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HYPODENSITIES WITHIN HEMATOMA PREDICT OUTCOME AFTER SPONTANEOUS INTRACEREBRAL HEMORRHAGE

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ABSTRACT

Background and objective:
Not much is known about the prevalence and significance of hypodensities within hematoma after spontaneous intracerebral hemorrhage (ICH). The objective of this study was to determinethe prevalence of hypodensitieswithin hematoma after spontaneous ICH and their significance to predict poor outcome after ICH.

Methods:
This observational cross sectional study was conducted in the Department of Neurology, Pakistan Institute of Medical Sciences, Islamabad,fromOctober 2021to June 2022. Total 140 patients of acute stroke were included.Inclusion criteria was any patient of >20 years of age with confirmed diagnosis of ICH on imaging, non-traumatic, who presented within 24 hours after onset of symptoms. Data was analyzed by SPSS ver.23.0.

Results:
Total 150 patients were included in the study. The mean age of patients was 52.28 ± 1.29 years. There were 100 (71.4%) males and 40 (28.6%) females. Hypertension was the most common comorbid present in 87 patients (62.1%).55% of patients had on presentation National Institute of Health Stroke Scale (NIHSS) and modified Rankin Scale score of moderate severity. The mean ICH score on presentation was 2.64 +1.26. Hematoma expansion was present in 55(39.3%) patients while interventricular extension was seen in 100(71.4%) patients. Hypodensities were seen in 125(89.3%) patients(p value 0.001). When hematoma volume were compared in both groups it was also significant (p value 0.002).

Conclusion:
We conclude that hypodensities within hematoma are a reliable marker of hematoma expansion after spontaneous ICH. Such reliable marker can be easily employed in resource-poor countries where CT angiography is not available everywhere. The higher NIHSS score and low GCS are significantly associated with hypodensities within hematoma.

Key words: Acute stroke, Hypodensity, Stroke score

INTRODUCTION

Nearly 20 % of strokes occurring each year are intracerebral hemorrhage (ICH).1ICH is one of the most fatal type of stroke with a mortality rate of 40% and survivors usually have very poor functional outcome i.e. only 20% are independent after six months as reported in literature.[1,2] ICH outcome depends on many factors like location of hematoma and volume but hematoma expansion is an important independent prognostic factor. Hematoma expansion usually occurs in 33% of patients suffering from ICH and is a usual target site to improve prognosis.[3] Early identification of patients who may develop hematoma expansion and early prompt treatment may result in better prognosis and may

improve functional outcome in ICH patients.[4] Many predictors have been reported in different studies which are reliable predictor of hematoma expansion like intraventricular extension, baseline volume and spot sign on CT angiography (CTA).[5,6]Out of these predictors, spot sign on CTA is one of the most reliable predictor but availability of CTA in resource poor country like Pakistan is questionable, also it requires use of IV contrast andmany centers do not favor its usage in acute phase.[3,7] So other predictors of non-contrast enhanced CT scan like swirl sign, blend sign and black hole sign which can easily predict hematoma expansion are favored in some studies.[8,9]

In available studies the comparison of these different markers of non-contrast CT (NCCT) was done but their correlation with functional outcome and after Intracerebral hemorrhage is still not well reported. So in search of a more reliable marker which can easily tell about hematoma expansion and correlate it with functional outcome Du et al. reported in their study that hypo-densities within hematoma after acute Intra-cerebral hemorrhage are reliable marker in telling about hematoma expansion and are correlated with poor functional outcome[10.]

As brain has got very low ischemia time so different scoring systems like BAT (blend sign, any hypo density and time lapse between onset to NCCT) and Brain (Baseline ICH volume, Recurrent ICH, Anticoagulation with warfarin at onset, Intraventricular extension and number of hours to baseline NCCT since symptoms)use time lapse since onset of symptoms to NCCT with shorter the time lapse being related with higher chances of hematoma expansion.[11-13]

There is very less available literature on correlation of hypo-densities within hematoma with time lapse of NCCT after onset of symptoms.We have conducted this study to provide comprehensive data on prevalence of hypo-densities within hematoma on baseline CT scan with time and its utilization in prediction functional outcome and hematoma expansion after acute intracerebral hemorrhage. It will in turnhelp in proper management of patients after ICH which will improve their quality of life after stroke.

METHODS

Study design: Prospective cross-sectional observational study.

Place and duration of study: We have conducted this study in Department of Neurology, Pakistan Institute of Medical Sciences Islamabad from Oct 2021 to June 2022 after getting approval from the hospital ethical committee.

Sample size: A sample size of 130 patients was calculated by keeping 80% power of study, 5% significance level andhematoma expansion i.e. 54% in hypodensity group vs 29% in non hypodensity group[1].
Sampling technique: Non-probability consecutive sampling.

