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Association between Migraine and Cardiovascular Diseases among Women of a Tertiary Care Hospital, Hyderabad – A Case–Control Study

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ABSTRACT

Objectives: Women tend to have a higher risk of migraine compared to men. Apart from the conventional risk factors, this study aims to provide insight into the association between migraine and cardiovascular diseases (CVDs). The aim of this study was to assess the association between CVDs and migraine along with other conventional factors among migraineurs with and without aura.

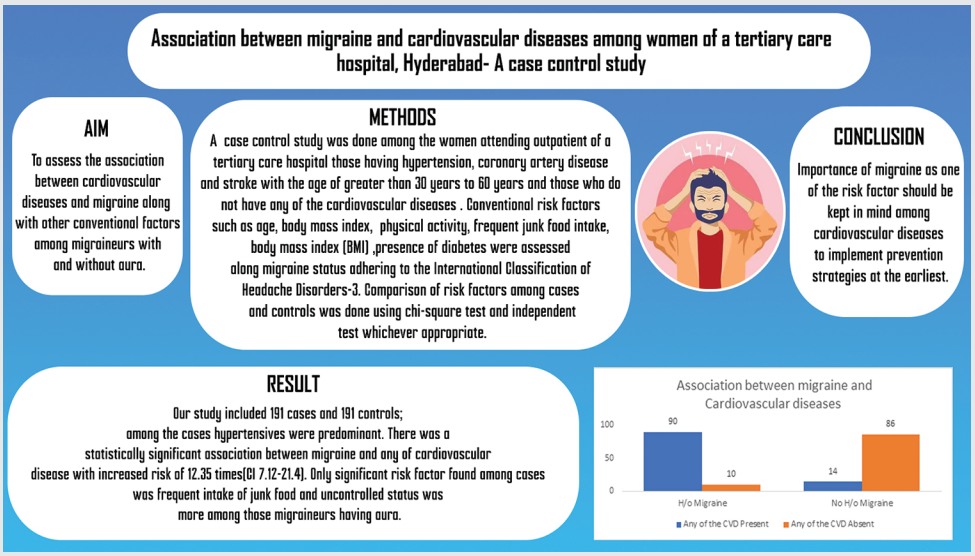
Materials and Methods: A case–control study was done among the women attending outpatient of a tertiary care hospital those having hypertension, coronary artery disease, and stroke at the age of >30–60 years, and those who do not have any of the CVDs. Conventional risk factors such as age, body mass index (BMI), physical activity, frequent junk food intake, BMI, and presence of diabetes were assessed along with migraine status adhering to the International Classification of Headache Disorders-3. Comparison of risk factors among cases and controls was done using the Chi-square test and independent *t*-test whichever was appropriate.

Results: Our study included 191 cases and 191 controls; among the cases, hypertensives were predominant. There was a statistically significant association between migraine and any CVD with an increased risk of 12.35 times (confidence interval 7.12–21.4). The only statistically significant risk factor among the cases was the frequent intake of junk food and uncontrolled status was more among those migraineurs having an aura.

Conclusion: The importance of migraine as one of the risk factors should be kept in mind among CVDs to implement prevention strategies at the earliest.

Keywords: Migraine, Aura, Cardiovascular diseases, Risk factor

ABSTRACT IMAGE



INTRODUCTION

Migraine is a common, disabling, primary headache disorder with systemic vascular involvement, autonomic dysfunction, and a wide range of ischemic vascular disorders. Individuals with migraine particularly migraine with aura are at risk for both ischemic and hemorrhagic forms of stroke, hypertension, ischemic heart disease, myocardial infarction (MI), angina, coronary revascularization procedures, and vascular mortality.[1] Although the exact mechanisms to explain increased vascular events are not fully understood, hypertension, smoking, and the use of oral contraceptives have been found to increase the risk of ischemic stroke for young women with migraine.[2] The poor control of blood pressure may exacerbate the frequency and severity of migraine when they are coexistent.[3]

Although the absolute effect of migraine on "vascular risks" is small, good practice parameters dwell on treating and reducing existing cardiovascular risk factors through lifestyle modification, encouraging smoking cessation, and advocating the wise use of agents such as ergot alkaloids and oral contraceptives, after a risk-benefit analysis.[4]

Therefore, this study was taken with a primary objective to compare the association between cardiovascular diseases (CVDs) and migraine along with other conventional risk factors among the cases and controls. A secondary objective was to evaluate the risk factors among cases having migraine with and without aura.

MATERIALS AND METHODS

Study design

This was a case–control study.

