"COMPARISON OF SERUM CALCIUM LEVELS AMONG PATIENTS WITH ALCOHOL RELATED SEIZURES AND PRIMARY SEIZURES"

Dissertation submitted to

THE TAMILNADU

DR M.G.R MEDICAL UNIVERSITY

CHENNAI

In partial fulfillment of regulations

For award of the degree of

M.D (GENERAL MEDICINE)

BRANCH – 1

GOVERNMENT KILPAUK MEDICAL COLLEGE

CHENNAI

APRIL 2014

BONAFIDE CERTIFICATE

This is to certify that dissertation named **"COMPARISON OF SERUM CALCIUM LEVELS AMONG PATIENTS WITH ALCOHOL RELATED SEIZURES AND PRIMARY SEIZURES"** is a bonafide work performed by Dr.V.Priyadarshini , post graduate student , Department of Internal medicine , kilpauk Medical College, Chennai – 10 , under my guidance and supervision in fulfilment of regulations of the Tamilnadu Dr.M.G.R Medical University for the award of **MD Degree Branch I (General Medicine)** during the academic period from May 2011 TO April 2014.

PROF. DR.N.GUNASEKARAN M.D , DTCD,
Director and Superintendent,
Institute of Non Communicable diseases,
Government Royapettah hospital,
Unit Chief and Head of the Department of Medicine,
Kilpauk Medical College,
Chennai – 600 010

PROF.DR.P.RAMAKRISHNAN MD, DLO
DEAN
Government Kilpauk Medical College
Chennai – 600 010

DECLARATION

I solemnly declare that the dissertation **"COMPARISON OF SERUM CALCIUM LEVELS AMONG PATIENTS WITH ALCOHOL RELATED SEIZURES AND PRIMARY SEIZURES"** was prepared by me at Government Kilpauk Medical College and Hospital , Chennai , under the guidance and supervision of **Prof Dr.N.Gunasekaran M.D, DTCD,** Director and Superintendent , Government Royapettah Hospital, Professor and HOD, Department of Internal Medicine, Kilpauk Medical College, Chennai.

This dissertation is submitted to The Tamil Nadu Dr.M.G.R Medical University , Chennai in partial fulfilment of the university regulations for the award of the degree of M.D Branch I (General Medicine).

Place : Chennai

Date (Dr. V.PRIYADARSHINI)

ACKNOWLEDGEMENT

At the outset , I would like to thank my beloved Dean , **Prof. Dr.P.Ramakrishnan MD, DLO**, Kilpauk Medical College for his kind permission to conduct the study in Kilpauk Medical College.

"The mediocre teacher tells. The good teacher explains. The superior teacher demonstrates . The great teacher inspires ". Words cannot express the amount of admiration , respect and gratitude I have for **Prof. Dr. N. Gunasekaran MD, DTCD ,Professor and HOD , Department of General Medicine , Director , Institute of Non Communicable diseases, Superintendent , Government Royapettah hospital** for being a great teacher who has been an embodiment of motivation and inspiration for me throughout. I would also like to thank him for permitting me to conduct this study and for his continuous encouragement and guidance through out the study.

"Ideal teachers are those who use themselves as bridges over which they invite their students to cross , then having facilitated their crossing , joyfully collapse , encouraging them to create bridges of their own ".I also express my special thanks to **Prof.Dr.K.T.Jayakumar MD., Prof.Dr.R.Sabaratnavel MD and Prof.Dr.S.Mayilvahanan MD**. I am extremely thankful to Assistant Professors of medicine , **Dr.K.Manickam MD,**

Dr.S.Gopalakrishnan MD, Dr.V.Madhavan MD, and Dr.S.Malathi MD for their assistance and guidance.

I extend my heartful thanks to my seniors , juniors, my batchmates for their help and support throughout my course. I would like to extend my special thanks to my co postgraduate Dr.K.Venkatraman who would always be remembered with extreme sense of thankfulness for his co-operation, affection and support he showed throughout this course.

"I have grown up with the wisdom of your words , the cheerfulness of your laughter , the strength of your mind and the warmth of your love ".I would like to thank my father Dr.N.Varadaraj M.tech, PhD, my mother Mrs. Dhana varadaraj BSc, B.Ed, my husband Dr.M.Haneesh MDS ,my brother V.Chakravarthy MS,MBA and all my in laws for fulfilling my dreams and for all their support and timely help.

Finally , I thank God Almighty for giving me the time and inclination to finish this dissertation successfully with in the stipulated time and for providing me the right wisdom and for making me what I am today.

CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF CHARTS

INTRODUCTION

An epileptic seizure is the result of a temporary physiologic dysfunction of the brain caused by a self-limited, abnormal, hypersynchronous electrical discharge of cortical neurons. A seizure is a transient epileptic event, a symptom of disturbed brain function. Seizures may be self-limited in that they occur only during the course of an acute medical or neurologic illness; they do not persist after the underlying disorder has resolved.

Parathyroid harmone and vitamin D are the two primary regulators of

TURNITIN ORIGINALITY REPORT

COMPARISON OF SERUM CALCIUM LEVELS AMONG PATIENTS WITH ALCOHOL RELATED SEIZURES AND PRIMARY SEIZURES

By Priyadarshini Varadaraj 20111114 M.D. General Medicine

From Medical (TNMGRMU APRIL 2014 EXAMINATIONS)

- Processed on 08-Dec-2013 15:10 IST
- ID: 379087114
- Word count : 10831

Similarity Index **21%**

Similarity by source

Internet sources **15%**

Publications **16%**

Student papers **9%**

Sources :

1 2% match ()
http://www.nuts.cc

2 1% match (Internet from 19-Apr-2011)
http://professionals.epilepsy.com

3 1% match (Internet from 31-Oct-2013)
http://www.pn.psychiatryonline.org

4 1% match (Internet from 29-May-2009)
http://www.efns.org

5 1% match (student papers from 24-Mar-2013)
Submitted to Fiji School of Medicine

“COMPARISON OF SERUM CALCIUM LEVELS AMONG PATIENTS WITH ALCOHOL RELATED SEIZURES AND PRIMARY SEIZURES”

ABSTRACT

BACKGROUND:

Hypocalcemia can be a contributory factor for epilepsy and previous studies showed that ethanol decreases plasma calcium. Alcohol-related seizures are defined as adult onset seizures that occur in the setting of chronic alcohol dependence. Alcohol-related seizures are typically brief, generalized tonic-clonic seizures that occur 6 to 48 h after the last drink. Alcohol overconsumption induces multiple effects on kidney function as well as on water, electrolyte and acid base homeostasis. Among the electrolyte abnormalities observed in alcoholic patients, Hypocalcemia is a common feature. Thus, the basis of this study is to establish the prevalence of Hypocalcemia in the general convulsive population and to ascertain if there was a specific group of risk for Hypocalcemia among alcoholics.

AIM OF THE STUDY:

To establish the role of hypocalcemia in alcohol related seizures in contrast to non alcoholic primary idiopathic seizures. To study the prevalence of

hypomagnesemia in hypocalcemic patients in both alcohol related seizures and primary idiopathic seizures.

MATERIALS AND METHODS:

This study was formulated as an analytical case control study. Based on previous records and by obtaining past history of any CNS infections, cerebrovascular accidents, head injury, structural brain lesions, metabolic diseases and illicit drug abuse ,patients with all negative history were screened with investigations such as serum electrolytes, random blood sugar ,serum amylase, serum bilirubin and CT- brain . Among these patients, patients who had all values within normal limits were taken into study population.

Among the patients in study population, patients with no history of alcohol consumption with all screening blood investigations within normal limits and those with EEG and CT Brain findings suggestive of primary seizures were grouped into control population. Patients satisfying CAGE criteria with screening blood investigations and CT-Brain normal were grouped into case population. Then, serum calcium levels, serum albumin levels and serum magnesium levels were measured in both cases and controls. Corrected calcium will be calculated in case of hypoalbuminemia. Serum calcium levels were compared in both cases and controls. The prevalence of hypomagnesemia in these patients and their association with hypocalcemia were also assessed

secondarily. The results were tabulated and their statistical significance were calculated using pearson's chi square tests.

RESULTS:

On comparing the case and control group , 65.2 % of the hypocalcemic patients were in the case group. Only 34.8 % of the patients were in the control group. On applying the chi-square tests, the p value is found to be 0.240. Thus, there is no statistically significant difference in the prevalence of hypocalcemia among the case and control group. On comparing the prevalence of hypomagnesemia among hypocalcemic patients in the case group, the p value is found to be 0.03 which is statistically significant, but p value was not significant in the control group.

CONCLUSION:

A **high prevalence of Hypocalcemia** among alcohol related seizures were identified in this study ,though a statistical significance against primary seizures could not be proven. **The prevalence of Hypomagnesemia was statistically significant in the Hypocalcemic alcoholic patients**. Thus, hypomagnesemia as a cause of seizures in these patients needs further studies.

KEY WORDS :

Alcohol related seizures, hypocalcemia , hypomagnesemia.

INTRODUCTION

An epileptic seizure is the result of a temporary physiologic dysfunction of the brain caused by a self-limited, abnormal, hypersynchronous electrical discharge of cortical neurons. A seizure is a transient epileptic event, a symptom of disturbed brain function. Seizures may be self-limited in that they occur only during the course of an acute medical or neurologic illness; they do not persist after the underlying disorder has resolved.

Parathyroid hormone and vitamin D are the two primary regulators of calcium homeostasis. It is the free ionized calcium fraction and not protein-bound calcium which is responsible for the excitability of muscle cells and neurons. The symptoms of Hypocalcemia depends on two factors

1. the degree of reduction in serum calcium level and
2. the acuteness of the fall in serum ionized (free) calcium concentration.

Acute hypocalcemia causes neurologic symptoms primarily because of increased neuromuscular excitability. Symptoms are:

1. Circumoral paresthesia - .numbness and tingling sensation of the circumoral region fingers and toes
2. Muscle cramps
3. Carpopedal spasm

4. Tetany producing flexor spasms in the arms and extensor spasms in the legs
5. Laryngeal stridor
6. Tremors
7. Chorea and
8. Seizures.

Seizures may occur either in the presence or absence of tetany. The various types of seizures in Hypocalcemia are generalized tonic-clonic, focal motor, atypical absence and less frequently akinetic seizures.[1,2,3] Majority of the patients presenting with hypocalcemia in the medical emergency, nearly about 20 – 25 % had seizures.[4]

Alcohol when consumed distributes throughout the body. It affects almost all the systems of the body. It alters nearly every neurochemical process in the central nervous system .Alcoholism temporarily mimics many medical (eg.diabetes mellitus) and psychiatric (eg. Depression) conditions

Ethanol and its oxidative metabolite acetaldehyde has a direct effect on both the developing and mature nervous system. Alcohol contains non nutritive calories, hence alcohol abuse is complicated by vitamin deficiencies and malnutrition. Alcohol overuse causes epileptic seizures.[5]

Alcohol-related seizures are typically brief. It is usually a generalized tonic-clonic seizures that occur within 6 to 48 hours after the last drink. Without

treatment , approximately 60% of patients develop multiple seizures. The interval between the first and the last seizure is typically less than 6 hours. Alcohol related seizures usually occurs in the absence of other signs of alcohol withdrawal and sympathetic activity such as tachycardia, hypertension and fever.[6]

Alcohol abuse causes multiple effects on renal function as well as on water, electrolyte and acid base homeostasis. Hypocalcemia is a common electrolyte abnormalities observed in alcoholic patients and may be evoked by various pathophysiologic mechanisms .

DEMOGRAPHY

Epilepsy , a chronic neurological disease is one of the oldest known disease to mankind. Epilepsy is the most common neurological disorder affecting people of all ages. It is estimated that at any given time about 50 million people are diagnosed to have epilepsy , with about 80% of these individuals residing in developing countries. Seizures accounts for about 1 % of the global burden of diseases.[7,8] In these countries, although most cases can be treated, around 75% of people with epilepsy are not receiving appropriate treatment.[9] There is a disparity in the incidence and prevalence of the disease across the world. Increased prevalence and incidence can be attributed to factors such as low socioeconomic status, infections such as neurocysticercosis and access to health care.

In the integrated disease surveillance project (IDSP) , non-communicable disease risk factors survey conducted by Ministry of Health & Family Welfare in seven states namely Tamil Nadu, Andhra Pradesh, Kerala, Madhya Pradesh, Maharashtra, Mizoram and Uttarakhand in the year 2007-08[10] , the consumption of alcohol was about 15% of the surveyed population in past 12 months and 11% in last 30 days preceding the survey. Among the males about 6 % were past drinkers. Among the surveyed population , the habit of alcohol consumption was higher among men with 30% in past 12 months as compared to only 0.1% among women. The average number of drinks consumed was two drinks on a drinking day. Binge drinking (high drinking) was seen in less than five percent of current drinkers. This statistics signifies the burden of alcoholism and the health related problems due to alcoholism in our country.

AIM OF THE STUDY:

- To establish the role of hypocalcemia in alcohol related seizures in contrast to non alcoholic primary idiopathic seizures.
- To study the prevalence of hypomagnesemia in hypocalcemic patients in both alcohol related seizures and primary idiopathic seizures.

REVIEW OF LITERATURE

SEIZURES

A seizure (from the Latin sacire, "to take possession of") is a paroxysmal event due to abnormal excessive or synchronous neuronal activity in the brain.

The incidence of epilepsy in different populations throughout the world is 0.3 – 0.5 %, and the prevalence of epilepsy has been estimated to be 5–10 persons per 1000.

CLASSIFICATION OF SEIZURES

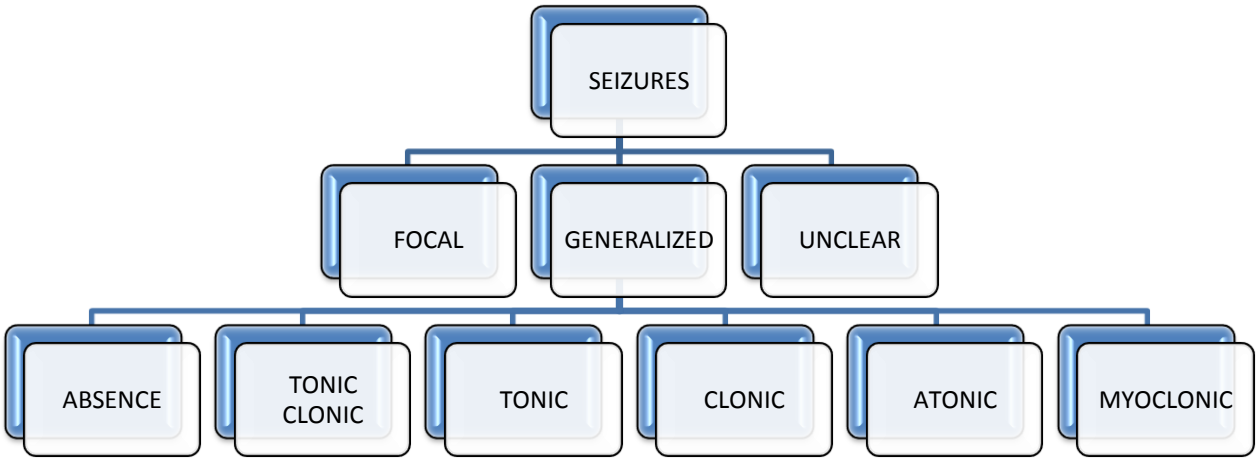


Fig 1: Classification of seizures

Focal seizures are those which originate within networks limited to one cerebral hemisphere . Generalized seizures arise within the cerebral hemisphere

and rapidly engage networks distributed across both hemispheres. Structural abnormalities of the brain are usually associated with focal seizures whereas generalized seizures may result from cellular, biochemical or structural abnormalities that may have a more widespread distribution.

