Modifiable Risk Factors for Dementia in Indonesia's Urban Population

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ABSTRAK

Latar belakang: Indonesia merupakan satu dari sepuluh negara di dunia yang diestimasi memiliki jumlah kasus demensia melebihi satu juta orang. Jumlah penduduk lansia di perkotaan Indonesia sudah melebihi jumlah lansia yang tinggal di pedesaan, namun Indonesia masih kekurangan data yang dapat mewakili populasi dominan tersebut tentang faktor risiko demensia yang dapat dimodifikasi. Pencegahan demensia penting dilakukan. Studi ini mengidentifikasi faktor risiko demensia yang dapat dimodifikasi pada populasi perkotaan di Indonesia. Metode: penelitian kasus-kontrol ini menggunakan data 5 tahun Rumah Sakit Umum Pusat Nasional dengan melacak kembali buku rekam medis individu berusia 60 tahun ke atas di klinik rawat jalan geriatri hingga data kunjungan pertama. Analisis statistik bivariat serta multivariat digunakan untuk mengontrol faktor perancu dengan tepat. Subanalisis dilakukan untuk demensia vaskular. Hasil: data 345 pasien menunjukkan bahwa faktor risiko demensia yang dapat dimodifikasi adalah riwayat merokok (adjusted OR 2.860, 95% CI 1.559-5.246), riwayat penurunan pendengaran (adjusted OR 7.962, 95% CI 3.534-17.941), riwayat depresi (adjusted OR 12.473, 95% CI 2.533-61.417), hipertensi (adjusted OR 1.751, 95% CI 1.006-3.048), dan diabetes melitus (adjusted OR 2.561, 95% CI 1.482-4.425). Pasien demensia memiliki median durasi diabetes melitus lebih lama (12 tahun) dibanding lansia tanpa demensia (9 tahun). Kondisi underweight atau tingkat pendidikan rendah sendirinya tidak berhubungan dengan demensia di perkotaan. Faktor risiko demensia vaskular mirip dengan demensia pada umumnya. Kesimpulan: pada populasi perkotaan di Indonesia, faktor risiko demensia yang dapat dimodifikasi adalah riwayat merokok, penurunan pendengaran, depresi, hipertensi, dan diabetes melitus.

Kata kunci: faktor risiko, demensia, Indonesia, perkotaan, Jakarta.

ABSTRACT

Background: Indonesia is one of ten countries in the world with estimated number of dementia case exceeding a million. The number of elderly population living in Indonesian cities has exceeded the number in rural areas, but the country lacks data representing the urban population better related to modifiable risk factors for dementia, prevention of which is crucial. We aimed to identify the modifiable risk factors for dementia in Indonesia's urban population. Methods: this case-control study used five-year data in Indonesia's national general hospital by tracing back medical record books of individuals aged 60 years and above in geriatric medicine outpatient clinic to the first hospital visit. Statistical analyses included bivariate and multivariate analyses to adjust for confounding factors appropriately. Results: data from 345 patients suggested that the significant risk factors for dementia were history of smoking (adjusted OR 2.860, 95% CI 1.559-5.246), history

*of hearing loss (adjusted OR 7.962, 95% CI 3.534-17.941), history of depression (adjusted OR 12.473, 95% CI 2.533-61.417), hypertension (adjusted OR 1.751, 95% CI 1.006-3.048), and diabetes mellitus (adjusted OR 2.561, 95% CI 1.482-4.425). Dementia patients had longer median duration of diabetes mellitus (12 years) than elderly without dementia (9 years) before the diagnosis of dementia. Single point late-life underweight condition and low educational attainment were not associated with dementia in Indonesia's urban setting. The risk factors for vascular dementia were largely similar to those of dementia. **Conclusion:** in Indonesian urban population, history of smoking, hearing loss, depression, hypertension, and diabetes mellitus are associated with dementia.*

*   **Keywords**: risk factor, dementia, Indonesia, urban, city, Jakarta.*

INTRODUCTION

The greatest challenge for social care and healthcare worldwide in the 21st century is dementia. Prevention is currently better than cure for dementia.[1] Asia Pacific region in general has the fastest growing population of dementia patients in the world.[2] Indonesia is one of ten countries in the world with estimated number of dementia case exceeding a million.[3] The number of population of older people nationwide in 2020 reached approximately 27.08 million (9.99% of total population)[4] and accounts for about two-fifths of the total elderly population in South-East Asia.[3] Previous local study in Yogyakarta, Indonesia reported several risk factors associated with dementia with most of the subjects residing in rural areas.[5] In fact, the number of urban population in Indonesia exceeded that of rural community.[6] There is also paucity of data representing the urban community of Indonesia better.

