

Wake Up and Non-Wake up stroke: A comparative Hospital Based Study

Mohamad Akram¹, Deepak Goel², Manish Mittal³

¹Senior Resident Department of General Medicine, Himalayan Institute of medical sciences, Dehradun, India.

²Professor, Department of General Medicine, Himalayan Institute of medical sciences, Dehradun, India.

³Associate Professor, Department of General Medicine, Himalayan Institute of medical sciences, Dehradun, India.

ABSTRACT

Background: Almost 25% of all acute ischemic strokes occur during sleep with the patients or relatives become aware of the neurological deficits as they wake up. The present study was conducted with an aim to find out the prevalence of wakeup stroke along with clinical profile and outcome of wake up stroke as compared to non-wake up stroke. **Methods:** All patients of age group 18 years or more presenting with stroke during the 12-month study period were included. Data was compared with non-wakeup stroke by applying Chi square test, Fischer exact test and Yates corrections was used to evaluate the association between the variables defining the clinical profile and outcome. **Results:** Patients of non wake-up stroke were higher (63%) as compared to wake-up stroke (37%). Out of 37 wake-up stroke patients, ischemic stroke was found in 23(62.16%) and hemorrhagic stroke in 14(37.83%) patients. Out of 14(37.83%) wakeup strokes; in 8(57.14%) patients lesion was parenchymal and in 5(35.71%) multiple lesions were present. Higher incidence of diabetes mellitus in wake up strokes was found. Atherothrombotic and cardioembolic strokes contribute to majority of the cases of ischemic stroke. **Conclusions:** The incidence of stroke increases dramatically with advancing age irrespective of gender. Diabetes mellitus emerged as the main risk factor in wake-up stroke. In wake up hemorrhagic stroke, the higher percentage of thalamic bleed was found. Improvement was appreciated more in non wake-up stroke as compared to wake-up stroke.

Key words: Stroke outcome, Stroke Severity, Wake-up stroke

INTRODUCTION

Stroke is the third leading cause of death after heart disease and cancer. According to the American stroke Association nearly 8,00,000 Americans suffer from stroke each year, approximately one every 40 seconds.^[1] Up to 25% of all acute ischemic strokes occur during sleep with the patients or relatives become aware of the neurological deficits once they wake up.^[2]

Mechanisms that precipitate stroke during sleep may have some influence immediately after getting up. Therefore sleep-related stroke was defined in two ways; a sleep related stroke occurring only during sleep and noticed immediately on awakening and onset of symptoms during the first 30 minutes after awakening.^[3] The most important factor determining the treatment plan and outcome is the duration of stroke symptoms in acute ischemic stroke. E.g. thrombolytic therapy is useful only upto 3 – 4.5 hours of acute ischemic stroke

After 24 hours of acute ischemic stroke, there is need for prophylaxis and supportive care only. Thus, the management and outcome of patients grossly depends on the time of presentation.^[4] It has been observed in clinical practice that a good proportion of strokes occur in the morning hours but so far to the best of our knowledge no Indian study focused on this aspect.

A recent population based study on wake up stroke among residents of the Greater Cincinnati/Northern Kentucky region (population 1.3 million) in 2005 showed that 14 % of ischemic strokes are wake-up strokes and there were no differences between wake up stroke and other stroke types with regard to clinical features except for minor difference in age and baseline retrospective NIH stroke scale score. Some studies suggest that wake up strokes have greater initial stroke severity and were more likely to have a poor outcome.

