FACTORS ASSOCIATED WITH PAROXYSMAL VERTIGO AMONG URBAN-DWELLERS AGED 55 YEARS AND OVER IN THE MALAYSIAN ELDERS LONGITUDINAL RESEARCH (MELOR) STUDY

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Abstract

Background: Paroxysmal Vertigo (PV) negatively affects life quality and increases in prevalence with age, but the risk factors remain inconclusive.

Objective: The present study aimed to investigate the risk factors of PV among a multi-ethnic urban population in late mid-life and late life within a middle-income Southeast-Asian country.

Methods: Cross-sectional data from the first wave of the Malaysian Elders Longitudinal Research (MELoR) study were utilized for this study involving randomly sampled participants aged 55 years and over. Socio-demographics, comorbidities, and psychological status were obtained through home-based computer-assisted interviews.

Results: Based on an analysis of 1530 participants, mean age (SD) = 68.81 (7.49), 64.9% female; 32.9% Malay, 34.6% Chinese), the lifetime prevalence of PV was 12.1%. The risk factors associated based on multivariate analysis were hypertension, osteoarthritis, depression, and vitamin B12 Deficiency. Chinese ethnicity (OR = 0.582; 95% CI = 0.390 to 0.870) and smoking (OR = 0.377; 95% CI = 0.223 to 0.637) were protective factors against PV.

Conclusions: While the risk factors reported are similar to other studies, the lower prevalence of PV among ethnic Chinese and smokers had not previously been reported. Our study highlighted potential genetic and lifestyle links to PV which should be evaluated in future studies.

Keywords: Paroxysmal Vertigo, Dizziness, Geriatric

Introduction

Benign positional vertigo (BPV) represents the most common diagnosis for patients presenting with dizziness, accounting for 51% of all cases of dizziness presenting to a specialist clinic (1). BPV is an inner ear condition associated with recurring episodes of positional dizziness provoked by positional changes of the head and accompanied by characteristic nystagmus (2). BPV can occur at any age however, its peak onset occurs in the fifth and sixth decades of life (3). The lifetime prevalence of BPV has been reported as 2.4% (4).

In the United States, BPV results in a disproportionately large healthcare expense in the United States (US) amounting to almost $2 billion each year and is expected to rise further as the population ages (3). Furthermore, month-long delays in the diagnosis and treatment of BPV may often lead to profound financial impact and quality of life implications for both patients and their caregivers. Patients with undiagnosed and untreated BPV are at increased risk of falls, fractures, and severely compromised patient's quality of life (5, 6). Furthermore, BPV is prone to occur and recur in people of senior age (6).

With the global population aging, the prevalence of BPV is, therefore expected to rise. Individuals aged 60 years and above made up 10% of the world's population in 1999 and are expected to rise above 22% by 2050 (7). In Malaysia, the population aged 60 years and over has doubled from around 1 million to 2.2 million between 1991 and 2010, and this figure is expected to climb to 7 million by 2040 (5).

To date, relatively few studies with limited sample sizes have evaluated risk factors for BPV, with a recent systematic review highlighting female gender, osteoporosis, diabetes mellitus, hypertension, vitamin D deficiency, and hyperlipidemia as potential risk factors (8). Prevalence studies for BPV, however, are challenging due to the highly transient nature of the condition and difficulty in confirmation of diagnosis with a Hallpike's maneuver in a population-based study. We, therefore, interrogated a large cross-sectional dataset obtained from a middle-income country in Southeast Asia to determine the prevalence of the symptoms of vertigo lasting seconds or paroxysmal vertigo (PV) and its associated risk factors among urban-dwelling individuals at late mid-life to late-life.