ALCOHOL RELATED SEIZURES

Alcohol related seizures may be either due to alcohol intoxication or alcohol withdrawal. After a period of heavy alcohol consumption , one or more generalized tonic-clonic seizures may occur within 48 hours of cessation of alcohol consumption. Such patients should be hospitalized for observation for atleast 24 hours to follow the severity of withdrawal symptoms. If the seizures is consistently of focal type, the possibility of an associated structural abnormality which is often traumatic in origin, must be ruled out. In patients with new onset of generalized seizures and whenever there are focal features associated with seizures Head CT scan or MRI should be performed . Anticonvulsant drugs is generally not required for alcohol withdrawal seizures as they are mostly self-limited. Benzodiazepines are the drug of choice and safe for preventing further seizures. Status epilepticus may rarely occur following alcohol withdrawal . Further attacks are not imminent if the patient abstains from alcohol.

ALCOHOLISM

Alcohol when consumed distributes throughout the body. It affects almost all organs in the body. It affects the brain by altering nearly every neurochemical process. Ethanol is likely to exacerbate most of the medical conditions. It affects almost any drugs metabolized in the liver. It temporarily mimics many medical diseases (e.g., diabetes) and psychiatric (e.g., depression) illnesses. Almost 80% of people in Western world have consumed alcohol in their lifetime , and two-thirds have been drunk in the last year, almost 20% for men and 10% for women have the lifetime risk for repetitive serious alcohol related problems , regardless of a person's education status or income. Though low doses of alcohol have some health benefits, consumption of more than three standard drinks per day on a regular basis increases the risk for cancer, cardiovascular and cerebrovascular disease. Alcohol related disorders decrease the life span of an individual by about 10 years.

Alcohol abuse is defined as repetitive problems with alcohol in any one of four areas of life—social, interpersonal, legal, and occupational—or repeated use in hazardous situations such as driving while intoxicated in an individual who is not alcohol dependent. About 50% of those with alcohol abuse continue to have alcohol problems 2–5 years later, but only 10% of these patients including adolescents go on to develop alcohol dependence.

ICD-10 DIAGNOSTIC CRITERIA FOR ALCOHOL DEPENDENCE

EUROPEAN VERSION

A definite diagnosis of alcohol dependence should usually be made only if three or more of the following have been experienced or exhibited at some time during the previous year:

a. A strong desire or sense of compulsion to take alcohol;

b. Difficulties in controlling alcohol-taking behaviour in terms of its onset, termination, or levels of use;

c. A physiological withdrawal state when alcohol use has ceased or been reduced, as evidenced by: the characteristic withdrawal syndrome for alcohol; or use of the alcohol with the intention of relieving or avoiding withdrawal symptoms;

d. Evidence of tolerance, such that increased doses of alcohol are required in order to achieve effects originally produced by lower doses (clear examples of this are found in alcohol-dependent individuals who may take daily doses sufficient to incapacitate or kill nontolerant users);

e. Progressive neglect of alternative pleasures or interests because of alcohol use, increased amount of time necessary to obtain or take alcohol or to recover from its effects;

f. Persisting with alcohol use despite clear evidence of overtly harmful consequences, such as harm to the liver through excessive drinking; efforts should be made to determine that the user was actually, or could be expected to be, aware of the nature and extent of the harm.

PHARMACOLOGY AND NUTRITIONAL IMPACT OF ETHANOL

Ethanol level in blood is expressed as grams per decilitre. One typical drink results in 0.02 gm/dl of blood alcohol level.

340 ml beer	10-15 gms of ethanol (one standard drink)
115 ml nonfortified wine	
43 ml whisky Gin Vodka	

Table 1 :Alcohol content in various beverages.

The alcoholic beverages have additional components called congeners. These include methanol, butanol, acetaldehyde, histamine, iron, lead, and tannins. They affect the taste and also contributes to the adverse effects of alcohol on the body. Alcohol acutely decreases neuronal activity,

METABOLISM OF ALCOHOL

Alcohol is absorbed at various levels of the gastrointestinal tract. Small amount from mouth and esophagus, modest amount from stomach and large

bowel and the major site is proximal portion of the small intestine. Rapid gastric emptying and absence of proteins , fats or carbohydrates which interferes with absorption all increases the rate of absorption.

Between 2% and 10 % blood alcohol concentration , ethanol is excreted through lung , urine or sweat. Ethanol is primarily metabolised in the liver. The major pathway occurs in the cell cytosol where ethanol is converted to acetaldehyde by alcohol dehydrogenase (ADH), which is then rapidly metabolised in cytosol and mitochondria by aldehyde dehydrogenase (ALDH). A second pathway called microsomal ethanol – oxidizing system occurs in the microsomes of smooth endoplasmic reticulum which metabolises >10 % of ethanol at high blood alcohol concentration.

Alcohol supplies empty calories , that is calories devoid of nutrients such as proteins, minerals and vitamins. Alcohol also interferes with absorption of micronutrients in the small intestine and reduces the storage in the liver with modest effect on thiamine (B1), pyridoxine (B6), folate and vitamin A.

Chronic alcohol abuse causes thiamine deficiency which accelerates the metabolism of ethanol and increases the synthesis of acetaldehyde. Inturn, acetaldehyde induces the transketolase activity by acetylation, which is a thiamine dependant enzyme . Certain genetic factors also play an important role in affecting the transketolase enzyme which makes certain alcoholics more susceptible to development of neurological complications.

EFFECT OF ALCOHOL ON BLOOD SUGAR

A heavy ethanol load in a healthy fasting individual produces transient hypoglycaemia within 6 – 36 hours due to acute actions of ethanol on gluconeogenesis. To measure actual blood glucose levels in alcoholics, patients has to be abstained from alcohol for 2-4 weeks. The effect of alcohol on gluconeogenesis results in temporary abnormal glucose tolerance tests resulting in erroneous diagnosis of diabetes mellitus. Alcoholism causes recurrent vomiting, poor diet and decrease in fatty acid oxidation resulting in alcohol ketoacidosis which can be misdiagnosed as diabetic ketoacidosis. In alcoholic ketoacidosis patients have increase in serum ketones with mild increase in serum glucose levels with a large anion gap. There is mild to moderate increase in serum lactate and a beta-hydroxybuterate / lactate ratio of 2:1 to 9:1 (normal is 1:1).

ACUTE ALCOHOL INTOXICATION

DSM-IV CRITERIA FOR ALCOHOL INTOXICATION

A. Recent ingestion of alcohol.

B. Clinically significant maladaptive behavioural or psychological changes (e.g., inappropriate sexual or aggressive behaviour, mood lability, impaired judgment, impaired social or occupational functioning) that developed during, or shortly after alcohol ingestion.

C. One (or more) of the following signs, developing during, or shortly after, alcohol use:

1. Slurred speech

2. Incoordination

3. Unsteady gait

4. Nystagmus

5. Impairment in attention or memory

6. Stupor or coma

D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

Mild	0.5 – 1.5 %
Moderate	1.5 – 2.5 %
Severe	>2.5 %

Table 2 : Severity and blood alcohol level

Mild	1.impaired concentration , behaviour and self control 2.decreased psychomotor activity 3.black-outs 4.minimal cerebellar symptoms – nystagmus

	5.extreme excitement, violence and psychotic reaction 6.hangover symptoms- nausea, vertigo,malaise, headache, tremors, lack of concentration
Moderate	1.psychosocially uncontrolled 2.aggressive on exogenous stimuli 3.euphoria, dysphoria or depression 4. nystagmus, slurred speech, ataxia, vertigo 5. nausea, tachycardia, sweating
Severe	1.disorientation, somnolescence and coma 2.marked cerebellar and autonomic symptoms 3.fatal respiratory paralysis

Table 4: Severity and symptoms of alcohol intoxication

DISORDERS OF CNS

ALCOHOL INDUCED SEIZURES

Seizures are the most common neurological effect of chronic alcohol abuse regardless of the duration of abuse.[11,12] The prevalence rate is about 20-35 %. Both alcohol intoxication as well as alcohol withdrawal can cause seizures. Usually cessation of alcohol for about one to two days can lead to generalised tonic clonic seizures or focal seizures. The pathophysiological mechanisms causing seizures in alcoholics remains unknown, but dysregulation

of potassium, magnesium , calcium and neurotransmitters such as glutamate and GABA are being proposed.

Clinical examination reveals no neurological deficits. EEG is normal. Minor EEG slowing and decreased alpha activity may be seen in some patients. EEG and CT scan-brain diagnosis is required to exclude focal brain injury in new onset epileptic seizures. Status epilepticus may occur in about 2 to 10% of the patients. About 30% of the patients with withdrawal seizures may progress to delirium tremens.[13]

Focal seizures are suggestive of focal brain injury such as head injury, haemorrhage, encephalopathy, malignancy and metabolic disorders such as hypoglycemia and electrolyte disturbances. Clinical examination shows focal neurological signs, such as motor, sensory or cranial nerve dysfunction. Therefore, laboratory investigations, CT scan and EEG should be performed. EEG may show paroxysmal or non-paroxysmal, focal or diffuse abnormalities. Depending on detected focal brain injury, further investigations or procedures may be considered. In general, these patients require hospital admission.

In addition, seizures due to pre-existing genuine epilepsy may be provoked or unmasked by alcohol abuse. EEG may show focal spiking. The first appearance of an seizure requires a detailed examination and investigations, but usually no acute treatment for the seizure is necessary . If patient has symptomatic epilepsy or develops status epilepticus , treatment is

necessary. If the history is unreliable, antiepileptic drugs can be given for a short duration, but long-term treatment is usually not indicated for alcohol-induced seizures because of usually coexisting alcoholic liver disease and poor compliance. Prophylactic anticonvulsant therapy are recommended in alcoholics with known withdrawal seizures during detoxification.

CEREBROVASCULAR DISEASES

Chronic alcohol abuse has an increase in the risk of intracerebral and subarachnoid haemorrhages. It lowers the prognosis of bleeding from intracerebral aneurysms and also increases the relapse rate.[14] The factors responsible for higher incidence of acute intracerebral haemorrhage and chronic subdural hematoma are head injury , seizures and concomitant liver disease due to alcohol abuse. Chronic alcohol abusers are more prone for ischemic disorders due to elevated blood pressure, changes in renin, aldosterone, cortisol and vasopressin levels and due to alteration in adrenergic transmitter system.[15] Arterial hypertonia and cerebral vasospasm due to sympathetic activation may occur in alcohol intoxication as well as alcohol withdrawal.[16] Excess smoking habit among alcoholics increase the risk of atherosclerosis. However , cerebrovascular and cardiovascular protective effect has been demonstrated when alcohol is taken in small amounts on a regular basis.[17]

CEREBELLAR DEGENERATION

Cerebellar atrophy may develop in about 30% of patients with chronic alcohol intake beyond fourth decade. Patients may progressively develop stance and gait ataxia , tremors , nystagmus and dysarthria. On alcohol abstinence , thiamine therapy and physiotherapy initial stages may be reversible.

DEMENTIA AND ENCEPHALOPATHY

Cognitive impairment is seen in about 75% of chronic alcohol abusers.[18] Wernicke's encephalopathy is characterised by triad of global confusion , ataxia and ophthalmoplegia.[19] Only about 10 % of the patients exhibit all the three features. Korsakoff's psychosis is characterised by memory impairment, confabulation, confusion and personality changes . In about 80 % of the patients MRI shows atrophy of mammillary bodies.[20] In acute phase the mortality of Wernicke's encephalopathy varies between 10 to 20 % due to midbrain haemorrhage.[21] Another important cause of encephalopathy in these patients are due to hepatic damage.

ALCOHOL WITHDRAWAL SYNDROME

A state in patients consuming alcohol for prolonged periods ,who suddenly stops the intake or reduces the amount of alcohol is referred to as Alcohol withdrawal syndrome (AWS). About 50% of alcohol dependent patients shows the symptoms and signs of AWS after stoping or reducing the

amount of alcohol depending on the total duration of alcohol consumption and quantity of alcohol consumed.[22] The correct dose of alcohol causing physical dependence is unclear and widely varies. Patients with moderate to severe AWS consumes approximately 300 g of alcohol per day.[23.24] It takes atleast 6 years for the appearance of first withdrawal symptom on cessation of alcohol ,from the onset of alcohol abuse.[25]

DSM-IV CRITERIA FOR ALCOHOL WITHDRAWAL

A. Cessation of (or reduction in) alcohol use that has been heavy and prolonged.

B. Two (or more) of the following, developing within several hours to a few days after

criterion A:

1. Autonomic hyperactivity (e.g., sweating or pulse rate greater than 100)

2. Increased hand tremor

3. Insomnia

4. Nausea or vomiting

5. Transient visual, tactile, or auditory hallucinations or illusions

6. Psychomotor agitation

7. Anxiety

8. Grand-mal seizures

C. The symptoms in criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

Symptoms of AWS

- ✓ Tremors
- ✓ Nausea / vomiting
- ✓ Increased sweating
- ✓ Tachycardia
- ✓ Lack of sleep
- ✓ Headache
- ✓ Fever
- ✓ anxiety
- ✓ Psychomotor agitation
- ✓ Lack of orientation
- ✓ Attention deficit
- ✓ Hallucinations
- ✓ Seizures

Abnormal Laboratory Parameters in AWS

- Increase in liver enzymes (AST, ALT, GGT)
- Increased alkaline phosphatase
- Reduced platelet count
- Dimorphic anemia (MCV, MCH)
- Increase in serum ammonia and bilirubin
- Electrolyte abnormalities (hypokalemia, hypocalcemia, hypomagnesemia, hyponatremia)

TREATMENT OF AWS

Clinical Institute Withdrawal Assessment Scale for Alcohol, revised (CIWA-Ar) is an objective criteria for assessment of the severity of AWS and is also used as a guide for the treatment of AWS.[26] The scale can be applied hourly or on a daily basis in patients suffering from AWS and is helpful in dosing the medications according to the severity.

The following factors determines the decision to treat AWS as an inpatient or outpatient , with or without a pharmacological agent

1. The duration of alcohol abuse,
2. Presence of concomitant diseases, and
3. Previous history of AWS.[27]

Factors responsible for the development of severe withdrawal syndrome are seen in patients with

- History of alcohol abuse for more than 6 years,
- Elderly,
- History of seizures,
- Delirium
- History of detoxifications .

