolled blood glucose increase incidence of dementia, and in turn dementia can result in poor self-management of diabetic patients due to deterioration of cognitive functions. Thus, poor management of blood glucose can be considered the main risk factor for the development of dementia in diabetic patients⁽²²⁾.

CONCLUSION

This review supported the evidence of the association between diabetes mellitus and occurrence of dementia based on the findings of recent epidemiological studies.

Conflict of interests

The authors declared that no financial support was provided and no conflict of interests

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