

## Electrocardiographic Changes in Patients with Seizure Disorder-A Hospital Based Study

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### ABSTRACT

**Objective:** To study the clinical and electrocardiographic changes in patients with seizure disorder and to find the relationship between seizure disorder and electrocardiographic abnormality, if any.

**Methods:** We analyzed 206 patients with seizures in whom pre-ictal electrocardiogram was available for comparison with post-ictal electrocardiogram. Arrhythmias, repolarization abnormalities, and PR and QTc intervals were determined for pre-ictal and post-ictal periods.

**Results:** The most common abnormality was sinus tachycardia (heart rate >100bpm) which was present in 160 patients (77.7%) followed by sinus arrhythmia in 19 patients (9.2%). CHB and bifascicular block remained in 9 patients each. APD's were present in 18 patients (8.7%), VPD's in 6 patients (2.9%). RBBB was present in 11 patients (5.3%), LBBB in 8 patients (3.9%), AF in 5 patients (2.4%), PSVT and T wave inversion in 1 patient each. ST segment elevation of 2mm was seen in 3 patients (1.5%) and ST segment depression in 4 patients (1.9%). The mean heart rate was 96.6 seconds and mean QTc interval was 396.4 seconds.

**Conclusion:** Cardiac rhythm and conduction abnormalities are common during seizures particularly if they are generalized and these abnormalities may contribute to SUDEP.

**Keywords:** ECG in seizure disorder, SUDEP, conduction abnormality.

### INTRODUCTION

It has long been recognized that changes in heart rate and rhythm may accompany epileptic seizures (Jackson et al 1932, Erikson et al 1939). During the last few years a number of case reports of seizure-associated cardiac arrhythmias have been published which are of interest for two main reasons (Dasheiff RM et al 1986, Smaje JC et al 1987). Firstly, it has been suggested that these arrhythmias may be the cause of some sudden unexplained deaths in epileptic (Leestma JE et al 1989). Secondly,

seizure-associated arrhythmias may lead to misdiagnosis. The symptoms of partial seizures and of cardiac arrhythmias overlap and can easily be confused. An increase in heart rate has been described in a high proportion of seizures and the timing of these changes may provide useful clinical information (Reeves AL et al 1996, Galimberti CA et al 1996). Although heart rate changes have often been described in seizures, the specific timing of these changes has not been reported. If the increase is at the onset or even before a

seizure it could be a helpful additional clinical sign in determining seizure onset.

While most studies have noted increase in heart rate around some seizures, there are also incidences of decreased heart rate, and an increased occurrence of serious ECG abnormalities (Nei M et al 2000, Opherk C et al 2001). Sudden unexpected death in epilepsy (SUDEP) is a major cause of death in patients with epilepsy, especially in patients with intractable epilepsy (Ficker DM 2000, Langan Y 2000) and SUDEP occurs much more when patients are having seizure (Nilsson L et al 1999). Cardiac and respiratory changes could possibly contribute to SUDEP (Nashef L et al 1995) and it is known that ECG abnormalities occur often during or after seizures. Cardiac arrests and severe bradyarrhythmias also occur during seizures and ECG abnormalities appear to occur more often during generalized seizures and within seizures of longer duration (Reeves AL et al 1996, Lathers CM et al 1997).

**OBJECTIVE:**

To study the clinical and electrocardiographic changes in patients with seizure disorder and to find the relationship between seizure disorder and electrocardiographic abnormality, if any.

**MATERIALS AND METHODS**

This prospective study was carried out in the Post Graduate Department of Medicine of S.M.H.S hospital of Government Medical College, Srinagar, India. All patients with seizures attending medical OPD and In-patient department were included in the study irrespective of their age and sex.

All patients underwent:

1. Detailed history.

2. Detailed clinical examination with emphasis on neurological and cardiovascular system.
3. Electrocardiogram.
4. EEG during interictal period and video EEG (where ever necessary).
5. Serum electrolytes- sodium, potassium, calcium, magnesium (wherever necessary).

