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Assessment of prognosis of intracerebral haemorrhage with respect to clinical, biochemical and radiological parameters: a study in a tertiary health care centre in Eastern India

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ABSTRACT

Introduction: The main objective of the study was to evaluate, compare and correlate clinical, biochemical and Radiological [Computerized Tomography (CT) scan/Magnetic Resonance Imaging (MRI)] findings in patients with intracerebral haemorrhage (ICH) with their outcomes at least 15 days in a hospital-based prospective study.

Material and methods: This was a prospective study carried out at the Department of Medicine at KPC medical college and hospital among 128 patients having haemorrhagic CVA based on CT/MRI findings. After proper ethical clearance from the Institutional Ethics Committee of KPC Medical College & Hospital (No: KPCMCH/IEC/470), informed consent was taken from all patients. Pre-designed, pre-tested and semi-structured proforma with a checklist was used to collect data regarding demographic and clinical variables. Random blood sugar, total cholesterol, HDL, LDL, TRIGLYCERIDE and VLDL were performed in each participant from the hospital laboratory. CT Scan/ MRI findings were used to calculate the site of the haematoma, the side of the haematoma and the volume of the haematoma. In this study, 67 (52%) patients had left-SIDED HAEMATOMA and 61(48%) patients had right-SIDED HAEMATOMA.

Results: In this study, 4 (8.0%) patients were < 40 years old, 11 (22.0%) patients were forty-one to fifty years old, 19 (38.0%) patients were fifty-one to sixty years old, 5 (10.0%) patients were sixty-one to seventy years old and 11 (22.0%) patients were more than seventy-one years old. In this study, 33 (26%) patients had APHASIC SPEECH, 36 (28%) patients had DYSARTHIC SPEECH, 32 (25%) patients could not be examined (ENP) and 27 (21%) patients had NORMAL SPEECH. In this study, 10 (8%) patients had BILATERAL, 56 (44%) patients had COMPLETE, 6 (4%) patients had NORMAL and 56 (44%) patients had VARIABLE motor weakness. In this study, 18 (14%) patients had decreased DTR OF AFFECTED SIDE and 110 (86%) patients had Exaggerated DTR OF AFFECTED SIDE. In this study, 18 (14%) patients had Extensor B/L, 51 (40%) patients had Extensor Left and 59 (46%) patients had Extensor Right.

Conclusions: It was found that a longer duration of a stroke at the time of initial evaluation was associated with higher mortality which was statistically significant. It was found that altered sensorium, level of consciousness at presentation, hypertension and h/o stroke were significantly associated with mortality.

Keywords: Intracerebral haemorrhage, stroke, assessment, outcome

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Introduction

As one of the most common subtypes of stroke, intracerebral haemorrhage (ICH) is also considered a critical disease which can lead to severe disability and even death. Intracerebral haemorrhage is more common in low- and middle-income countries in advanced-aged men, especially among Asians. A higher fatality rate was observed among ICH patients which is as high as 40% at one month and 54% at one year and long-term functional independence can be achieved by only 12% to 39% of survivors [1]. Risk factors of ICH

are hypertension, current smoking, excessive alcohol consumption, hypocholesterolaemia, and drugs [1, 2].

Intracerebral haemorrhage results from the rupture of an intracerebral vessel leading to the formation of haematoma within the brain substance. It is the most common type of intracranial haemorrhage [3]. It accounts for 10% of all strokes and is associated with almost 50% of the case fatality rate. Incidence rates are particularly high among Asians and the black population. Hypertension, trauma and cerebral amyloid angiopathy cause the majority of these haemorrhages. Advancing age and uncontrolled alcohol consumption increase the risk whereas cocaine and amphetamine addiction are the most important causes in the young population.

Prognostic models for mortality and functional outcome after intracerebral bleeding were proposed from time to time based on the neurological features at the time of presentation. Marquardsen (1969), a pioneer in this field, observed that in the acute phase of stroke, the single most important prognostic factor is the level of consciousness of the patient. The ICH score is a simple clinical grading scale that allows risk stratification on presentation with ICH[4]. The use of this type of scale could improve the standardization of treatment protocols and clinical research studies on ICH [5–8]. The initial ICH volume is one of the most important prognostic factors to determine the severity of ICH in patients. ICH volume is one of the three most important predictors of mortality in ICH patients; others are the level of consciousness and age [9, 10].