Indonesia is seldom involved in multinational studies related to dementia. Studies in high-income,[1] as well as other low- and middle- income countries, have analyzed the relationship between several modifiable risk factors (abnormal body mass index [BMI], low educational attainment, history of smoking, hearing loss, hypertension and diabetes mellitus [DM]) and dementia.[7] The aforementioned risk factors may also confound each other's link with dementia.[8–25] Therefore, a local study about alterable risk factors for dementia in urban settlement with appropriate adjustment for potential confounders is needed.

We aimed to identify the modifiable risk factors for dementia in Indonesia's urban setting, by utilizing data from the national general hospital in Jakarta, the capital city of Indonesia.

The center is a favorable study location due to its variability of patient characteristics to estimate and represent the real condition of population well. The study variables were late-life underweight condition, low educational attainment, history of smoking, history of hearing loss, hypertension, and DM. As vascular dementia was among the commonest type of dementia in previous study of Indonesia's geriatric medicine outpatients.[26] Subanalysis was also done to identify the modifiable risk factors for vascular dementia.

METHODS

Data Source

We investigated the effect relationship of the modifiable risk factors and dementia in Indonesian clinical cohort of patient with and without dementia. A hospital-based case-control study design was conducted in Indonesia's national general hospital, Cipto Mangunkusumo Hospital (RSCM) using five-year data between January 2014 and December 2018. We selected the centre due to its variable characteristics of patient to estimate and represent the real condition of population well. Ethical approval was granted by The Ethics Committee of the Faculty of Medicine, Universitas Indonesia (protocol number 20-03-0384).

We included all prevalent dementia cases in this study. Patients in control group attended the same outpatient service with no history of dementia and were selected with simple random sampling technique. We included patients 60 years of age and older, and excluded patients with incomplete medical record. We manually opened medical record books of patients in

outpatient geriatric medicine clinic to obtain the information by tracing back to the first hospital visit of each patient. Such data collection method was an attempt to avoid potential bias from possible mistake in data input to the underdeveloped electronic health record system. In addition, we verified the diagnoses by rereading the subjective and objective findings in the care plans of each patient.

We collected data related to body mass index, educational attainment, history of smoking, history of hearing loss, hypertension, and DM. We also documented the durations of hypertension and DM up until the diagnosis of dementia or simply the duration until 1 March 2020 for the control group. The durations were based on local hospital data and memory recall during history taking.

Dementia and depression diagnoses were made by physician as per Diagnostic and Statistical Manual of Mental Disorders IV (DSM IV) and Indonesia's own guideline Pedoman Penggolongan dan Diagnosis Gangguan Jiwa III (PPDGJ III). The suspected type of dementia was based on clinical judgement by physicians and supported by appropriate diagnostic tool (e.g. brain MRI), without post-mortem brain study. We considered late-life body mass index as underweight if it was <18.5 kg/m^2. Low educational attainment was defined as history of primary school completion only or no formal education at all. Smoking was obtained by self-report and classified as the presence or absence of history of smoking. History of hearing loss was recorded as yes or no, depending on diagnosis made by physicians. The diagnoses of hypertension and DM were made on the basis of Joint National Committee 7 (JNC 7) criteria and American Diabetes Association (ADA) 2010 criteria, respectively.