Other investigations where ever necessary:

1. 24 hour Holter monitoring.
2. Echocardiography.
3. Exercise tolerance test.

Two hundred and six patients (206) were included in the study in whom pre seizure electrocardiograms were available for comparison with post seizure electrocardiograms.

**Statistical analysis:** Data was described as mean ± standard deviation and percentage. Inter group variance was measured at 95% confidence interval. Metric data was compared by students-t test whereas non metric data was compared by Mann Whitney U test and chi square test. Data analysis was performed with the help of statistical package for social sciences (SPSS-20) and Microsoft excel.

**RESULTS**

Study sample comprised of 206 patients with seizures of which 117 (56.7%) were males and 89 (43.3%) were females. The mean age was 32.3 years with a standard deviation of 15.1 years. The minimum and maximum age of the patient was 16 years and 84 years respectively. There was statistically no significant difference as per age distribution in our study (p value=0.703).

Age and Gender distribution of the Seizure Patients							
Age (yr)	Male		Female		Total		p value
	n	%	n	%	n	%	
≤ 20	32	27.4	15	16.9	47	22.8	0.703 (NS)
21 to 30	22	18.8	34	38.2	56	27.2	
31 to 40	20	17.1	10	11.2	30	14.6	
41 to 50	18	15.4	11	12.4	29	14.1	
51 to 60	18	15.4	15	16.9	33	16.0	
> 60	7	6.0	4	4.5	11	5.3	
Total	117	56.8	89	43.2	206	100.0	
mean ± SD	35.6 ± 15.2 (16,84)		34.8 ± 15.0 (16,69)		32.3 ± 15.1 (16,84)		

Out of 206 patients, 97 patients (47%) had partial seizures, 66 patients (32%) had generalized seizures and 43 patients (21%) had undetermined seizures. Simple partial seizures were present in 20 patients (9.7%), complex partial seizures in 53 patients (25.7%) and partial seizures with secondary generalization were present in 24 patients (11.7%).

Tonic seizures were present in 12 patients (5.8%), clonic seizures in 10 patients (4.9%), tonic clonic seizures in 32 patients (15.5%), myoclonic, absence and astatic seizures were present in 6, 5 and 1 patient respectively.

Type of Seizure			
		n	%
Partial seizure (n=97)	Simple Partial Seizure	20	9.7
	Complex Partial Seizure	53	25.7
	Partial Seizure with Secondary Generalization	24	11.7
Generalized seizure (n=66)	Tonic Seizure	12	5.8
	Clonic Seizure	10	4.9
	Tonic Clonic Seizure	32	15.5
	Myoclonic Seizure	6	2.9
	Absence Seizure	5	2.4
	Astatic Seizure	1	0.5
Undetermined (n=43)	Undetermined	43	20.9

11 clinical variables in history were analyzed. Loss of consciousness, post ictal confusion and urinary/fecal incontinence were the most common clinical manifestations and were present in 137 patients (66.5%), 136 patients (66.0%) and 90 patients (43.7%) of the patients respectively. Frothing was present in 78 patients (37.9%), tongue bite in 71 patients (34.5%), headache and vomiting in 50 patients (24.3%) and 30 patients (14.6%) respectively. Other clinical features included weakness of any side, fever and trauma.

Presenting complaints		
	n	%
Loss of Consciousness	137	66.5
Post Ictal Confusion	136	66.0
Urine/Fecal Incontinence	90	43.7
Frothing	78	37.9
Tongue bite	71	34.5
Headache	50	24.3
Vomiting	30	14.6
Weakness of any side	25	12.1
Fever	12	5.8
Trauma	7	3.4
Drugs/Toxins	5	2.4

