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# ROLE OF PROLACTIN: A COMPARATIVE STUDY BETWEEN GRAND MAL EPILEPTIC AND PSEUDO-SEIZURES PATIENTS

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**Abstract:**

Epilepsy is a condition of the brain characterized by abnormal, recurrent and excessive discharge from living neurons of brain. It comes in attacks or fits which lasts for a few seconds to a few minutes. It is important to distinguish generalized tonic-clonic seizures (GTCS) from either psychogenic nonepileptic seizures (PNES).

This study is designed to determine the level of prolactin hormone in females suffering from Grand Mal epilepsy and Pseudo seizures.

**Methodology:** After getting approval from Ethical Review Board, this cross-sectional study was conducted in a tertiary care medical teaching hospital over a period of 2 years. A total of Ninety (90) female subjects were enrolled in this study and they were divided in three groups equally. :**Group-1(n=30)** included patients with known cases of grand mal seizures as well as recently diagnosed cases of GTCS. **Group-2 (n=30)**: Patients with previous history of pseudo seizures.**Group-3 (n=30):** Control group, healthy females of comparable age. Quantitative data was presented as Mean ± SD and ANOVA was used to compare the results of the different groups. Statistical significance was set at p- value $\leq 0.001$.

**Results:** The results showed significant difference of serum prolactin levels among three groups (p value 0.0001). Serum prolactin level was higher in epileptic group as compared to pseudo-seizures and control group ($p < 0.001$).

**Conclusion:** It is concluded that serum prolactin may be used as a sensitive biochemical marker in the diagnosis of grand mal seizures in females and is also helpful in differentiating it from pseudo-seizures

**Key words:** Prolactin, Generalized Tonic-Clonic Seizures, Pseudo-Seizures.

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**INTRODUCTION:**

Grand mal epilepsy, also known as generalized tonic-clonic seizure (GTCS) — is caused by abnormal electrical activity throughout the brain (1).

During the attack, the classical epileptic seizure includes a phase of tonicity showing contraction of facial, jaw, limbs and trunk muscles, followed by jerking of the limbs in the clonic phase. At the beginning of the tonic phase, which usually last for about 15-30 seconds, the patients may utter a cry as air is forced out their lungs, bite their tongue, then become cyanosed as apnoea continues in a position of forced expiration. As the tonic phase passes into clonic phase, the patients may pass urine or occasionally open bowels. The rhythmic jerking of the clonic phase gradually subsides, leaving the patient unconscious or in a state of confusion which may last for some minutes or hours, after which the patients may complain of headache or painful back (2).

Pseudoseizures (also called psychogenic non-epileptic seizures) are involuntary behavioral changes having no organic cause, showing resemblance to epileptic seizures and are not accompanied by the ictal, pericta and interictal electroencephlical changes(spikes and slowing) that characterize epilepsy. Pseudo seizures can look like any kind of epileptic seizures and thus can be mistaken for generalized tonic-clonic seizures, absence seizures and simple partial seizures. Pseudoseizure symptoms include indifferent staring, slight motor movements, weird behavior and sweeping movements. Prevalence of non-epileptic seizures in general population all over the world ranges from 2 to 33 cases per 100,000 persons. It is noted that 75 to 85% of the patients of psychogenic non-epileptic seizures are found to be females. These seizures have a tendency to begin in middle age, though the seizures may occur in any age. Psychogenic non-epileptic seizures are found to be more in patients suffering from head injuries, problems of learning or isolated neuropsychologic insufficiency.(3).