Study setting

This study was General Medicine and Cardiology Outpatient Block, ESIC Medical College and Hospital, Hyderabad, Telangana, India.

Study participants

All the women having CVDs and not having any of the CVDs attending general medicine and cardiology outpatient department above the age of 30 years and up to 60 years and given informed consent forms in both groups were included in the study.

Exclusion criteria

Critically ill, other headaches, and above 60 years of age group were excluded from the study.

Sample size

Using the formulae n(Each Group)=(p0q0 + p1q1) (z 1-a+z 1-b)/(p1-p0)2 where p0 is 9% with a history of migraine with aura compared to those without migraine and p1 is 21% with a history of migraine without aura compared to those

Table 1: General characteristics of the participants.

Variables	Any of the CVD present (cases) *n*=191	Any of the CVD absent (controls) *n*=191	*P*-value
Age	50.95±5.29	42.79±6.40	0.0001
Educational (illiterates)	98 (51.3)	93 (48.7)	0.0001
Occupation (House Wives)	171 (75.3%)	56 (24.7%)	0.0002
Diabetes (Yes)	104 (70%)	43 (30%)	0.0003
Physical activity (Yes)	7 (43.8%)	9 (56.3%)	0.801
Family/History (Yes)	48 (76.2%)	15 (23.8%)	0.038
Body mass index (Mean±SD)	23.29±3.5	22.11±2.99	0.007

Categorical variables-Chi-square test, Continuous Variables-"t" test, (Variables such as education, occupation, diabetes, physical activity are categorical wheres age and body mass index are continuous variables), CVD: Cardiovascular disease, Body mass index (Mean±SD): Mean scores with standard deviation in each group

without migraine and the calculated sample size was 191 in each group, so a total 382.[5]

Methodology in detail

A pre-designed and pre-tested questionnaire was used as a data collection tool. This contains sociodemographic details, conventional risk factors such as lifestyle factors, personal factors, frequent intake of at least one item of junk food >3 days a week which included instant noodles, biscuits, cookies, chips lay, chocolates, ice cream, cake, momo, samosa, coke, burgers, pizza, canned foods, fried potatoes, and meat products; physical activity in the form of walking, jogging, yoga for at least 5 times a week for 30 min, height and weight measurements with body mass index (BMI) as per the World Health Organization-Asians classification,[6] and blood pressure measurement were done using standardized protocol.

Migraine status was based on a self-report using a questionnaire, with additional questions closely adhering to the International Classification of Headache Disorders (ICHD)-2 criteria for migraine without aura and ICHD-3 for migraine with aura was used.[7] Migraine without aura was defined as a recurrent headache with attacks lasting 4–72 h; unilateral, pulsating, aggravated by physical activity, and associated with nausea and/or photophobia and phonophobia. Migraine with aura is defined as a recurrent headache with attacks of completely reversible focal neurological symptoms lasting <60 min following aura symptoms. Aura was defined as visual changes such as spots, stars, lines, or flashing lights. The primary dependent variable of interest is migraine (yes vs. no), and secondary outcomes were migraine with aura and migraine without aura, individually compared to those with aura by their disease status.

Data analysis

Data was entered into Microsoft Excel 2019 and was analyzed using the OpenEpi calculator. Descriptive statistics such as mean standard deviation were used wherever required. A comparison of dependent variables between those with CVDs and those not having CVDs was done using the t-test and Chi-square for categorical variables. The status of migraine among them was compared by checking the association using a Chi-square test. Further, the status was assessed among those with migraine associated with aura and without aura to check the plausibility by comparison using an odds ratio (OR).

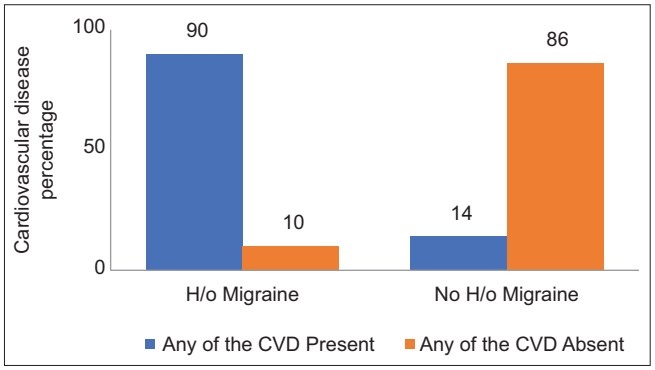


Figure 1: Association between migraine and cardiovascular diseases. (Chi-square=98.95 chi-square used to show association between cardiovascular disease presence and absence with and without history of migraine. ie 2x2 table; *P* value 0.0001, CVD-Cardiovascular disease, H/o-History of migraine).