Statistical Methods

Sample size calculation relied on the formula for case-control study.[27] We expected the number of individuals in control group to be twice as many as in case groups. P1 was the proportion of dementia elderly exposed to hypertension (0.72),[26] whereas P2 was 0.478.[28]

The minimum number of sample in dementia group was 62. Data were finally obtained from 115 patients with dementia and 230 patients without dementia. We analyzed the data utilising IBM® SPSS® Statistics Version 20 involving bivariate and multivariate analyses. The crude OR of each variable was appropriately adjusted for other study variables in multivariate analysis. We provided subanalysis result to identify the role of the potential risk factors for vascular dementia. We considered p-value < 0.05 as statistically significant.

RESULTS

We collected data from 345 subjects. The characteristics of study participants are shown in **Table 1**. Nearly half of all subjects were 70-79 years old (47.0%). A majority of older people completed senior high school education (40.9%). Most of all older people had BMI of 18.5 kg/m^2 or higher (86.1%). Among all subjects, 20%, 11.9%, 58.3%, and 32.8% had history of smoking, hearing loss, hypertension, and DM, respectively. Only 4.9% of elderly had history of depression.

Table 1. Characteristics of Subjects (n = 345).

Characteristics	All subjects (n = 345)	
	n	%
Age		
60-69 years	103	29.9
70-79 years	162	47.0
80 years and older	80	23.2
Sex		
Male	190	55.1
Female	155	44.9
Body mass index		
≥18.5 kg/m^2	297	86.1
Underweight (<18.5 kg/m^2)	48	13.9
Last completed formal education		
No formal education	19	5.5
Primary school	58	16.8
Junior high school	34	9.9
Senior high school	141	40.9
Higher education	93	27.0
History of smoking	69	20.0
History of hearing loss	41	11.9
History of depression	17	4.9
Hypertension	201	58.3
Diabetes Mellitus	113	32.8

Among dementia patients (n=115), the most common types of dementia were vascular dementia (54.8%) and Alzheimer's disease (17.4%). Among all dementia patients, 2.6% and 1.7% were diagnosed with dementia with Lewy bodies and frontotemporal dementia, respectively. On the other hand, 23.5% of patient's dementia type remained unspecified. A majority of patient (70.4%) was diagnosed with dementia for the first time when they were 70 years old or older. Forty percent dementia patients completed higher education and 74.8% of dementia patients had high educational attainment. The numbers of participant in each variable, bivariate, and multivariate analysis results related to dementia in general are shown in **Table 2**, whereas it is shown in **Table 3** for vascular dementia. Most

dementia patients in the city had normal BMI, high educational attainment, and without the history of smoking, hearing loss, as well as depression. A majority of dementia patients had late-life hypertension (70.4%), whereas the proportions of dementia patient with and without documented DM were similar (47.8% vs 52.2%). Likewise, similar proportions were also seen in vascular dementia patients, except much higher proportion of vascular dementia patients had late-life hypertension (82.5%). The median (range) duration of hypertension was 7 years (1.47 years) in control group, whereas it was 6 years (0.36 years) in dementia patients. In control group and dementia group, the durations of DM were 9 years (1.47 years) and 12 years (0.37 years), respectively.

Table 2. Crude Odds Ratio (OR) and Adjusted OR of Modifiable Risk Factors for Dementia.

Variables	Patient without dementia (n= 230) n (%)	Patient with dementia (n=115) n (%)	Crude OR (95% CI)	p value of crude OR	Adjusted OR (95% CI)[a]	p value of adjusted OR
Body mass index						
≥18.5 kg/m^2	200 (87)	97 (84.3)	1.237	0.510	1.608	0.190
Underweight (<18.5 kg/m^2)	30 (13)	18 (15.7)	(0.657-2.329)		(0.791-3.271)	
Educational attainment						
High educational attainment	183 (79.6)	86 (74.8)	1.313	0.313	1.272	0.440
Low educational attainment	47 (20.4)	29 (25.2)	(0.774-2.228)		(0.690-2.342)	
History of smoking						
No history of smoking	196 (71)	80 (69.6)	2.522	0.001	2.860	0.001
Documented smoking history	34 (49.3)	35 (30.4)	(1.471-4.323)		(1.559-5.246)	
History of hearing loss						
No history of hearing loss	220 (95.7)	84 (73)	8.119	<0.001	7.962	<0.001
Documented history of hearing loss	10 (4.3)	31 (27)	(3.813-17.288)		(3.534-17.941)	
History of depression						
No history of depression	228 (99.1)	100 (87)	17.100	<0.001	12.473	0.002
Documented history of depression	2 (0.9)	15 (13)	(3.838-76.180)		(2.533-61.417)	
Hypertension						
No hypertension	110 (47.8)	34 (29.6)	2.184	0.001	1.751	0.048
Late-life hypertension	120 (52.2)	81 (70.4)	(1.356-3.518)		(1.006-3.048)	
Diabetes Mellitus						
No diabetes mellitus	172 (74.8)	60 (52.2)	2.718	<0.001	2.561	<0.001
Documented diabetes mellitus	58 (25.2)	55 (47.8)	(1.696-4.357)		(1.482-4.425)	