Clinicians are often faced with the challenging task of distinguishing between PNES and epileptic seizures (ES). Clinical features of ictal events correctly differentiate PNES from ES in less than 70% of cases.(4,5) Even when a patient's typical events are recorded during video-EEG, artifacts often obscure scalp EEG during violent motor movements. Serum prolactin, a pituitary hormone that is elevated during generalized ES, has been reported to differentiate epileptic from hysterical seizures.(6) However, subsequent studies demonstrated that serum prolactin was elevated in temporal lobe epilepsy but not frontal lobe epilepsy, which may lead to erroneous diagnosis of the latter as PNES.(7)

The American Academy of Neurology (AAN) guidelines on the use of serum prolactin in diagnosing ES stated that elevated serum prolactin 10–20 minutes after a clinical event is probably useful in differentiating ES from PNES (Level B).(8)

Literature review revealed that a lot of previous trials have studied the relationship of serum PRL levels with epileptic events but use of serum PRL levels in clinical practice to diagnose epilepsy or to discriminate epileptic seizures from psychogenic seizures is still controversial because of some limitations which have been described by authors of different studies(9,10). One of these limitations includes intrapersonal and interpersonal variations in the basal serum PRL levels, so it is difficult to label significant PRL rise in different individuals. Moreover, most of the seizures occurred at home or non-hospital settings where it is not feasible to measure serum postictal PRL levels, while in hospitals settings video EEG monitoring facility is present which is considered a better tool for this purpose(10).

The present study is designed to determine and compare the level of serum prolactin in female atients suffering from Grand Mal epilepsy and Pseudo seizures.

**Methodology:**

This cross sectional study was conducted at Kind Edward Medical University, Lahore in the Department of Physiology over a period of 2 years. Registered subjects were selected from the indoor as well as outdoor, Emergency Department of Internal Medicine and Psychiatry Department after getting approval from the Ethical Committee of King Edward Medical University Lahore and Mayo Hospital Lahore.Healthy females were recruited from general population. We included young female of child bearing age (16 to 35 years), having history of Grand Mal epilepsy and Pseudo seizures.. Patients with history of head trauma, brain tumor, meningitis, cerbro vascular accidents, metabolic disorders(Hypoglycemia, hypocalcaemia), muscle injuries and mental impairment were excluded. Pregnant and lactacting females were also excluded.

The written consent was obtained from the subjects and their guardians at the spot.

Ninety female subjects were enrolled and they were divided in three gr equally.

**Group1(n=30)**: Previous and recently diagnosed patients of grand mal seizures

**Group-2 (n=30)**: Known cases of pseudo seizures.

**Group-3 (n=30):** Healthy Females (Control)

Under aseptic measures , five millilitres (5ml) of blood sample was collected within 30 minutes of a seizure or pseudo seizure. The samples were sent to center of Nuclear Medicine (CENUM) of Mayo Hospital, and pathology department of King Edward Medical University Lahore for further processing within 24 hours. Serum prolactin was determined by radioimmununo assay(RIA) using an automated Gamma Counter machine (Model- Genesys TM 5000 Series LTI U.S.A). 2 to 29 ng/mL was taken as normal range for prolactin in nonpregnant females:

Data was entered and analysed by Statistical Package for the Social Sciences for Windows 16.0 (SPSS Inc., Chicago, IL, USA).

**RESULTS:**

The mean age of female included in control, pseudo-seizure and epileptic group was 23.4± 4.7 year, 21.9 ± 5.5 year and 21.6 ± 4.1 year respectively. The age limit in all female was 16 to 35 years. The mean age in both pseudo-seizure group and epileptic group was not significantly different (P=0.792) but was lower than the control group without significant difference (p= 0.25 & 0.098 respectively). (Table 1)

Mean serum prolactin level was found to be 44.5±5.3 ng/100ml in group 1(epileptic) , 8.2±4.8 ng/100ml, in group 2( pseudoseizure) , and 4.6±3.2 ng/100ml, and in group 3 (control) respectively. On applying analysis of variance (ANOVA) we found significant difference between the mean levels of prolactin among three groups. Further statistical analysis showed that prolactin was significantly higher in epileptic group as compared to pseudo-seizures groups and control (p-value < 0.001) and prolactin was also higher in pseudo-seizures when compared to control group (p-value < 0.001). ( Table 2, Fig 1).