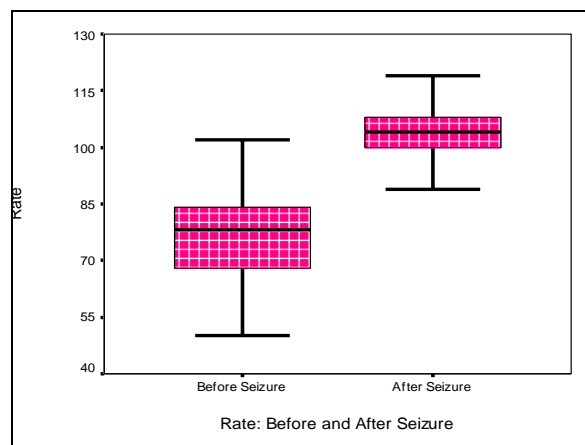
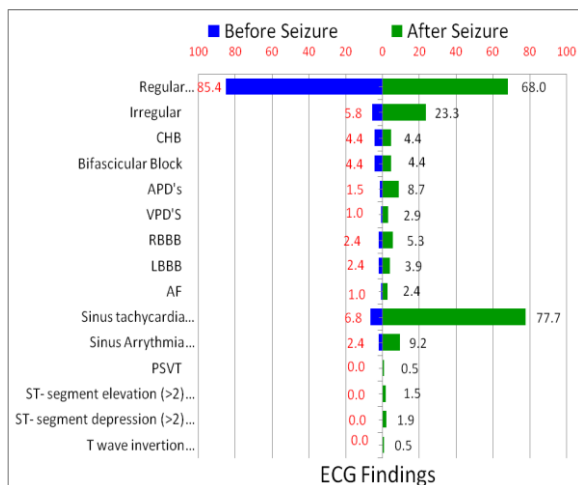
Thorough CNS examination was done in all patients. Higher mental functions were abnormal in 84% of patients on admission. 10 patients had cranial nerve palsy while 14 patients had right hemiparesis and 6 patients had left hemiparesis. Plantar response was flexor in 41.7% patients and extensor in 48.5% patients on admission and meningeal signs were present in 12 patients.

CNS Examination			
		n	%
Higher Mental Function	Normal	33	16.0
	Abnormal	173	84.0
Speech	Normal	180	87.4
	Abnormal	26	12.6
Cranial Nerves	Normal	196	95.1
	Abnormal	10	4.9
Motor System	Normal	186	90.3
	Right Hemiparesis	14	6.8
	Left hemiparesis	6	2.9
DTR	Present	200	97.1
	Absent	6	2.9
Plantars	Flexor(b/l)	86	41.7
	Extensor(b/l)	100	48.5
	Right ext, Left flex	14	6.8
	Right flex, Left ext	6	2.9
Meningeal Signs	Present	12	5.8
	Absent	194	94.2

**ECG findings:** ECG findings were compared before and after (within 3 hours) the seizure to see the changes on electrocardiogram induced by the seizure. The most common ECG abnormality after seizure was sinus tachycardia in 160 patients (77.6%) followed by sinus arrhythmia in 19 patients ( 9.2%), Right Bundle branch block in 11 patients (5.3%) , Left bundle branch in 8 patients (3.9%). Atrial Premature Depolarization in 18 patients (8.7%), ST segment elevation/depression in 7 patients (3.3%), VPD's in 6 patients (2.9%), AF in 5 patients (2.4%), PSVT was observed in 1 patient (0.5%) and T inversion in 1 patient (0.5%). Mean QTc before and after seizure was 377.4 ms and 396.4 ms respectively. QTc interval was abnormal in 2.4%, borderline high in 6.3% and normal in 91.3% patients after seizure. Mean heart rate before seizure was 75.2 seconds and after seizure was 96.6 seconds which was statistically significant. Complete heart block was present in 9 patients (4.4%), symptomatic bifascicular

block in 9 patients (4.4%) and required pacemaker.