Intraventricular extensions (IVE) are also another important predictor of stroke severity. The association of IVE with other independent risk factors results in the death of the patients.

Independent predictors of mortality following an ICH are age, hypertension, intraventricular blood extension and stroke severity.

Intracerebral haemorrhage (ICH) is defined as the spontaneous extravasation of blood into the brain parenchyma. Non-traumatic forms of ICH account for 10% to 30% of all stroke hospital admissions [11], leading to catastrophic disability, morbidity, and mortality of 30% to 50% at 30 days [11]. Death at 1 year varies by different location: 42% for cerebellar, 51% for deep, 65% for brain stem haemorrhages and 57% for lobar [12]. Twelve to fifteen cases per 100,000 population were estimated as the overall incidence of ICH as per a recent population-based study [13]. USD 125,000 was the estimated cost per person per year to treat ICH with a total cost of USD 6 billion per year in the United States alone [14] related to the loss of productivity with the enhancement of both acute and chronic medical care cost.

Depending on the underlying cause of haemorrhage, ICH may be classified as primary when it originates from the spontaneous rupture of small arterioles damaged by chronic hypertension or cerebral amyloid angiopathy, representing at least 85% of all cases; or secondary when associated with vascular malformations, bleeding related to an ischaemic stroke, tumours, abnormal coagulation, trauma [15], or vasculitis. In approximately 40% of the cases, blood may also extend into the ventricles – intra-ventricular haemorrhage (IVH) — potentially leading to neurological death related to acute obstructive hydrocephalus resulting in a substantial worsening of the prognosis [16–19]. Although several randomized therapeutic trials for ICH were published, neither surgical nor medical treatments were shown conclusively to benefit patients. However, early surgical intervention shown mild statistically significant improvement in clinical outcomes. Prognostic factors for predicting functional outcome and mortality thus play a major role in determining the treatment outcome.

The main objective of the study was to evaluate, compare and correlate clinical, biochemical and Radiological [Computerized Tomography (CT) scan/Magnetic Resonance Imaging (MRI)] findings in patients with intracerebral haemorrhage (ICH) with their outcomes at least 15 days in a hospital-based Prospective study.

Material and methods

This was a prospective study carried out at the Department of Medicine at KPC medical college and hospital among 128 patients having haemorrhagic CVA based on CT/MRI findings. After proper ethical clearance from the Institutional Ethics Committee of KPC Medical College & Hospital (No: KPCMCH/IEC/470), informed consent was taken from all patients.

The main inclusion criteria of the study included patients admitted to the department of medicine with a history of suggestive stroke of less than 7 days duration. Patients in whom a subsequent CT/MRI of the brain confirmed the diagnosis were taken up for the study. Only new cases were enrolled in the study.

The main exclusion criteria of the study included brain tumours, haemorrhagic transformation of cerebral infarct, aneurysmal or vascular malformation rupture, haematologic malignancies, subdural haematoma and cerebral amyloid angiography.

To collect data from the participants researchers used pre-designed semi-structured proforma. Demographic details like sex, age, addiction to alcoholism and smoking etc and clinical variables like blood pressure (BP), pulse rate (PR), respiratory rate (RR), level of consciousness, temperature, pupil size, ocular posture, speech abnormalities, degree of motor weakness, side of motor weakness, etc. were in the above-mentioned semi-structured proforma. Random blood sugar, total cholesterol, HDL, LDL, TRIGLYCERIDE, and VLDL were performed in each participant from the hospital

laboratory. CT Scan/MRI findings were used to calculate the site of the haematoma, the side of the haematoma and the volume of the haematoma.

The volume of the haematoma was calculated by using a simple and easily reproducible bedside method (Kothari, Brott, Broderick; ABC's of measuring intracerebral volume). In this method, the CT slice with the largest area of haemorrhage was first identified. Therefore, the largest diameter (A) of the haemorrhage on this slice was measured. On the same slice, the largest diameter 90° to A was measured next (B). Lastly, of 10-mm slices on which the ICH was seen the approximate number was calculated (C). C was calculated by a comparison of each CT slice with the largest haemorrhage on that scan. If the haemorrhage area for a particular slice was greater than 75% of the area seen on the slice where the haemorrhage was largest, the slice was considered 1 haemorrhage slice for determining C. If the area was approximately 25% to 75% of the area, the slice was considered half a haemorrhage slice; and the slice was not considered a haemorrhage slice if the area was less than 25% of the largest haemorrhage. To determine the value for C, these CT haemorrhage slice values were then added. All measurements for A and B were made with the use of the centimetre scale on the CT scan to the nearest 0.5 cm. A, B, and C were then multiplied, and the product was divided by 2, which yielded the volume of haemorrhage in cubic centimetres.