Benzodiazepines are the first drug of choice in the treatment of AWS.[28] They are the most effective drug in treating withdrawal symptoms such as tremors, anxiety, insomnia, for prevention of seizures and in reducing the risk of developing delirium tremens.[29] Diazepam are most efficient against withdrawal seizures than lorazepam or oxazepam.[30] . Intravenous benzodiazepines are better choice in severe withdrawal symptoms and delirium.[31] The various parenteral formulations available are diazepam, chlordiazepoxide, midazolam and lorazepam.

Among the anticonvulsants, carbamazepine has been proved to be very helpful in AWS. However , it is not helpful in case of delirium tremens. It is also useful in preventing seizures and has no cross-tolerance with ethanol .[32]

As an add on therapy to benzodiazepines, antipsychotics (e.g., haloperidol) can be used in case of delirium. Hallucinations can be treated with haloperidol successfully. Sympatholytics for symptomatic improvement.

MECHANISM OF HYPOCALCEMIA IN ALCOHOLICS

Alcohol abuse leads to multiple effects on kidney functions including water, electrolyte and acidbase balance.[33-35] Among the electrolyte abnormalities noted in alcoholic patients, hypocalcemia is a common finding and may be as a result of various pathophysiologic mechanisms, which are not yet well understood.

i. Magnesium depletion could lead to decreased calcium levels largely due to impaired release of parathormore (PTH) and also due to skeletal resistance to the action of PTH .[36]
ii. The tubular reabsorption of calcium in kidneys is reduced due to the effect of ethanol in decreasing the Na+,K+-ATPase activity in the proximal tubular cells .[37]
iii. The suppressed secretion of PTH resulting from acute alcohol consumption[38] or hypomagnesemia could further contribute to the decreased tubular reabsorption of calcium.
iv. Renal PTH resistance is induced by severe respiratory alkalosis resulting in hyperphosphatemia, calciuria and hypocalcemia.[39]

v. chronic pancreatitis in alcoholics can cause vitamin D3 deficiency due to its decreased intestinal absorption .[40]

DIAGNOSIS OF ALCOHOL RELATED SEIZURES

HISTORY TAKING

A detailed drinking history that indicates alcohol overuse should be obtained to make a clinical diagnosis of alcohol related seizures. Frequently the true levels of alcohol consumption are under reported. A detailed history of recent alcohol intake should be asked whenever possible. History of alcohol withdrawal symptoms should be obtained.

A detailed drinking history should include both the frequency and quantity of alcohol intake during the past 5 days, any changes in drinking pattern as well as the time of last alcohol intake should be asked.

Many legal or illegal pharmacological agents have the tendency to cause seizure due to their direct neurotoxic effect (eg: antidepressants, antipsychotics) or either due to withdrawal (eg:benzodiazepines). Thus, history of any other drug abuse should be asked for as they can complicate the clinical picture.

QUESTIONNAIRES

Alcohol overuse and dependence as well as excessive alcohol consumption can be graded and revealed by using structured questionnaires. Questionnaires should be brief and reliable. The most commonly used four simple question questionnaire is the CAGE criteria.[41] It is easy to remember and has a fair accuracy. Sensitivity and specificity data for the CAGE range from 73 to 97% and 72 to 96%, respectively . But, the drawback of this questionnaire is that it fails to recognise binge drinking. This can be assessed by asking the history of taking largest number of drinks in one single occasion.

CAGE QUESTIONNAIRE:

Cut down	1. Have you ever felt that you ought to cut down on your drinking?
Annoyed	2. Have people annoyed you by criticizing your drinking?
Guilty	3. Have you ever felt bad or guilty about your drinking?
Eye opener	4. Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover?

Table 4 : CAGE criteria

Another commonly used questionnaire model is published in 1989 by the World Health Organization [42.43] the Alcohol Use Disorder Identification Test (AUDIT) consists of ten questions assessing frequency and quantity of alcohol use, dependence symptoms, personal and social harm attributed to excessive alcohol use. This is a 10 item model which takes about 2-3 minutes to interview. It is graded from 0 -40. Responses to individual questions are given a score varying from 0 to 4, with a test score of 8 or higher indicating the presence of hazardous drinking. For patients consuming lower drinking levels, AUDIT has a better accuracy than CAGE criteria . the major disadvantage is it is difficult to remember and consumes more time to interview amidst busy medical settings.

AUDIT

1.How often do you have a drink containing alcohol?	(0) Never (1) Monthly or less (2) Two to four times a month (3) Two to three times a week (4) Four or more times a week
2. How many drinks containing alcohol do you have on a typical day when you are drinking?	(0) 1 or 2 (1) 3 or 4 (2) 5 or 6 (3) 7 to 9 (4) 10 or more

3. How often do you have six or more drinks on one occasion?	(0) Never (1) Less than monthly (2) Monthly (3) Weekly (4) Daily or almost daily
4. How often during the last year have you found that you were not able to stop drinking once you had started?	(0) Never (1) Less than monthly (2) Monthly (3) Weekly (4) Daily or almost daily
5.How often during the last year have you failed to do what was normally expected from you because of drinking?	(0) Never (1) Less than monthly (2) Monthly (3) Weekly (4) Daily or almost daily
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?	(0) Never (1) Less than monthly (2) Monthly (3) Weekly (4) Daily or almost daily
7. How often during the last year have	(0) Never

you had a feeling of guilt or remorse after drinking?	(1) Less than monthly (2) Monthly (3) Weekly (4) Daily or almost daily
8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?	(0) Never (1) Less than monthly (2) Monthly (3) Weekly (4) Daily or almost daily
9. Have you or someone else been injured as a result of your drinking?	(0) No (2) Yes, but not in the last year (4) Yes, during the last year
10. Has a relative or a friend, or a doctor or other health worker, been concerned about your drinking or suggested you cut down?	(1) Now (2) Yes, but not in the last year (4) Yes, during the last year

Table 5: AUDIT criteria

Other questionnaires available widely are MICHIGAN ALCOHOLISM SCREENING TEST (MAST) and Munich Alcoholism Test (MALT). If time consumption is of a concern, two abbreviated versions of the MAST, the ten-question Brief MAST (BMAST) and the thirteen question Short

MAST(SMAST), have been developed and can be widely used as a suitable alternative measures.

BIOCHEMICAL PARAMETERS USED FOR DIAGNOSIS OF ALCOHOLISM

•Alcohol levels in

- ✓ breath, blood, urine

•Blood constituents

- ✓ Total Proteins
- ✓ Albumin
- ✓ Globulins (gamma and alpha)
- ✓ Carbohydrate-deficient transferrin (CDT)

•Complete blood count

- ✓ Erythrocyte count
- ✓ Leukocyte count
- ✓ Packed cell volume
- ✓ Mean corpuscular hemoglobin (MCH)
- ✓ Mean corpuscular volume (MCV)

•Blood lipids

- ✓ Total Cholesterol

- ✓ Triglycerides
- ✓ HDL and LDL- cholesterol

•Liver function tests

- ✓ Aspartate aminotransferase (AST)
- ✓ Alanine aminotransferase (ALT)
- ✓ AST:ALT ratio
- ✓ Alkaline phosphatase(ALP)
- ✓ gamma-glutamyl transferase (GGT)
- ✓ GGT:ALP ratio
- ✓ Glutamate dehydrogenase

Though questionnaire-based interview model is more sensitive than using biomarkers for detecting alcohol overuse , these biomarkers can be used when information on alcohol consumption is not reliable or unavailable.[44-47]

The most recently identified biochemical marker for alcohol abuse has been found out to be carbohydrate-deficient transferrin. Normal human transferrin contains three or more sialic acid residues. In individuals with excessive alcohol abuse there is an elevated concentrations of transferrin isoforms with a decreased content of sialic acids and other carbohydrate residues.[48]

The two sensitive markers for alcohol overuse is carbohydrate deficient transferrin (CDT) and gamma glutamyl transferase (GGT). Both the biomarkers have poor accuracy in screening alcohol related seizures.[49] A combination of both tests have increased sensitivity.[50-52] As the level of intoxication is very important in any alcohol related seizures , blood alcohol levels should be measured whenever possible.[53]

PATIENT EXAMINATION AND OBSERVATION

The clinical institute withdrawal assessment scale (CIWA-Ar) questionnaire model can be used to grade the severity of alcohol withdrawal symptoms.[54] This can be used as a supportive tool to make decision regarding whether to keep or discharge the patient. This model takes about 2-5 minutes to administer. The grading of severity varies from 0-67 .

Nearly 90% of the alcohol withdrawal seizures occur in the first 48 hours of stopping prolonged drinking. The patient should be observed for atleast 24 hours as inpatient. A clinical assessment should be made later depending on the development of symptoms of alcohol withdrawal.

The symptoms and signs used to differentiate the post-ictal state of primary seizures and the early alcohol withdrawal syndrome are as follows. In a patient with primary seizure , the patient will have post ictal sleep or drowsiness with a calm mood whereas patients in alcohol withdrawal will be sleepless with

an anxious mood. Tremors and sweating are usually absent in primary seizures whereas it is a predominant feature in alcohol withdrawal. On examination the pulse rate and blood pressure will be normal in primary seizures whereas alcohol withdrawal can have tachycardia and increased blood pressure. Alcohol withdrawal can have increased temperature and their arterial blood analysis may show respiratory alkalosis.

NEUROIMAGING

Any patient presenting with first episode of alcohol related seizures should have their cerebral computed tomography (CT) done , as the incidence of structural intracranial lesions is very high in alcohol overusing patients.[55,56] Etiologies other than simple alcohol withdrawal such as brain contusion, subdural hematoma, combined drug and alcohol overuse are possible causes for seizures later than 48 hours .[57] Repeat neuroimaging is not necessary in patients presenting with repeated typical alcohol related seizures . Repeat neuroimaging is necessary in the following situations:

1. Change in seizure type and frequency
2. Seizures occurring later than 48 hours after cessation of alcohol consumption.
3. Unusual presentations.

ELECTROENCEPHALOGRAPHY (EEG)

The incidence of EEG abnormalities is lower in patients with alcohol related seizures when compared with patients with seizures of other etiologies. Thus, EEG is done in patients presenting with first episode of alcohol related seizures to rule out other possible aetiologies of seizures. Repeat investigation is necessary only if alternative aetiology is suspected in patients with repeated alcohol withdrawal seizures.

PATIENT MANAGEMENT

The acute management of alcohol related seizures focuses on the complications of alcohol abuse and dependence such as

- ✓ Thiamine deficiency
- ✓ Electrolyte disturbance
- ✓ Infections
- ✓ Acute intracranial lesions
- ✓ Presence of alcohol withdrawal syndrome

THIAMINE THERAPY

Excessive alcohol consumption causes thiamine deficiency both by reducing absorption and by increasing excretion. The incidence of Wernicke's encephalopathy is about 5-14%. About 80% of patients having CNS pathology suggestive of thiamine deficiency are chronic alcohol abusers. Identification of

patients with thiamine deficiency is very difficult, but the consequences of thiamine deficiency undertreated is very severe. Therefore, wherever suspected, treatment of thiamine deficiency should be initiated.

In chronic alcoholics the intestinal absorption of thiamine is severely impaired , hence oral administration of thiamine is insufficient.[58] In a recent Cochrane review , it could be concluded that dose of 200 mg thiamine daily was better than 5 mg daily.[59] Amny trials on imminent and manifest Wernicke's encephalopathy suggest a daily dose of about 200 mg parenteral thiamine for about 5 days . Few studies recommend continued treatment for period of 2 weeks or longer.

Thus any patients presenting in the emergency department with symptoms of alcohol overuse or alcohol related seizures, should be treated with prophylactic thiamine therapy before starting any carbohydrate containing fluids or food.

TREATMENT OF ELECTROLYTE DISTURBANCES

Due to large quantity of fluid intake, alcoholic abusers are more prone for hyponatremia. Hyponatremia in alcoholics generally have a benign course clinically[60] which usually gets corrected on alcohol cessation and on restoration of normal diet.[61] If correction is needed , the rate of sodium correction should

not be more than 10 mmol/day.[62] Rapid correction of hyponatremia can lead to central pontine myelinolysis.[63]

Hypomagnesemia and respiratory alkalosis may be present in alcohol withdrawal. Hypomagnesemia correction may increase the threshold for seizures in the initial phase of ethanol withdrawal.[64] Hypomagnesemia can cause unresponsiveness to parenteral thiamine therapy.[65] There is no sufficient data supporting the routine correction of hypomagnesemia in alcoholics.

PRIMARY PREVENTION OF ALCOHOL WITHDRAWAL SEIZURES

When pharmacological treatment is needed, benzodiazepines should be drug of choice for the primary prevention of seizures in a person with alcohol withdrawal, as well as for treatment of the alcohol withdrawal syndrome. The drugs of choice are diazepam and lorazepam.

SECONDARY PREVENTION

Following a withdrawal seizure, the recurrence risk within the same withdrawal episode is 13 – 24%.[66] For the secondary prevention of AWS, benzodiazepines should be used. Lorazepam reduces recurrence risk significantly . [67]Phenytoin will not prevent the relapse of seizures in individuals who had several episodes during the same withdrawal episode.

MANAGEMENT OF SEIZURES IN PATIENTS WITH CURRENT ALCOHOL OVERUSE

The management of epilepsy in patients with alcohol abuse includes detailed counselling and information about the seizure - precipitating effect of ethanol. The concurrent withdrawal of alcohol and anticonvulsant drugs may lead to serious effects. Prescription of antiepileptic drugs to alcohol abusers is often useless, which may increase the occurrence of seizures due to drug - alcohol interactions, poor compliance and drug overuse.[68] The anticonvulsant drugs prescribed for such patients should be tolerated well when taken with ethanol and should have a benign side effect and should be safe in overdose also[69], and should have a suppressive action on drinking behaviour. In a few studies, sodium valproate, carbamazepine , gabapentin, and pregabalin have been reported to decrease alcohol consumption [70-73] , and topiramate has been shown to reduce alcohol craving recently . [74]

DISTRIBUTION OF CALCIUM AND CALCIUM HOMEOSTASIS

Most calcium is bound and associated with bone structures (99%). The majority of free calcium, either in diffusible non ionized form or in ionized form (Ca2+), is found in the intracellular and extracellular fluid compartments. There is a steep concentration gradient of Ca2+ between the intracellular and the extracellular milieu.