RESULTS

Our study included 382 women, 191 cases of those having any of the CVDs and 192 as controls without having any of the CVDs. Among the CVDs – hypertensives were 189 (99.4%), stroke 1 (0.3%), and coronary artery disease 1 (0.3%); on comparison of general characteristics among cases and controls, there was a statistically significant association between age, educational status, occupation, physical activity, family history, BMI, and CVDs [Table 1].

Among those with any of the CVDs, there was a statistically significant association with the presence of migraine [Figure 1]. The odds for the presence of migraine among those having any of the CVDs were 12.35 times compared to those without migraine (confidence interval [CI] 7.12–21.41).

Table 2: Various risk factors among the cases with the presence of migraine with aura and migraine without aura.

Risk factors	Cases having migraine with aura (*n*=109) (%)	Cases having migraine without aura (*n*=82) (%)	Odds ratio	*P*-value
Education				
Illiterates	57 (58.2)	41 (41.8)	0.912 (0.51–1.67)	0.433 (NS)
Literates	52 (55.9)	41 (44.1)		
Occupation				
Housewives	98 (57.3)	73 (42.7)	0.910 (0.359–2.319)	0.513 (NS)
Working women	11 (55)	9 (45)		
Based on the Asian classification of BMI				
Normal	55 (53.9)	47 (46.1)	0.889 (0.695–1.136)	0.214 (NS)
Overweight and obese	54 (60.7)	35 (39.3)		
Diabetes mellitus				
Presence	64 (61.5)	40 (38.5)	1.493 (0.839–2.659)	0.112 (NS)
Absence	45 (51.7)	42 (48.3)		
Physical activity				
Yes	3 (42.9)	4 (57.1)	0.552 (0.12–2.537)	0.346 (NS)
No	106 (57.6)	78 (42.4)		
Frequent junk food intake				
Yes	77 (62.1)	47 (37.9)	1.792 (0.982–3.269)	0.040 (S)
No	32 (47.8)	35 (52.2)		

NS-Non Significant (*P* value>0.05), S-Significant (*P*<0.05), BMI: Body mass index

Table 3: Association of the status of hypertension and migraine with and without Aura.

HTN status	Migraine with Aura (109) (%)	Migraine without Aura (82) (%)
Short duration controlled HTN	46 (53)	37 (47)
Long duration controlled HTN	47 (54)	37 (46)
Uncontrolled short duration HTN	9 (55)	4 (45)
Uncontrolled long duration HTN	7 (64)	4 (36)

Chi-square=1.442 - indicates statistically not significant, *P*=0.837 indicates statistically not significant, HTN: Hypertension

Among the cases-on evaluation of various risk factors for the status of migraine with aura and without aura, we found no significant association between education, occupation, presence of diabetes mellitus, regular physical activity, overweight, and obesity. Only a statistically significant association was found between frequent intake of junk food and migraine with aura having a higher percentage [Table 2]. Alcohol and tobacco consumption was found only among 2 of our study participants.

Since cases of hypertension were predominant, on subgroup analysis – we found uncontrolled hypertension to be more among those in migraine with Aura patients compared to those without aura. However, it was not statistically significant [Table 3].

DISCUSSION

Our case–control study included 191 cases having any of the CVDs; with predominant hypertensives constituting 98%, stroke at 1%, and coronary artery disease at 1%. Among the general characteristics, we found significant risk factors of increased age, illiterates, housewives, presence of diabetes mellitus, family history, and increased BMI having any of the CVD. There was a statistical association between migraine and CVD with an OR of 12.35 times (7.12–21.4). Among these cases, we found only regular intake of junk food to be the statistically significant factor among migraineurs with aura. A comparison of the status of hypertension with migraine status, it revealed that uncontrolled status was more predominant among migraineurs with aura compared to those without aura.

