Burden of comorbidities among older Malaysians with stroke: Associations with diabetes mellitus and frailty

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Abstract

Background and aims

The increasing prevalence of diabetes and the growing population of older people further adds to the complexities of stroke care. This study aimed to describe (1) prevalence of diabetes in older persons with stroke and (2) compare the burden of comorbidities and cardiovascular risk factors among patients with diabetes and frailty compared to those without these conditions.

Methods

We conducted an analysis of older patients aged ≥ 65 years. Comorbidities were assessed using the Charlson Comorbidity Index (CCI). Frailty assessments were performed using the Clinical Frailty Scale (CFS) version 2.

Results

A total of 384 participants were included for analysis, mean age of 81.11 ± 6.373. Diabetes was present in 45.1%. The prevalence of frailty was 81.3% in those with diabetes and 70.5% in those without diabetes. The mean CCI was highest for the frail and diabetic group (6.97 ± 1.97). Participants with diabetes also had a significantly higher prevalence of risk factors like hypertension (90.8% versus 74.4%, p <0.001) and cardiovascular disease like ischemic heart disease (27.2% versus 14.8%, p =0.003).

Conclusions

There was a very high prevalence of diabetes in older patients with stroke in this study. Besides the management of diabetes, frailty and cardiovascular risk factors are potential target areas that healthcare providers can strive to address to enhance the overall well-being and quality of life for older stroke survivors with diabetes.

Introduction

Stroke continues to be a major contributor to mortality and disability.1 Due to the nature of the disease, stroke patients experience loss of brain function that affects motor and cognitive function resulting in disabilities. Recent advancements have allowed improved care resulting in a growing number of stroke survivors.2 These stroke survivors may regain some motor capability depending on recovery.3 Factors influencing the prognosis of stroke recovery include, age, stroke severity, subtypes of stroke and comorbidities like diabetes.4,5

The prevalence of diabetes has increased considerably over recent decades.6,7,8 This has implications when considering management and prevention strategies for stroke. The high prevalence of diabetes among stroke in-patients specifically can increase complexities and healthcare utilization. Some studies
have reported how diabetes influences mortality and recurrent stroke, although this is usually limited to the younger population.\textsuperscript{9,10}

With most studies focusing on patients aged less than 65 years\textsuperscript{11}, there is currently limited data on in-hospital and long-term outcomes for older stroke patients with diabetes. This is partly contributed by the age limit set in some clinical trials.\textsuperscript{12} The growing number of older people and the fact that age is an irreversible risk factor for stroke, studies in this specific age group are needed to help guide future care. Especially when age-specific prevalence rates of diabetes are noted to be growing faster in the older population (≥ 65 years of age) when compared to those younger.\textsuperscript{13} Research prioritization exercises have also highlighted the lack of evidence to guide care for older people with diabetes and the need for more studies to explore how it relates to other comorbidities.\textsuperscript{14,15} The additional influence of frailty on health outcomes for an older person\textsuperscript{12,16} further increases the complexity but also shows the necessity for further studies.

Like many other regions, stroke and diabetes are growing public health concerns in Malaysia.\textsuperscript{17} Malaysia, has one of the highest rates of diabetes in the Western Pacific region.\textsuperscript{18} For broader stroke management strategies, this is critical as the prevalence of diabetes in hospitalized patients with strokes in Malaysia has been reported to be highest among Southeast Asian and East Asian countries.\textsuperscript{8} Stroke is also the second major cause of premature mortality among older adults in Malaysia.\textsuperscript{19} The growth of the older population has overtaken the younger population and it is estimated that the older population will make up almost 20% of the population by 2040.\textsuperscript{20} The continuous rise of diabetes and the growing ageing population in Malaysia further adds to challenges for broader stroke management.\textsuperscript{21} In 2016, more than 40% of hospital admissions for stroke in Malaysia were those 65 years and older.\textsuperscript{17} In this study of Malaysian older patients hospitalised with strokes, we aimed to: (1) describe the prevalence of diabetes and (2) compare the burden of comorbidities and cardiovascular risk factors among patients with diabetes and frailty compared to those without these conditions.