After proper ethical clearance from the Institutional Ethics Committee of KPC Medical College & Hospital (No: KPCMCH/IEC/470), informed consent was taken from all patients fulfilling inclusion/exclusion criteria presenting to indoor of the Department of Medicine and Department of Neurology, KPC Medical College and Hospital. Detailed history-taking will be done.

For statistical analysis, data were entered into a Microsoft Excel spreadsheet and then analysed by SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5. For numerical variables as mean and standard deviation data was summarized and for categorical variables it was counted and percentages were calculated. Two-sample t-tests, Paired t-test, Chi-squared test ($\chi 2$ test) and Fischer's exact test were used as appropriate. From Student's t-distribution by using a table of values a p-value can be found, once a t value is determined. Here, a p-value ≤ 0.05 was considered statistically significant.

Results

In this study, 4 (8.0%) patients were < 40 years old, 11 (22.0%) patients were 41–50 years old, 19 (38.0%) patients were 51–60 years old, 5 (10.0%) patients were 61–70 years old and 11 (22.0%) patient were > 70 old. Demographic details were listed in Table 1.

Table 1. Demographic details of the participants

Parameters	N (%)
Age in years	
< 40	10 (8%)
41–50	28 (22%)
51–60	49 (38%)
61–70	13 (10%)
> 71	28 (22%)
Distribution of sex	
Male	85v (45%)
Duration of stroke (in hours)	
< 48	102 (80%)
> 48	m6 (20%)
Distribution of speech	
A	33 (26%)
D	36 (28%)
ENP	32 (25%)
NOR	27c(21%)
Distribution of pupils	
CON	8 (6%)
DIL	18h(14%)
NOR	102 (80%)
Distribution of ocular posture	
HGP	28 (22%)
NOR	8dar (68%)
VIP	13 (10%)
Distribution of 7th nv palsy	
ENP	15 (12%)
UMN	113 (88%)
Distribution of motor weakness	
BIL	10 (8%)
COM	56 (44%)
NOR	6 (4%)
V	56 (44%)
Distribution of deep tendon reflex of affected side	
Decreased	18 (14%)
Exaggerated	110 (86%)
Distribution of plantar-flexor/extensor	
Extensor B/L	18 (14%)
Extensor Left	51 (40%)
Extensor Right	59 (46%)
Distribution of site of haematoma	
BG	59 (46%)
BS	5 (4%)
CER	5 (4%)
LB	28 (22%)
T	31 (24%)
Distribution of side of haematoma	
Left	67 (52%)
Right	61 (48%)