Inclusion criteria: Any patient of >20 years of age with diagnosis of stroke on imaging, non-traumatic, those patients who presented within 24 hours of onset of symptoms of stroke and patients with modified Rankin scale score of <2.

Exclusion criteria: Patients of trauma, those with Rankin scale score of >2 and drug addicts.

Data Collection: Informed written consent was taken from all included patients or their relatives. A non contrast CT brain was done at baseline and 24 hours after admission. The reporting of Ct scans was done by consultant radiologist. Following parameters were noted on CT scan. a) Presence of number and pattern of hypodensities within hematoma, b) any midline shift, c) location of hematoma with any extension if present, d) volume of hematoma present. Stroke severity was identified using National Institute of Health Stroke Scale (NIHSS) score and modified Rankin score [14,15].Included patients had undergone second NCCT on 7th day of admission and their findings were compared with the previous CT scan. Data was collected on proforma by postgraduate trainees on duty. Hematoma expansion was defined as increase in hematoma volume of more than 33% or more than 6 ml increase in volume from baseline scan. The hypodensity was defined as an area of hypodensity or isodensity present within hyperdense hematoma shadow in two consecutive 5mm axial slices.

Data analysis: Data was collected and later on entered and analyzed in SPSS v. 23. Mean and standard deviation was calculated for quantitative variables and frequency and percentages for qualitative variables. Students T test was applied for continuous variables and Fisher exact test was applied for categorical variables. P value <0.05 was considered as significant.

RESULTS

Total 140 patients were included in the study. 10 patients were removed as they had presented after 24 hours of onset of symptoms. The mean age of patients was 52.28 ± 1.29 years. There were 100 (71.4%) males and 40 (28.6%) females. Hypertension was the most common comorbid present in 87 patients (62.1%) followed by DM which was found in 76 patients (54.3%). Ischemic heart disease was present in 64 (45.7%) patients. The demographics of patients are mentioned in table 1.

Table 1: Demographics of patients

Variable	n %
No of patients	140
Age (years)	52.28 ± 1.29
Male	100 (71.4%)
Female	40 (28.6%)
Hypertension	87 (62.1%)
Diabetes Mellitus	76 (54.3%)
Ischemic Heart Disease	64 (45.7%)

Twenty-five patients had died before 7 days of admission so their second CT scan was not done. Out of 115 patients left there second CT scan was done on 7th day of admission and findings were compared with baseline CT scan. 40 patients had died during hospital admission showing a total mortality of 46.42%. 55% of patients had on presentation NIHSS and MRSS were of moderate category. The mean ICHS on presentation was 2.64 +1.26. Hematoma expansion was present in 55(39.3%) patients while intraventricular extension was seen in 100(71.4%) patients. Hypodensities were seen in 125(89.3%) patients which was statistically significant. (p value 0.001). One-hundred-fifteen (82.1%) patients had ICH in supratentorial region while 25(17.9%) had hematoma in infra tentorial region. Most common pattern of hypodensity seen was curvilinear which was present in 70(50%) patients. Midline shift and hydrocephalus was seen in 30(21.4%) and 35 (25%) patients respectively.

All other findings which were present at admission are mentioned in Table 2.

Table 2:Findings at admission

Variable		**n (%)**
Modified Rankin scale score	Mild	40 (28.6%)
	Moderate	50(35.7%)
	Severe	50(35.7%)
NIHSS	Mild	40(28.6%)
	Moderate	60 (42.9%)
	Severe	40(28.6%)
ICHS	Normal	2.64 ±1.26
Hematoma volume	<30 ml	55 (39.3%)
	30-60 ml	55 (39.3%)
	>60 ml	15(10.7%)
	>80 ml	15(10.7%)
Hematoma expansion	Yes	55(39.3%)
Intraventricular extension	Yes	100(71.4%)
Hypodensity	Yes	125(89.3%)
Location of hematoma	Supratentorial	115(82.1%)
	Infratentorial	25(17.9%)
Pattern of Hypodensity	Linear	25(17.9%)
	Curvilinear	70(50%)
	Globular	10(7.1%)
	Slit like	10(7.1%)
	Mix	25(17.9%)
Midline shift	Yes	30(21.4%)
hydrocephalus	Yes	35 (25%)

NIHSS: The National Institute of Health Stroke Scale

ICHS: Intracerebral hemorrhage score

Out of 25 who died, 20 had hypodensities present in their initial scan. When ICHS was compared in both groups it was 2.08 +1.41 vs 1.33 + 0.97 which was statistically significant (p value 0.05). When hematoma volume were compared in both groups it was also significant (p value 0.002). Most common pattern seen in hypodensity group was curvilinear present in 60 (48%) patients which was also statistically significant (p value 0.001). The comparison of different variables in both groups is mentioned in Table 3.