These findings were consistent with the Gupta and Srivastava study, namely, that migraineurs were at a higher risk of any of the CVDs than those without having an OR of 2.77 (1.56–4.90) in the fully adjusted model. Following subgroup analysis, migraineurs with aura had higher ORs than migraineurs without aura for the association between migraine or severe headache and CVD.[4]

This has also been supported by a Danish population-based cohort study wherein after 18 years of follow-up, migraine patients had an increased risk of MI (OR 1.49, CI 95%: CI: 1.36–1.64), ischemic stroke (OR 2.26, CI 95%: CI: 2.11–2.41), and hemorrhagic stroke (OR 1.94, 95% CI: 1.68–2.23).[8] In a study of 115,541 young,

middle-aged female nurses in the Nurses' Health Study II, which revealed a positive correlation between migraine and MI (OR 1.39, 95% CI: 1.18–1.64), stroke (OR 1.62, 95% CI: 1.37–1.92), angina pectoris/coronary revascularization (OR 1.73, 95% CI: 1.29–2.32), and cardiovascular mortality (OR 1.37, 95% CI: 1.02–1.83). The association between migraine and a higher risk of MI and stroke (including unspecified, ischemic, and hemorrhagic stroke) as well as a higher risk of death from cardiovascular causes was discovered by a recently published meta-analysis of 18 prospective cohort studies involving 1.6 million migraine sufferers. The majority of the explanations for the moderate to high degree of heterogeneity in cardiovascular outcomes seen in these studies are with migraineurs with the presence of aura.[9]

Although extensive literature has described the association between migraine and CVD in recent decades, the underlying mechanisms appear complex and multidimensional. From a pathophysiological perspective, the association between migraine and CVD may reflect the possibility that common cellular and molecular bases underlie the pathogenesis of both diseases. Decreased number and function of endothelial progenitor cells, endothelial dysfunction, limited vasoconstriction, platelet aggregation, and excessive activation of the coagulation cascade are key events closely linked to the pathogenesis of migraine, and these factors also play a crucial role in accelerating the development of CVD.[10-13] The cardiovascular system may be adversely affected by certain migraine treatments, including non-steroidal anti-inflammatory drugs, triptans, and ergotamine. This effect seems to worsen as migraine dosage and intensity increase.[14]

Furthermore, there is evidence that migraines may play a role in the development of CVD because they have been closely linked to established risk factors for CVDs, such as hypertension, diabetes, and hypercholesterolemia, all of which are more prevalent in individuals who experience aura-producing migraines by raising the risk profiles of other CVDs.[15]

In a study by Wang *et al*. about migraine and CVDs, there was a positive association between migraine and CVD.[16] Given the high frequency of migraine in the general population, the impact of increased cardiovascular risk associated with migraine appears to be minimal at the individual level; however, at the population level, migraine may result in a significant risk of CVD. The risk of CVD in male and female adult residents over the next 10 years was estimated using QRISK3 risk prediction models that included migraine as an indicator for cardiovascular risk stratification. These results suggest that migraine is becoming more widely acknowledged as a significant risk. It is essential in clinical practice to identify migraine patients who are at high risk of CVD, and it is a factor to take into account.[17] Early detection and identification of the CVD process in patients with migraine and early initiation of pharmacological interventions may also improve the prognosis of patients with migraine and CVD. As per the latest guidelines 2022 from the German Society of Neurology, the beta-blockers propranolol and metoprolol, the calcium antagonist flunarizine, as well as the anticonvulsants valproic acid and topiramate, and the antidepressant amitriptyline are effective in migraine prevention treatment.[18]

In contrast to all these studies, Sacco *et al*. in their review article on conventional vascular risk factors: Their role in the association between migraine and CVDs concluded from their review that there was no solid evidence to demonstrate an increased burden of conventional vascular risk factors in migraineurs, with the only significant have dyslipidemia and cigarette smoking.[19]

This extreme variation could be explained by the differences in selection criteria, study designs, operational definitions used to define migraine, and inadequate control of confounders such as age and gender.

Although we have attempted to review the literature and address potential risk factors as much as possible, given that CVD is an amalgamation of several complex and multifaceted diseases, there may still be unidentified or unmeasured confounders, which could also play a role in the pathogenesis of CVDs.

Limitations are we need to have cohort studies to establish biological plausibility in the near future. Moreover, since the self-reported question of migraine status was assessed, there are high chances of recall biases due to the retrospective nature of self-assessment measures.

CONCLUSION

This study showed that migraine with aura has a significant association with CVDs with 90% of women having a history of migraine, henceforth proving that women have a higher preponderance than men. Hence, migraine a benign and episodic condition can also be one of the risk factors for CVD, and determining whether prevention strategies in migraine patients can reduce the cardiovascular burden is of utmost importance. Modification of lifestyle factors including avoidance of frequent intake of junk food such as noodles, fried potatoes, chips, and coke can become a targeted intervention to reduce the risk. Physical activity on a regular basis is important along with adequate control of disease status that is crucial for the prevention of further complications.

Ethical approval

The research/study was approved by the Institutional Review Board at ESIC Medical College & Hospital, number ESICMC/SNR/IEC S0297/11-2023, dated November 28, 2023.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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