Methods

Study design and sample

This was a cross-sectional analysis conducted using data collected from the Malaysian Elders Longitudinal Research (MELoR) database. MELoR was a multi-disciplinary research study based in the Klang Valley of Malaysia to investigate the multi-dimensional elements of aging encountered by older individuals residing in urban communities (9). Information was gathered from individuals aged 55 years and above, stratified by three ethnic groupings and 10-year age groups, using simple random sampling from the 2012 electoral rolls of the parliamentary constituencies of Petaling Jaya North, Petaling Jaya South, and Pantai Valley. Individuals who were bedridden, unable to attend assessments, or who were unable to converse owing to advanced dementia or significant speech difficulties were excluded from the study. The University of Malaya Medical Centre Medical Ethics Committee approved this study (Ref: 925.4), which followed the Helsinki Declaration of 1975, which was amended in 1983. Written informed consent was obtained from the participants before the study was carried out. The age cut-off of 55 years was selected as that corresponded to Malaysia's mandatory retirement age at the time the study began.

Data collection

Eligible participants were contacted for a home visit at recruitment, through door-to-door visits and hand-delivered invitation letters. During the home visit, a computerized survey instrument was used to conduct structured interviews. Information on sociodemographics, medical history, and psychological status was obtained during the home-based interview. Medical history was obtained through self-reported, physician diagnosis of medical conditions identified through a detailed checklist.

Psychological status

The presence of anxiety, depression, and stress was determined using the 21-item Depression, Anxiety, and Stress (DASS-21) questionnaire. Each domain of anxiety, depression, and stress comprised seven items scored on a four-point Likert scale. The total score of each domain is computed separately and multiplied by two to obtain a maximal total score of 42 for each domain. A higher score indicated increased severity. The cut-off scores of up to 9, 7, and 14, above were utilized and depression, anxiety, or stress were considered present (10).

Paroxysmal vertigo

The presence of PV was identified using a three-staged questioning process. Participants were first asked if they had ever experienced symptoms of dizziness. Those who responded with the answer "yes", were then enquired on the duration of their dizziness" "seconds to minutes", "hours or days" or "continuous". An additional question, what their dizziness felt like, which yielded the responses, "room spinning", "light-headed", "unsteady" or "others" was also applied. The presence of PV was considered likely in individuals who responded positively to the presence of dizziness and selected the downstream responses of "seconds or minutes" and "room spinning".

Statistical analysis

Data analyses were conducted using SPSS V.27 (IBM). We categorized the participants into 5-year age bands: 55–59, 60–64, 65–69, 70–74, and ≥ 75 years. The prevalence of PV was calculated using weightages which were determined using the population breakdowns according to age and sex obtained from the 2010 national census (11). Univariate analyses were used to identify the variables with a significant relationship to PV. Variables with a significant relationship to PV were included in a multivariable logistic regression analysis. which were entered in a backward stepwise regression model. P-values of less than 0.05 were considered statistically significant.

Results

Prevalence of paroxysmal vertigo

Table 1 shows the univariate comparisons of sociodemographic factors, comorbidities, and psychological status among those with and without PV. Of 1530 individuals within our sample population, 185 (12.1%) reported ever having symptoms of room spinning lasting seconds or minutes. Weight adjustments for the population distribution of Kuala Lumpur according to five-year age brackets and ethnicity yielded an estimated true lifetime prevalence of 10.5%. Among the overall 185 individuals with PV, 62 (33.5%) were ethnic Malays, 45 (24.3%) Indians, and 78 (42.2%) Chinese.

'**Table 1:** Baseline characteristics and risk factors of participants.