**Methods**

This study was conducted using data from an observational study on the prevalence of pre-stroke frailty and its impact on outcomes in older patients hospitalised with strokes in Malaysia. Details of this study were published in 2023.\textsuperscript{22} In brief, patients from Universiti Malaya Medical Centre, a teaching hospital in Kuala Lumpur, Malaysia were included for analysis. The study period was from January 2016 to January 2020. Older patients aged ≥ 65 years admitted to the Geriatric Medicine Unit with acute stroke were eligible for the study. Patients underwent a Comprehensive Geriatric Assessment (CGA) at the point of admission where medical history and functional abilities before their stroke were recorded. Ethics approval was obtained from the Medical Research Ethics Committee of the University Hospital (MEC No: 201312-0636).

**Variable definitions**
Comorbidities were assessed using the Charlson Comorbidity Index, (CCI). The CCI is a widely used index and is considered to be the gold standard measure in predicting patient survivability in patients with multiple comorbidities in clinical research.  

Participants’ history of cardiovascular disease was collected using a predefined list of eight conditions, namely hypertension, previous stroke/transient ischemic attack, dyslipidaemia, chronic kidney disease (eGFR < 60mL/min), atrial fibrillation, ischemic heart disease, congestive heart failure and peripheral vascular disease.

Participants’ frailty status before their admission with stroke was assessed using the Clinical Frailty Scale (CFS) version 2. The CFS is a 9-point scale that can be used to summarize the level of frailty in an older person. The CFS score ranges from 1–9, and a score of 4 or greater indicates a frailty status. Briefly, scoring were as follows: 1 – very fit, 2 – well, 3 – managing well, 4 – living with very mild frailty, 5-living with mild frailty, 6-living with moderate frailty, 7- living with severe frailty, 8-living with very severe frailty, 9-terminally ill. For this study, the frail category includes CFS 4–8 and the non-frail category includes CFS 1–3. CFS 9 was excluded as it describes patients with limited life expectancy.

**Statistical analysis**

Data analysis was conducted using IBM SPSS Statistics version 26.0 (IBM Corp, Armonk, NY, USA). Comparisons between participants with and without diabetes were conducted using independent samples t-test for continuous variables and Chi-square tests or Fisher’s exact tests for categorical variables. P-value < 0.05 was deemed significant.

Participants were also classified into 4 groups according to their frailty status and whether they had diabetes or not: Group 1 – frail and diabetic, Group 2 – non-frail and diabetic, Group 3 – frail and non-diabetic, and Group 4 – non-frail and non-diabetic. Comparisons among these 4 groups were assessed using Chi-square tests or Fisher’s exact tests for categorical variables, and ANOVA test for continuous variables. Two-tailed P values < 0.05 were deemed statistically significant.

