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QUALITATIVE AND QUANTITATIVE (VOLUMETRIC) HIPPOCAMPAL MRI ASSESSMENT IN TEMPORAL LOBE EPILEPSY

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Abstract:
Objective: *To determine the accuracy of hippocampal quantitative (volumetric) assessment in diagnosing hippocampal atrophy in patients with temporal lobe epilepsy by comparing it with qualitative (visual) assessment on MRI.*
Materials and Methods: Setting*: Department of Radiology, Allied Hospital, Faisalabad.*
Duration: *Minimum 6 months after the approval of my synopsis.*
Study Design*: Cross sectional.*
Conclusion: *We can conclude that MRI based hippocampal volumetric assessment is a valuable tool for the detection of hippocampal atrophy in patients with refractory temporal lobe epilepsy who are candidates for surgery avoiding unnecessary supplementary tests including PET, SPECT & invasive EEG.*
Keywords: *Temporal lobe epilepsy, hippocampal volumetric assessment, hippocampal sclerosis.*

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INTRODUCTION:

Epilepsy is a familiar neurological disease characterized by recurrent seizures [1]. Partial-onset epilepsies account for about 60% of all adult epilepsy cases, and temporal lobe epilepsy (TLE) is the most common type of partial epilepsy [2]. Two main types of TLE have been recognized the commoner; Mesial temporal lobe epilepsy (MTLE), is an entity in which the most predominant seizures originate in limbic areas of the mesial temporal lobe, particularly in the hippocampus [3]. The hippocampus has been the focus of research since more than 80% of the cases of TLE are caused by Mesial temporal sclerosis (MTS) i.e. hippocampal sclerosis (HS) [4,8]. Classic findings of hippocampal sclerosis on MRI are atrophy of the hippocampal gray matter and increased hippocampal signal on T2-weighted images (T2WI) [5]

New MRI techniques demonstrate the structure of the brain in fine detail and help in understanding the underlying pathology [6]. Visual (qualitative) assessment of T2-weighted changes (hyper intense signal on T2-weighted images and atrophy) was the earliest method employed [1]. However, in a minority of cases of HS, these qualitative radiologic findings are not present. This dilemma led to the development of quantitative volumetric hippocampal analysis [5]. MR-based hippocampal volume measurement offers a practical and valuable method for both clinical and research purposes. This quantitative assessment may be helpful in establishing early and accurate diagnosis, measuring disease progression, detecting and assessing therapeutic effects and predicting prognosis in different disease [7].

Despite its known utility, hippocampal volumetry has been difficult to incorporate in clinical practice because of the time demands and the technical skills required however recent advances in technology have led to the development of automated software for generic quantitative morphometric. Recent studies have shown that these automated techniques can also detect hippocampal asymmetry and lateralize hippocampal atrophy accurately [9].

According to the study carried out by Singh P. at Baba Farid University of Health Sciences, Punjab, India, 65% of the patients with Temporal Lobe Epilepsy showed hippocampal atrophy both on visual and volumetric MRI assessments [1]. This Study is carried out to see how accurately different MRI imaging modalities detect hippocampal atrophy (indicator of hippocampal sclerosis) and quantify disease progression with special benefit to patients who have medically refractory epilepsy and are potential candidates for surgical cure of their illness. Most of these patients have good outcomes after surgery and this mainly depends on the pre surgical evaluation by EEG and MRI. Since no similar study has been carried out in Pakistan it is essential that such a study is initiated to benefit patients with both medically treated and medically refractory Epilepsy.

METHOD:

The patients were examined on 1.5 Tesla Achievaphilips scanner, visual assessment and volumetry will be performed on oblique coronal IR/T2W and FLAIR images perpendicular to the long axis of hippocampus with TE = 3000ms, TR =200ms, slice thickness = 1mm, Gap = 0. Visually the images will be assessed as per operational definition. Volumetric analysis will be done by measuring volume of both the hippocampi in these oblique coronal sections by the contour stack by drawing ROI's from one end of hippocampus to the other end (head to tail) and volume will be measured automatically by internal software system. For this purpose, the anterior boundary(head) and posterior hippocampal boundary (tail) will be defined as follows. On hippocampal head area the CSF in the uncal recess of the temporal horn when visible will be considered the most reliable boundary between the hippocampal head and the amygdala. If uncal recess is not visible, then the alveus will be used. To standardize the measurement, first section of the anterior hippocampus will be defined as point where the uncal recess or alveus first appears. Posterior margin of hippocampal volumetric measurement will be defined by MR image where crus of fornix is seen in full profile. Lateral and medial borders will be defined as CSF in temporal horn of lateral ventricle and CSF in uncal/ambient cisterns, respectively. Inferior border will be defined by grey -white matter junction between subiculum and white matter of Para hippocampal gyrus.