	Total (n = 1530)	No PV (n = 1345)	PV (n = 185)	p-value
Age (years), mean (SD)	68.81 (7.49)	68.74 (7.48)	69.26 (7.58)	0.334
Age categories (years), n (%)	1530			0.921
55-59		167 (12.4)	21 (11.4)	
60-64		281 (20.9)	37 (20.0)	
65-69		312 (23.2)	43 (23.2)	
70-74		311 (23.1)	41 (22.2)	
75+		274 (20.4)	43 (23.2)	
Race, n (%)	1530			0.002
Malay	503	441 (32.8)	62 (33.5)	
Chinese	530	485 (36.1)	45 (24.3)	
Indian	497	419 (31.2)	78 (42.2)	
Female gender, n (%)	1530	751 (55.8)	120 (64.9)	0.020
Single/widowed, n (%)	1530	324 (24.1)	47 (25.4)	0.695
Secondary/ tertiary education, n (%)	1530	993 (73.8)	124 (67.0)	0.051
Living alone, n (%)	1470	1222 (90.9)	164 (88.6)	0.319
Smoker, n (%)	1530	286 (21.3)	17 (9.2)	< 0.001
Alcohol consumption, n (%)	1530	394 (29.3)	40 (21.6)	0.030
Comorbidity, n (%)				
Hypertension	1525	708 (52.6)	121 (65.4)	0.001
Hypercholesterol	1525	715 (53.2)	120 (64.9)	0.003
Diabetes	1525	393 (29.2)	74 (40)	0.003
Osteoporosis	1525	123 (9.1)	16 (8.6)	0.814
Gout	1525	83 (6.2)	11 (5.9)	0.895
B12 Deficiency	1525	79 (5.9)	22 (11.9)	0.002
Osteoarthritis	1525	208 (15.5)	47 (25.4)	0.001
Thyroid	1525	53 (3.9)	10 (5.4)	0.353
Headache	1530	68 (5.1)	16 (8.6)	0.045
Head injury	1530	18 (1.3)	3 (1.6)	0.756
Hearing problem	1521	305 (22.7)	43 (23.2)	0.866
Psychological status, n (%)				
Depression	1530	110 (8.2)	35 (18.9)	< 0.001
Anxiety	1530	227 (16.9)	47 (25.4)	0.005
Stress	1530	69 (5.1)	22 (11.9)	< 0.001

Univariate analysis of associated sociodemographic, comorbidities, and psychological status factors

Risk factors associated with PV according to the univariate analysis included race (p = 0.002), female gender (p = 0.020), smoker (p < 0.001), hypertension (p = 0.001), hypercholesterolemia (p = 0.003), diabetes (p = 0.003), osteoarthritis (p = 0.001), presence of depression (p < 0.001), anxiety (p = 0.005) and stress (p < 0.001), B12 deficiency (p = 0.002), alcohol (p = 0.030) and headache (p = 0.045).

Multivariate Analysis

Table 2 summarizes the results of the multivariate analyses to examine the association between PV and its significant risk factors. Using a backward stepwise regression model, the final model for the multivariate analysis revealed that hypertension (OR = 1.491; 95% CI = 1.072 to 2.07), osteoarthritis (OR = 1.521; 95% CI = 1.044 to 2.217), depression (OR = 2.134; 95% CI = 1.377 to 3.305) and vitamin B12 Deficiency (OR = 1.844; 95% CI = 1.092 to 3.116) were independently associated with increased risk of PV after adjustment for all covariates. Conversely, Chinese ethnicity compared to Indian ethnicity (OR = 0.582; 95% CI = 0.390 to 0.870) and cigarette smoking (OR = 0.377; 95% CI = 0.223 to 0.637) emerged as protective factors for PV.

Table 2: Logistic linear regression model showing the variables predictive of and odds of developing paroxysmal vertigo.

	PV		
	Relative risk	**95% CI**	**p-value**
Ethnicity			
Indian (reference)			0.019
Malay	0.952	0.653 to 1.387	0.797
Chinese	0.582	0.390 to 0.870	0.008
Smoker	0.377	0.223 to 0.637	< 0.001
Hypertension	1.491	1.072 to 2.073	0.018
Osteoarthritis	1.521	1.044 to 2.217	0.029
B12 Deficiency	1.844	1.092 to 3.116	0.022
Depression	2.134	1.377 to 3.305	0.001

Discussion

This study identified that one in nine to one in 10 individuals aged 55 years and over in the Klang Valley had experienced symptoms suggestive of BPV in their lifetime. A previous study that examined the point prevalence of BPV suggested

a prevalence of 1.4% confirmed with a diagnostic maneuver (12, 13). The 2.4% lifetime prevalence suggested by von Brevern et al. (4) was comparatively lower but utilized a telephone interview rather than face-to-face interviews and utilized validated diagnostic criteria which required qualitative inquiry by trained medical students, but the strict criteria which were validated in a small sample within a dizziness clinic may have led to a difficulty in diagnosing benign positional vertigo.