		ECG Findings				p value
		Before Seizure		After Seizure (within 3hrs.)		
		n	%	n	%	
Rhythm	Regular	176	85.4	140	68.0	0.000 (Sig)
	Irregular	12	5.8	48	23.3	
	CHB	9	4.4	9	4.4	
	BifascicularBlock	9	4.4	9	4.4	
APD's		3	1.5	18	8.7	0.000(Sig)
VPD'S		2	1.0	6	2.9	0.102 (NS)
RBBB		5	2.4	11	5.3	0.014(Sig)
LBBB		5	2.4	8	3.9	0.083 (NS)
AF		2	1.0	5	2.4	0.083 (NS)
PSVT		0	0.0	1	0.5	0.317 (NS)
Sinus tachycardia		14	6.8	160	77.7	0.000(Sig)
Sinus Arrhythmia		5	2.4	19	9.2	0.001(Sig)
ST- segment elevation > 2mm		0	0.0	3	1.5	0.083 (NS)
ST-segment depression > 2mm		0	0.0	4	1.9	0.046(Sig)
T wave inversion		0	0.0	1	0.5	0.317 (NS)
Asystole		0	0.0	0	0.0	1.000 (NS)
Junctional escape		0	0.0	0	0.0	1.000 (NS)
Heart Rate (mean)		75.2 ±14.6(38,142)		96.6 ±20.4(40,158)		0.000(Sig)
Mean QT interval (ms)		364.9 ±49.8(138,556)		376.0 ±51.7(138,514)		0.000(Sig)
Mean QTc (ms)		377.4 ±44.1(128,478)		396.4 ±45.2(128,500)		0.000(Sig)

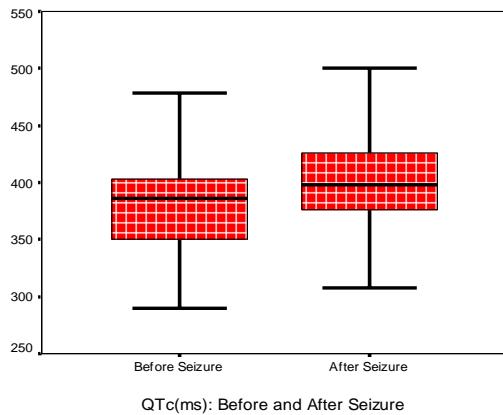


**Changes in heart rate after seizure are as follows:** Bradycardia was observed in only 4 patients (1.9%), tachycardia was observed in 160 patients (77.7%) and rate remained within normal limits in 42 patients (20.4%). Heart rate between 100-119 bpm was observed in 136 patients and rate more than or equal to 120 was seen in 21 patients.

Heart Rate After Seizure			
		N	%
Rate	Bradycardia	4	1.9
	Normal	42	20.4
	Tachycardia	160	77.7
Tachycardia	100 to 119	136	85.0
	≥ 120	24	15.0

**Changes in QTc after seizure are as follows:** QTc interval after seizure remained within normal limits in 188 patients (91.3%) of which 110 were males and 78 were females. It was borderline high in 13 patients (6.3%) out of which 5 were males and 8 were females. QT interval was abnormal in 5 patients (2.4%). Similar results were observed by Rainer Surges<sup>119</sup>. P value was 0.138 and it was not statistically significant.

	QTc Interval (ms) after Seizure						p value
	Male		Female		Total		
	n	%	N	%	n	%	
Normal	110	94.0	78	87.6	188	91.3	0.138 (NS)
Border Line High	5	4.3	8	9.0	13	6.3	
Abnormal	2	1.7	3	3.4	5	2.4	



**24 hour holter monitoring** was done in 40 patients, out of which it was normal in 19 patients (47.5%) and abnormal in 21 patients (52.5%). Abnormalities include APD's/VPD's in 7 patients, AV blocks in 10 patients, sinus pauses and AF/AFL in 2 patients each.

**Echocardiography** was done in 42 patients, out of which it was normal in 22 patients (52.3%) and abnormal in 20 patients (47.6%). Abnormalities include HTCVD, PAHTR, CAD and DCM. Exercise tolerance test was done in 16 patients, out of which it was normal in 12 patients (75%) and abnormal in 4 patients (25%).

**Electrophysiological study** was done in 21 patients, out of which it was normal in 12 patients (57.1%) and abnormal in 9 patients (42.9%).

