

AN ANALYSIS OF VARIOUS CLINICAL PRESENTATION, ETIOLOGICAL AND RISK FACTORS AMONG ACUTE ISCHEMIC STROKE PATIENTS ADMITTED AT A TERTIARY CARE HOSPITAL, IN NORTH INDIA.

Neurosurgery

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ABSTRACT

Background: South Asian countries constitute 22% of world population and 40% of developing world and account for more than 40% of global burden of stroke death¹. There are insufficient studies available on ischemic stroke in Asian countries including India.

Aims: The present study aimed at evaluating risk factors, clinical profile and stratification of ischemic Stroke subtypes based on TOAST categories among patients admitted in a tertiary care hospital, in North India.

Methods and Material: An Observational prospective hospital based Study was carried out on patients of acute Ischemic stroke admitted within 7 days of symptom onset to a tertiary care hospital during June 2015 to December 2016 who were suitable as per our inclusion and exclusion criteria.

Results: A total of 164 acute ischemic stroke patients were enrolled during the study period. Acute ischemic stroke was found comparatively more in Male patients [71%] than in females [29%]. More than one fourth of patients were between 61-70 years (28%) followed by 51-60 (23.8%). The most common risk factors were Hypertension (56.1%) followed by Diabetes (40.2%). The most common clinical presentation was limb weakness in (70.7%) of patients followed by dysarthria (58.5%). The most common subtypes of acute ischemic stroke was undetermined etiology (UDE) in 34.7% followed by Stroke of other determined etiology in 24.3%.

Conclusions: The present study suggests that male and middle aged individuals are at increased risk of having acute ischemic stroke. The commonest risk factor in our study was Hypertension, followed by diabetes, CAD, smoking and tobacco chewing. The most common etiology of ischemic stroke was stroke of undetermined etiology.

KEYWORDS

Ischemic stroke, risk factors, clinical presentation, hypertension, North India.

INTRODUCTION

Stroke is the 2nd leading cause of death and third leading cause of disability worldwide². Globally, 70% of strokes and 87% of both stroke-related deaths and disability-adjusted life years occur in low- and middle-income countries (LMIC)^{3,5}. The disability in LMIC like India, largely driven by demographic changes and further enhanced by the increasing prevalence of the key modifiable risk factors. So there is double whammy for LMIC as both primary prevention and stroke treatment is not up to the mark.

Hence the present study aimed at Stratification of ischemic Stroke subtypes and to identify the common modifiable and non- modifiable risk factors along with clinical presentation among ischemic stroke patients in North India.

Subjects and Methods

Study Population:-

The present study was undertaken after obtaining permission from the institution's research and ethical committee. Patients of acute Ischemic stroke admitted within 7 days of symptom onset to a tertiary care hospital during June 2015 to 31st December 2016 who were suitable as per our inclusion and exclusion criteria were included in the study.

Inclusion criteria:

- Patients of all age group diagnosed as having acute ischemic stroke within 7 days of symptom onset, based on the imaging study (MRI or CT scan) during the study period.

Exclusion criteria:

- All other patients not willing to give an informed consent, stroke mimics and ICH were excluded from the study.

Study Design:- Observational prospective hospital based Study

Sample Size

For the margin of error at 2% and confidence level of study at 99%, a minimum of 136 patients (calculated using Raosoft sample size calculator and based on similar previous studies reported prevalence of stroke is 83%)⁶ were required for Evaluation of clinical in different subtypes of ischemic stroke and to Assess Prognosis of patients in different sub types of ischemic strokes. So the sample size in our study was minimum of 136 patients.

Methodology-

- An informed consent of each patient studied prospectively was obtained.
- A detail history in terms of name, age, sex, chief complaints, past and family history was taken. History related to etiological factor like smoking, diabetes, hypertension, previous stroke, history of atrial fibrillation, dyslipidemia, malignancy etc. was noted.
- Diabetics- Patients who are known diabetics, or newly diagnosed (HbA1C $\geq$ 6.5%)
- Hypertension- Patients on antihypertensive medication or having previous history of hypertension.
- Dyslipidemia- Total cholesterol $>$ 200mg/dl and /or LDL cholesterol $>$ 100mg/dl.
- Smoking- 10 or more cigarette or Bidi per day for at least 6 months
- Alcoholic- on average $\geq$ 2 drinks/day for males and $\geq$ 1 drinks for females (previous drinker: ex drinker for more than 1 year).
- Tobacco Chewer – History of tobacco chewing
- Hypothyroidism- History of hypothyroidism or newly diagnosed
- Renal disease- History of chronic kidney disease (Stage I-V) or newly diagnosed.
- CAD- History of angiographically proven CAD.