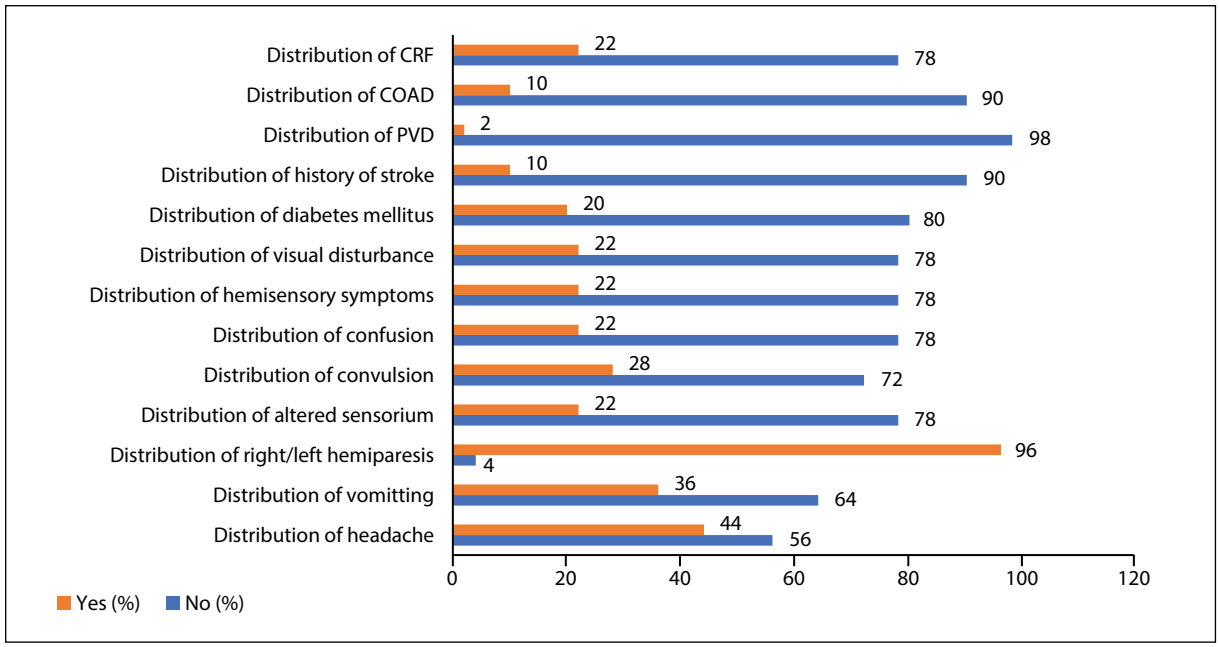

Figure 1. Distribution of demographical parameters

In this study, 33 (26%) patients had APHASIC SPEECH, 36 (28%) patients had DYSARTHIC SPEECH, 32 (25%) patients could not be examined (ENP) and 27 (21%) patients had NORMAL SPEECH. In this study, 8 (6%) patients had CONSTRICTED PUPILS, 18 (14%) patients had DILATED PUPILS and 102 (80%) patients had NORMAL PUPILS. In this study, 28 (22%) patients had Horizontal Gaze Palsy, 87 (68%) patients had NORMAL OCULAR POSTURE and 13 (10%) patients had Vertical Gaze Palsy. As per the Distribution of 7TH NV PALSY is concerned, in this study, 15 (12%) patients could not be examined and 113 (88%) patients had UMN. In this study, 10 (8%) patients had BILATERAL, 56 (44%) patients had COMPLETE, 6 (4%) patients had NORMAL and 56 (44%) patients had VARIABLE motor weakness. In this study, 18(14%) patients had decreased DTR OF AFFECTED SIDE and 110 (86%) patients had Exaggerated DTR OF AFFECTED SIDE. In this study, 18 (14%) patients had Extensor B/L, 51 (40%) patients had Extensor Left and 59 (46%) patients had Extensor Right. In this study, 59 (46%) patients had Basal Ganglia bleeding, 5 (4%) patients had Brain Stem bleeding, 5 (4%) patients had Cerebellar bleeding, 28 (22%) patients had Lobar bleeding and 31 (24%) patients had Thalamic bleeding. In this study, 67 (52%) patients had Left-SIDED HAEMATOMA and 61 (48%) patients had Right-SIDED HAEMATOMA.

Figure 1 demonstrates the distribution of demographical parameters. It was observed that the distribution of right/left hemiparesis was more distinct among participants.

The authors studied various variables to find out the associated mortality with the impact of individual risk factors, such as age, size of ICH, ICH score, GCS Score, and mean BP and they were subjected to multiple regression analysis in relation to clinical outcome as presented in Table 2.

Table 3 described an unadjusted logistic regression analysis of clinical features as a predictor of mortality. The increase in the size of ICH was significantly associated with increased mortality and poor clinical outcome in the present study. Moreover, the GCS score was featured as the most important predictor of clinical outcome (Tab. 3).

Table 4 demonstrated an unadjusted logistic regression analysis of Imaging as a predictor of mortality. The size of the ICH (cm^3) was high in patients who died (63.2 ± 55.7 cm^3) as compared to patients who survived (20.8 ± 18.8 cm^3) ($p < 0.001$) (Tab. 4). In the present study 24% patients had midline shift in the CT scan (Brain) who were alive. It was observed that the patients who were having a midline shift had bad outcomes whereas those who did not have a midline shift had met with good outcomes. The difference is statistically significant ($p < 0.001$) (Tab. 4).