**Table – 1: Pairwise comparison of age (mean ± SD years) among different groups**

| **Variable** | **Study group** | | **p-value** |
|---|---|---|---|
| **Age (years)** | Pseudo-seizures (21.90 ± 5.54 year) | Epileptic (22.03 ± 4.62 year) | 0.792 |
| | | Control (18± 1.17 year) | 0.25 |
| | Epileptic (22.03 ± 4.62 year) | Pseudo-seizures (21.90 ± 5.54 year) | 0.792 |
| | | Control (18± 1.17 year) | 0.098 |

**Table – 2: Pairwise comparison serum Prolactin among different groups**

| **Variable** | **Study group** | | **p-value** |
|---|---|---|---|
| **Prolactin** (ng/100ml) | Pseudo-seizure (8.2±4.8 ) | Epileptic (44.5±5.3) | 0.0001** |
| | | Control (4.6±3.2) | 0.001* |
| | Epileptic (44.5±5.3) | Pseudo-seizure (8.2±4.8) | 0.0001** |
| | | Control (4.6±3.2) | 0.0001** |

* Significant (P< 0.05)

** Highly significant (P< = 0.0001)

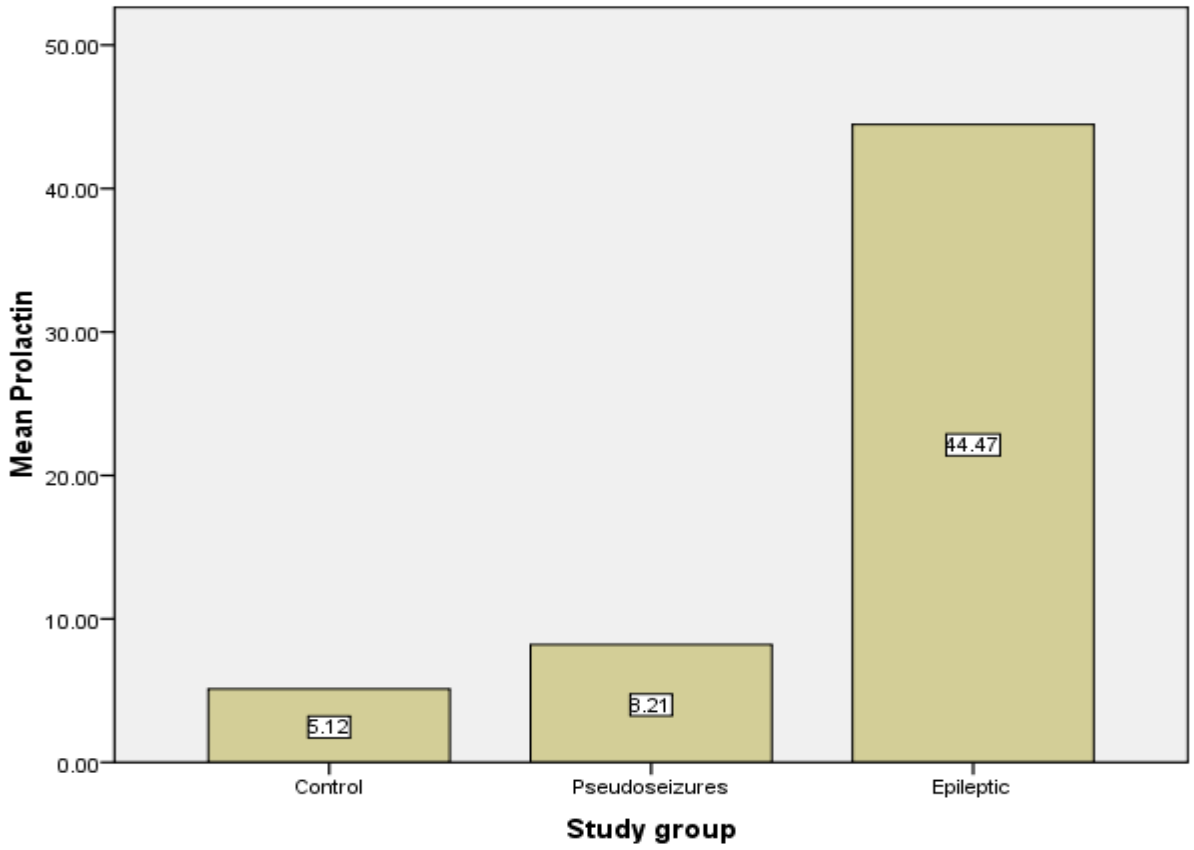


**Fig-1: Comparison of mean serum Prolactin in study groups**

**DISCUSSION:**

In our study, prolactin levels were significantly higher in epileptic group as compared to pseudo-seizures groups and control (p-value < 0.001) and prolactin was also higher in pseudo-seizures when compared to control group (p-value < 0.001).

Prolactin release from the pituitary is controlled by the hypothalamus through a PRL inhibitory factor, now believed to be dopamine,[11] it is possible that the generalized neuronal discharge of a seizure stimulates the hypothalamus either directly, through specific neurotransmitter changes, or through the release of other substances.[12]

Epilepsy and pseudo- seizures are important medical problems. Our findings were comparable to the findings of various study groups,[13,14] who concluded that if PRL was measured 10–20 min after an event, then it probably can be a useful measure to differentiate between a generalized tonic–clonic seizure and PNES. However, if the serum PRL test is taken 5 h after the event, then it is probably indicative of the baseline PRL level of that patient.

According to our results, a significant difference in the PRL levels between true epileptic patient (Grand mal) and those with pseudo seizers was noted. Levels of PRL were significantly higher in epileptic group than the pseudo seizure group and mean PRL level in both groups was higher as compared to the healthy control group. These results are in accordance to the finding of a recent study