The discovery of ethnic differences in the lifetime prevalence of PV represents an original finding. The MELoR study consists of three major racial groups which populate Asia today. The ethnic Chinese were found to have a 40% reduction in odds of reporting PV compared to Indians, with no difference in prevalence between the ethnic Malays and Indians. The mechanism behind this racial difference remains unclear. This finding contradicts the findings of a previous study involving 777 individuals with BPV which found the ethnic Chinese to be more prone to vestibular disorders (14). Moreover, SLC26A4 mutations were found to be much higher in East Asian populations, especially Chinese, at 89% (15). SLC26A4 mutations were linked to abnormal otoconia composition and distribution which can cause BPV (16). However, limited data regarding the frequency of SLC26A4 mutations were collected in Indians and Malays. The conflicting findings between the present and previous studies could be attributed to differences in health-seeking behavior between the ethnic groups. Further, non-communicable diseases including diabetes are more prevalent among the ethnic Indians and ethnic Malays compared to the ethnic Chinese, which may confound the reduced likelihood of PV among the ethnic Chinese (17).

The protective effect of smoking has not previously been reported. A previous study reported 2-3 times increased odds of peripheral vestibular disorder among smokers (18). As smoking has a causal link to arterial dysfunction, it was thought to be a risk factor for BPV. Counterintuitively, smoking can reduce monoamine oxidase activity in the brain which will lead to elevated dopamine (19). Dopamine was postulated to be able to protect the auditory neurons situated in the cochlea by inhibiting excess glutamate in acoustic trauma or ischemia from causing excitotoxicity toward the primary neurons (20). Furthermore, Meredith and Rennie (21) have further strengthened this theory by proving the role of dopamine in regulating Na+ current in rodent vestibular afferents. It would be unethical to propose cigarette smoking for BPV prevention. However, such a finding remains valuable with regard to identifying the potential mechanisms of BPV, which remains elusive, as well as potential therapeutic targets for the treatment of BPV.

We also examined other risk factors that might contribute to PV development. Hypertension was found to be significantly associated with the occurrence of PV. Hypertension in BPV has been widely researched and found to be important in previous studies (8, 22). It is believed that hypertension would induce labyrinthine ischemia which would lead to otoconial detachment.

Depression was found to double the risk of BPV occurrence and is consistently supported by other studies (23). There are a few explanations behind this association. Increased oxidative stress in depression is thought to play an important role in causing otolith dysfunction, vestibular hair cell, and inner ear neuronal damage which leads to the development of BPV (24, 25). Besides, the vascular changes in the inner ear induced by the hypothalamus–pituitary–adrenal axis dysfunction were postulated to impact otoconial homeostasis and inner ear fluid balance (26). Vestibular nucleus complexes which are highly serotonergic are theorized to be impacted by serotonin dysfunction in depression (27). The association of B12 deficiency was first described in 1970 by Mahmud et al. (28). However, the results of other studies have contrary outcomes, and the controversy between B12 deficiency and BPV remains elusive (29). Individuals with osteoarthritis were found to have a higher rate of PV. Limited evidence has been shown regarding the association between osteoarthritis and dizziness.

This study is limited by the difficulty in establishing a causal-and-effect relationship, in view of the cross-sectional nature of the MELoR study (30). The self-reported information is also inevitably associated with recall bias. A previous study in Thailand has revealed older persons are less likely to describe the classic symptom of vertigo that was specific to BPV compared to younger individuals (31). The detection of BPV relied on the presence of rotatory symptoms and duration of symptoms to determine the potential presence of BPV, without taking into account precipitants of positional change, with no confirmatory maneuver, which was not possible considering we were estimating lifetime prevalence. However, the risk factors established in this study were similar to those of previous studies, hence suggesting that our detection method had accurately identified the correct population. Prospective follow-up studies should be carried out to evaluate the longitudinal relationship of the risk factors of BPV. Moreover, this study is being conducted exclusively in an urban setting, so the data in rural or semi-urban areas should be investigated in the future. Further studies will be needed to explain the underlying ethnic differences in BPV prevalence and determine whether these differences still exist in prospective studies with the use of rigorous diagnosing method for BPV that includes diagnostic maneuvers and diagnostic questionnaires.