Discussion

Among 50 studied cases, the incidence of intracerebral haemorrhage was found to have increased with advancing age. The mean age found in the present study was 58.1200 ± 13.1903 years. Various other

Table 2. Unadjusted logistic regression analysis of demographic and risk factors as predictors of mortality

Demographic and risk factors	Survival (N = 110)	Died (N = 18)	P-value	OR (95% CI)
Age (years)	58.12 ± 13.19	54.23 ± 18.05	0.084	0.97 (0.95–1.004)
Sex (male)	74 (86.1%)	12 (66.7%	0.142	0.57 (0.27–1.19)
DM	6 (5.5%)	14 (77.8%)	0.011	0.38 (0.30–0.48)
HTN	38 (34.5%)	10 (55.6%)	0.0121	1.7 (0.8–3.7)
Smoking	32 (29.1%)	8 (44.4%)	0.002	0.25 (0.10–0.61)
Alcohol	24 (21.8%)	3 (16.6%)	0.046	0.31 (0.1–1.0)
Poor treatment compliance	55 (50%)	18 (100%)	< 0.001	2.7 (1.9–4.1)

CI — confidence intervals; DM — diabetes mellitus; HTN — hypertension; OR — odds ratio

Table 3. Unadjusted logistic regression analysis of clinical features as a predictor of mortality

Clinical features	Survival (N = 110)	Died (N = 18)	P-value	OR (95% CI)
Headache	36 (32.7%)	8 (44.4%)	0.361	1.4 (0.7–2.9)
Vomiting	62 (56.7%)	17 (94.4%)	< 0.001	8.7 (2.9–26.8)
Loss of consciousness	31 (28.2%)	15 (83.3%)	< 0.001	13 (5.2–31.8)
Focal neurological deficit	110 (100%	9 (50%)	< 0.001	4 (2.8–5.7)
GCS (median)	15.7 (5.9–15.4)	4.3 (5.8–12.2)	< 0.001	0.721 (0.51–0.81)
ICH score	1.1 ± 0.7	3.2 ± 1.7	< 0.001	4.96 (2.70 –9.07)
Infection	31 (28.2%)	10 (55.6%)	0.26	0.37 (0.17–0.85)

CI — confidence intervals; GCS — Glasgow coma scale; ICH — intracerebral haemorrhage; OR — odds ratio

Table 4. Unadjusted logistic regression analysis of Imaging as a predictor of mortality

Imaging features	Survival (N = 110)	Died (N = 18)	P-value	OR (95% CI)
Infratentorial location	0	4 (22%)	< 0.001	–
Hydrocephalus	0	7 (38.9%)	< 0.001	–
Midline shift	24 (21.8%)	10 (55.5%)	< 0.001	2.6 (1.6–4.3)
IV extension	19 (17.27%)	10 (55.5%)	0.001	2.1 (1.3–3.3)
ICH volume (cm^3)	20.8 ± 18.8	63.2 ± 55.7	< 0.001	1.035 (1.016–1.054)

CI — confidence intervals; ICH — intracerebral haemorrhage; OR — odds ratio

studies also support the present study observation. Rohit Bhatia et al. (2013) [13] noted a mean age of 57.32 ± 12.84 years in his work. Similarly, Ji Woong Oh et al. (2012) [14] found patient's mean age was 58.2 years and Qureshi et al. (1997) [15] found a mean age of 56.4 years. However, most of the European studies have a higher incidence in the elderly. Celikbilek A et al. (2013) [16] found the mean age of study in his patients was 65.9 years, Similarly, Daniel Agustin Godoy et al. (2006) [17] also noted the mean age was 66–12 years. Due to lower life expectancy, this age discrepancy is probably observed in the Indian population. Almost 60% of patients in the present study were found in the 50–69 years of age group; 33.3% were distributed in the 50–59 years and 26.7% in the 60–69 years age group. The present observation is also supported by Kumaravelu et al. (2001) [18], who found 64% of the cases were more than 50 years of age. Similarly, Celikbilek A et al. (2013) [16] found 85% of the cases were 50 years of age and Daverat et al. (1991) [19] 26 got 87% patients of age more than 50 years.

