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Silent Brain Infarcts in Patients with Non-Specific Neurological Symptoms: 1-Year Cross-Sectional Study

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Abstract
Background: *Silent brain infarctions are considered as a preclinical warning of symptomatic strokes and multiple deep infarct-relatedbrain damage.Limitation of studies on risk factors and non-specific neurological symptoms in the Indian population led to the formulation of the present study.*
Aim: *To evaluate the presence of silent brain infarctions in patients with non-specific neurological symptoms and association with cardiovascular risk factors.*
Methods: *This cross-sectional study was conducted from January to December 2010, including patients with non-specific neurological symptoms (n = 51). General and neurological assessment with Mini-Mental Scale Examination were conducted after recording the demographic data, body mass index, and cardiovascular risk factors. T2-weighted magnetic resonance imaging was performed with repetition time of 4500 ms and echo time of 116 ms. Scans were processed with double-blind method. Particle-enhanced turbidimetric immunoassay technique was performed for assessing high-sensitivity C-reactive protein.*
Results: *The major non-specific neurological symptoms were headache (54.90%), dizziness (23.53%),and vertigo (25.49%). Out of 51 patients, 29.41% were diagnosed with silent brain infarction. Cortical (26.6%) and sub cortical (73.4%) nature of infarction was recorded. The association of risk factors with silent brain infarction was not significant.*
Conclusion: *Patients with non-specific neurological symptoms should be examined for silent brain infarction. Follow-up study can be conducted with large sample size to evaluate the association of the risk factors with infarction and stroke.*
Keywords: *Silent brain infarction; high-sensitivity C-reactive protein; MRI.*

Introduction

Silent brain infarctions (SBIs) are the asymptomatic parenchymal lesions believed to be caused by occlusion of the small blood vessels [(1, 2)]. The asymptomatic nature of SBIs can be attributable to long-term ischemic tolerance and chronic ischemic pre conditioning[(1)]. However, it can be identified only with the help of different

signals obtained on diffusion-weighted magnetic resonance imaging (MRI) [1, 2].

SBIs has been associated with an increased risk of cognitive decline and stroke[3]. To prevent such consequences, it is important to identify, characterize, and manage SBI. Despite being asymptomatic, the occurrence of SBIs have been associated with the development of certain non-specific neurological symptoms such as dizziness, forgetfulness, age, and hypertension, as reported by Hougaku et al[4]. Even though several studies have been conducted on association of migraine and SBI[5], there is lacuna in studies exploring the association of other non-specific neurological symptoms in patients diagnosed with SBI. Therefore, this study examines the patients with non-specific neurological symptoms for the presence of SBIs and is believed to be the first Indian study to assess the role of these symptoms in diagnosing SBIs.

In addition, recent studies have focused on the involvement of inflammatory processes and the association of risk factors such as obesity, hypertension, and dyslipidemia in patients with SBIs[6,7]. This study was also conducted to explore and ascertain the presence of these associations, especially in an Indian population.

Materials and Methods

This1-year cross-sectional study was conducted from January to December 2010 at KLE's Dr Prabhakar Kore Hospital and Medical Research Centre, Belgaum. The study included51 inpatients and outpatients with non-specific neurological symptoms.

Patients with a history of non-specific neurological symptoms such as headache, vertigo, dizziness, tinnitus and syncope, and asymptomatic during the time of examination were enrolled for the study. Patients with stroke, infection, claustrophobia, and the presence of implanted devices sensitive to strong magnetic fields were excluded.

The study was conducted in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving human subjects. Approval for the study was provided by the Ethical and Research Committee of Jawaharlal Nehru Medical College, Belgaum. Written consent was obtained from all the patients before the start of the study. Demographic data (sex and age of the patients) and history of non-specific neurological symptoms, alcohol consumption, and smoking were recorded.

Detailed general and neurological examination was performed by conducting Mini-Mental Scale Examination (MMSE) followed by routine investigations of hemoglobin, total and differential count white blood cell count, erythrocyte sedimentation rate, urine routine and microscopy, fasting blood sugar, and lipid profile. MMSE is performed with the help of questionnaire to establish the presence of impairment in brain. The scores allotted for each question is summed at the end of the examination and the patients are categorized on the basis of the scores obtained. Score of 30 indicates minimal degree of impairment, 25-30 score indicates mild degree of impairment, 10-20 score and 0-10 score are indicative of moderate and severe degree of impairment, respectively [8].