In USA, 14 % of patients found to have wake up stroke without any clinical difference from non-wake up stroke.^[5] As this type of statistics is not available in India, the present study was conducted with an aim to find out the prevalence of wakeup stroke in hospital setting along with the clinical profile and

Name & Address of Corresponding Author

Dr Mohamad Akram
Senior Resident
Department of General Medicine,
Himalayan Institute of medical sciences, SRHU
Dehradun, Uttarakhand ,INDIA.
Email: akrampmedicine@gmail.com

MATERIALS AND METHODS

The study was conducted in the Department of Medicine, Himalayan Institute of Medical Sciences, Jollygrant, Dehradun over a period of 12 months. All the stroke patients admitted to the neurology ward were screened. After obtaining written informed consent, they were recruited to detailed history, thorough clinical examination and investigations as per the working proforma. Prior approval from Ethical committee was also obtained. It was an observational and cross sectional study with a samples size of 100. All patients more than 18 years of age of either gender admitted during the study period, fulfilling the inclusion criteria and willing to give informed consent were included in the study. Exclusion criteria include all cases of meningitis, secondaries in brain, primary brain tumour, diabetic ketoacidosis, hypoglycemia, metabolic encephalopathy, septic encephalopathy, electrolyte imbalance, post-ictal phase seizure, and post head injury infarction. Case reporting form was used to collect the data.

Patient's functional and clinical status has been assessed according to Modified Rankin Scale, National Institute of Health Stroke scale, and Glasgow Coma scale at the time of admission. Relevant Blood Investigation and Radiological Imaging have been done. Patients received standard treatment for acute ischemic stroke as per American Academy of Neurology guidelines, year 2007. The patients have been classified in to two groups as wake-up stroke and non wake-up stroke. Wake-up stroke is defined as stroke occurring during sleep and noticed immediately on awakening. It also include strokes with an onset of symptoms during the first 30 minutes after awakening. This was followed by the interpretation and analysis of clinical profile and radiological findings of wakeup stroke.

Data Management and statistical analysis: Statistical analysis was done by using statistical software (SPSS -19). Data was expressed in the terms of frequency and percentage. Chi-square test, Fischer exact test and Yates corrections was used to evaluate the association between the variables mentioned above.

RESULTS

Out of 37% patients of wake up stroke, maximum number of patients 78% were between the age of 51-79 years while and 63% of non-wakeup stroke

majority were between the age of 51-64 years. Out of 37 wakeup stroke patients 23 were of ischemic stroke while 14 were hemorrhagic stroke. Thalamus is the most common location for wakeup stroke; 5 (13.5%) while putamen; 15 (23.8%) was the most common location for non-wakeup stroke. For both wake up; 14(37.8%) and non-wake up stroke; 13(20.63%) anterior circulation is the most common location of ischemic stroke. For ischemic stroke; athrothrombotic; 10(43.47%) stroke forms the most common etiology whereas cardioembolic stroke; 13(40.62%) was the most common reason for non-wake up stroke. For hemorrhagic stroke; hypertension forms the most common etiology for both wake up; 10(71.42%) and non wake up stroke; 25(80.64%).

For GCS score, out of 37 patients of wake-up stroke 33(89.18%) were having GCS score >8 and 4(10.81%) having GCS score <8. Out of 63 patients of non-wake-up stroke, in 50(79.36%) GCS score was >8 and in 13(20.63%) patients GCS score was <8 (p=0.206). For NIHSS score, out of 23(62.16%) of wakeup ischemic stroke, in 18(78.26%) patients was NIHSS score was between 7-25 and in 20(62.5%) NIHSS score was 62.5%. In 5(21.73%) of patients NIHSS was <7. Out of 32(50.79%) non wakeup in 20(62.50%) NIHSS score was between 7-25 and in 12(37.5%) NIHSS score was <7. For MRS score, out of 23(62.16%) patients of wakeup stroke, in only 1(4.34%) patients MRS score was <2 and in 22(95.65%) patients was >2. Out of 32(50.79%) of non-wakeup ischemic stroke, in only 1(3.12%) patients MRS score was <2 and in 31(96.87%) MRS score was >2. For HSCRCP score, out of 23(62.16%) ischemic wakeup stroke in 14(60.86%) patients, value of HSCRCP was more than 10 and in 9(39.13%) patients, value of HSCRCP was less than 10 of 32(50.79%) of ischemic non wakeup stroke in 18(56.25%) patients HSCRCP value was more than 10 and in 14(43.75%) patients HSCRCP score was less than 10.