RESULTS:

A total of 90 patients were included in this study over a period of 2 years and 7 months from 1-09-2014 to

30-4-2017. Patients were divided into two groups according to their age. Majority of the patients were <35 years (71.1 %) whereas the rest (28.9%) were > 35 years. Mean age was 28.93 (Table-1 & 2). Distribution of patients according to gender showed 47 (52.2%) were male and 43 (47.8 %) were females (Table-3). Mean volume of right sided hippocampus was2.1071 and mean volume of the left sided hippocampus was 2.2098 (Table-4). Hippocampal atrophy was detected in 45 (50%) patients by visual assessment and in 75 (83.3%) patients by volumetric assessment. 45(50%) patients showed no hippocampal atrophy on visual assessment and 15(16.7%) patients showed no Atrophy on volumetric assessment (Table-5 & 6).

Amongst the 90 patients under study 41 (45.6%) were true positives, 10(11.1%) were true negatives, 4(4.4%) were false negatives and 35(38.9%) were false positives (Table-7). The true positives, true negatives, false negative and false positive were than stratified into two groups according to age, among those who were <35 years; 28 (43.8%) were true positives, 7(10.9%) were true negatives, 3(4.7%) were false negative and 26(40.6%) were false positive. Among those who were >35 years; 13(50%) were true positives,3(11.5%) were true negatives,1(3.8%) were false negatives and 9(34.6%) were false positive. P value was 0.947 indicating that there is no statistical significance. (Table-8). Among the males 21(44.7%) were true positives, 7 (14.9%) were true negatives,2(4.3%) were false negatives and 17 (36.2%) were false positives. Among the females 20 (46.5%) were true positives, 3 (7%) were true negatives,2(4.7%) were false negatives and 18 (49.9%) were false positives. P value was 0.687 indicating that there is no statistical significance. (Table-9).

Out of the 90 patients who had the clinical symptoms/EEG findings consistent with temporal lobe epilepsy 41 patients showed hippocampal atrophy on both visual and volumetric assessment and 11 didn't show hippocampal atrophy on quantitative or qualitative assessment while 4 patients had hippocampal atrophy on visual assessment which was not detected on volumetric assessment and 11 patients showed hippocampal atrophy only on volumetric assessment but not on visual assessment (Table-10). Out of 64 patients who were <35 years; 28 showed hippocampal atrophy both on visual and volumetric assessment,25 showed atrophy on volumetric assessment but visual assessment failed to detect them,3 were picked up by visual assessment but showed normal volume on volumetry,8 were normal on both visual and volumetric assessment. Accuracy of these results was 56.25%. Out of 26 patients who were >35 years; 13 showed hippocampal atrophy both on visual and volumetric assessment,9 showed atrophy only on volumetric assessment,1 showed atrophy only on visual assessment and 3 showed no atrophy on either of the methods. Accuracy of the results was 61.54 %. (Table-11).

Among the 47 males 21 showed hippocampal atrophy both on visual and volumetric assessment,17 showed atrophy only on volumetry2 showed only on visual assessment and 7 didn't show atrophy on either of the methods. Accuracy of these results was 59.57%. Among the 43 females 20 showed atrophy both on visual and volumetric assessment,17 showed atrophy only on volumetry,2 were only detected by visual assessment and both volumetry and visual assessment failed to detect atrophy in 4 patients. Accuracy of these results was 55.81%.