Cardiovascular risk factors including blood pressure, fasting blood sugar level, serum high-density lipoprotein level, triglyceride levels, and body mass index were assessed. Hypertension was defined as the blood pressure ≥ 140/90 mmHg according to Joint National Committee VII criteria [9]. Diabetes mellitus was defined as the fasting blood sugar level ≥ 100 mg/dL (International Diabetic Federation criteria)[10], Dyslipidemia with serum high-density lipoprotein (HDL) level < 40 mg/dL, and triglyceride levels > 150 mg/dL (International diabetic Federation criteria).Body mass index (BMI)was calculated for all the patients by recording their weight and height. Obesity was defined as BMI> 30 kg/m^2, according to WHO criteria[11].

Patients underwent a brain MRI by following the standard procedure using 1.5-Tesla MRI system

(Siemens Magnetom Symphony, Siemens Medical Solutions, USA Inc., Malvern, Pennsylvania). T2(transverse relaxation time)-weighted coronal MRI scans employed in the form of dual spin-echo pulse sequence were acquired. The contiguous slices (3-5 mm of thickness) were obtained from the nasion to the occiput with a repetition time of 4500 ms and echo time of 116 ms.MR images with slices more than 3 mm thick were considered for diagnosis of SBIs[12] and those distinctly separated from circle of Wills' vessel and having cerebrospinal fluid density on the subtraction images were suspected as basal ganglion infarcts. Double-blind method was followed for processing and analyzing the scans obtained. The investigators were also masked from the stroke risk factor of the patients while analyzing the scans.

Blood samples from the patients were drawn with minimal traumatic venepuncture for quantification of high-sensitivity C-reactive protein (hsCRP).The blood was centrifuged at 3000 rpm for 15 min at 4˚C; the aliquots were stored at −70˚C. hsCRP was quantified by using particle-enhanced turbidimetric immunoassay (PETIA)technique with a sensitivity of 0.5 mg/dL[3]. Patients with hsCRP concentration > 0.3 mg/dL are said to have higher hsCRP range than normal, indicative of infections, tissue injury, or non-infectious inflammatory processes.

Data obtained were tabulated in excel spreadsheet and expressed as rates, ratios, and percentages. Mean blood pressure was calculated in terms of mean ± standard deviation.Fischer exact test using SPSS 15 was employed for the analysis of data. *P* ≤ 0.05 was considered as statistically significant.

Results

The demographic characteristics of the patients is shown in Table 1. The risk factors contributing to the development of SBI represented shown in Table 2. Mean blood pressure calculated for 51 patients was 126.1± 14.08 mmHg (systolic) and 77.53 ± 9.65 mmHg (diastolic).MMSE scores revealed a total of 38 patients demonstrating a minimal degree of impairment (MMSE score =30) and 13 patients with mild to severe degree of impairment(MMSE score < 30).

Assessment of 51 patients and their neurological examination with MMSE and MRI revealed the presence of SBI in 29.41% patients, in which 26.6% of patients had cortical and 73.4% had sub-cortical SBIs.

The association of distribution of SBI with risk factors such as triglycerides, hsCRP, age, BMI, hypertension, and HDL has been shown in Table 3. Out of 51 patients, 33.3% and 50% of patients had cortical and sub cortical SBI, respectively with raised hsCRP and triglyceride levels. However, 66.67% patients with cortical SBI and 50% patients with subcortical SBI had high hsCRP and low triglycerides levels. .High triglycerides and low hsCRP was present in 6.25% patients with cortical SBIs and 33.33%patients with subcortical SBI. The MMSE revealed mild to severe degree of impairmentin 75% patients with cortical SBI and 27.27% patients with subcortical SBI. No association was observed between the distribution of SBI with the risk factors.

Table 1. Distribution of demographic variables, body mass index and history of non-specific neurological complaints in the patients

Variables	Distribution (%)
Sex distribution	
Male	26 (50.98)
Female	25 (49.02)
Age distribution	
< 18	2 (3.92)
18-30	13 (25.49)
31-45	16 (31.37)
46-60	10 (19.61)
≥61	9 (17.65)
Non-specific neurological symptoms	
Headache	28 (54.90)
Vertigo	13 (25.49)
Tinnitus	7 (13.73)
Syncope	5 (9.80)
Dizziness	12 (23.53)
Transient motor disturbances	2 (3.92)
Transient sensory disturbances	4 (7.84)
Transient loss of memory	6 (11.76)
Body mass index	
< 19.5	0 (0)
19.5–24.99	41 (80.39)
25–29.99	4 (7.84)
≥ 30	6 (11.76)