[a] Mutually adjusted odds ratios (with 95% confidence intervals) derived from logistic regression model which included all of other variables for which results are presented.

The crude odds ratio (OR) and adjusted OR of the risk factors for dementia were shown in **Table 2**. Results showed that history of smoking (adjusted OR 2.860, 95% CI 1.559-5.246), history of hearing loss (adjusted OR 7.962, 95% CI 3.534-17.941), history of depression (adjusted OR 12.473, 95% CI 2.533-61.417), hypertension (adjusted OR 1.751, 95% CI 1.006-3.048), and DM (adjusted OR 2.561, 95% CI 1.482-4.425) were significant modifiable risk factors for dementia. In contrast, underweight (adjusted OR 1.608, 95% CI 0.791-3.271) and low educational attainment (adjusted OR 1.272, 95% CI 0.690-2.342) were not significant risk factors for dementia in this study. Similarly, significant risk factors for vascular dementia were also history of smoking, hearing loss, depression, hypertension, and DM. (**Table 3**) The adjusted OR of hypertension (adjusted OR 3.305, 95% CI 1.576-6.931) as a risk factor for vascular dementia was higher than for dementia in general, whereas the role of depression as a risk factor for vascular dementia was insignificant.

DISCUSSION

The most common type of dementia in this study was vascular dementia. The modifiable risk factors for dementia in Indonesia's urban population are history of smoking, hearing loss, depression, hypertension, and DM. In this study, the role of underweight state or low educational attainment as the risk factor for dementia was not significant. Longer median duration of DM was seen in dementia patients (12 years) than in elderly without dementia (9 years).

In this study, we identified risk factors similar to those found in studies in high[1] and low-income countries,[7] except the findings related to body mass index and low educational level. We found

Table 3. Crude Odds Ratio (OR) and Adjusted OR of Modifiable Risk Factors for Vascular Dementia.

Variables	Patient without vascular dementia (n= 282) n (%)	Patient with vascular dementia (n=63) n (%)	Crude OR (95% CI)	p value of crude OR	Adjusted OR (95% CI)[a]	p value of adjusted OR
Body mass index						
≥18.5 kg/m^2	242 (85.8)	55 (87.3)	0.880	0.758	1.240	0.638
Underweight (<18.5 kg/m^2)	40 (14.2)	8 (12.7)	(0.390-1.985)		(0.506-3.042)	
Educational attainment						
High educational attainment	222 (78.7)	47 (74.6)	1.260	0.476	1.162	0.679
Low educational attainment	60 (21.3)	16 (21.1)	(0.668-2.377)		(0.569-2.373)	
History of smoking						
No history of smoking	235 (85.3)	41 (65.1)	2.683	0.001	2.922	0.002
Documented smoking history	47 (16.7)	22 (34.9)	(1.465-4.915)		(1.478-5.778)	
History of hearing loss						
No history of hearing loss	259 (91.8)	45 (71.4)	4.504	<0.001	4.262	<0.001
Documented history of hearing loss	23 (8.2)	18 (28.6)	(2.252-9.010)		(1.942-9.350)	
History of depression						
No history of depression	273 (96.8)	55 (87.3)	4.412	0.003	2.303	0.162
Documented history of depression	9 (3.2)	8 (12.7)	(1.631-11.939)		(0.715-7.419)	
Hypertension						
No hypertension	133 (47.2)	11 (17.5)	4.220	<0.001	3.305	0.002
Late-life hypertension	149 (52.8)	52 (82.5)	(2.114-8.423)		(1.576-6.931)	
Diabetes Mellitus						
No diabetes mellitus	204 (72.3)	28 (44.4)	3.269	<0.001	2.882	0.001
Documented diabetes mellitus	78 (27.7)	35 (55.6)	(1.865-5.731)		(1.528-5.434)	