Subtypes of ischemic stroke

Clinical examination of patient was done including general physical and neurological examination with parameters like baseline NIHSS, Pupils, Cranial nerves examination, Muscle Tone, Power in limbs, Deep tendon reflexes, Sensory examination, Cerebellar signs. Based on clinical and radiological findings patients were classified in different TOAST categories

Data processing and analysis

All the analysis was carried out on SPSS 16.0 version (Chicago, Inc., USA) with statistical significance at $<$ 0.05.

Results

A total 164 acute ischemic stroke patients were enrolled during June 2015 to December 2016 and were evaluated for risk factors, clinical presentation and stroke subtype.

Demographic profile

In the current study, acute ischemic stroke patients was found comparatively more in Male patients i.e. 117 [71%] than in female

patients 47 [29%]. The male to female ratio was 2.49:1. The mean age was 57.77 ± 15.16 years for males and 62.19 ± 14.54 years for females. More than one fourth of patients were between 61-70 years (28%) followed by 51-60 (23.8%), >70 (22%), <40 (14%) and 41-50 (12.2%) years. (Figure 1-3)

Risk factor profile

Among ischemic stroke patients, 92 (56.1%) were hypertensive, 66 (40.2%) were diabetic and 24 (14.6%) had dyslipidemia. History suggestive of coronary artery disease was present in 36 (22%) patients, atrial fibrillation was present in 16 (9.8%) patients, and 10 (6.1%) patients each had rheumatic heart disease and Renal disease. Family history suggestive of stroke was present in 23 (14%) patients and previous history of stroke was found in 14% patients. Smoking habit was seen in 12.8% patients and tobacco chewing habit was seen in 6.1%. Alcoholic were 3%. (Figure 4-6)

Figure 7 is showing distribution of patients with recurrent stroke according to the time interval from the previous stroke. Maximum (39.1%) patients had previous stroke between 1-5 years followed by 30.4% of patients within 3 months to 1 year and 26.1% before 5 year. Only 4.3 % of patients were having stroke within 3 months of previous stroke.

Clinical presentation

Figure 8 is showing distribution of symptoms in acute ischemic stroke. Acral weakness was the most common symptom present in 70.7% of patients followed by dysarthria (58.5%), aphasia (22.6%) and ataxia (11.6%). Other uncommon symptoms were Loss of consciousness (11%), headache (7.3 %), vertigo (1.8%), seizure (1.2%), visual loss (1.2%), and altered sensorium (0.6%).

Ischemic stroke subtype

An important objective of our study was to classify the patients in to subtypes of acute ischemic stroke. Despite extensive evaluation , etiology remained undetermined in 34.7% (UDE). Stroke of other determined etiology in 24.3%, small vessels (20.7%), large artery atherosclerotic disease in 12.8% and Cardio-embolic in 7.3 % patients were seen. Stroke of other determined etiology was identified in 40 patients (24.3%), which included hyperhomocysteinemia in 33 (82.5%), malignancy in 4(10%), Antiphospholipid syndrome in 1 (2.5%), dissection in 2(5%) patients. (Figure 9-10)

DISCUSSION

The present observational prospective hospital based Study provides advance and unique data on clinical presentation, etiological and risk factors of ischemic stroke in a section of Indian population. Out of 164 acute ischemic stroke patients, 117 [71%] were male and 47 [29%] were female ($p = 0.08$). Male to female ratio in our study was 2.49:1. This gender differentiation is similar to other studies reported by Raghuvanshi S. et al⁷, Marulaiah S.K. et al⁸ and Kashinkunti et al⁹. The male to female ratio is comparable to other studies conducted by Raghuvanshi S. et al⁷, from Bhopal and Parvaiz A Shah et al¹⁰, from Kashmir showing a M:F ratio of 2.89:1 and 2.4:1 respectively. The above studies concluded that stroke is more common among men than women. Male sex is one of the strong risk factor for stroke. Women have lower stroke incidence than men because of genetic factors, positive effects of estrogen on the cerebral circulation, and low blood pressure levels. Moreover, ischemic heart disease, peripheral artery disease and cigarette smoking are more prevalent among male stroke patients¹¹. This gender difference probably resulted from inherent social bias, in which female patients are less likely to be admitted to hospital compared to male patients which is less likely in urban setting. This observation is in contrast to the study done by Yadav R.S. et al¹² in which there was female predominance in ischemic stroke patients; may be due to disorders related to pregnancy, excess use of contraceptive pills and also stroke in females due to migraine in these studies.