**Results**

A total of 384 participants were included in our study. They had a mean age of 81.11 (SD 6.373), and 57% were female. A diagnosis of diabetes was recorded in 45.1% of the participants (173/384).
<table>
<thead>
<tr>
<th>Variables</th>
<th>All participants (N = 384)</th>
<th>Participants without diabetes (N = 211)</th>
<th>Participants with diabetes (N = 173)</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>81.11 ± 6.373</td>
<td>81.95 ± 6.182</td>
<td>80.09 ± 6.471</td>
<td>0.004</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>165 (43.0%)</td>
<td>91 (43.1%)</td>
<td>74 (42.8%)</td>
<td>0.945</td>
</tr>
<tr>
<td>Female</td>
<td>219 (57.0%)</td>
<td>120 (56.9%)</td>
<td>99 (57.2%)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>86 (22.4%)</td>
<td>44 (20.9%)</td>
<td>42 (24.3%)</td>
<td>0.103</td>
</tr>
<tr>
<td>Chinese</td>
<td>210 (54.7%)</td>
<td>126 (59.7%)</td>
<td>84 (48.6%)</td>
<td></td>
</tr>
<tr>
<td>Indian</td>
<td>82 (21.4%)</td>
<td>37 (17.5%)</td>
<td>45 (26.0%)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>6 (1.6%)</td>
<td>4 (1.9%)</td>
<td>2 (1.2%)</td>
<td></td>
</tr>
<tr>
<td>Residence status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>346 (91.5%)</td>
<td>193 (92.8%)</td>
<td>153 (90.0%)</td>
<td>0.333</td>
</tr>
<tr>
<td>Nursing home</td>
<td>32 (8.5%)</td>
<td>15 (7.2%)</td>
<td>17 (10.0%)</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>24 (6.3%)</td>
<td>16 (7.6%)</td>
<td>8 (4.7%)</td>
<td>0.251</td>
</tr>
<tr>
<td>Polypharmacy (≥ 5 medicines)</td>
<td>150 (39.4%)</td>
<td>55 (26.2%)</td>
<td>95 (55.6%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Stroke subtype</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total/partial anterior circulatory ischaemic</td>
<td>67 (17.4%)</td>
<td>37 (17.5%)</td>
<td>30 (17.3%)</td>
<td>0.217</td>
</tr>
<tr>
<td>Posterior circulatory ischaemic</td>
<td>20 (5.2%)</td>
<td>11 (5.2%)</td>
<td>9 (5.2%)</td>
<td></td>
</tr>
<tr>
<td>Lacunar ischaemic</td>
<td>249 (64.8%)</td>
<td>130 (61.6%)</td>
<td>119 (68.8%)</td>
<td></td>
</tr>
<tr>
<td>Haemorrhagic</td>
<td>48 (12.5%)</td>
<td>33 (15.6%)</td>
<td>15 (8.7%)</td>
<td></td>
</tr>
</tbody>
</table>

Compared to participants without diabetes, those with diabetes were younger (mean age 80.09 ± 6.47 compared to 81.95 ± 6.18, respectively, p = 0.004). Age distribution of the participants is presented in Fig. 1.
The distribution of the Clinical Frailty Scale score in participants with and without diabetes is present in Fig. 2. Using the cut-off point of 4, the prevalence of frailty was 75.3% in all participants, 81.3% in those with diabetes and 70.5% in those without diabetes (p = 0.015).

The burden of comorbidities among 384 participants

The mean Charlson Comorbidity Index was 5.97 ± 2.05 in all participants. Compared to participants without diabetes, participants with diabetes had a higher Charlson Comorbidity Index (6.82 ± 2.02 versus 5.28 ± 1.80, p < 0.001).

Among 384 participants with strokes, 139 (36%) were classified into Group 1 – frail and diabetic, 32 (8%) were classified into Group 2 – non-frail and diabetic, 148 (39%) were classified into Group 3 – frail and non-diabetic, and 62 (16%) were classified into Group 4 – non-frail and non-diabetic. When comparing the four groups of frailty-diabetes, participants with diabetes and frailty had the highest comorbidity burden, as shown with the highest Charlson Comorbidity Index mean score in Fig. 3. The mean CCI was for the frail and diabetic group was 6.97 ± 1.97, followed by non-frail and diabetic, 6.00 ± 2.02, frail and non-diabetic, 5.49 ± 1.79, and non-frail and non-diabetic, 4.74 ± 1.68.

The burden of cardiovascular disease and risk factors

Among the history of cardiovascular diseases and risk factors, the most prevalent was hypertension (81.8%), followed by previous stroke/TIA (48.2%), dyslipidaemia (39.8%), chronic kidney disease (39.3%), atrial fibrillation (21.9%), ischemic heart disease (20.4%), heart failure (3.6%), and peripheral vascular disease (2.9%).

Participants with diabetes had a significantly higher prevalence of hypertension (90.8% versus 74.4%, p < 0.001), ischemic heart disease (27.2% versus 14.8%, p = 0.003), congestive heart failure (5.8% versus 1.9%, p = 0.043), and chronic kidney disease (45.1% versus 34.6%, p = 0.036).