Conclusion

The lower prevalence of PV among ethnic Chinese and smokers had not previously been reported. Our study highlighted potential genetic and lifestyle links to BPV which should be evaluated in future studies. In addition, appropriate management of the risk factors of hypertension, osteoarthritis, vitamin B12 replacement, and

depression should be explored as primary and secondary prevention strategies for BPV.

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Competing interests

All authors have no conflicts of interest.

Data Availability

Data were retrieved from the Malaysian Elders Longitudinal Research (MELoR) database.

Ethical Clearance

The study was conducted in accordance with the Declaration of Helsinki. The study was exempt from IRB review was no confidential patient information was involved.

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References

1. Philip R, Prepageran N. Dizziness, a review of walk-in patients at a specialised neurotology clinic. Med J Malaysia. 2009; 64(1):56–8.
2. Bhattacharyya N, Gubbels SP, Schwartz SR, Edlow JA, El-Kashlan H, Fife T, et al. Clinical practice guideline: Benign paroxysmal positional vertigo (update). Otolaryngol Head Neck Surg. 2017; 156(3):S1–S47.
3. Kim HJ, Park J, Kim JS. Update on benign paroxysmal positional vertigo. J Neurol. 2021; 268(5):1995–2000.
4. von Brevern M, Radtke A, Lezius F, Feldmann M, Ziese T, Lempert T, et al. Epidemiology of benign paroxysmal positional vertigo: a population-based study. J Neurol Neurosurg Psychiatry. 2007; 78(7):710–5.
5. Tey NP, Siraj SB, Kamaruzzaman SBB, Chin AV, Tan MP, Sinnappan GS, Müller AM. Aging in Multi-ethnic Malaysia. Gerontologist. 2016; 56(4):603–9.
6. Lindell E, Kollén L, Johansson M, Karlsson T, Rydén L, Falk Erhag H, et al. Benign paroxysmal positional vertigo, dizziness, and health-related quality of life among older adults in a population-based setting. Eur Arch Otorhinolaryngol. 2021; 278(5):1637–44.
7. Tinker A. The social implications of an ageing population. Introduction. Mech. Ageing Dev. 2002; 123(7):729–35.
8. Chen J, Zhang S, Cui K, Liu C. Risk factors for benign paroxysmal positional vertigo recurrence: a systematic review and meta-analysis. J Neurol. 2021; 268(11):4117–27.
9. Lim LM, McStea M, Chung WW, Nor Azmi N, Abdul Aziz SA, Alwi S, et al. Prevalence, risk factors and health outcomes associated with polypharmacy among urban community-dwelling older adults in multi-ethnic Malaysia. PloS one. 2017; 12(3):e0173466.
10. Lovibond PF, Lovibond SH. The structure of negative emotional states: comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. Behav Res Ther. 1995; 33(3):335–43.
11. Department of Statistics Malaysia. Preliminary Count Report, Population and Housing Census, Malaysia. 2011. Accessed 12 September 2022.
12. Kim H-J, Song J-M, Zhong L, Yang X, Kim J-S. Questionnaire-based diagnosis of benign paroxysmal positional vertigo. Neurology. 2020; 94(9):e942–e9.
13. van der Zaag-Loonen HJ, van Leeuwen RB, Bruintjes TD, van Munster BC. Prevalence of unrecognized benign paroxysmal positional vertigo in older patients. Eur Arch Otorhinolaryngol. 2015; 272(6):1521–4.
14. Wahat NHA, Sevasankaran R, Abdullah A, Ali RA. Prevalence of vestibular disorders among otology patients in a tertiary hospital in Malaysia. Int Med J. 2013; 20:312–4.
15. Wu C-C, Lu Y-C, Chen P-J, Yeh P-L, Su Y-N, Hwu W-L, et al. Phenotypic analyses and mutation screening of the SLC26A4 and FOXI1 genes in 101 Taiwanese families with bilateral nonsyndromic enlarged vestibular aqueduct (DFNB4) or Pendred syndrome. Audiol Neurootol. 2010; 15(1):57–66.
16. Dror AA, Taiber S, Sela E, Handzel O, Avraham KB. A mouse model for benign paroxysmal positional vertigo with genetic predisposition for displaced otoconia. Genes Brain Behav. 2020; 19(5):e12635.
17. Chiang PPC, Lamoureux EL, Cheung CY, Sabanayagam C, Wong W, Tai ES, et al. Racial differences in the prevalence of diabetes but not diabetic retinopathy in a multi-ethnic Asian population. Invest Ophthalmol Vis Sci. 2011; 52(10):7586.
18. Wada M, Takeshima T, Nakamura Y, Nagasaka S, Kamesaki T, Kajii E, Kotani K. Association between smoking and the peripheral vestibular disorder: a retrospective cohort study. Sci Rep. 2017; 7(1):1-6.
19. Miroshnychenko A, Uhlman K, Malone J, Waltho D, Thoma A. Systematic review of reporting quality of economic evaluations in plastic surgery based on the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. J Plast Reconstr Aesthet Surg: JPRAS. 2021; 74(10):2458–66.