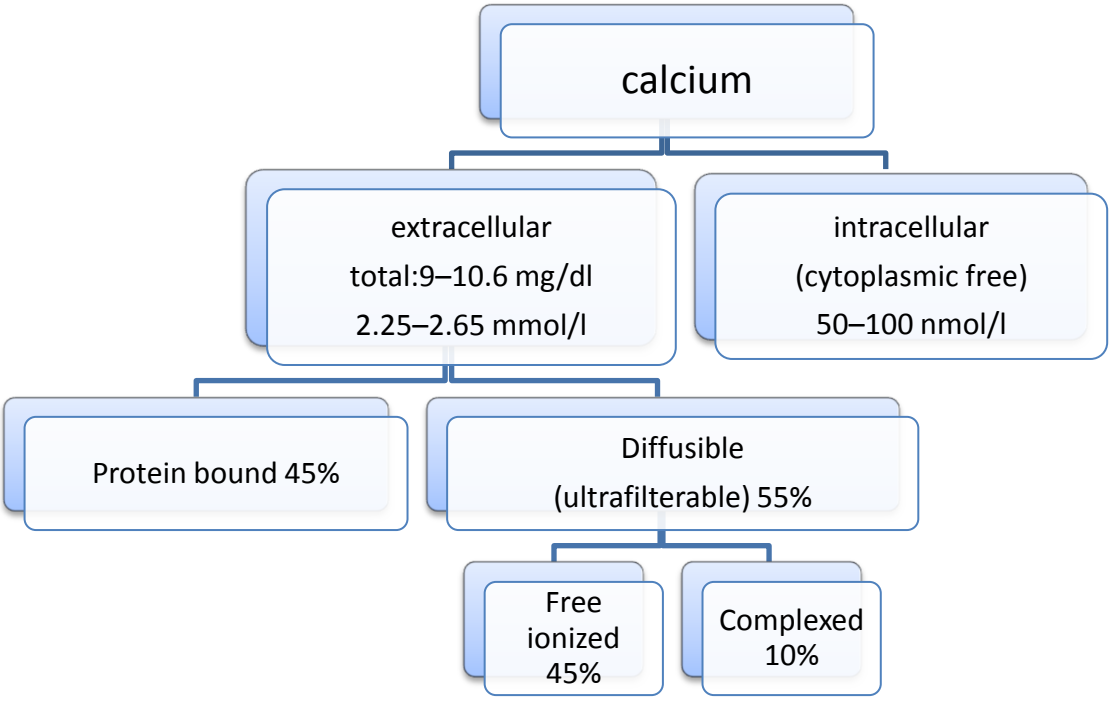


Fig 2: Distribution of calcium in extracellular and intracellular spaces.

The plasma concentration of Ca^{2+} is tightly regulated by the actions of parathyroid hormone (PTH) and calcitriol (1,25-dihydroxycholecalciferol). The physiologic role of other calcium regulatory hormones, such as calcitonin, estrogens, and prolactin, is less clear.

Figures 3 and 4 demonstrate the physiologic defence mechanisms used to counter changes in serum Ca2+ levels. Serum Ca2+ levels are also influenced by acid-base status; alkalosis causes a decrease in Ca2+, and acidosis has the opposite effects.

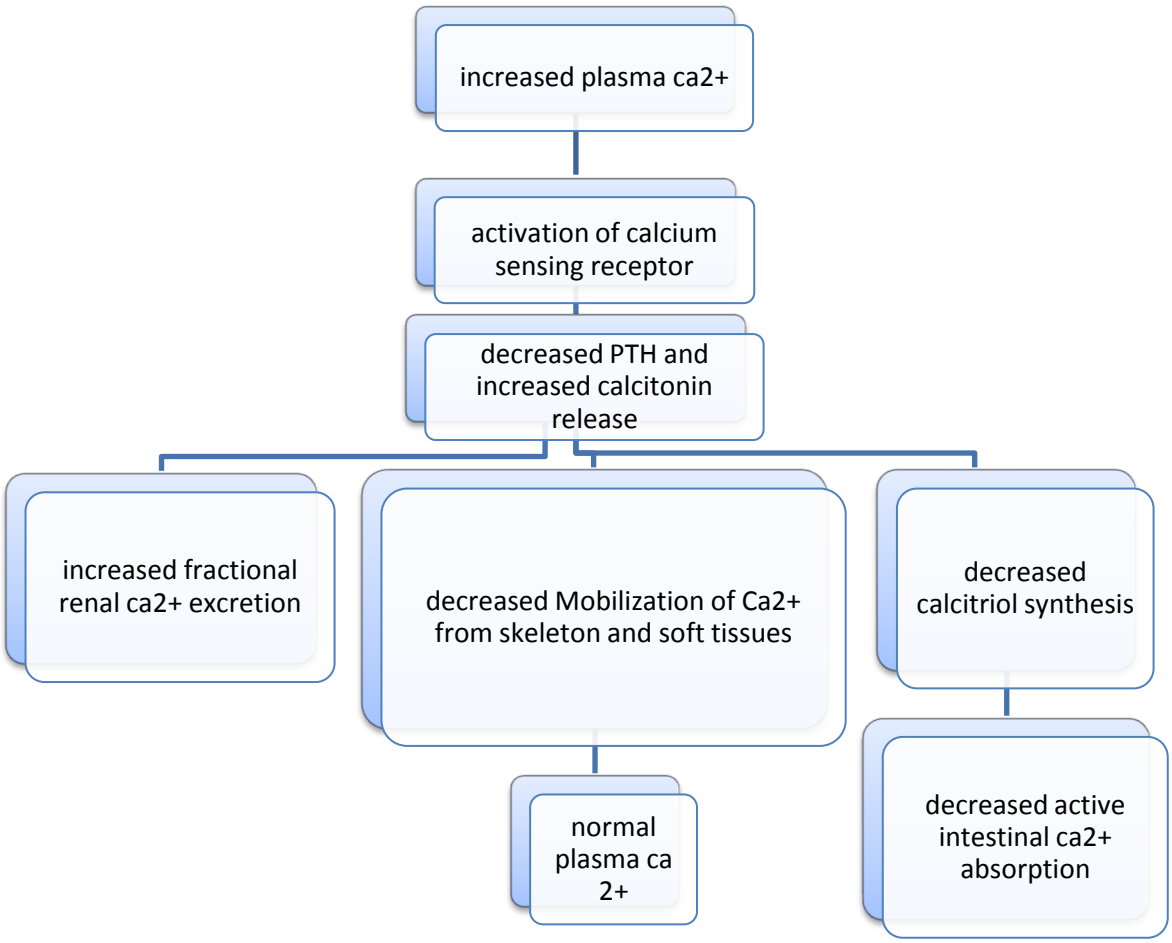


Fig 3 : Defence against hypercalcemia

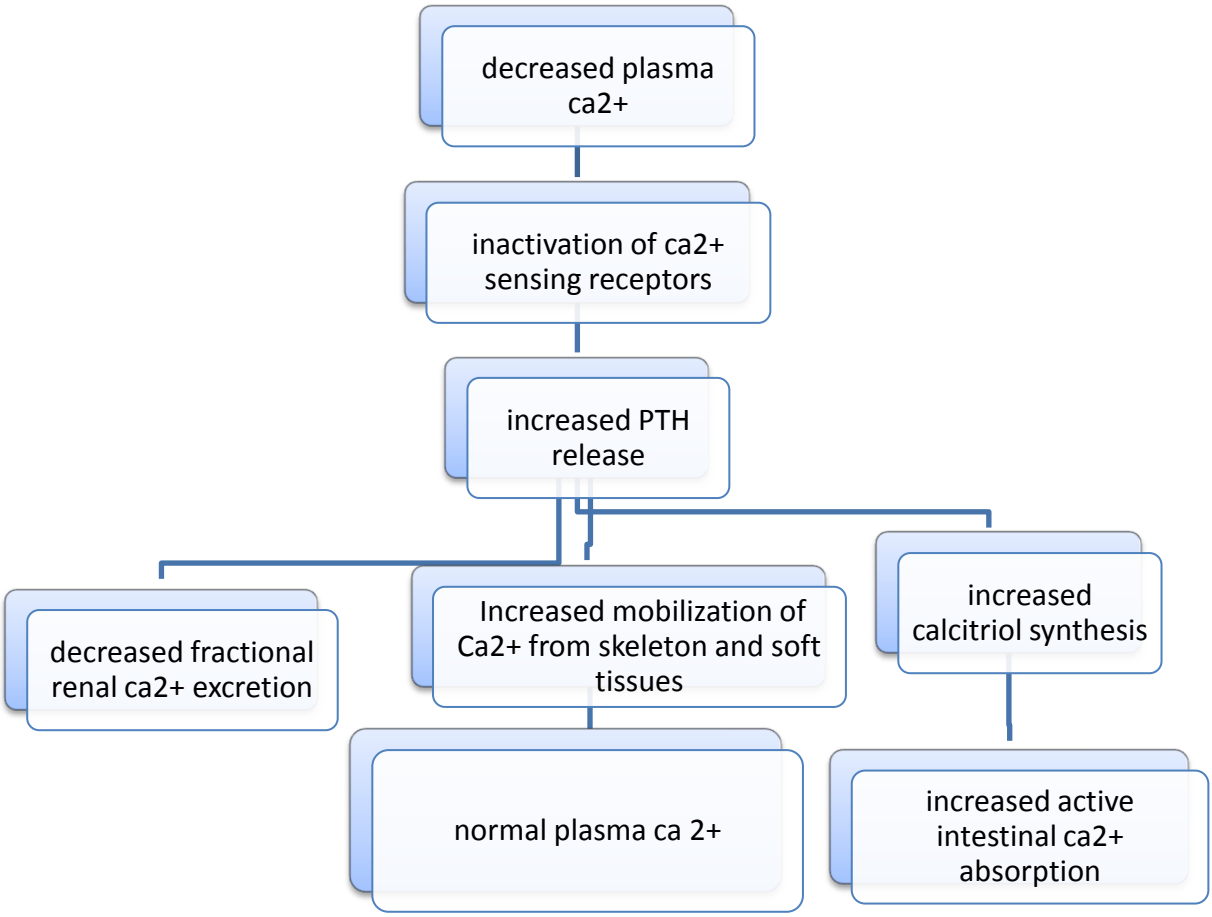


Fig 4: Defence against hypocalcemia

Long-term maintenance of calcium homeostasis depends on the adaptation of intestinal Ca2+ absorption to the needs of the organism, on the balance between bone accretion and resorption, and on urinary excretion of calcium (fig 5).

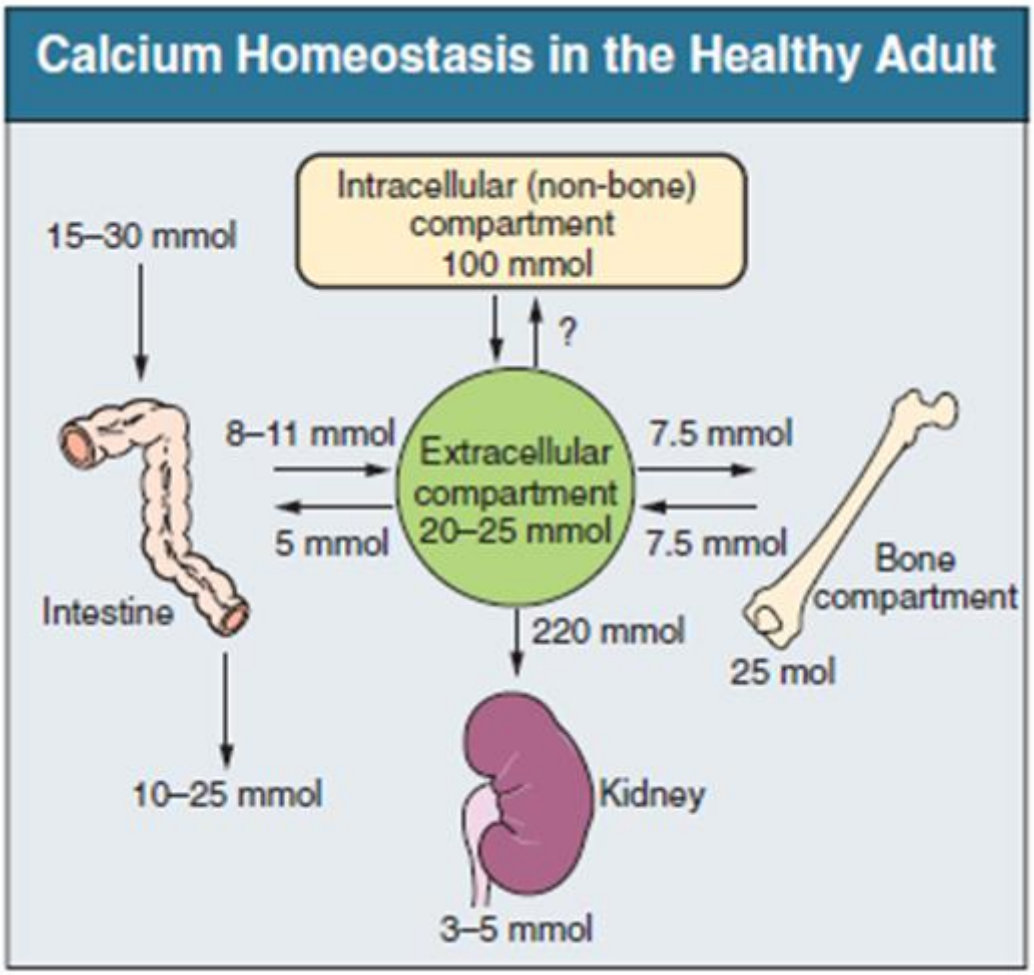


Fig 5: Calcium homeostasis in the healthy adult. Net zero Ca2+ balance is the result of net intestinal absorption (absorption minus secretion) and urinary excretion.

INTESTINAL, SKELETAL, AND RENAL HANDLING OF CALCIUM

Gastrointestinal calcium absorption is a selective process; only about 25% of total dietary calcium is absorbed. Ca2+ transport across the intestinal wall occurs in two directions: absorption and secretion. Absorption can be subdivided into transcellular and paracellular flow .[75] Transcellular calcium flux takes place through the recently identified TRPV6 calcium channel. Calcitriol is

its most important hormonal regulatory factor.[76] After binding to and activating the vitamin D receptor (VDR), calcitriol increases active transport by inducing the expression of TRPV6, calbindin D9k, and Ca2+-ATPase (PMCA1b). Other hormones, including estrogens, prolactin, growth hormone, and PTH, also stimulate Ca2+ absorption, either directly or indirectly. The amount of dietary calcium intake also regulates the proportion of calcium absorbed through the gastrointestinal tract.