The cardiovascular risk factors and disease burden across the four groups of frailty-diabetes are presented in Fig. 4. Across the four groups, hypertension was the most prevalent. Frail participants (with or without diabetes) had a higher prevalence of previous stroke/TIA, while ischemic heart disease was most prevalent in the non-frail and diabetic groups.

Discussion

In this study in 384 older Malaysian admitted to hospital due to strokes, we found a high prevalence of diabetes (45.1%) among patients with strokes. Patients with diabetes had a higher burden of frailty, higher Charlson Comorbidity Index score, cardiovascular risk factors such as hypertension and CKD, and disease burden such as IHD and heart failure, and were at a younger age at the time of stroke. More than one-third (36%) of the patients had both diabetes and frailty.
The prevalence of diabetes in stroke inpatients in our study was higher compared to other countries in the Southeast Asian region. The mean age of our study participants is 81 years of age. As such, the results of our analysis provide an evidence base for the older old population with participants in similar studies having a mean age ranging from 57–68 years.\textsuperscript{4,28–32} Analysis from the National Neurology Registry for Acute Stroke in Malaysia showed estimates of diabetes prevalence ranged from 24.9–53.3% depending on first or recurrent stroke across ischemic and haemorrhagic stroke.\textsuperscript{33} Studies in neighbouring countries such as Thailand, Indonesia and Singapore have reported prevalence ranging from 17.1–38.5%.\textsuperscript{4,28,29} Similar studies in other countries such as Ethiopia, Pakistan and China have also reported a prevalence ranging from 8.1–35.46%.\textsuperscript{30–32} In a study of 208 stroke patients in a hospital in the city of Yogyakarta, Indonesia, the prevalence of diabetes was found to be 34.1% with common comorbidities including hypertension, dyslipidaemia and cardiac diseases like atrial fibrillation.\textsuperscript{4} In another analysis of 9766 patients across 3 hospitals in Singapore, the prevalence of diabetes in stroke inpatients was found to be 38.5%.\textsuperscript{28} With diabetes influencing stroke prevalence and outcomes, countries like Malaysia, Indonesia and Singapore face similar challenges in managing the growing impact of non-communicable diseases like diabetes.

Older people in Malaysia were more than 10 times more likely to have diabetes compared to younger people.\textsuperscript{18} There is growing evidence of the association of diabetes with frailty in the older population.\textsuperscript{34} In a study among community-dwelling older adults in Malaysia, the prevalence of frailty was found to be 18.3% and the top 2 comorbidities associated were diabetes and hypertension.\textsuperscript{35} With the growing population of older people in Malaysia, there is a need to have routine frailty assessments when providing care for older persons with diabetes. Evidence-based interventions can be tailored to the different frailty groups.

Research on the role of frailty in stroke outcomes is still growing. In a study of 433 individuals with ischaemic stroke, the 28-day mortality was noted to be higher in frail participants compared to non-frail participants.\textsuperscript{36} A separate study also reported higher one-year mortality in frail participants.\textsuperscript{22} In another study of 530 patients in China, it was found that frailty was an independent risk factor for one-year all-cause mortality among older stroke patients.\textsuperscript{37} A systematic review and meta-analysis described how the prevalence of frailty in acute stroke ranged from 2.2–54%, with outcomes inconsistently reported.\textsuperscript{38} Studies that met inclusion criteria appeared to be mainly from higher-income countries although the methodology was designed to be inclusive and global.\textsuperscript{38} Age being an irreversible risk factor for stroke highlights the need for studies in the older population, especially in low to middle-income countries such as Malaysia.

In patients with diabetes, frailty was found to be associated with an increased risk of all-cause mortality, cardiovascular-related mortality, major adverse cardiovascular events and hypoglycaemia.\textsuperscript{39} It does highlight the need for frailty assessment and management to be incorporated into routine diabetes care. The results of our analysis demonstrate a significant association between diabetes and increased frailty among older people with stroke. This aligns with previous studies that have further described the link
between diabetes and frailty.\textsuperscript{40} The presence of diabetes appears to influence frailty potentially due to metabolic and inflammatory interactions which may exacerbate age-related decline in physiological reserves. The accelerated pace of muscle wastage, decreased physical function and heightened vulnerability to stressors in individuals with diabetes could contribute to the increased likelihood of a stroke attack.