In our study, the mean age of patients of acute ischemic stroke at presentation was 57.77 ± 15.16 years for males and 62.19 ± 14.54 years for females. More than half of the patients were in the age group of 51–70 years (51.8%). Young patients with ischemic stroke (age ≤ 50 years) comprised of 26% of the cohort while 7.3% were in age group of >80 year. The above mentioned observations are similar to studies conducted by Grau AJ et al¹³, Acciarresi M et al¹⁴, in which ischemic stroke mean age for males was lower females (59.3 ± 13.6 versus 66.85 ± 14.9). This is dissimilar to studies conducted by Al-Rajeh S et

al¹⁵, El Sayed MM et al¹⁶, in which stroke occurred at a younger age in women than men. The age distribution in our study is similar to studies carried out by Yadav R.S. et al¹² and Marulaiah S.K. et al⁸, with 45.5% were 51-70 years, and 51% patients in 51-70 years, respectively. The data of young ischemic stroke is comparable with the studies done by Misbach and Wendra et al¹⁷, and Eapen et al¹⁸, with incidences of young patients with ischemic stroke were 12.9% and 15.4% respectively. Stroke at earlier age has been shown by various studies conducted in India⁷.

The mean age of stroke in present study was 59.04 ± 15.07 years which is comparable to study conducted by Raghuvanshi S. et al⁷ (Indians) 53.02 ± 12.45 years versus (Americans) 71 ± 13 years. In comparison with the studies carried out by Kissela et al¹⁹, and Baidya et al²⁰, the mean age of the patients with stroke is relatively lower in our study. It is possibly because of lack of preventive strategies in place regarding various risk factors of stroke at the population level.

In the present study, hypertension was the most common risk factor among the stroke patients (56.1%). Diabetes was the second most common (40.2%) and CAD was the third most common disease (22%). This is similar to study conducted by Nadia Aquil et al²¹, in which hypertension was most common with (55%), diabetes mellitus (49%), CAD in (30%) and dyslipidemia in 22% patients. Similar trend was seen in study conducted by N.A. Syed²², in which hypertension was reported as the most commonest risk factor (66.2%), followed by diabetes mellitus in 41.5% patients. In study by Marwat et al²³, hypertension was the most common risk factor (75%) followed by diabetes mellitus (54.5%), IHD (36.3%), hyperlipidemia (13.6%) and valvular heart disease (6.8%).

In contrast to the present study, Vaidya et al²⁴, reported that the most common risk factor was hypertension with (30.1%) incidence, second most commonest was CAD (16.1%), dyslipidemia (15.6%) and diabetes mellitus in 10.8% patients. A study by Misbach and Wendra et al¹⁷, hypertension was the most important risk factor for ischemic stroke, as other risk factors were hyperlipidemia, diabetes mellitus, IHD and atrial fibrillation.

Hypertension has been observed the most common risk factor of ischemic stroke in various studies. This alarmingly high prevalence of hypertension in patients with ischemic stroke calls for need of treatment of major public health problems and indicates the need to incorporate treatment of hypertension into health care policy measures in order to reduce morbidity and mortality of stroke. Also the risk of stroke in diabetic patients is about double than that found in non-diabetic individuals²⁵.