Table 2: Distribution of risk factors for development of silent brain infarct

Risk factors	Distribution (%)
Body mass index > 30 kg/m^2	6 (11.76)
Alcohol	1 (1.96)
Smoking	2 (3.92)
Hypertension	7 (13.78)
High density lipoprotein level < 40 mg/dL	31 (60.68)
Triglycerides level > 150 mg/dL	15 (29.41)
High sensitivity C-reactive protein level > 0.3 mg/dL	32 (62.75)

Table 3. Association of silent brain infarcts with risk factors

Risk factors	Silent brain infarct		*P* value
	Cortical (%)	Subcortical (%)	
Triglycerides (mg/dL)			
<150 mg/dL	2 (50)	6 (54.55)	0.662
>150mg/dL	2 (50)	5 (45.45)	
High density lipoprotein (mg/dL)			
> 40 mg/dL	1 (25)	5 (45.45)	0.47
< 40 mg/dL	3 (75)	6 (54.55)	
High sensitivity C-reactive protein (mg/dL)			
< 3	1 (25)	3 (27.27)	0.725
> 3	3 (75)	8 (72.73)	
Age (years)			
18–30	1 (25)	2 (18.18)	0.14
31–45	0 (0)	4 (36.36)	
46–60	0 (0)	3 (27.27)	
≥ 61	3 (75)	2 (18.18)	
Hypertension			
Present	2 (50)	5 (45.45)	0.87
Absent	2 (50)	6 (54.55)	
Body mass index (kg/m^2)			
< 19.5	0 (0)	0 (0)	0.62
19.5–24.99	3 (75)	9 (81.82)	
25–29.99	0 (0)	1 (9.09)	
≥ 30	1 (25)	1 (9.09)	

Discussion

The study results showed that non-specific neurological symptoms were associated with SBIs. The association of cortical and subcortical SBIs with various risk factors was also determined and analyzed to ascertain their importance in diagnosing and the management of SBIs. This study is, to the best of our knowledge, the first Indian study to assess the importance of non-specific neurological symptoms in diagnosing SBI in an Indian population.

Hougake et al. first reported the relation of non-specific neurological symptoms with SBI. They observed that prevalence of SBI was common in patients with headache (18%), and forgetfulness and dizziness (40%). They also reported the correlation of age, stroke, and hypertension with SBI[4]. In contrast, researchers have argued that it is the deep white matter lesions on MRI and not SBIs that produces the dizziness and headache of non-specific cause [13,14]. Further, Gaist et al., in a recent study, have reported the lack of evidence of an association between the white matter hyperintensities, SBIs, and migraine with aura[5]. The present study has, therefore, taken into consideration the non-specific neurological symptoms for analyzing their role in the incidence of SBIs. The most commonly observed non-specific neurological symptom in the present study were headache (54.90%), dizziness (23.53%), and vertigo (25.49%).

Studies reporting the risk factors for SBI have always implicated hypertension, age, and BMI [1, 2, 7]. In the present study, HDL, triglyceride, and

hsCRP levels are the major risk factors for development of SBIs in the patients along with BMI and high blood pressure unlike factors such as smoking and alcohol consumption. The non-specific neurological symptoms reported in the present study might have a significant association with the development of these risk factors [15-17], which might be the cause of high distribution of the patients in the current study.

In the current study, higher distribution of patients with abnormal levels of HDL, triglycerides, hsCRP, and blood pressure were diagnosed with SBIs. The association of these risk factors with SBIs was not statistically significant, which contrasts with the results of the similar studies on SBIs[18]. Similar results with respect to levels of triglycerides and low HDL levels in association with SBI was also reported by Kato et al. [19]. Level of hsCRP is usually reported to be high in SBI indicating the involvement of inflammatory processes[20], as is also evident in present study. However, the level of hsCRP was also not significant in the study of SBI reported by Umemura et al. [21] confirming the results of the present study.

Smaller sample size was among the limitations of the study. A larger sample size could have helped in the establishment of the presence/lack of association of non-symptomatic neurological symptoms and risk factors with SBI.

Conclusion

The NSNCs evaluated in the study should be considered for diagnosis of SBIs with or without the incidence of the risk factors mentioned. The findings of this study could further be strengthened by determining the role of these risk factors with larger smaller size in a follow-up study. Further, studies can also be conducted to evaluate the presence of association in patients presenting with NSNCs and SBI with traditional risk factors of stroke.

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