In hemorrhagic stroke type, improvement in wake-up stroke was 20% and non wake-up was 48.88%. In ischemic stroke type, improvement in wake-up stroke was 29.09% and non wake-up stroke was 43.63%. This show that improvement was appreciated more in non-wake-up stroke as compared to wake-up stroke. Not much difference was found in the outcome of LAMA (Leaving against medical advice) and expired patients between wake-up and non-wake-up stroke amongst hemorrhagic and ischemic stroke.

Table 1: General Characteristics of stroke patients

Parameters	Wake up stroke	Non-wake up stroke
Number (total 100)	37 (37%)	63 (63%)
Age range		
< 50 years	4 (11%)	17 (27%)
51-64 years	14 (38%)	26 (41%)
ears	15 (40%)	17 (27%)
>80 years	4 (11%)	3 (5%)
Location of hemorrhagic stroke		
Putamen	4 (10.8%)	15 (23.8%)
Thalamus	5 (13.5%)	12 (19.0%)
Cerebellar	1 (2.7%)	1 (1.5%)
Pontine	0	1 (1.5%)
Lobar	4 (10.8%)	2 (3.1%)
Location of ischemic stroke		
Anterior circulation	14(37.8%)	13(20.63%)
Posterior circulation	1(2.7%)	3(4.7%)
Multifocal	8(21.6%)	16(25.4%)
Etiology of ischemic stroke		
Athrombotic	10(43.47%)	11(34.37%)
Cardioembolic	9(39.13%)	13(40.62%)
Lacunar Syndrome	2(8.69%)	5(15.62%)
Young stroke with known etiology	1(4.34%)	0
Young stroke with unknown etiology	1(4.34%)	3(9.37%)
Etiology of hemorrhagic stroke		
Hypertensive	10(71.42%)	25(80.64%)
Coagulopathy	1(7.14%)	2(6.45%)
Vascular malformation	2(14.28%)	3(9.67%)
Drug induce	1(7.14%)	1(3.22%)

Table 2: Parameters showing severity of stroke

PARAMETERS	Wake stroke (n=37)		Non-wake stroke (n=63)	
	<8	>8	<8	>8
GCS	4(10.81%)	33(89/18%)	13(20.63%)	50(79.36%)
NIHSS	<7 5(21.73%)	7-25 12(37.5%)	<7 18(78.26%)	7-25 20(62.5%)
MRS	<2 1(4.34%)	>2 22(95.65%)	<2 1(3.12%)	>2 31(96.87%)
HS CRP	<10 9(39.13%)	>10 14(60.86%)	<10 14(60.86%)	>10 18(56.25%)

Table 3: Parameters showing outcome of stroke

	Hemorrhagic (n=45)		Ischemic (n=55)	
	Wakeup	Non-wake up	Wakeup	Non-wake up
Improved	9 (20%)	22 (48.88%)	16 (29.09%)	24 (43.63%)
LAMA (Leaving against medical advise)	3 (6.66%)	4 (8.88%)	4 (7.27%)	3 (5.45%)
Expired	2 (4.44%)	5 (11.11%)	3 (5.45%)	5 (9.09%)
Total	14 (31.11%)	31 (68.88%)	23 (41.81%)	32 (58.18%)

DISCUSSION

The present study evaluates the profile and outcome of wake-up stroke is compared to non-wake-up stroke, and prevalence of wake-up stroke in hospital setting. 100 stroke patients including ischemic and

hemorrhagic stroke were studied with respect to prevalence of risk factors, time of onset of stroke, radiological findings of CT Scan Head, scale of severity and effect of time of onset on the outcome of stroke.