Out of 164 patients, 21 (12.8%) were smokers, 6.1% patients were tobacco chewer and only 3% patients were alcoholic. This is comparable to the study done by Deepa Dash et al²⁶ and Azra Zafar et al²⁷, who found smoking in 9.5% and 7.2% patients respectively but is in contrast to studies conducted by Raghuvanshi S et al⁷ and Yadav RRS et al¹², in which the smoking rate was much higher i.e. 44% and 23.8% respectively. The observation of tobacco chewing habit is comparable to the study conducted by Raghuvanshi S et al⁷, in which 10% patients were tobacco chewer, a slight high rate of tobacco chewing is noticed in study conducted by Yadav RRS et al¹², i.e. 14.8%. The alcoholics (3%) are comparable to the study done by Vaidya C et al²⁵, with 6.6%. This is much lower than the studies conducted by Eapen RP et al¹⁸, and Naik M et al²⁸, who found 35.3% and 30.5% alcoholics respectively. The current study had a reduced frequency of smoking, tobacco chewing and alcoholics compared to previous Indian studies. A bias due to suppression of history of addiction may be responsible for some reduction.

In the present study, previous history of stroke was found in 14% patients. This figure is generally in agreement with studies conducted by Raghuvanshi S et al⁷, and Yadav RSS et al¹², with history of stroke in 13.7%, and 9.8% patients respectively. Maximum (39.1%) patients had previous stroke between 1-5 years followed by 30.4% of patients within 3 months to 1 year and 26.1% before 5 year. Only 4.3 % of patients were having stroke within 3 months of previous stroke in the present study.

The most common stroke subtype in the present study was undetermined etiology (34.7%) followed by stroke of other determined cause (24.3%), small vessel disease (20.7%), large vessel disease

(12.8%) and cardioembolic stroke (7.3%). This is comparable with the study done by Yatsu FM et al²⁹ and Kunitz SC et al³⁰ in which 33% and 33% patients were remained in stroke of undetermined etiology. This is much higher than the previous studies done by Kaul S. et al¹ in 27%, Raghuvanshi S et al⁷ in 21.7% and Nadia et al²¹ in 18% patients. The most common reason for categorizing these patients as having an undetermined etiology was due to fact that a large number of patients had two or more etiological possibilities and some patients could not be evaluated extensively for stroke subtypes on account of various reasons. (Table1)

Stroke of other determined etiology was identified in 40 patients (24.3%). The most common etiology in this group was hyperhomocysteinemia in 33(82.5%), followed by cancer in 4(10%), Antiphospholipid syndrome in 1 (2.5%), dissection in 2(5%) patients. Similar to the study conducted by Kaul S et al¹, in which Stroke of other determined etiology was identified in 17 patients (4%), in which hyperhomocysteinemia was the most common etiology ie in 8 (47.1%) patients, followed by anticardiolipin antibody in 4(23.5%) and dissection in 2(11.7%). A study conducted by Kumar SSS et al³², hyperhomocysteinemia (55%) was predominantly seen followed by Protein S deficiency, Protein C deficiency and antithrombin III deficiency in 21%, 14% and 7% patients respectively and Antiphospholipid antibody (APLA) was positive in 3% . In contrast to the study conducted by Deepa Dash et al²⁶, reported the most common etiology in patients with ODC to be dissection (51.3%). Increased incidence of hyperhomocysteinemia in our study is probably due to slight higher incidence of smoking.

Third most common cause of ischemic stroke was small vessels etiology (20.7%). This is comparable to 18% reported previously by Parvaiz AS.etal¹⁰, however, lower than 43% and 42.7% reported by Nadia et al²¹ and Syed NA²² et al respectively.

The frequency of cardioembolic stroke was 7.3% in this study. This is much lower than that reported from Sacco RL et al³³ (19%) and Raghuvanshi S et al⁷ (16%) but comparable to 6% by Syed et al²² and 10% by Kaul et al³¹.

Most common symptom at presentation amongst patients of acute ischemic stroke was hemiparesis (70.7%) followed by dysarthria (58.5%) which was similar to the findings in study done by Vaidya.etal²⁴. Weakness and dysarthria (58.5%) were also the most common symptoms in the study performed by Kumar NSSetal³² where they found motor weakness in 94% of cases and dysarthria in 72% of cases. The higher occurrence of these symptoms in this study may be related to the higher percentage of anterior circulation stroke (86%) of patients. Other uncommon symptoms were aphasia (22.6%) loss of consciousness (11%), headache (7.3 %), vertigo (1.8%), seizure (1.2%), visual loss (1.2%) and altered sensorium (0.6%). Headache ataxia, vertigo and visual loss were associated with posterior circulation stroke.