Hypodensity present

Table 3:Comparison of variables in both groups

Variable		**Hypodensity present**	**Hypodensity absent**	**P value**
Modified Rankin scale score	Mild	35 (28%)	-	0.96
	Moderate	35 (28%)	5(12.5%)	
	Severe	35 (28%)	5(12.5%)	
NIHSS	Mild	30 (26.08%)	5(4.3%)	0.01
	Moderate	45 (39.13%)	5(4.3%)	
	Severe	30 (26.08%)	-	
ICHS	Normal	2.08±1.41	1.33 + 0.97	0.05
Hematoma volume	<30 ml	35 (28%)	10 (8.6%)	0.002
	30-60 ml	40 (32%)	-	
	>60 ml	15 (12%)	-	
	>80 ml	15 (12%)	-	
Hematoma expansion	Yes	50 (40%)	15(10.7%)	0.11
Intraventricular extension	Yes	85 (68%)	15(10.7%)	0.04
Location of hematoma	Supratentorial	85 (68%)	20(10.5%)	0.17
	Infratentorial	10 (16%)	-	
Pattern of Hypodensity	Linear	15 (12%)	-	0.001
	Curvilinear	60 (48%)	-	
	Globular	10(8%)	-	
	Slit like	10(8%)	-	
	Mix	10(8%)	10(8%)	
Midline shift	Yes	22(81.5%)	10(18.5%)	0.13
hydrocephalus	Yes	35(87.5%)	10 (12.5%)	0.17

NIHSS: The National Institute of Health Stroke Scale

ICHS: Intracerebral hemorrhage score

Some representative NCCT images are shown in Figure 1.