In our study, out of 100 patients, 37 patients were of wake-up stroke and 63 were non wake-up. Percentage of patients of non wake-up stroke was higher (63%) compared to wake-up stroke (37%) (Non wake-up:Wake-up stroke ratio = 1.7:1). This result is in accordance with a study by Silva G S et al which found approximately 25% of patients with ischemic stroke awaken with neurological deficits.^[6] The high proportion of wake-up in our study is supposed to be due to difference in our case definition i.e. we have included cases, which had stroke within half an hour of awakening. We found that out of 37 wake-up stroke, ischemic stroke was found in 23(62.16%) and 14(37.83%) was found in hemorrhagic stroke. Some studies have estimated that wake up strokes comprises 8% - 28% of all ischemic strokes, but these studies were either too small or non-population based.^[7] We found that out of 14 (37.83%) wakeup strokes, in 8 (57.14%) patients lesion was parenchymal and in 5 (35.71%), there were multiple lesions present. In only 1(7.14%) patients SAH/IVH lesion was found. And our result of non wake up stroke, out of 31(49.20%) non wakeup stroke, in 19 (61.29%) patients the lesion was parenchymal, in 8(25.80%) lesion was multiple and in 4(12.90%) lesion was SAH/IVH. We couldn't find any evidence supporting the aforementioned findings. Most of the patients had parenchymal hypertensive hemorrhage with or without intraventricular hemorrhage. Out of 23(62.16%) wakeup stroke, in 18(78.26%) patient lesion was multiple and in 5(21.73%) there were subcortical lesions and out of 32(50.79%) non wakeup stroke, in 24(75%) patients, the lesion was multiple and in 7(21.87%) patients there was subcortical lesion. Only one patient (3.12%) of non wakeup stroke was recorded with lesion in cortex. No evidence was again found for the results obtained.

In patients of nonwake-up ischemic strokes the anterior circulation involvement had found to be in highest percentage i.e. 49.20% followed by multiple and middle circulation strokes and least common case of ischemic non wake-up stroke had found in posterior circulation territory. Our results showed higher incidence of diabetes mellitus in wake up strokes as compared to non wake up strokes. This result is comparable with a study done by Yee SN et al in 2007 with 19.7% patients of ischemic stroke having diabetes mellitus.^[8] Another study by Mats E et al had similar results in which 24.24% of ischemic stroke patients had diabetes mellitus.^[9] The higher incidence of diabetes mellitus in patients of wake-up stroke in comparison to nonwake-up was one of the most important finding in our study. Diabetes mellitus showed higher sympathetic activity and early morning hours exhibit sympathetic over activity

thus evincing strong coalition between wake up stroke and diabetes mellitus.^[10]

Our results showed increased level of blood pressure in both wake up and non wake up stroke. Similar results were shown by a study conducted by Yee SN et al in which most common risk factor was hypertension involving 70.6% of patients.^[8] Also Nadeau et al reported that patients on awakening have higher levels of blood pressure.^[11] Another study by K Sabareesh et al show same results, stroke risk factors included hypertension 21 patients (70%).^[12] Thus, there is a fourfold increase in the relative risk of cardiovascular event among patients with diabetes and hypertension as compared to those without the two conditions.^[13] No difference in snoring, alcoholism and smoking was found between wake up and non wake up stroke. Our results suggested that majority of patients were hypertensive i.e. wakeup (71.42%) and non-wakeup (80.64%). The common sites of hypertensive hemorrhage are deep grey matter constituting 65% of stroke etiology which is in close resemblance with our results.^[14] Other etiologies such as coagulopathy (wakeup: 7.14% and non wakeup 6.45%), vascular malformation (wakeup 14.28% and non wakeup 9.67%) and drug induced (wakeup 7.14% and non wakeup 3.22%) contribute less in causing haemorrhagic stroke. Upto 25% of ICH are attributable to bleeding from rupture of aneurysms and A-V malformation (14). Evidence suggests that cocaine and methamphetamine are common causes of stroke in <45 years of age (15). About 10% of ICH are attributable to coagulopathies resulting from anti couagulations.^[14] Our result suggested that atherothrombotic and cardioembolic strokes contribute to majority of the cases of ischemic stroke with a contribution of (wakeup 43.49% and non wakeup 34.37%) and (wakeup 39.13% and non wakeup 40.62%) respectively. Evidence suggests that atherothrombotic is responsible for 60%^[16] and cardioembolic strokes contributes to 20% of all ischemic strokes.^[15] Yet another study suggests cardioembolic stroke contributes to 43% of etiology of WUS.^[17] This result is in contrast to the previous evidence. Lacunar syndrome (small vessel stroke) contributes to (wake up 8.69%, non wakeup 15.62%) in our results. Lacunar stroke contributes to around 20 % of all strokes.^[15] Young stroke with known etiology (wakeup 4.34% and non wakeup 0) and young stroke with unknown etiology exhibit minimum contribution.