Strength and limitations of the study

This is a prospective study with a relatively large sample size and also ensured uniform data collection of various risk factors related to stroke ,we obtained reliable information about clinical characteristics risk factors to achieve the goals of our study. This will in turn help the health care authorities to formulate the preventive strategies for management of risk factors and will also decrease the gravities effect of stroke by having overview knowledge about clinical characteristics of stroke.

There are certain limitations of our study. First, this study was confined to a single tertiary care hospital and thus represents a limited population. Moreover, this Hospital is a specialized neurology and neurosurgery hospital of India. The patients treated here are usually in a more critical condition as these patients are referred from the adjacent peripheral areas including rural and urban areas in and around metropolitan city, also referred from other neighbouring states and this may result in selection bias.

CONCLUSION

Our study suggests that acute ischemic stroke was maximum in male and middle aged patients. The most common preventable stroke risk factors were smoking, HTN, diabetes and CAD. The most common clinical presentation was limb weakness and dysarthria. Our study

showed that most common subtype of acute ischemic stroke was stroke of undetermined etiology.

Considering the high morbidity and mortality associated with stroke, a large scale community based health awareness programme should be launched with the help of social group, local political leaders and healthcare workers. So that stroke can be recognized at its early stage and available treatment should be offered to the patients. It is also important for the local health care workers to know the acute ischemic stroke treatment guidelines.

To conclude, further similar studies on ischemic stroke, its clinical profile, risk factors should be encouraged, so that local risk factors of the defined area could be identified and shared with frontline healthcare workers, so that screening and management of common risk factors can be executed at the community level.

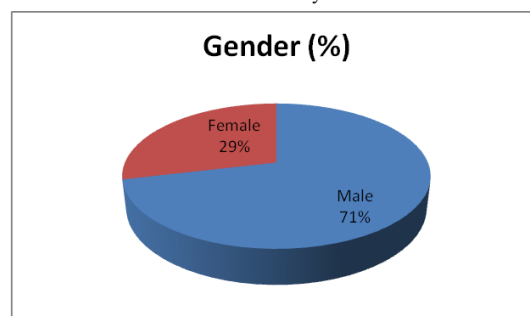


Figure -1: Gender distribution of acute ischemic stroke patients

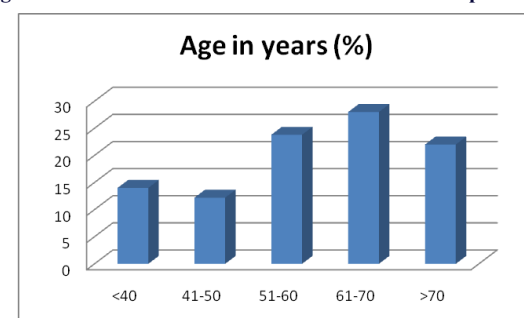


Fig. 2: Age distribution of acute ischemic stroke patients

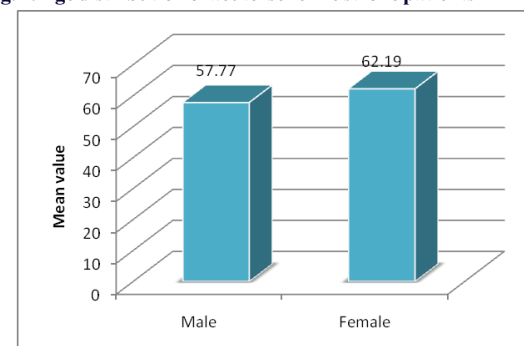


Fig. 3: Mean and SD of age according to gender

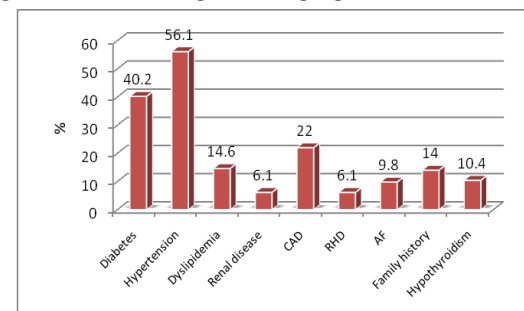


Fig. 4: Distribution of patients according to comorbid illness and other risk factors