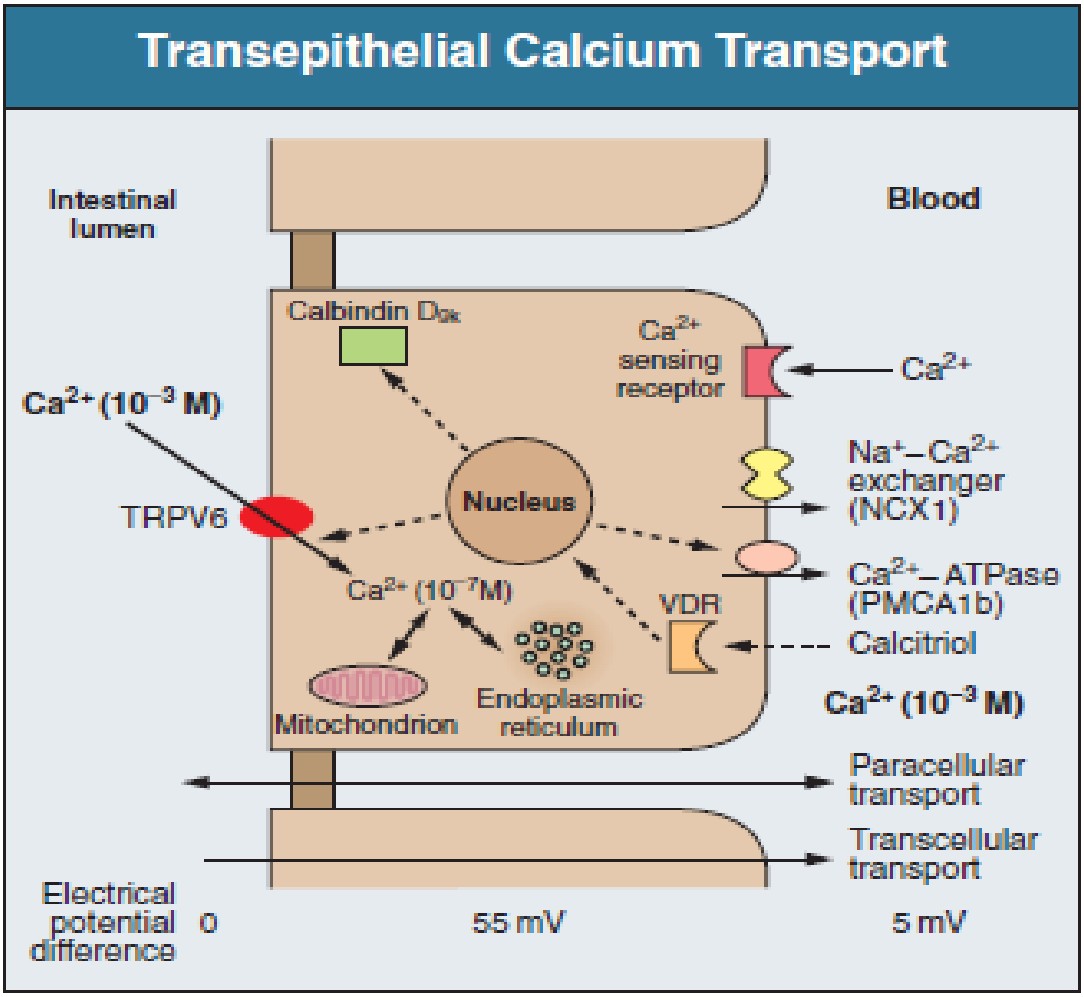


Fig 6: Transepithelial calcium transport in the small intestine

Cutaneous synthesis on exposure to UV light converts 7-dehydrocholesterol to vitamin D substrate (cholecalciferol). Cholecalciferol has minimal inherent biologic activity and requires two hydroxylation steps for full hormonal activity. 25-Hydroxylation occurs in the liver. Further hydroxylation to 1,25-dihydroxyvitamin D (calcitriol) occurs predominantly in the kidney, but also occurs in non-renal tissues.

Increased calcium absorption is required in puberty, pregnancy, and lactation. In all these states, calcitriol synthesis is increased. Intestinal Ca2+ absorption is also increased in vitamin D excess and acromegaly. Rarely, the ingestion of calcium and alkali in large quantities can overwhelm gastrointestinal checks on calcium absorption, resulting in hypercalcemia (milk-alkali syndrome); however, innate limitations on gastrointestinal calcium absorption prevent this condition from occurring in most individuals.

A decrease in intestinal Ca2+ transport occurs in a low Ca2+/phosphate ratio in the food, a high vegetable fibre and fat content of the diet, corticosteroid treatment, estrogen deficiency, advanced age, gastrectomy, intestinal malabsorption syndromes, diabetes mellitus, and renal failure. The decrease in Ca2+ absorption in the elderly probably results from multiple factors in addition to lower serum calcitriol and intestinal VDR levels.[77] The net balance between Ca2+ entry and exit fluxes is positive during skeletal growth in children, zero in young adults, and negative in the elderly.

Exchangeable skeletal Ca2+ contributes to maintenance of extracellular Ca2+ homeostasis. Several growth factors, hormones, and genetic factors participate in the differentiation from the mesenchymal precursor cell to the osteoblast and the maturation of the osteoclast from its granulocyte macrophage precursor cell . The regulation of bone formation and resorption involves a large number of hormones, growth factors, and mechanical factors.[78]

The kidneys play a major role in the minute-by-minute regulation; the intestine and the skeleton ensure homeostasis in the mid and long term. To perform its task, the kidney uses a complex system of filtration and reabsorption. The adjustment of blood Ca2+ is mainly achieved by modulation of tubular Ca2+ reabsorption in response to the body's needs, perfectly compensating minor increases or decreases in the filtered load of calcium at the glomerular level, which is normally about 220 mmol (8800 mg) in 24 hours.

In the proximal tubule, most of the Ca2+ is reabsorbed by convective flow (as for Na+ and water); in the distal segments of the tubule, the transport mechanisms are more complex. States of excess volume delivery to the kidney, such as a high-sodium diet, diminish the concentration gradient between proximal tubule and peritubular capillary, reducing calcium absorption and increasing calcium in the urine. This mechanism is thought to play a role in the pathogenesis of calcium-based kidney stones. On the other hand, volume

depletion states increase salt, water, and (by convection) calcium reabsorption in the proximal tubule, exacerbating states of hypercalcemia.

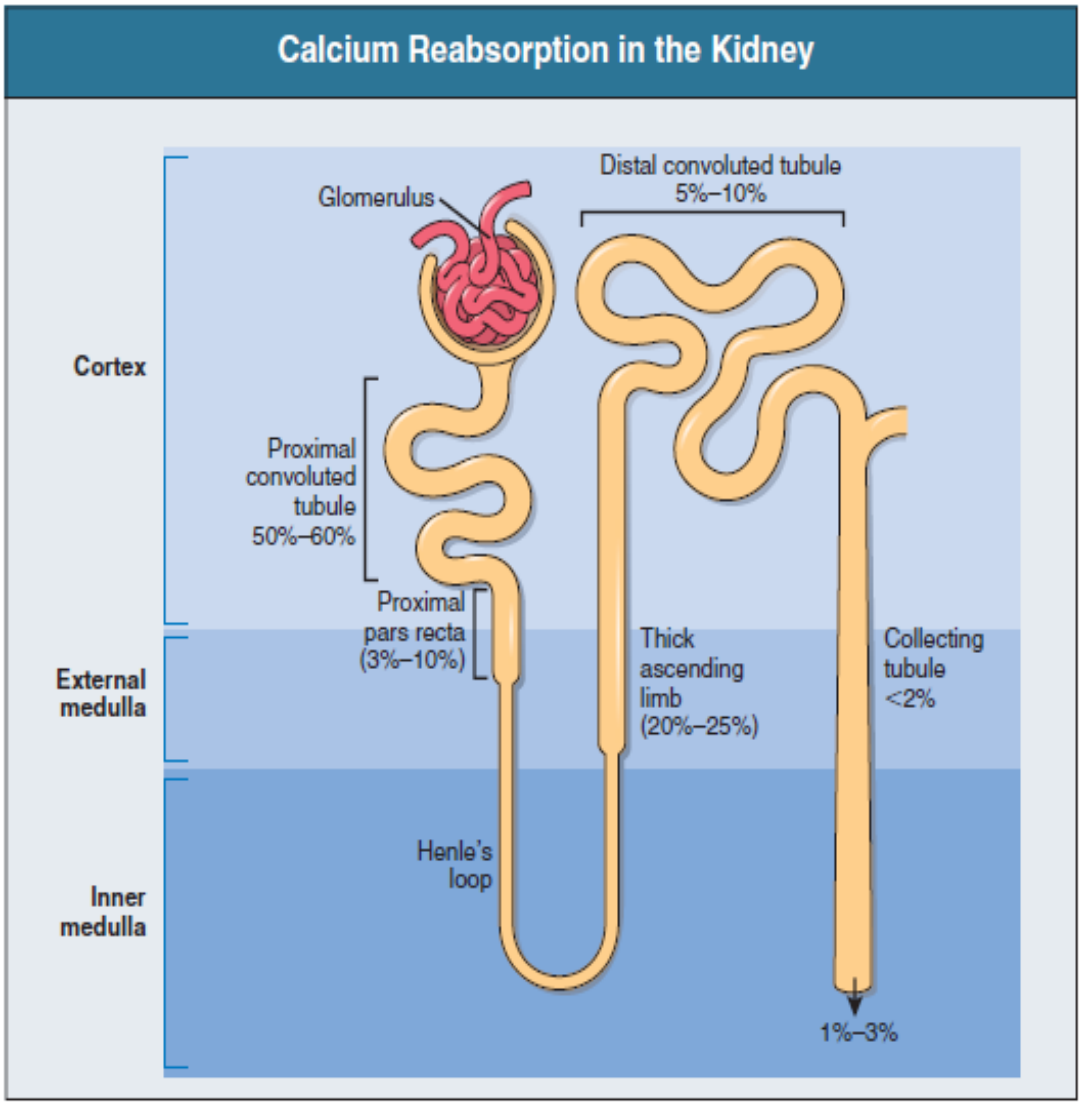


Fig 7: Sites of calcium reabsorption in various segments of the renal tubule

In the thick ascending loop, the transport of Ca2+ is primarily passive by the paracellular route, depending on the electrical gradient, with the tubular

lumen being positive, and also on the presence of claudin 16 in the tight junction. At this step, Ca^{2+} transport is enhanced by PTH, probably through an increase in paracellular permeability, but it is reduced by an increase in extracellular Ca^{2+} involving the Ca^{2+}-sensing receptor (CaRG). Specifically, stimulation of CaRG by elevated serum calcium levels decreases the activity of rectifying K^+ channels (ROMK), resulting in less Na^+-K^+-$2Cl^-$ cotransporter activity and less calcium reabsorption in this segment. In the distal tubule, Ca^{2+} transport is primarily active by the transcellular route, through TRPV5 located in the apical membrane and coupled with a specific basolateral Ca^{2+}-ATPase (PMCA1b) and a Na^+-Ca^{2+} exchanger (NCX1). Both PTH and calcitriol regulate distal tubular transport.

Numerous factors control the glomerular filtration and tubular reabsorption of Ca^{2+}. Elevated renal blood flow and glomerular filtration pressure (during extracellular fluid volume expansion) lead to an increase in filtered load, as do changes in the ultrafiltration coefficient Kf and an increase in glomerular surface. True hypercalcemia also increases ultrafilterable calcium, whereas true hypocalcemia decreases it. PTH decreases glomerular Kf and thus reduces the ultrafiltered calcium load; it also increases Ca^{2+} reabsorption in the distal nephron. However, PTH and PTH-related peptide (PTHrP) also induce hypercalcemia, and because of the increase in serum calcium, the excretion of filtered calcium is elevated overall. Both extracellular Ca^{2+} and intracellular

Ca^{2+} reduce tubular calcium reabsorption by activating CaRG, and the effect of extracellular Ca^{2+} is enhanced by calcimimetics.

Metabolic and respiratory acidosis lead to hypercalciuria, respiratory acidosis through an increase in plasma Ca^{2+} and metabolic acidosis through calcium release from bone and an inhibitory effect on tubular Ca^{2+} reabsorption. Conversely, alkali ingestion reduces renal excretion of calcium. The enhancing effect of phosphate depletion on urinary calcium elimination can partly occur through changes in PTH and calcitriol secretion.

Dietary factors modify urinary excretion of calcium, mostly by their effects on intestinal Ca^{2+} absorption. Several classes of diuretics act directly on the tubules: loop diuretics and mannitol favor hypercalciuria, with a major impact on the thick ascending limb, whereas the thiazide diuretics and amiloride induce hypocalciuria.

HYPERCALCEMIA

Increased plasma total calcium concentration can result from an increase in plasma proteins (false hypercalcemia) or from an increase in plasma ionized Ca^{2+} (true hypercalcemia). Only the latter leads to clinically relevant hypercalcemia. When only the value for the total plasma calcium concentration is available rather than the free level ions, plasma Ca^{2+} can be estimated by

taking into account plasma albumin: an increase in albumin of 1.0 g/dl reflects a concomitant increase of 0.20 to 0.25 mmol/l (0.8 to 1.0 mg/dl) in plasma calcium

ETIOLOGIES OF HYPERCALCEMIA

- ✓ Primary hyperparathyroidism
- ✓ Primary adenoma
- ✓ Primary diffuse hyperplasia
- ✓ Primary adenocarcinoma
- ✓ Multiple endocrine neoplasias (MEN-1, MEN-2A)

Other endocrinopathies

- ✓ Hyperthyroidism
- ✓ Acromegaly
- ✓ Pheochromocytoma
- ✓ Acute adrenal insufficiency
- ✓ Tertiary hyperparathyroidism
- ✓ Chronic renal failure

Neoplastic diseases

Solid tumors

- ✓ Breast cancer
- ✓ Bronchial cancer

- ✓ Renal cancer
- ✓ Thyroid cancer

Neoplasias of hematopoietic system

- ✓ Myeloma
- ✓ Lymphoma
- ✓ Leukemia

Vitamin intoxication

- ✓ Hypervitaminosis D
- ✓ Hypervitaminosis A

Familial hypocalciuric hypercalcemia

Granulomatous diseases

- ✓ Sarcoidosis
- ✓ Tuberculosis
- ✓ Berylliosis
- ✓ Coccidioidomycosis
- ✓ Histoplasmosis
- ✓ Leprosy
- ✓ Silicon-induced granulomas

Pseudohyperparathyroidism (Jansen's disease)

Others

- ✓ Immobilization
- ✓ Treatment with certain medications (thiazides, lithium, theophylline)
- ✓ Milk-alkali syndrome
- ✓ Recovery phase of acute renal failure (rhabdomyolysis)
- ✓ False hypercalcemia (by hemoconcentration)

Clinical Manifestations

The severity of clinical symptoms and signs caused by hypercalcemia depends not only on the degree but also on the velocity of its development. Severe hypercalcemia can be accompanied by few manifestations in some patients because of its slow, progressive development, whereas much less severe hypercalcemia can lead to major disorders if it develops rapidly.

First symptoms

- ➢ increasing fatigue,
- ➢ muscle weakness,
- ➢ inability to concentrate,
- ➢ nervousness,
- ➢ increased sleepiness,
- ➢ depression.

- gastrointestinal signs- constipation, nausea and vomiting
- peptic ulcer disease
- pancreatitis.
- Renal-related signs include polyuria (secondary to nephrogenic diabetes insipidus),
- urinary tract stones and their complications,
- tubulointerstitial disease with medullary and to a lesser extent cortical deposition of calcium (nephrocalcinosis).
- Neuropsychiatric manifestations include headache, loss of memory, somnolence, stupor, and, rarely, coma.
- Ocular symptoms include conjunctivitis from crystal deposition and, rarely, band keratopathy.
- Osteoarticular pain
- High blood pressure
- Soft tissue calcifications can occur with long-standing hypercalcemia.
- Electrocardiography may show shortening of the QT interval and coving of the ST wave.
- Hypercalcemia may also increase cardiac contractility and can amplify digitalis toxicity.

HYPOCALCEMIA

Symptomatic hypocalcemia is defined as reduction in the serum ionized (free) calcium concentration, or as a serum calcium level less than 8.5 mg/dL in the presence of normal levels of serum proteins. The total serum calcium concentration is reduced by approximately 0.8 mg/dL for every 1 g/dL reduction in serum albumin concentration. Occasionally, symptomatic hypocalcemia can occur with normal total serum calcium concentration .