[a] Mutually adjusted odds ratios (with 95% confidence intervals) derived from logistic regression model which included all of other variables for which results are presented.

that dementia patients were not more likely to have late-life underweight condition (adjusted OR 1.608, 95% CI 0.791-3.271). The result of subanalysis for vascular dementia also suggested similar finding. This is contrary to the results of a longitudinal study conducted by Fitzpatrick and colleagues, including the evidence that people with late-life underweight condition had higher risk of dementia (HR 1.62, 95% CI 1.02-2.64).[29] This finding may suggest less contribution of single measurement of BMI in increasing the risk of dementia in Indonesian urban population aged 60 years and above. Rather than single measurement, lifetime trends in weight may improve the prediction. Monitoring of BMI is thus needed, seeing that BMI loss is a marker of incipient dementia.[30]

The odds of low educational attainment among dementia patients are similar to the odds among controls (adjusted OR 1.272, 95% CI 0.690-2.342). Likewise, the result of subanalysis for vascular dementia also suggested insignificant role of low educational attainment in early life as an alterable risk factor. In contrast, a cross-sectional study in Indonesia with most of the subjects residing in rural area reported inverse association between dementia and educational level.[5] Our study showed that almost half of the dementia patients in our urban population completed higher education. In addition, Jakarta has the highest net enrolment ratio of senior and junior high school among other provinces. Earlier study in Jakarta also showed no significant relationship between educational level and memory impairment among elderly with normal Mini-Mental State Examination (MMSE) result.[31] In another urban setting in Manado, Indonesia, there was also no correlation between educational level and dementia.[32] The findings in the Indonesian cities collectively suggest that people in the city regardless of their educational attainment may also develop dementia, whilst other risk factors may be more prominent. Years of schooling might not represent the quality of education, which is possibly a more important factor.[33] On the other hand, we hypothesised that the result of this study may be affected by presumed underdetection of dementia in urban

population with low educational level. There is limited data to support this conjecture and researchers have yet to analyse the associated risk factors for underdetection of dementia in Indonesia, owing to the fact that different income may partly affect the detection of dementia in different countries. For instance, low levels of education, occupational class and income in China are strongly associated with greater risk for having undetected dementia.[34]

Dementia patients are nearly three times more likely to have a history of smoking (adjusted OR 2.860, 95% CI 1.559-5.246). Similar result was seen for vascular dementia. Cigarette smoke contains neurotoxins increasing the risk for dementia.[35] The proportion of elderly with history of smoking in Indonesia's urban population was 22.54%,[36] similar to the finding in this study (20%). The link between smoking and dementia may also be due to the relationship between smoking and cardiovascular diseases.[1] Smoking increases fibrinogen levels, induces hypercoagulable state, and results in oxidative damage. The risk of cardiovascular pathology is lowered as smoking cessation reduces oxidative stress and inflammatory markers. In Asian population, a prolonged period of smoking cessation ($\geq$ 4 years) is beneficial to lower the risk of dementia.[37] Nevertheless, not smoking increases health in ageing as well as life expectancy.[1] Strategy regarding the prevention and cessation of smoking should be emphasised in all age groups.