Our findings highlight the compounded cardiovascular disease burden in older stroke survivors with diabetes and frailty. This is also similar to another study in an Egyptian population.\textsuperscript{41} The synergistic relationship between diabetes and cardiovascular disease burden has been extensively documented with diabetes serving as a significant risk factor for the development and progression of cardiovascular complications. In the context of stroke survivors, diabetes may also exacerbate underlying vascular damage, leading to greater impairment in vascular integrity and contributing to recurrent cardiovascular events. The increased prevalence of comorbidities such as hypertension, IHD, CCF, PVD, dyslipidaemia, cerebrovascular disease (including TIA) and chronic kidney disease observed in individuals with diabetes could further contribute to the amplified cardiovascular disease burden observed in our study population.

**Clinical implications**

Implications of our findings underscore the need for tailored interventions and management strategies for older stroke survivors with diabetes. Furthermore, goals of treatment differ in people with varying levels of frailty, with many not tolerating the usual targets of treatment at the higher frailty levels. The integration of multidisciplinary approaches, encompassing medical management, lifestyle modifications and rehabilitative interventions becomes imperative in addressing the intertwined challenges of frailty and cardiovascular disease burden. Optimizing appropriate glycaemic control and managing cardiovascular risk factors through appropriate pharmacological and lifestyle interventions could help reduce the adverse outcomes associated with diabetes in this population. This is more relevant as control rates for diabetes in the older population in Malaysia were reported to be low (21.8\%)\textsuperscript{42} in comparison with neighbouring countries like Thailand reporting higher rates (26.4\%).\textsuperscript{43}

Moreover, the findings emphasize the importance of early identification and screening for diabetes and frailty in the older population. Timely diagnosis and management of diabetes could potentially mitigate the progression of frailty and help reduce the impact of stroke. Routine comprehensive geriatric assessment that incorporates frailty assessment and cardiovascular risk assessment should be further encouraged even in non-routine settings. This can aid in identifying high-risk individuals who may benefit from early targeted interventions.

**Strengths and limitations**

Our study findings provide insights into the complex interplay between diabetes, frailty, and comorbidities, particularly cardiovascular health, and further shed light on the multifaceted challenges in this vulnerable population. It also highlights the critical need for diabetes management particularly with
the high prevalence of diabetes reported in Malaysia. Our study was conducted in a very old population in Malaysia and contributed to the evidence on the epidemiology of stroke, diabetes and comorbidities in low- and middle-income countries.

However, our study was a single-site study and results may not be generalisable to other health settings. The cross-sectional design prevents any establishment of a causal relationship between diabetes, frailty and cardiovascular disease burden. Future prospective studies with larger sample sizes and longitudinal follow-up can help to elucidate the temporal relationships and mechanisms underlying the observed associations. Although our study did not explore the influence of diabetes on the likelihood of stroke, it does describe the higher prevalence of frailty and cardiovascular comorbidities burden in those with diabetes. The results of our analysis do provide an opportunity for this area to be further explored and its influence on the management of post-stroke outcomes.

**Conclusion**

There was a very high prevalence of diabetes in older patients with stroke in this study. This study provides further evidence of the intricate interplay between diabetes, frailty and comorbidity burden in older individuals with stroke. Besides the management of diabetes, frailty and cardiovascular risk factors are potential target areas that healthcare providers can strive to address to enhance the overall well-being and quality of life for older stroke survivors with diabetes.

**Declarations**

**Competing interests:**

The authors declare no competing interests.

**References**


**Figures**

![Figure 1](image-url)

*Figure 1*
Age distribution among participants with and without diabetes

Figure 2

The distribution of the Clinical Frailty Scale in participants with and without diabetes

Figure 3

The mean Charlson Comorbidity Index score among the four groups of frailty-diabetes
Figure 4

Cardiovascular risk factors and disease burden across the four frailty-diabetes groups (*p-value<0.05)