Like hypercalcemia, hypocalcemia can be secondary either to reduced plasma albumin (false hypocalcemia) or to a change in ionized Ca2+ (true hypocalcemia). False hypocalcemia can be excluded by direct measurement of plasma Ca2+, by determination of plasma total protein or albumin levels, by the clinical context, or by other laboratory results. Corrected calcium levels in case of hypoalbuminemia can be calculated using the following formula:

[4- patient serum albumin] * 0.8 + patient serum calcium level.

Acute hypocalcemia is often observed during acute hyperventilation and the respiratory alkalosis that follows, regardless of the cause of hyperventilation. Hyperventilation can occur secondary to cardiopulmonary or cerebral diseases. After exclusion of false hypocalcemia linked to hypoalbuminemia, hypocalcemia can be divided into that associated with elevated and that associated with low plasma phosphate concentration.

CAUSES OF HYPOCALCEMIA

Associated with normal/low plasma phosphate

1. Vitamin D deficiency: decreased intake or decreased absorption

(postgastrectomy, primary biliary cirrhosis, intestinal Ca malabsorption)

2. Decreased 25-hydroxyvitamin D generation (liver disease, anticonvulsants)

3. Decreased calcitriol formation (renal failure, type 1 vitamin D–dependent rickets)

4. Resistance to calcitriol (type 2 vitamin D–dependent rickets)

5. Acute pancreatitis

6. Magnesium deficiency

7. Hungry bone syndrome (postsurgical treatment of hyperparathyroidism or vitamin D deficiency)

Associated with high plasma phosphate

1. Idiopathic or sporadic hypoparathyroidism

2. Postoperative hypoparathyroidism

3. Acquired hypoparathyroidism (postirradiation, amyloidosis)

4. Pseudohypoparathyroidism: type 1 or 2

5. Chronic renal failure, advanced stage

6. Acute renal failure, oligoanuric stage

Associated with hypoalbuminemia

1. Hemodilution
2. Nephrotic syndrome
3. Exudative enteropathy
4. Cirrhosis

CLINICAL MANIFESTATIONS

As with hypercalcemia, the symptoms of hypocalcemia depend on the rate of its development and its severity.

1. fatigue
2. muscle weakness
3. increased irritability
4. loss of memory
5. a state of confusion
6. hallucination, paranoia, and depression.

Clinical signs

1. Chovstek's sign - tapping of facial nerve branches leads to twitching of facial muscle and
2. Trousseau's sign - carpal spasm in response to forearm ischemia caused by sphygmomanometer cuff.

In acute hypocalcemia

1. Paresthesias of the lips and the extremities
2. Muscle cramps
3. Tetany
4. Laryngeal stridor
5. Convulsions.

Chronic hypocalcemia

1. Cataracts
2. Brittle nails with transverse grooves
3. Dry skin and
4. Decreased or even absent axillary and pubic hair.

Tetany, often mistaken for motor seizures, are as a result of spontaneous action potentials originating in peripheral nerves when the serum ionized calcium concentration falls below 4.3 mg/dL which usually corresponds to a total serum calcium concentration of 7.0-7.5 mg/dL. Tetany can also be induced by hypomagnesemia, hypokalemia and respiratory alkalosis.

LABORATORY AND RADIOGRAPHIC SIGNS

- ✓ Plasma phosphate is elevated in hypoparathyroidism, pseudohypoparathyroidism, and advanced CKD, whereas it is decreased in steatorrhea, vitamin D deficiency, acute pancreatitis, and the polyuric phase during recovery from AKI.
- ✓ Plasma PTH is reduced in hypoparathyroidism and also during chronic magnesium deficiency, whereas it is normal or increased in pseudohypoparathyroidism and in CKD.
- ✓ Urinary calcium excretion is increased only in the treatment of hypoparathyroidism with calcium and vitamin D derivatives, in which it may lead to nephrocalcinosis; it is low in all other cases of hypocalcemia.
- ✓ Fractional urinary calcium excretion is high in hypoparathyroidism,in the polyuric phase during recovery from AKI, and in severe CKD; it is low in all other cases of hypocalcemia.
- ✓ Urinary phosphate excretion is low in hypoparathyroidism, pseudohypoparathyroidism, and magnesium deficiency; it is high in vitamin D deficiency, steatorrhea, and CKD and during phosphate administration. Determination of serum 25-hydroxyvitamin D and calcitriol levels may also be useful.

- ✓ Intracranial calcifications, notably of the basal ganglia, are observed radiographically in 20% of patients with idiopathic hypoparathyroidism but much less frequently in patients with postsurgical hypoparathyroidism or pseudohypoparathyroidism.
- ✓ On electrocardiography, the corrected QT interval is frequently prolonged, and there are sometimes arrhythmias.
- ✓ Electroencephalography shows nonspecific signs, such as an increase in slow, high-voltage waves.

TREATMENT

- ➢ The basic treatment is that of the underlying cause.
- ➢ Severe and symptomatic (tetany) hypocalcemia requires rapid treatment.
- ➢ Acute respiratory alkalosis, if present, should be corrected, if possible.
- ➢ When the cause is functional, the simple retention of carbon dioxide (e.g., by breathing into a paper bag) may suffice.
- ➢ In other cases and to obtain a prolonged effect, intravenous infusion of calcium salts is most often required.
- ➢ In the setting of seizures or tetany, calcium gluconate should be administered as an intravenous bolus (for instance, calcium gluconate, 10 ml 10% w/v [2.2 mmol of calcium], diluted in 50 ml

of 5% dextrose or isotonic saline), followed by 12 to 24 g during 24 hours in 5% dextrose or isotonic saline. Calcium gluconate is preferred to calcium chloride, which can lead to extensive skin necrosis in accidental extravasation.

- Treatment of chronic hypocalcemia includes oral administration of calcium salts, thiazide diuretics, or vitamin D. Several oral preparations of calcium are available, each with its advantages and disadvantages. The amount of elemental calcium of the various salts differs greatly. For example, the calcium content is 40% in carbonate, 36% in chloride, 12% in lactate, and only 8% in gluconate salts.
- The daily amount prescribed can be 2 to 4 g elemental calcium. Concurrent magnesium deficiency (serum Mg^{2+} <0.75 mmol/l) should be treated either with oral magnesium oxide (250 to 500 mg every 6 days) or with magnesium sulfate: intramuscular (4 to 8 mmol/day) or intravenous (2 g i.v. over 2-4 hours, then as needed to correct deficiency).
- Treatment of hypocalcemia secondary to hypoparathyroidism is difficult as urinary calcium excretion increases markedly with calcium supplementation and can lead to nephrocalcinosis and loss of renal function. To reduce urinary calcium concentration,

thiazide diuretics can be used in association with restricted salt intake and high fluid intake.

- Lastly, treatment with active forms of vitamin D, calcitriol or its analogue 1α-hydroxycholecalciferol (0.25 to 1.0 μg/day), is the treatment of choice at present for idiopathic or acquired hypoparathyroidism because these compounds are better tolerated than massive doses of calcium salts. Administration of vitamin D derivatives generally leads to hypercalciuria and, rarely, to nephrocalcinosis. It requires regular monitoring of the serum calcium concentration to avoid hypercalcemia.

MAGNESIUM HOMEOSTASIS

Magnesium is the fourth most abundant cation in the body and the second most abundant cation intracellularly. It is often referred to as the "forgotten cation ". Magnesium plays a vital role in many functions of the cell including protein, carbohydrate and fat metabolism , maintenance of normal cell membrane function and most importantly the regulation of parathyroid hormone secretion. It is involved in the regulation of mitochondrial function, inflammatory processes and immune defence, allergy, growth, and stress, and in the control of neuronal activity, cardiac excitability, neuromuscular transmission, vasomotor tone, and blood pressure.

HYPOMAGNESEMIA AND MAGNESIUM DEFICIENCY

Magnesium deficiency is defined as a decrease in total body magnesium content. Poor dietary intake of magnesium is usually not associated with marked magnesium deficiency because of the remarkable ability of the normal kidney to conserve Mg2+.Hypomagnesemia is encountered in about 25% to 35% of patients with acute pancreatitis, is frequently observed in patients with chronic alcoholism, and can also be present in patients with poorly controlled diabetes mellitus. Hypomagnesemia can also be observed in patients with hypercalcemic disorders and in primary aldosteronism.

ETIOLOGY

Decreased intake

- ✓ Starvation
- ✓ Alcohol dependence
- ✓ Total parenteral nutrition

Gastrointestinal diseases

- ✓ Malabsorption syndromes - nontropical sprue, steatorrhea
- ✓ Massive resection of the small intestine
- ✓ Intestinal and biliary fistulae
- ✓ Excessive use of purgatives

Increased urinary losses

- ✓ Drug administration – Aminoglycoside, Amphotericin, Cisplatin, Cyclosporine, Pentamidine, Thiazide diuretics
- ✓ High urinary output states (polyuric phase of acute renal failure, postobstructive polyuria ,post-transplantation polyuria)
- ✓ Hypercalcemic states
- ✓ Primary aldosteronism
- ✓ Metabolic acidosis
- ✓ Diabetes (glycosuric and ketoacidotic states)
- ✓ Hyperthyroidism
- ✓ Phosphate depletion
- ✓ Idiopathic renal wasting
- ✓ Gitelman's syndrome

Miscellaneous

- ✓ Acute pancreatitis
- ✓ Chronic alcoholism
- ✓ Bartter syndrome
- ✓ Idiopathic hypomagnesemia

CLINICAL MANIFESTATIONS

Specific clinical manifestations of hypomagnesemia may be difficult to appreciate because of concomitant hypocalcemia and hypokalemia.

Moderate to severe magnesium depletion causes

- ✓ General weakness ,
- ✓ Neuromuscular hyperexcitability with hyperreflexia ,
- ✓ Carpopedal spasm,
- ✓ Seizure,
- ✓ Tremor,
- ✓ tetany.

Cardiac findings

- ✓ prolonged QT interval and ST depression
- ✓ predisposition to ventricular arrhythmias
- ✓ potentiation of digoxin toxicity.

Magnesium deficiency can also be associated with hypocalcemia (decreased PTH release and end-organ responsiveness) and hypokalemia (urinary loss).The diagnosis of moderate degrees of magnesium deficiency is not easy because clinical manifestations may be absent and blood Mg^{2+} levels may not reflect the state of body magnesium. Severe magnesium deficits, however, are associated with hypomagnesemia.

TREATMENT

Magnesium deficiency is managed with the administration of magnesium salts. Magnesium sulfate is generally used for parenteral therapy (1500 to 3000 mg [150 to 300 mg elemental magnesium] per day). A variety of magnesium salts are available for oral administration, including oxide, hydroxide, sulfate, lactate, chloride and carbonate. Oral magnesium salts often are not well tolerated. All of them may induce gastrointestinal intolerance, in particular diarrhea.

Green vegetables such as spinach are good sources of magnesium. Some legumes (beans and peas), nuts and seeds, and whole, unrefined grains are also good sources of magnesium.

METHODS AND MATERIALS

Study group

- Case : Patients with alcohol related seizures satisfying CAGE criteria.
- Control : Patients with primary idiopathic seizures.

Study design : Analytical case control study

(Cross sectional study)

Place of Study : Govt. Royapettah Hospital

Duration of study : 6 months

Conflict of interest : Nil.

Hazards of study : Nil

METHODOLOGY

This study was formulated as an analytical case control study. Ethical committee approval was obtained from Institutional Ethical Committee, Kilpauk Medical College, Chennai-10. This study was conducted in Government Royapettah hospital in the department of General Medicine between May and December 2013.

Patients presenting with seizures to the emergency department were screened after obtaining written informed consent.

Inclusion criteria :

Case : Patients (with age >18 yrs) satisfying CAGE criteria of alcohol dependence and who had seizures.

Control : Patients (with age >18 yrs) with primary idiopathic seizures

Exclusion criteria:

Patients with

1. Previous head injury
2 Metabolic diseases
3. Stroke
4. Structural brain lesions
5.CNS infections
6.Other illicit drugs

Based on previous records and by obtaining past history of any CNS infections, cerebrovascular accidents, head injury, structural brain lesions, metabolic diseases and illicit drug abuse ,patients with all negative history were screened with investigations such as serum electrolytes, random blood sugar

,serum amylase, serum bilirubin and CT- brain . Among these patients, patients who had all values within normal limits were taken into study population.

Among the patients in study population, patients with no history of alcohol consumption with all screening blood investigations within normal limits and those with EEG and CT Brain findings suggestive of primary seizures were grouped into control population. Patients satisfying CAGE criteria with screening blood investigations and CT-Brain normal were grouped into case population. Then, serum calcium levels, serum albumin levels and serum magnesium levels were measured in both cases and controls. Corrected calcium will be calculated in case of hypoalbuminemia. Patients with serum calcium levels between 8.7 - 10.2 mg/dl were taken as normal. Patients with levels 8.6 md/dl or less were taken as hypocalcemic range and 10.3 mg/dl and above as hypercalcemic range. Serum calcium levels were compared in both cases and controls. The prevalence of hypomagnesemia in these patients and their association with hypocalcemia were also assessed secondarily. The results were tabulated and their statistical significance were calculated using pearson’s chi square tests.

RESULTS

Total of 182 patients presenting with seizures in the emergency department were screened. Total of 110 patients were taken into study population and 72 patients were excluded due to other causes .

Of the 110 patients 56 were grouped into cases and 54 into control group.