In the present study, 14.00% adverse outcome was found. In the study of Rohit Bhatia et al. (2013) [13] got in-hospital mortality of 32.7%. Similarly, Khan FY et al. (2008) [20], reported 40.54% in-hospital mortality in the patients with haemorrhagic stroke in his work. Likewise, C Fieschi et al. (1988) [21] also found 30% early mortality in his study.

Weakness of the limb was the most common presenting symptom found in 96% of the patients in the present study that was followed by headache (44%), vomiting (36%), convulsions (28%), altered sensorium (22%), confusion (22%), visual disturbances (22%) and hemisensory symptoms (22%). Similar observations were also found in Sahani R, (2007) [22] with hemiparesis/plegia in 80% of cases, headache in 45%, impaired consciousness in 48%, dizziness in 14%, seizure in 14%, visual symptoms in 2% and hemisensory symptoms in 6% of patients. Also, Gregoire et al. (2011) [23] found hemiparesis or hemiplegia (78%) as the commonest presenting feature followed by speech dysfunction (60%). Likewise, Siddique et al. (2009) [24] also found hemiparesis in 100% of patients, headache in 60% of patients and vomiting in 75% of the patients. Moreover, Feigin et al. (2003) [25] found headaches in 36% of patients, vomiting in 44%, and convulsions in 7% of patients; Kumar HH et al. (2011) [26], noted in his study that 100% of patients had hemiplegia, out of which 56% were right-sided and 44% were left-sided hemiplegia. Patients with vomiting and convulsions had relatively poor outcomes (45% and 48% respectively) in the present study.

The present study found that unfavourable outcome was associated with low GCS at presentation. The patients who were having a mean GCS of 10.1163 ± 3.1938 met with a favourable outcome whereas patients with a mean GCS of 3.7143 ± 0.9512 ended up having a poor outcome. With a GCS of 3–5, 76% had a poor outcome. A statistically significant difference was noted in regard to these groups ($p < 0.0001$). Other studies also found an increase in mortality with low GCS at presentation. Godoy et al. (2006) [17] found 96% adverse outcomes in the patients with GCS 3–5 and 11.1% adverse outcomes with GCS 13–15. Similarly, Portenoy et al. (1987) [27] got 97% adverse outcomes in patients with GCS 3–5 in contrast to 14% with GCS 13–15. Likewise, Celikbilek A et al. (2013) [16] also found 100% adverse outcomes with GCS < 8 and 11.3% adverse outcomes with GCS > 12. Moreover, Franke et al. (1992) [28], Lisk et al. (1994) [29] and Yair Lampel et al. (1995) [30] also found poor outcomes with low admission GCS.

In the present study, 7 patients had an ICH score of 0, 19 had a score of 2, 7 had a score of 3, 12 had a score of 1, 2 had a score of 4 and 3 had a score of 5. All the patients with a score < 4 had a good prognosis. All the patients having an ICH score of > 4 died. The worst outcome was associated with an increase in ICH score. Various other studies also support this result. Hemphill et al. (2001) [4] observed that the 30-day mortality increased progressively with increasing ICH scores. In their series of patients, all patients with an ICH score = 0 survived and all those with ICH score = 5 died.

Despite every sincere effort, the present study has lacunae. The major notable shortcoming of this study is the small sample size; 50 cases are not sufficient for this kind of study. This was a single-centre study, carried out in a tertiary care hospital, so a hospital bias cannot be ruled out.

Conclusions

It was found that a longer duration of stroke at the time of initial evaluation was associated with higher mortality which was statistically significant. It was found that altered sensorium, level of consciousness at presentation, hypertension and h/o stroke were significantly associated with mortality. The present study found that a history of smoking was associated with poor outcomes in haemorrhagic CVA patients. Presentations like SPEECH and PUPIL abnormalities were found to be higher in the Haemorrhagic CVA mortality group and were statistically significant.

It was found that low mean GCS, MOTOR WEAKNESS, higher baseline ICH volume, presence of IVH, vol of haematoma and midline shift were significantly associated with Haemorrhagic CVA and are independent predictors of mortality.

Article information

Ethical approval: *Ethical clearance to conduct this study was obtained from the Institutional Ethics Committee of KPC Medical College & Hospital (No: KPCMCH/IEC/470). Ethical Review Committee Board.*

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