Cardiac Evaluation			
		N	%
24 hr holter monitoring (n=40)	APD's/VPD's	7	3.4
	Sinus Pause	2	1.0
	AV Block	10	4.9
	AF/AFL	2	1.0
	Normal	19	9.2
	Not needed	166	80.6
Echocardiography (n=42)	HTCVD	5	2.4
	PAH TR	6	2.9
	CAD	6	2.9
	DCM	3	1.5
	Normal	22	10.7
	Not needed	164	79.6
Exercise tolerance test (n=16)	Normal	12	5.8
	Abnormal	4	1.9
	Not needed	190	92.2
EPS (n=21)	Normal	12	5.8
	Abnormal	9	4.4
	Not needed	185	89.8

### Seizure duration

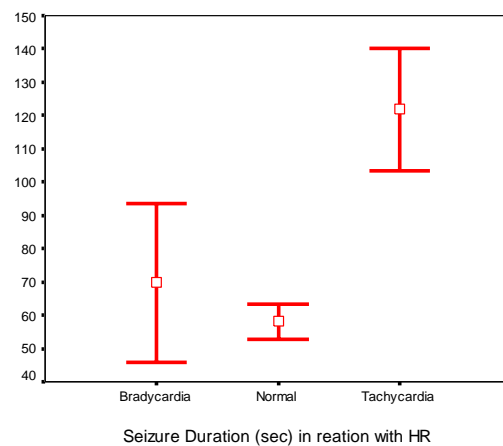
The mean seizure duration was 107.9 seconds. The patients in whom QTc interval

remained within normal limits had a mean seizure duration of 83.3 seconds, in whom QTc interval was border line high had a mean seizure duration of 259.9 seconds and in whom it was abnormal had a mean seizure duration of 262.6 seconds and the difference was statistically significant.

Seizure Duration (sec) in relation with QT Interval.		
	Mean ± SE	p value
Normal	83.3 ± 5.7 (33, 600)	0.000 (Sig)
Border Line High	259.9 ± 50.6 (55, 469)	
Abnormal	262.6 ± 126.4 (56, 598)	
Total	107.9 ± 7.4 (33, 600)	

Mean seizure duration of 69.7 seconds was observed in patients with post ictal bradycardia and 58.2 seconds was observed in those whose rate was within normal limits. Mean seizure duration of 120.1 seconds was observed in patients who had post ictal tachycardia and this difference was statistically significant.

Seizure Duration (sec) in relation with Heart Rate		
	Mean ± SE	p value
Bradycardia	69.7 ± 7.5 (52, 85)	0.000 (Sig)
Normal	58.2 ± 2.6 (33, 89)	
Tachycardia	120.1 ± 9.0 (33, 600)	



### Type of seizure and heart rate

The relationship between type of seizure and heart rate was also analyzed. 84.8% of generalized seizures were associated with tachycardia whereas 78.4% of partial seizures were associated with tachycardia and 65.1% of undetermined were associated with tachycardia. These findings were statistically significant.

Type of seizure in relation with Heart Rate							
	Bradycardia		Normal		Tachycardia		p value
	n	%	n	%	n	%	
Partial seizure	2	2.1	19	19.6	76	78.4	0.000 (Sig)
Generalized seizure	0	0.0	10	15.2	56	84.8	
Undetermined	2	4.7	13	30.2	28	65.1	

Patients with cardiac origin of seizures were 23 in number (11.2%). Abnormal QTc prolongation was seen in 5 patients. Complete heart block was seen in 9 patients (4.3%) and other AV blocks were seen in 9 patients (4.3%). Patients with CHB and symptomatic AV blocks were put on pacemaker (8.6%).

Patients with cardiac origin of seizures (n=23)		
	n	%
QTc prolongation	5	2.4
CHB	9	4.3
AV Blocks	9	4.3
Total	23	11.2

## DISCUSSION

The present study is one of the few studies to describe the clinical and electrocardiographic abnormalities in patients with seizure disorder. A total of 206 patients were taken in the study.

**Age and Gender:** In this study the mean age was  $32.3 \pm 15.1$  years. Out of 206 patients males were 117 (56.8%) and females were 89 (43.2%). The difference was not statistically significant.