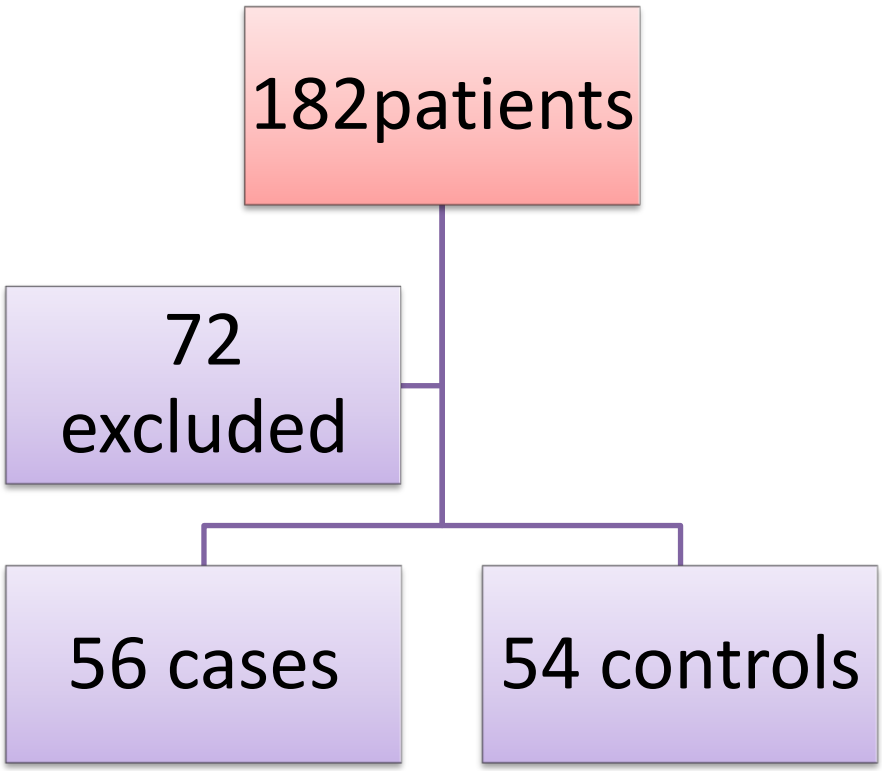


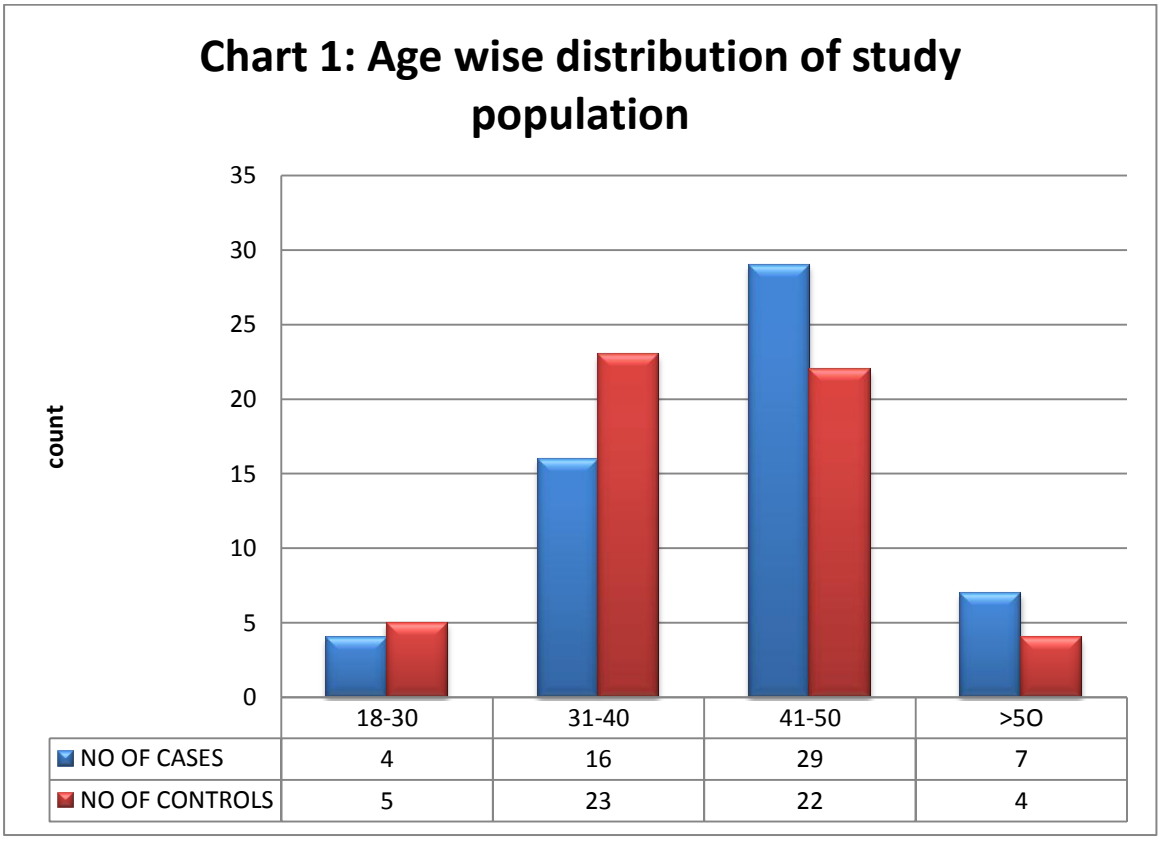
Fig 8 : Study population

DESCRIPTIVE STATISTICS

The mean age of the case group is 42.821 years (min 29 yrs and max 53 yrs). The mean age of the control group is 40.574 years (min 17 yrs and max 55 yrs)

	N	Minimum	Maximum	Mean
Case	56	29	53	42.821
Control	54	17	55	40.574

Table 6 : Mean age of study population



Among the cases and controls all patients included in the study group had normal levels of random blood sugar, serum sodium, serum potassium, serum amylase , serum bilirubin and CT brain.

In the case group the mean RBS was 110.310 , mean serum sodium – 139.8 , mean S.potassium – 3.978, mean S.amylase -51.035 and mean serum bilirubin was 0.7. in the control group the mean values of RBS, S.sodium, S.potassium, S.amylase and S,bilirubin were 111.592, 138.259, 4.064, 42.296 and 0.659 respectively.

	CASE		CONTROL		MEAN	
	MIN	MAX	MIN	MAX	CASE	CONTROL
RBS	80	152	80	163	110.310	111.592
Serum sodium	135	145	135	145	139.8	138.259
Serum potassium	3.5	4.9	3.5	4.9	3.978	4.064
Serum bilirubin	0.3	1.1	0.3	1.1	0.7	0.659
Serum amylase	24	90	26	72	51.035	42.296

Table 7 : Mean lab values of study population

The mean calcium values in the case and control population were 9.200 and 9.065 respectively

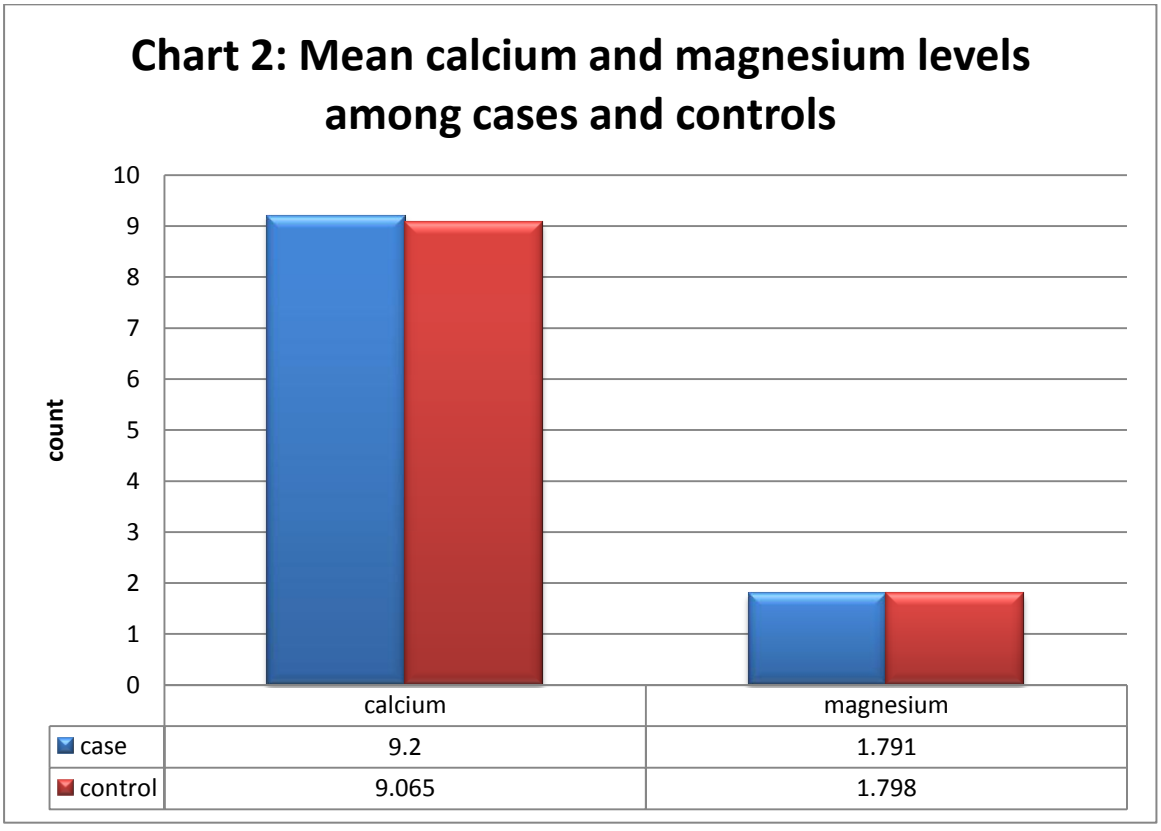
	Group	N	**Mean**	Std. Deviation	Std. Error Mean
Serum Calcium	Control	54	**9.065**	.4149	.0565
	Cases	56	**9.200**	.5530	.0739

Table 8 : Mean serum calcium values of study population

The mean magnesium values in the case and control population were 1.791 and 1.798 respectively.

	Group	N	**Mean**	Std. Deviation	Std. Error Mean
Serum Magnesium	Control	54	**1.798**	.4708	.0641
	Cases	56	**1.791**	.2776	.0371

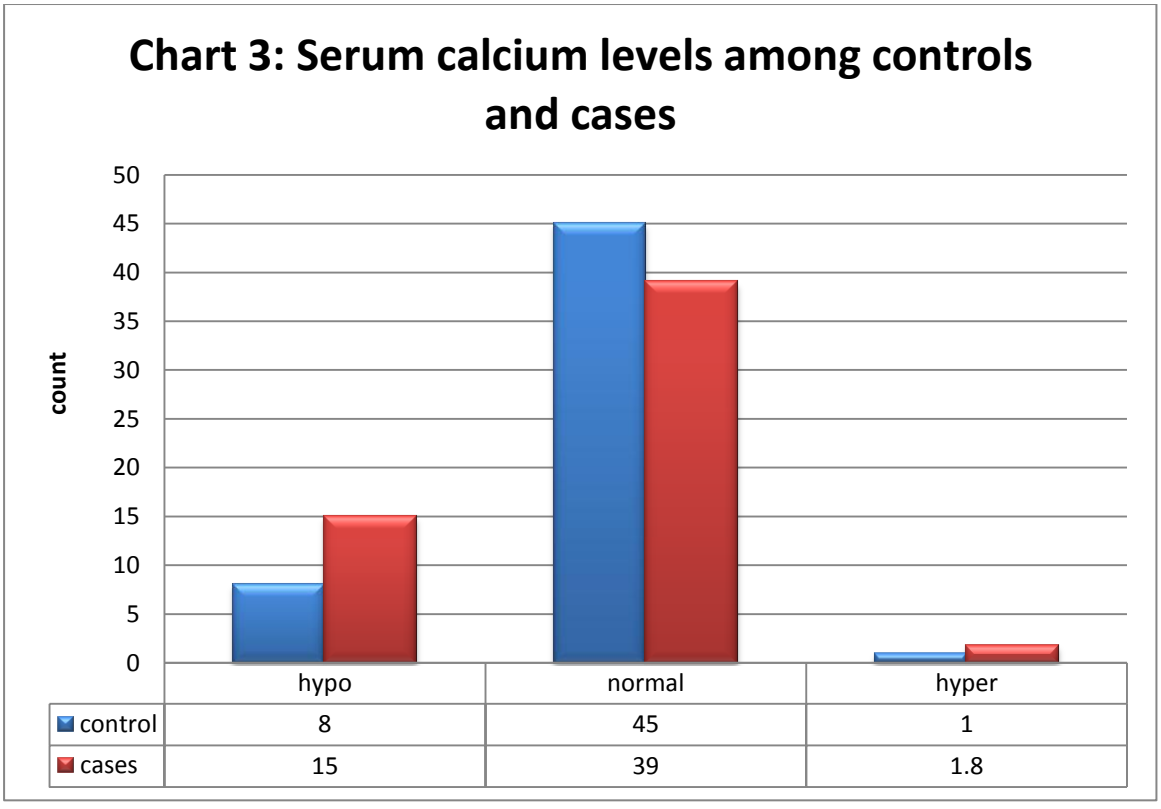
Table 9: Mean serum magnesium values of study population



There is no significant difference in the mean serum calcium and magnesium levels among cases and controls.

In the case group out of 56 patients , 39 patients had normal calcium level, 15 were in hypocalcemic range and 2 had hypercalcemia. Thus, about 26.8 % of the cases were in hypocalcemic range, 69.6% in normocalcemic range and 3.6% in hypercalcemic range.

In the control group of 54 patients , the number of patients in normocalcemic, hypocalcemic and hypercalcemic range were respectively 45,8 and 1. The percentage of patients presenting with hypo, normo and hypercalcemic range within the control group were 14.8 %, 83.3 % and 1.9 % respectively.



			Group		Total
			Control	Cases	
Serum Calcium	Hypo	Count	8	15	23
		% within Serum Calcium	34.8%	65.2%	100.0%
		% within Group	14.8%	26.8%	20.9%
	Normal	Count	45	39	84
		% within Serum Calcium	53.6%	46.4%	100.0%
		% within Group	83.3%	69.6%	76.4%
	Hyper	Count	1	2	3
		% within Serum Calcium	33.3%	66.7%	100.0%
		% within Group	1.9%	3.6%	2.7%
Total		Count	54	56	110

Table 10 : Comparison of serum calcium values in cases and controls

CHI-SQUARE TESTS

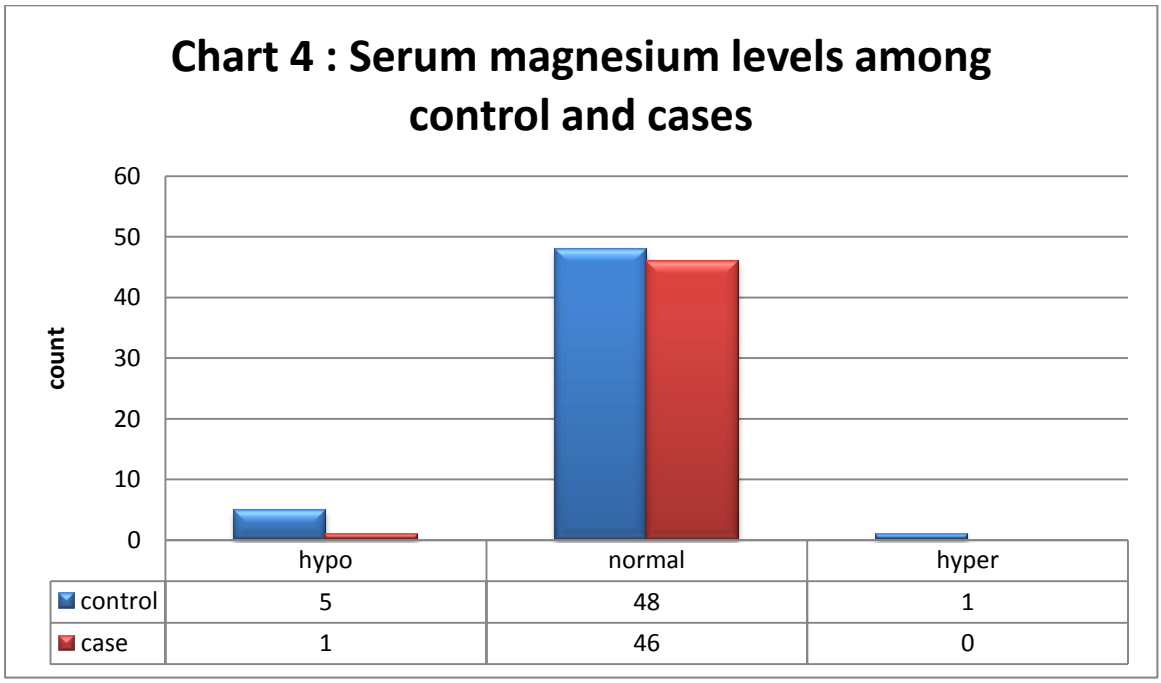
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	2.857(a)	2	.240
Likelihood Ratio	2.897	2	.235
Linear-by-Linear Association	1.408	1	.235
N of Valid Cases	110		

On comparing the case and control group , 65.2 % of the hypocalcemic patients were in the case group. Only 34.8 % of the patients were in the control

group. On applying the chi-square tests, the p value is found to be 0.240. Thus, there is no statistically significant difference in the prevalence of hypocalcemia among the case and control group.