conducted by Priyanka et al (15) in which PRL was 37 ng/ml in patients of generalized clonic seizures, while in patients of psychogenic non-epileptic seizures the level was 16.8 ng/ml and in control subjects it was 16.5 ng/ml respectively. Epileptic seizures lead to increase the level of serum PRL hormone due to dissemination of epileptic action typically from temporal lobe to hypothalamic-pituitary axis. PRL elevation was seen in 60% of complex partial seizures which is due to intensity of epileptic discharges by Bauer in 1996. As there was no rise of PRL hormone observed after psychogenic seizures, so postictal PRL levels can be used to distinguish epileptic from psychogenic seizures. It is also observed that PRL secretion may decline in repetitive seizures like in cases of status epilepticus possibly due to reduced spread of ictal discharges during the course

of status epilepticus (16). Malkowicz et al (17) determined the PRL levels were after 24 hours seizures which were monitored by video EEG intracranial monitoring. It was seen there was a significant postictal PRL elevations in those patients having longer seizures free intervals while the PRL responses were reduced in subjects having shorter seizures free intervals suggesting that amount of PRL hormone released from the hypothalamus is depleted by seizures or by PRL inhibit feedback mechanism (17). In another study conducted in children it was observed that mean PRL level was 28.6 ng/ml in epileptic while in pseudo-seizure and in control groups PRL was 10.4 ng/ml and 9.8 ng/ml respectively. It was proposed that abnormal electrical discharge in epileptic seizures passes through the hypothalamic nuclei responsible for elevation of PRL (18). Ahmad et al (19) stated parallel results viewing that generalized epileptic seizure cause noticeable early increase of PRL with more increase following prolonged seizures in children. Thus it may be concluded from these studies that serum PRL is a valuable biochemical indicator to differentiate between epileptic and pseudo-epileptic seizures

**CONCLUSION:**

An elevation of serum prolactin can be taken as a predictor of epilepsy. Maximum elevation of prolactin is seen within 15 to 30 minutes post ictally. Misdiagnosis of PNES has substantial morbidity, social effect, and economic burden on the health care system.

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