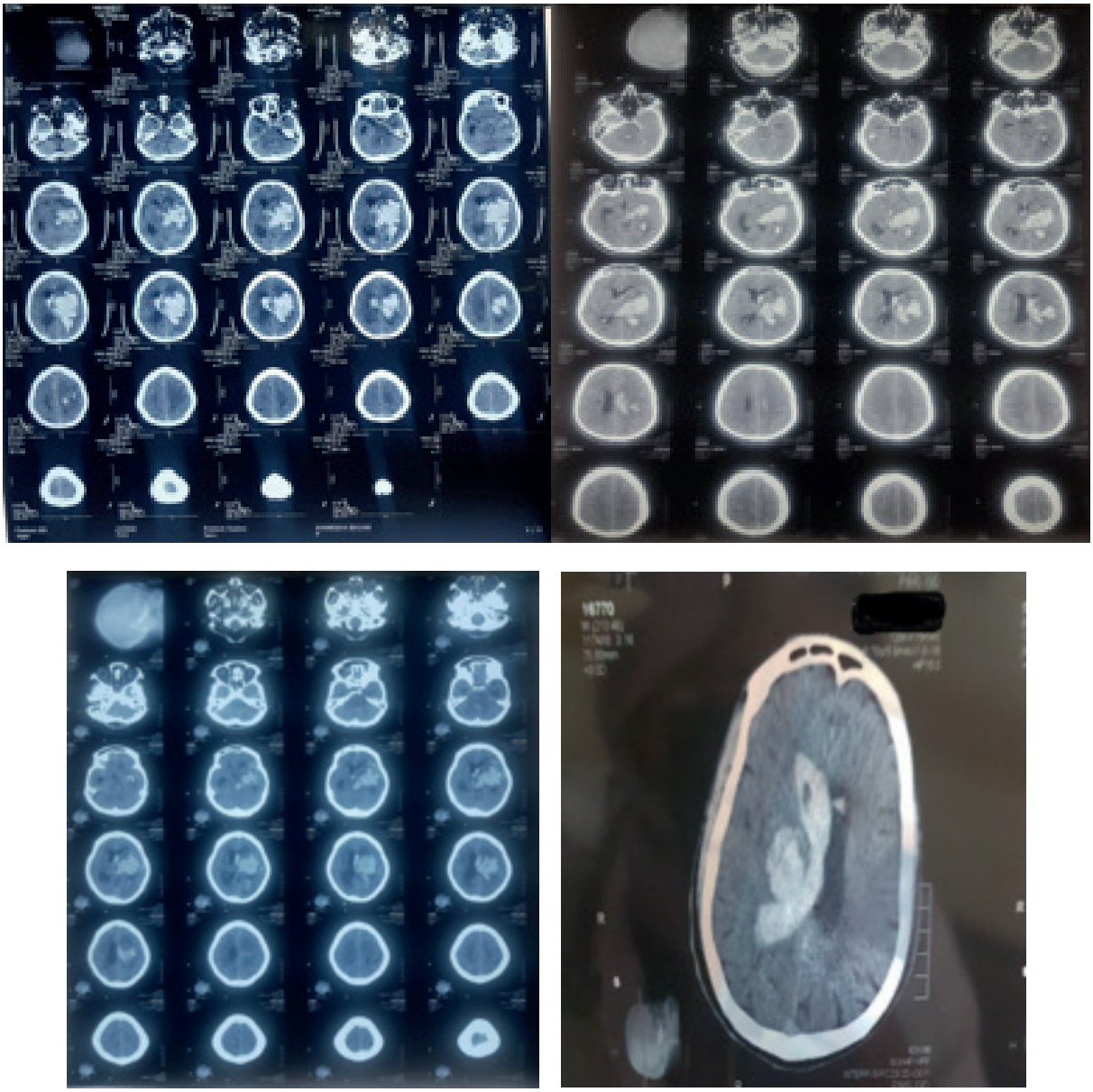

Figure 1: Non-contrast CT images showing hypodensities within hyperdense areas of bleeding

DISCUSSION

Hypodensities within a hematoma after ICH are independent factor associated with hematoma expansion. As NCCT is commonly performed after acute ICH and is widely available in resource poor countries so detection of hypodensities is of valuable significance which may help to target the patients at risk.[3] Such findings have been reported by many studies available which shows a valuable significance of hypodensities in relation to patient outcome.[16,17] The exact pathophysiology of hypodensities is still unknown.[18] They are generally related to shorter time to CT scan after ICH, anticoagulation, and large hematomas therefore recommended as an easily assessed acute phase prognostic sign.[18] A study by Newet al showed that hypodensities may represent unclotted blood i.e. .more recent bleeding.[19] A study by Boloiouset al inferred that hypodensities are a different neuroimaging feature as it may be present with spot sign or not and is independently associated with hematoma expansion and poor functional outcome.[3]

In our study mean hematoma volume was higher in hypodensity group as compared to hypodensity negative group. Out of 115 survivals patients only 10 patients(8.6%) had no hypodensity seen and their volume was less than 30 ml while in hypodensity positive group 70 patients (60.8%) had volume in between 30 to 80 ml which was statistically significant (p value 0.002). These results are similar to results shared by Leiraet al in their study who showed that hypodensities were associated with significantly higher hematoma volume and large volumes are associated with hematoma expansion and poor prognosis.[20] Similarly, a study by Boloiuoset al showed that 65% of patients who had hypodensity in NCCT showed unfavourable outcome and had hematoma volume between 24-74 ml (mean 48) which are comparable to our results.[21] Two different studies by Vedarthamet al and Duet al showed that patients of hypodensity positive hematoma had volume of more than 30 ml with more chances of hematoma expansion and poor functional outcome over 3 months.[1,22] Lawet al shared the similar results that presence of hypodensities within hematoma are a predictor of poor outcome in ICH patients.[23]

In our study 75 patients (65.21%) on presentation had GCS less than 9 which were hypodensity positive on NCCT which was statistically significant. Similarly those patients with hypodensity positive had mean ICHS of 2.08 + 1.41 vs 1.33 + 0.97 which was statistically significant (p value 0.05). These findings are similar to results shared by different studies that patients with hypodensity positive NCCT had statistically low GCS with maximum patients having NIHSS of moderate and severe category and a high ICHS.[1,18,24]

Spornset al concluded in their study that hypodensities within hematoma are the most reliable marker of functional outcome out of all NCCT markers studied.8Our results also support the similar results that hypodensities capture new onset hematomas. Such patients are at higher risk of hematoma expansion with poor clinical outcome. In resource poor countries like Pakistan where CTA is not available everywhere and is costly, hypodensities in NCCT may help us to select patients at risk and find a better level of care after ICH. It may be that when resources are limited, patients can be stratified to regular stroke unit care vs intensive care based on their risk of expansion and deterioration.

The limitation of our study is that it was conducted in a single hospital with small sample size. Also it does not include patients follow up after discharge. So long term functional outcome after three and six months cannot be predicted based on our study.

CONCLUSION

We conclude thathypodensities within hematoma are a reliable marker of hematoma expansion after spontaneous ICH. Such reliable marker can be easily employed in resource poor countries where CTA is not available everywhere. The higher NIHSS score and low GCS are significantly associated with hypodensities within hematoma.

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Maryam Khalil; concept, data collection, data analysis, manuscript writing, manuscript review
Sumaira Nabi; data collection, data analysis, manuscript writing, manuscript review
Amjad Mahmood Khan; concept, data analysis, manuscript review
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Samar Naik; data collection, data analysis, manuscript writing
Zaid Waqar; data collection, data analysis, manuscript writing
Malik Muhammad Adil; concept, manuscript review
Mazhar Badshah; concept, manuscript review