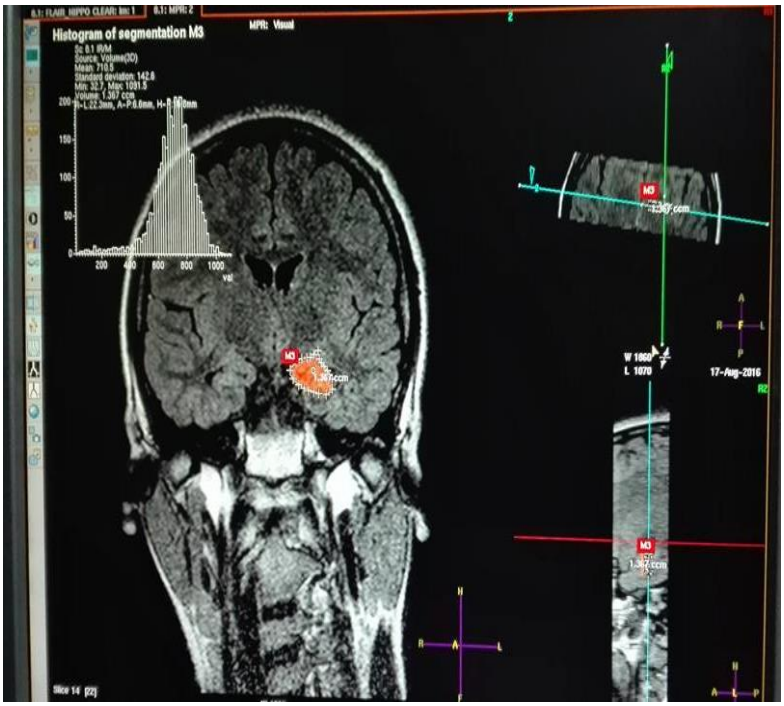

FIGURE 1: {Case no.1} Coronal FLAIR image showing bilateral hippocampal atrophy. Volume of left hippocampus is 1.367 and volume of right hippocampus is 1.719.

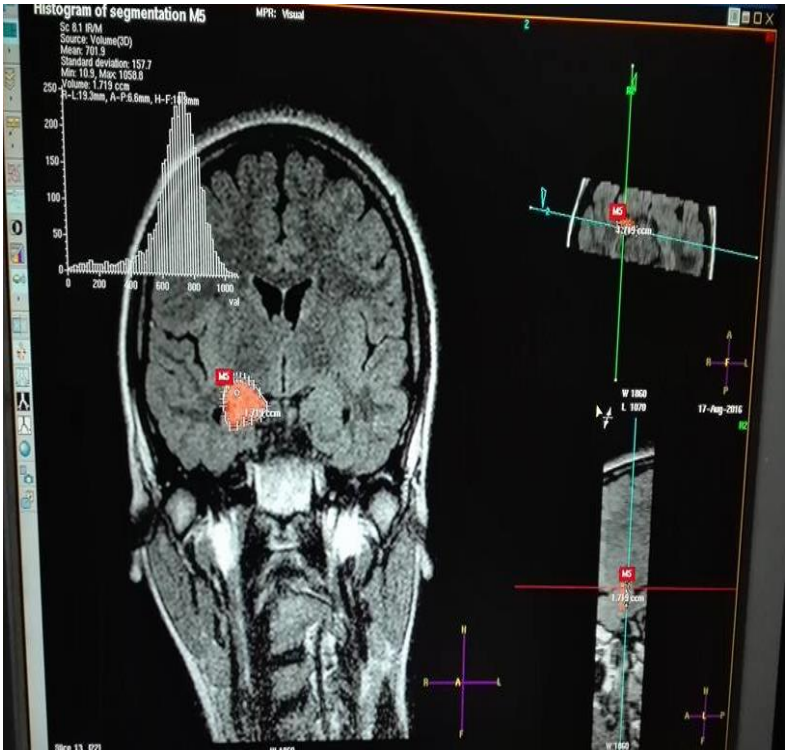

FIGURE2: {Case no.1} Coronal FLAIR image showing bilateral hippocampal atrophy. Volume of left hippocampus is 1.367 and volume of right hippocampus is 1.719.