In this study, hearing loss was not divided into central and peripheral impairment. Hearing loss itself may lead to depression or social disengagement. Furthermore, it may cause alterations in the brain through the cognitive load of the vulnerable brain. Microvascular pathology and older age heighten the risk of peripheral hearing loss and dementia, which may confound the association between the two.[1] However, even after adjustment for potential confounders in this study, the odds of having hearing loss among dementia patients were significantly higher than controls (adjusted OR 7.962, 95% CI 3.534-17.941), whereas the adjusted OR was lower in terms of vascular dementia (adjusted OR 4.262, 95% CI 1.942-9.350). Preliminary

result of other study suggested that mitigation of the risk of dementia from hearing loss can be achieved by hearing aid.[7] However, in the case of central hearing loss, hearing aid does not improve hearing. Thus, central hearing loss is unlikely to be modifiable since comprehension of speech in noise is impaired due to noncochlear pathology. Nevertheless, the relationship between depression and dementia can be bidirectional, since Alzheimer's disease may affect central auditory area. Thus, hearing loss could be a prodromal symptom of the dementia as well.[1]

We suggest an association between history of depression and dementia (adjusted OR 12.473, 95% CI 2.533-61.417). A systematic review suggested a link between depressive mood and air pollution, noise pollution, lack of green areas, as well as poor housing quality [38], which are all common in Indonesian urban setting. A cohort study suggested that only 10 years prior to the incidence of dementia that depression is more common in elderly with dementia than those without dementia. The risk of dementia is increased through the impact on stress hormones, hippocampal volume, and neuronal growth factor.[39] Similar to hearing loss, the association between the cognitive decline and depressive symptoms may also be bidirectional. In regards to the effort to lower the risk of dementia, the effect of antidepressants remains controversial.[1] Interestingly, depression is not a significant risk factor for vascular dementia (adjusted OR 2.303,95% CI 0.715-7.419). We hypothesised that depression may occur later in vascular dementia, instead of being an independent variable prior to vascular dementia. One study suggested that depressive symptoms were more prevalent in patients with vascular dementia compared to Alzheimer's disease. In addition, the depressive symptoms may also be more severe in vascular dementia patients.[40]

The odds of having hypertension is almost two times higher among dementia patients than controls (adjusted OR 1.751, 95% CI 1.006-3.048). On the other hand, the odds of having hypertension is 3.3 times higher among vascular dementia patients than controls in this study (adjusted OR 3.305, 95% CI 1.576-6.931). The median duration of hypertension was 7 years in control group, whereas it was only 6 years in dementia patients. The duration may be affected by recall bias.

In general, both the detection of hypertension and the blood pressure control are protective against later-life cognitive decline.[41] Fortunately, the awareness and treatment of hypertension in Indonesia's urban population is already higher than in rural parts. Indonesia's community-based integrated coaching posts may contribute to the community participation in the early detection of hypertension.[42] The issue in Asian countries is that not many people are aware of the relationship between hypertension and dementia / cognitive impairment.[41] Blood pressure control can be achieved by combining pharmacological and non-pharmacological approach.[43] Among all antihypertensives, angiostensin receptor blockers (ARBs)[44] and calcium channel blockers (CCBs)[45] have a more pronounced protective effect to reduce the risk of dementia. Older people with hypertension may not meet the target of recommended physical activity for young adults, thus functional capacity and preferences of each individual should be considered. Lifestyle changes that are recommended to patients with hypertension in general, including dietary salt restriction, Dietary Approaches to Stop Hypertension (DASH) diet, may be detrimental to older people.[43]

Ambulatory adults with hypertension may benefit from treatment with a goal of SBP <120 mm Hg to reduce the risk of mild cognitive impairment (MCI) significantly in comparison with antihypertensive drug treatment with higher goal SBP (>140 mm Hg) (HR 0.81, 95% CI 0.69-0.95).[46] However, the relationship in studies conducted in older adults was variable. Although at least a trial of elderly patients showed no significant difference in dementia incidence between antihypertensive treatment and placebo groups, the result of meta-analysis of trials favoured treatment (HR 0.87, 95% CI 0.76-1.00, p = 0.045).[47] A recent meta-analysis of cohort studies showed that antihypertensive drug in older people is associated with reduced risk for dementia (RR 0.86, 95% CI 0.75-0.99, p = 0.033), but not with the risk for cognitive

impairment, cognitive decline and Alzheimer's disease.[48]