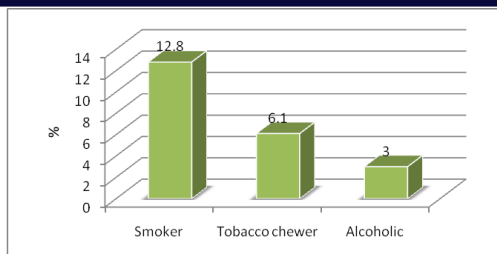


Fig. 5: Distribution of patients according to addiction habit

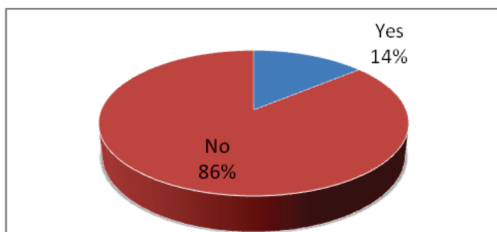


Fig. 6: Distribution of patients according to previous history of stroke

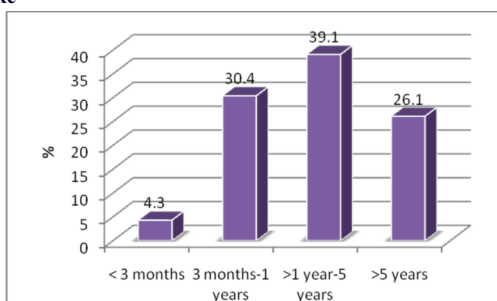


Figure 7 Distribution of the patients according to the time interval of the previous stroke

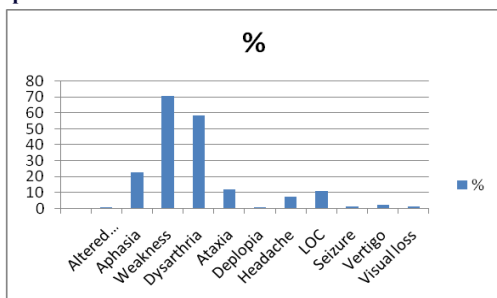


Figure 8 :Distribution of the patients according to the presenting symptoms

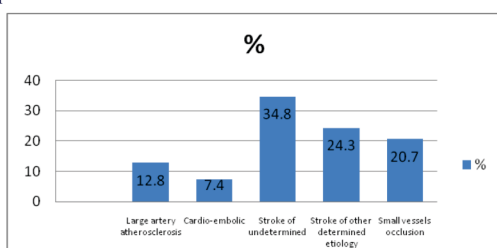


Fig. 9: Stroke Subtype by TOAST criteria

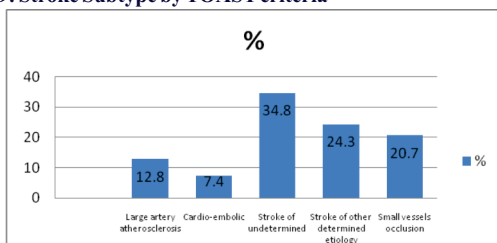


Figure-10: Distribution of stroke of other determined etiology

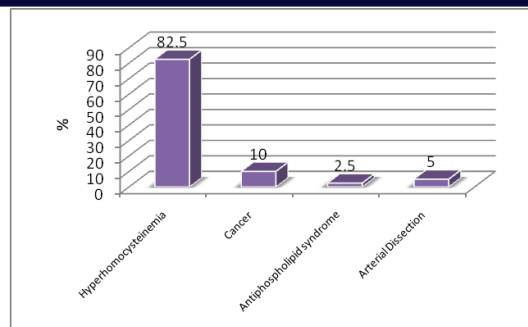


Table 1-Comparative analysis of present studies Vs previous studies

Study	Patient No	Large Vessel Disease (%)	Small Vessel Disease (%)	Cardioembolic (%)	Other Determined Etiology (%)	Undetermined Etiology (%)
Sacco RL et al ¹⁴	1273	14	27	19	-	40
Yatsu FM et al ¹⁹	3727	50	-	-	17	33
Kunitz SC et al ¹⁰	708	24	14	-	28	33
Kaul S. et al ¹¹	392	41	18	10	4	27
Raghuvanshi S et al ⁷	175	41.1	15.4	16	2.2	25.1
Syed NA et al ²²	393	26.9	42.7	6.1	-	20.3
Nadia et al ²¹	100	31	43	8	1	18
Parvaiz AS. et al ¹⁸	3837	1.6	17.9	2.3	25.1	1.5
Present study	164	12.8	20.7	7.3	24.3	34.8

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