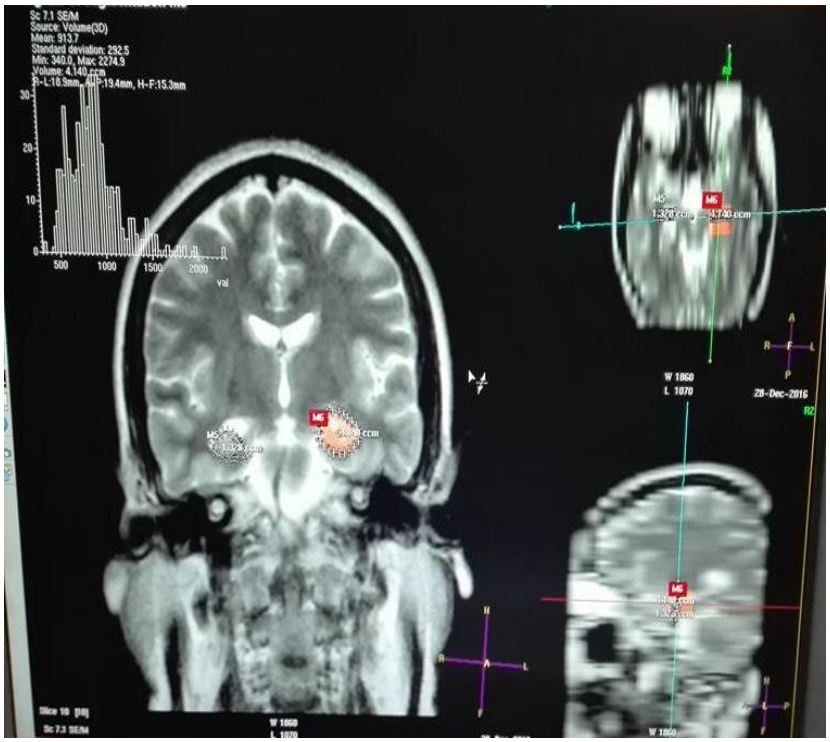

FIGURE 3: {Case no.2} Coronal T2W image showing unilateral hippocampal atrophy; right hippocampal volume is 1.326 and left sided volume is 4.140.
e is 4.140.

Table 1

	N	Minimum	Maximum	Mean	Std. Deviation
Age	90	11	59	28.93	12.254

Table 2

	n	Minimum	Maximum	Mean	Std. Deviation
Volume of hippocampus of right side	90	.38	4.27	2.1071	1.02248
Volume of hippocampus of left side	90	.48	4.04	2.2098	1.02031

Table 3

Age distribution	Frequency	Percent
< 35 years	64	71.1
≥ 35 years	26	28.9
Total	90	100.0

Table 4

Gender	Frequency	Percent
Male	47	52.2
Female	43	47.8
Total	90	100.0

Table 5

Hippocampal atrophy on visual assessment	Frequency	Percent
Yes	45	50
No	45	50
Total	90	100.0

Table 6

Hippocampal atrophy at volumetric assessment	Frequency	Percent
Yes	75	83.3
No	15	16.7
Total	90	100.0

Table 7

Variables	Frequency	Percent
True positive	41	45.6
True negative	10	11.1
False negative	4	4.4
False positive	35	38.9
Total	90	100.0

Table 8

Variables	Age distribution		Total	p-value
	< 35 years	≥ 35 years		
True positive	28 43.8%	13 50.0%	41	
True negative	7 10.9%	3 11.5%	10	0.947
False negative	3 4.7%	1 3.8%	4	
False positive	26 40.6%	9 34.6%	35	
Total	64	26	90	

Table 9

Variables	Gender		Total	p-value
	male	female		
True positive	21 44.7%	20 46.5%	41	0.687
True negative	7 14.9%	3 7.0%	10	
False negative	2 4.3%	2 4.7%	4	
False positive	17 36.2%	18 41.9%	35	
Total	47	43	90	

Table 10

		hippocampal atrophy on visual assessment		Total
		yes	no	
hippocampal atrophy at volumetric assessment	yes	41	34	75
	no	4	11	15
Total		45	45	90

$$\text{Accuracy} = \frac{TP+TN}{TP+FN+FP+TN} = \frac{52}{90} \times 100 = 57.78\%$$

Table 11

age distribution	hippocampal atrophy at volumetric assessment	hippocampal atrophy on visual assessment		Total	Accuracy
		Yes	No		
< 35 years	Yes	28	25	53	56.25%
	No	3	8	11	
	Total	31	33	64	
≥ 35 years	Yes	13	9	22	61.54%
	No	1	3	4	
	Total	14	12	26	

Table 12

Gender	hippocampal atrophy at volumetric assessment	hippocampal atrophy on visual assessment		Total	Accuracy
		yes	no		
Male	Yes	21	17	38	59.57%
	No	2	7	9	
	Total	23	24	47	
Female	YES	20	17	37	55.81%
	NO	2	4	6	
	TOTAL	22	21	43	

DISCUSSION:

The detection of MR imaging signs of hippocampal sclerosis can help to define seizure etiology and indicate surgical treatment for patients with drug-resistant mesial temporal lobe epilepsy. In the present study, we used MRI based visual analysis and hippocampal volumetry to evaluate the occurrence of hippocampal atrophy/sclerosis in 90 patients with clinical symptoms /EEG findings consistent with temporal lobe epilepsy. There has been extensive discussion relating to the variety of methods of MR-based volume estimates of the hippocampi. Obviously with different imaging parameters and quantification techniques, different results would be expected. [1] We used a manual hippocampal tracing method to measure hippocampal volume and detect hippocampal atrophy. Multiple similar studies have been done in the past to evaluate various MR techniques and methods. In a study done by Singh P. et al 65% of the patients with temporal lobe epilepsy showed hippocampal atrophy on visual assessment and 75% showed atrophy on volumetric assessment. [1] According to our study 83.3% patients showed atrophy on volumetric assessment whereas visual assessment detected abnormality in only 50% of the cases. From this we can infer that in TLE patients, hippocampal volumetry provides maximum concordance with EEG/clinical findings, this correlated well with the previous studies. In a study conducted by Coan *et al.*, hippocampal volumetry identified hippocampal sclerosis in 95% of patients with visually detected hippocampal sclerosis and in 13% visually normal MR imaging findings. [11] Thus quantitative techniques can detect mild abnormalities, undetectable on visual assessment and therefore are better.

Another study done by Azab.et al showed that the accuracy of a volumetric fully automated computer assessment of hippocampal volume asymmetry was 79.4% and the estimated accuracy of the neuro radiologist was 72.6%. Neuro radiologists can often detect even small temporal lobe volumetric changes visually. [12] Study done by Cheon.et al gave an accuracy of 81% for volumetric assessment. [10] According to our study the calculated diagnostic accuracy of manual hippocampal volumetric assessment is 57.78%. False positives in our study were 38.9% whereas they were 18% in the study done by Cheon et al, false negatives in our study were only 4.4% in comparison to 19% in the study of Cheonet al. This difference may be attributed to inter observer measurement errors in the manual tracing of hippocampi which can be reduced by using semi-automated and automated software's for volume measurement however still one can't deny the better results achieved by manual volumetric assessment as compared to qualitative assessment alone.

Although MR volumetry is known to improve the diagnostic accuracy in detection of hippocampal sclerosis by a small incremental amount, this technique is not currently used as a routine procedure in most institutions. [10] Temporal lobe resection gives a complete or almost complete control of seizures in about 70% to 80% of patients. The success of surgery relies on tests that can help identify the source and side of the seizures.[13]Theoretically it is conceivable that ,MRI volumetry may obviate the supplementary examinations such as ictal single-photon emission computed tomography(SPECT), positron emission tomography(PET) and invasive EEG in selective

patients with visually normal hippocampal volumes.[10] Brain perfusion single photon emission computed tomography (SPECT) is an accurate method for detecting the origin of the seizure. These epileptogenic foci classically appear as a region of normal perfusion or hypo perfusion in the interictal study that becomes hyper perfused in ictal study. The specificity of this combination is nearly 100% by visual analysis alone while the sensitivity of the evaluation of the ictal SPECT study alone has a sensitivity of nearly 96%. PET, particularly PET/computed tomography (PET/CT) provides better quality and higher resolution images as compared to SPECT and allows quantitative measurements. Imaging brain glucose metabolism with [10] Fluoro-2-deoxyglucose (FDG) PET is the most commonly utilized technique in routine clinical practice. In normal adult brain, there is high FDG uptake in cerebral and cerebellar cortices and sub cortical gray matter with mild FDG uptake in the white matter. PET images are usually obtained in interictal phase. Interictal FDG-PET images usually demonstrate focal hypometabolism. Ictal PET shows complex pattern of increased and decreased metabolism. Postictal PET can demonstrate complex pattern of increased and decreased metabolism or only increased or decreased metabolism depending on the time of injection after seizure. [14] From a practical point of view surgical resection is not done without positive findings from other supplementary studies because concordance between ictal EEG and imaging findings including MR imaging, ictal SPECT and/or PET is important in the laterization of epileptogenic focus. Currently, a set of preoperative examinations is conducted in most patients in search of concordance. Considering the trend of cost containment efforts in health care, selective use of imaging studies before epilepsy surgery will be demanded in the future. [10]

CONCLUSION:

To sum up hippocampal volumetry provides a practical and valuable tool to aid us in identifying patients with hippocampal sclerosis and when compared with the visual assessment it gives better results and detects patients with hippocampal atrophy that were not diagnosed on visual assessment alone. Although the manual hippocampal volumetry is time consuming and requires skills it is still better than visual assessment in detection of the disease. Nowadays automated software's are being studied which give results in much less time and avoid errors. Hippocampal volumetry can enables us to avoid supplementary examinations like PET, SPECT and invasive EEG which are routinely done in the preoperative evaluation of patients with intractable temporal lobe epilepsy to localize the epileptogenic focus.

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