In the present study, HSCR in ischemic stroke (n=55), out of 23(62.16%) ischemic wake-up stroke in 14(60.86%) patients, value of HSCR was more than 10 and in 9(39.13%) patients, value of HSCR was less than 10. Also, out of 32(50.79%) of

ischemic non wakeup stroke in 18(56.25%) patients HSCRP value was more than 10 and in 14(43.75%) patients HSCRP score was less than 10. Our study says that the high value of HSCRP was found in ischemic wake-up stroke in higher proportion in comparison to ischemic non-wake-up stroke patients. A study by Idicula TT has similar findings i.e. ischemic stroke patients showing high CRP levels at admission are associated with more severe stroke, cardioembolic etiology, poor functional outcome and high mortality. The high CRP group had higher frequency of stroke of cardioembolic origin (38% in the high CRP group vs. 21% in the low CRP group). CRP was associated with short-term functional outcome on mRS ($p = 0.04$), with the high CRP group having a 44% risk for a poor outcome vs. 26% for the low CRP group.^[18]

Our results showed that in hemorrhagic stroke type, improvement in wake-up stroke was 20% and non wake-up was 48.88% and in ischemic stroke type, improvement in wake-up stroke was 29.09% and non wake-up stroke was 43.63%. The ratio of improved patients of wake-up to non-wake stroke in hemorrhagic stroke type is 1:2.44, and in ischemic stroke type is 1: 1.5. Our study showed that improvement was appreciated more in non-wake-up stroke as compared to wake-up stroke. Another study by Adams H P et al suggest poor outcome of wake-up strokes, in which among the wake-up group (4 of 43 [9.3%]) were worse than the non-wake-up group (221 of 758 [29.2%]; $P_{0.005}$). The baseline characteristics of the wake-up group of subjects were similar to those of persons enrolled in the non-wake-up group, their outcomes were much poorer.^[19] Not much difference was found in the outcome of expired patients between wake-up and non-wake-up stroke amongst hemorrhagic and ischemic stroke.

Thus it can be said that wake up stroke was associated with increased incidence of diabetes mellitus, higher value of HSCRP (>10) and carries a poor prognosis as compared to non wake up stroke.

ACKNOWLEDGEMENT

The authors thank the participants and all the faculty members of department of Medicine for their invaluable patience and co-operation.