20. Andrianov GN, Ryzhova IV, Tobias TV. Dopaminergic modulation of afferent synaptic transmission in the semicircular canals of frogs. Neurosignals. 2009; 17(3):222–8.
21. Meredith FL, Rennie KJ. Dopaminergic inhibition of Na+ currents in vestibular inner ear afferents. Front Neurol. 2021; 15:710321.
22. Sreenivas V, Sima NH, Philip S. The role of comorbidities in benign paroxysmal positional vertigo. Ear Nose Throat J. 2021; 100(5):225–30.
23. Kim SK, Hong SM, Park I-S, Lee H-J, Park B, Choi HG. Mood disorders are associated with increased risk of BPPV: A national sample cohort: Mood disorder increase risk of BPPV. Laryngoscope. 2021; 131(2):380–5.
24. Black CN, Bot M, Scheffer PG, Cuijpers P, Penninx BWJH. Is depression associated with increased oxidative stress? A systematic review and meta-analysis. Psychoneuroendocrinology.2015; 51:164–75.
25. Şahin E, Deveci İ, Dinç ME, Özker BY, Biçer C, Erel Ö. Oxidative status in patients with benign paroxysmal positional vertigo. J Laryngol Otol. 2018; 14(2):299–303.
26. Varghese FP, Brown ES. The hypothalamic-pituitary-adrenal axis in major depressive disorder: A brief primer for primary care physicians. Prim Care Companion CNS Disord. 2001; 3(4):151–5.
27. Smith PF, Darlington CL. A possible explanation for dizziness following SSRI discontinuation. Acta Otolaryngol. 2010; 130(9):981–3.
28. Mahmud K, Ripley D, Doscherholmen A. Paroxysmal positional vertigo in vitamin B12 deficiency. Arch Otolaryngol Head Neck Surg. 1970; 92(3):278–80.
29. Çelik H, Yardım A, Ertaş A, Varışlı B, Ocak Ö. Evaluation of serum 25-hydroxyvitamin vitamin D, vitamin B12, and folate levels in patients with benign paroxysmal positional vertigo. Eurasian J. Emerg. Med. 2021; 20(1):19–24.
30. Rindfleisch A, Malter AJ, Ganesan S, Moorman C. Cross-sectional versus longitudinal survey research: Concepts, findings, and guidelines. J Mark Res. 2008; 45(3):261–79.
31. Plodpai Y, Atchariyasathian V, Khaimook W. The characteristic differences of benign paroxysmal positional vertigo among the elderly and the younger patients: A 10-year retrospective review. J Med Assoc Thai. 2014; 97(8):850–5.