**Type of Seizure:** Out of 206 patients, partial seizures were present in 47.1% patients, 32% had generalized seizures and undetermined seizures in 20.9%. Similar findings were observed by King et al, 1998 who observed 25% of cases with generalized seizures.

**Symptomatology:** We analyzed 11 clinical variables in patients. Overall loss of consciousness was the most common clinical finding and was found in 137 patients (66.5%). Post ictal confusion was present in 136 patients (66.0%). Other findings were urine/faecal incontinence which was present in 90 patients (43.7%), frothing in 78 patients (37.9%), tongue bite in 71 patients (34.5%), headache in 50 patients (24.3%). Other clinical features were vomiting, Todd's palsy, fever and trauma. These clinical features have been

described in standard text books on Epilepsy.

## Electrocardiographic Changes-

**Pre Ictal ECG:** Out of 206 patients, 152 had normal ECG (73.8%). Abnormalities include- sinus tachycardia in 14 patients (6.8%), CHB and bifascicular block in 9 patients each (4.4%), sinus arrhythmia, RBBB, LBBB in 5 patients each (2.4%), APD's in 3 patients and VPD's in 2 patients. The mean heart rate was 75.2 beats per minute and mean QTc was 377.4 milli seconds

**Post Ictal ECG:** The most common abnormality was sinus tachycardia (heart rate >100bpm) which was present in 160 patients (77.7%) followed by sinus arrhythmia in 19 patients (9.2%). CHB and bifascicular block remained in 9 patients each. APD's were present in 18 patients (8.7%), VPD's in 6 patients (2.9%). RBBB was present in 11 patients (5.3%), LBBB in 8 patients (3.9%), AF in 5 patients (2.4%), PSVT and T wave inversion in 1 patient each. ST segment elevation of 2mm was seen in 3 patients (1.5%) and ST segment depression in 4 patients (1.9%). The mean heart rate was 96.6 seconds and mean QTc interval was 396.4 seconds.

The results of our study were similar to that conducted by Maromi Nei et al, 2004 who studied ECG changes after the seizure and found that sinus tachycardia was present in 53% of patients, APD's in 18.6% and sinus arrhythmia in 14%, bundle branch block in 6.9%, AF and PSVT in 2% patients each.

Maeike Zijlmans et al, 2002 conducted a study on 81 patients and found that sinus tachycardia was present in 76.5% patients after the seizure. Sinus arrhythmia was present in 23.4% patients, APD's in 14.8% patients, VPD's in 8.6% patients, ST segment elevation/depression in 3.7% patients.

Marshall J. Keilson et al,1989 conducted a study in which they found that 93% of seizures were associated with tachycardia.

LM li et al,1995 found that 90% seizures were associated with tachycardia.

**QTc Interval after Seizure:** Out of 206 patients 188 had normal QTc interval(91.3%). QTc was borderline high in 13 patients (6.3%) and abnormally high in 5 patients (2.4%). Similar results were observed by M. Borzoe et al,2003 in which they observed 11.7% of patients with prolonged QTc interval.

**Type of Seizure in Relation with Heart Rate:** 84.8% of generalized seizures were associated with tachycardia, 78.4% of partial seizure patients were associated with tachycardia and 65.1% of undetermined seizures were associated with tachycardia. Similar results were observed by Maromi Nei et al,2004.

**Patients with Cardiac Origin of Seizures:** Patients with cardiac origin of seizures were 23 in number (11.2%), out of which 5 had prolonged QTc interval, 9 had CHB and 9 patients had symptomatic AV blocks.

## CONCLUSION

Partial seizures constituted the major seizure group in our study with loss of consciousness and post ictal confusion as most common clinical manifestation. EEG, CT head and MRI brain are important tools in the evaluation of patients with seizure disorder. Seizure duration is more in patients with borderline high to abnormal QTc interval and abnormal QT interval may have a role in SUDEP. Generalized seizures and prolonged seizures are more often associated with tachycardia. Cardiac rhythm abnormalities should be kept in mind while evaluating a patient with seizure disorder especially refractory seizures.

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