REFERENCES

1. Patients who wake up with stroke may be candidate for clot busters. Health and medicine. <http://www.physorg.com/news156094923html>. Accessed on Aug 10 2011.
2. Breur L, Huttner HB, Dorfler A, Schellinger PD, Kohrmann M. Wakeup stroke: overview on diagnostic and therapeutic options ischemic stroke on awakening. *FortschrNeurolPsychiatr.* 2010; 78: 101-6.
3. Palomaki H, Partinen M, Juvela S, Karte M. Snoring as a risk factor for sleep related brain infarction. *Stroke.* 1989; 20: 1311-5.
4. Benavente O, Hart RG. Stroke part II management of acute ischemic stroke. *AmFam Phys.* 1999; 59: 2828-34.
5. Mackey J, Kleindorfer D, Suchare MH, Moomaw CJ, Kissela BM, Alwell K, et al. Population based study of wakeup strokes. *Neurology.* 2011; 76: 1662-7.
6. Silva GS, Lima FO, Camargo ECS, Smith WS, Singhal AB, Greer DM, et al. Wake up stroke: clinical and neuroimaging characteristics. *Cerebrovasc Dis.* 2010; 29: 336-42.
7. Mackey J, Kleindorfer D, Sucharew H, Moomaw CJ, Kissela BM, Alwell K et al. Population- based study of wake- up strokes. *Neurology.* 2011; 76:1662-7.
8. Yee SN, Stein J, Ning MM, Randie M. Black-Schaffer. Comparison of Clinical Characteristics and Functional Outcomes of Ischemic Stroke in Different Vascular Territories. *Stroke.* 2007; 38; 2309-14.
9. Eliasson M, Lindahl B, Lundberg V, Stegmayr B. Diabetes and obesity in Northern Sweden: occurrence and risk factors for stroke and myocardial infarction. *Scand J Public Health.* 2003; 31: 70.
10. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. *Circulation* 1996; 93:1043-65.
11. Nadeau JO, Fang J, Kapral MK, Silver FL, Hill MD. Registry of the Canadian Stroke Network. Outcome after stroke upon awakening. *Can J Neurol Sci.* 2005; 32:232-6.
12. Sabareesh K, Natarajan KV, Snyder AH, Siddiqui AH, Jonita CC, Hopkins LN et al. Safety and effectiveness of endovascular therapy after 8 hours of acute ischemic stroke onset and wake-up strokes. *Stroke.* 2009; 40: 3269-74.
13. Biller J, Love BB, Schneck MJ. Vascular diseases of the nervous system: ischemic cerebrovascular disease. In: Bradley WG, Daroff RB, Fenichel GM, Jankovic J, editors. *Neurology in clinical practice*. 5th ed. Vol 2. Elsevier: Philadelphia; 2008. p. 1165-94.
14. Srivastava MVP, Garg A. Haemorrhagic cerebrovascular disease. In: Munjal YP, editor. *API textbook of medicine.* 9th ed. Jaypee Brothers Medical Publishers (p) Ltd. New Delhi; 2012. p. 1411-3.
15. Smith WS, English JD, Johnston SC. Cerebrovascular diseases. In: DL Longo DL, Kasper

- DL, Jameson JL, Fauci AS, Hauser SL, Loscalzo J, editors. Harrison's principles of internal medicine. 18th ed. Vol2. McGraw Hill: USA; 2012. p. 3270-97.
16. Dalal PM. Ischemic vascular diseases. In: Munjal YP, editor. API textbook of medicine. 9th ed. Jaypee Brothers Medical Publishers (p) Ltd. New Delhi; 2012. p. 1401.
 17. Andrew D, Barreto S, Hallevi H, Miriam M, Morales AT, Abraham AR, et al. Thrombolytic therapy for patients who wake up with stroke. *Stroke*. 2009; 40: 827-32.
 18. Idicula TT, BroggerJ, NaessH, Andreassen UW, Thomassen L. Admission C – reactive protein after acute ischemic stroke is associated with stroke severity and mortality: The 'Bergen stroke study'. *BMC Neurology*. 2009; 9:18.
 19. Adams HPJ, Leira EC, Torner JC, Barnathan E, Padgett L, Effron MB et al. Treating patients with wake-up stroke: the experience of the abest-II trial. *Stroke*. 2008; 39: 3277-82.

How to cite this article: Akram M, Goel D, Mittal M. Wake Up and Non-Wake up stroke: A comparative Hospital Based Study. *Ann. of Int. Med. & Den. Res.* 2015;1(2):82-7.

Source of Support: Nil, **Conflict of Interest:** None declared