Despite the controversial results regarding the beneficial effect of antihypertensive drugs on the reduction of dementia risk, we still emphasise the importance of antihypertensive treatment in all patients with hypertension. The reasons include the potential damage of the brain in cases of hypertension. Hypertension is associated with incidence of stroke. Once stroke occurs, there is sixfold higher risk of developing dementia at 5 years. Stroke may have impact on the white matter and hippocampus, leading to post-stroke cognitive impairment.[41] A systematic review and metaregression analysis showed that antihypertensive treatment lowered the risk for disabling or fatal stroke (RR 0.71, 95% CI 0.59-0.85, p < 0.001) as well as the risk for recurrent stroke (RR 0.73, 95% CI 0.62-0.87, p < 0.001).[49] Stroke prevention is crucial, since it is a risk factor for dementia. In fact, blood pressure variability in Asian older adults is still an issue. Diurnal blood pressure variation is associated with silent cerebrovascular damage and may lead to the development of dementia in the form of Alzheimer's disease. Strict nocturnal blood pressure control has a neuroprotective effect on the brain to prevent the incidence of dementia.[41.] A multicentre study in low- and middle-income countries not involving Indonesia suggested hypertension and hearing loss as initial targets for dementia prevention strategies. The prevention potential of the modifiable risk factors for dementia in those countries is even greater than in high-income countries.[7]

The odds of having DM among dementia patients in general and vascular dementia patients are nearly three times higher than controls (adjusted OR for dementia 2.561, 95% CI 1.482-4.425; adjusted OR for vascular dementia 2.882, 95% CI 1.528-5.434). In controls and dementia group, the median duration of DM were 9 years (range 1, 47 years) and 12 years (range 0, 37 years), respectively. Diabetes has adverse effects seen from vascular, degenerative and metabolic point of view. Atherosclerosis and cerebrovascular diseases may result in vascular dementia, whereas altered insulin metabolism, impaired amyloid clearance, and p-tau play role

in the development of Alzheimer's disease.[50] Peripheral insulin anomalies lead to lower production of brain insulin causing impairment in amyloid clearance. From metabolic point of view, high blood sugar level and inflammatory state in diabetic patients also impair cognition.[1] Oxidative stress, advanced glycation end product (AGE), and glucose toxicity are all involved in the pathophysiology of the newly proposed type of dementia, namely diabetes-related dementia. Patients with diabetes-related dementia are characterised by less severe medial temporal lobe atrophy and less word recall impairment, but patients may have impaired executive function and attention. Patients with this type of dementia is typically old with long duration of diabetes, high haemoglobin A1C, high frequency of insulin therapy, and low frequency of apolipoprotein E4 carrier.[50] Interestingly, a 24-week randomised controlled trial analysing the oral hypoglycaemic drug rosiglitazone in older people did not show beneficial effect of the treatment on the reduction of dementia risk.[51] Another commonly prescribed drug for diabetic patient, statin, is also ineffective for the risk reduction in the elderly.[52]

To date, we believe that our study is the only primary observational study taking account data related to various reported multiple risk factors at once to identify the modifiable risk factors for dementia in Indonesia's urban setting. We also avoided overadjustment and under-adjustment for potential confounders. However, we acknowledge the limitations of this study. First, wide confidence interval is an issue in mainly two study variables (history of hearing loss and depression). Second, the study result might be affected by presumed underdetection of dementia in city dwellers with low educational attainment. Third, we only took account one-time BMI measurement for the analysis. Fourth, we have not incorporated other potential risk factors in our study, including low social contact, physical inactivity, living near major roads, and alcohol consumption. To overcome the limitations, studies should have larger sample size and follow up the changes of study variables. Moreover, future studies have yet to elaborate more on other potential risk

factors for dementia, as well as the potential risk factors for underdetection of dementia. Improved detection of dementia may bring about higher reliability of study result.

CONCLUSION

The odds of having either hypertension, DM, history of smoking, hearing loss, or depression are significantly higher among dementia patients in Indonesia's urban population than controls. The role of underweight state or low educational attainment as the risk factor for dementia was not significant. The study result provides information to physicians and patients for the detection of modifiable risk factors before the occurrence of dementia. Prolonged smoking cessation (≥4 years), hearing aid, and antihypertensive drugs (angiostensin receptor blockers and calcium channel blockers) may be beneficial for the significant reduction of dementia risk.

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