			Group		Total
			Control	Cases	
Serum Magnesium	Hypo	Count	5	10	15
		% within Group	9.3%	17.9%	13.6%
	Normal	Count	48	46	94
		% within Group	88.9%	82.1%	85.5%
	Hyper	Count	1	0	1
		% within Group	1.9%	.0%	.9%
Total		Count	54	56	110

Table 11 : Comparison of serum magnesium values in cases and controls

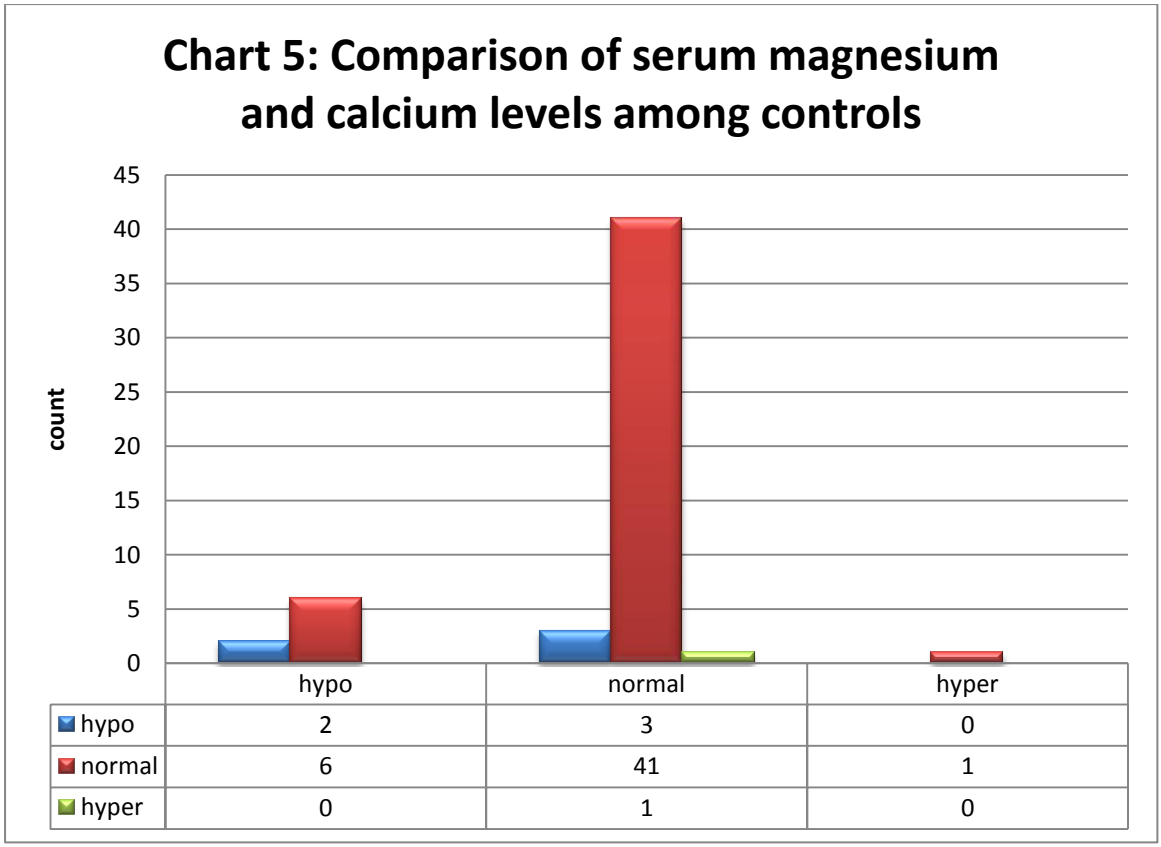


The prevalence of hypomagnesemia in the case and control group is 17.9 % and 9.3 % respectively. On applying the chi-square test, the p value is 0.263 which is >0.05, thus there is no statistical difference in the prevalence of hypomagnesemia among cases and control.

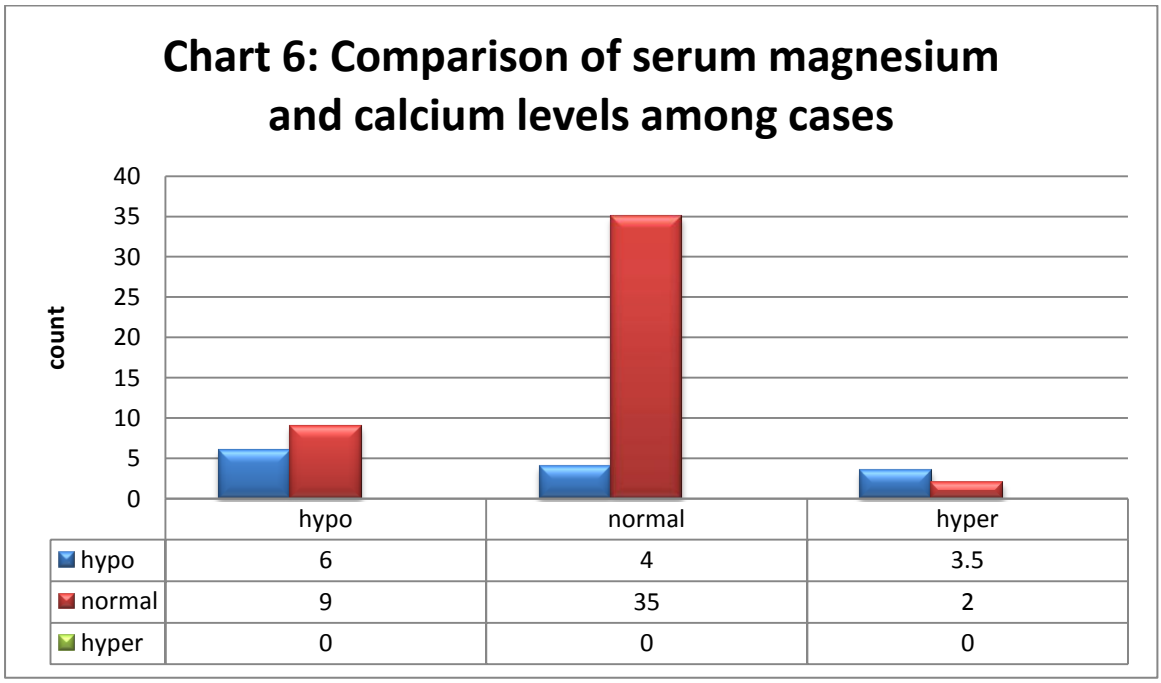
Group			Serum Magnesium			Total
			Hypo	Normal	Hyper	
Control	Serum Calcium	Hypo	2	6	0	8
		Normal	3	41	1	45
		Hyper	0	1	0	1
	Total		5	48	1	54
Cases	Serum Calcium	Hypo	6	9	0	15
		Normal	4	35	0	39
		Hyper	0	2	0	2
	Total		10	46	0	56

Table 12 : Comparison of serum calcium and serum magnesium levels

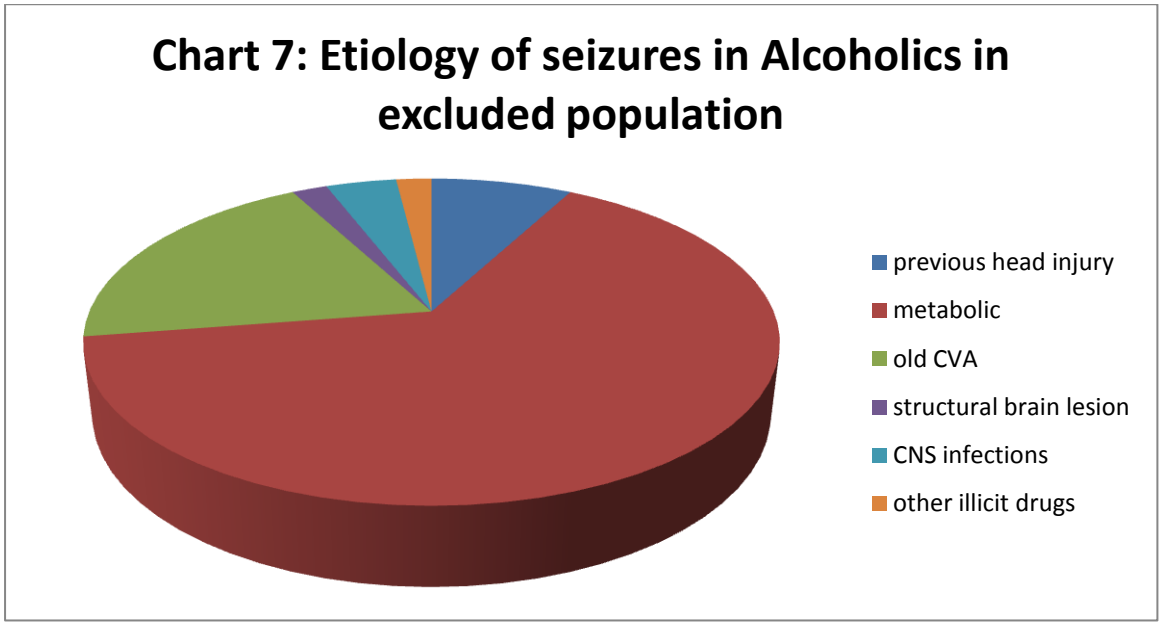
On comparing the prevalence of hypomagnesemia among hypocalcemic patients in the case group, the p value is found to be 0.03 which is statistically significant.

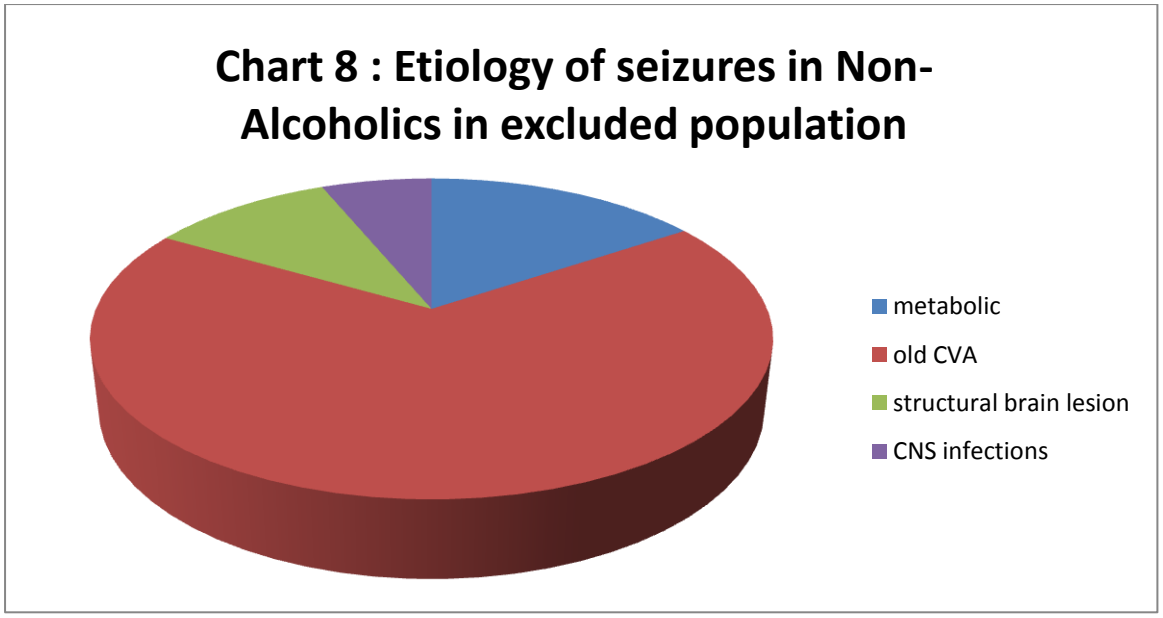


Among controls the p-value is 0.562 , thus the prevalence of hypomagnesemia among hypocalcemic patients is statistically insignificant.



Among the 72 patients excluded from the study, 51 patients satisfied CAGE criteria and 21 patients were non alcoholics. Among the alcoholics , the most common cause of seizures was found to be metabolic (hypoglycaemia) and among the nonalcoholics previous cerebrovascular accident was the common cause.





DISCUSSION

It is a well known fact since Hippocratic times that ethanol overuse produces seizures. Alcohol related seizures may be either due to alcohol intoxication or alcohol withdrawal. Alcohol related seizures accounts for about one third of seizure related admissions. Seizures occur in alcoholics as an effect of alcohol intoxication or alcohol withdrawal. The diagnosis of alcohol related seizures is primarily based on history taking and examination. The concurrent risk factors in these group of patients are pre-existing epilepsy, structural brain lesions , head injury, metabolic diseases and use of illicit drugs.

It is also known fact that various electrolyte abnormalities can lead to seizures , especially hypocalcemia. In the study conducted by Gordon et al, it has been proven that alcohol can interfere with calcium metabolism in several ways, acute alcohol consumption causes transient parathormone deficiency and increases the urinary calcium excretion , resulting in calcium loss from the body. Chronic alcohol abuse causes disturbance in vitamin D metabolism producing inadequate dietary calcium absorption.

The purpose of this study is to find the prevalence of hypocalcemia among alcohol related seizures after excluding the secondary causes of seizures and after excluding other electrolyte abnormalities and to compare with primary seizures disorder patients who were not alcoholics . Hypocalcemia as a

cause of seizure in neonates is well documented whereas hypocalcemia as a cause of seizures in adults is still underestimated. The study also aims to find the prevalence of hypocalcemia in seizure patients due to any cause after excluding other electrolyte abnormalities. Other factors responsible for provoking seizures in alcoholics were also analysed .

In a study conducted by kayath et al , it was proven that hypocalcemia is an important factor in the alcoholic convulsive population. As ethanol reduces both calcium and magnesium levels . a high prevalence of hypocalcemia was found in alcoholic convulsive population in contrast with the non alcoholic convulsive group and alcoholic non convulsive group. This study emphasized the importance of serum calcium measurement in alcoholic seizure patients and suggested that hypocalcemia correction may be considered in these patients.

In this study a total of 182 seizure patients were screened in the emergency department of which 72 were excluded from the study due to secondary causes and the presence of other biochemistry abnormalities. Among the 110 patients in study population, 56 patients satisfied CAGE questionnaire of alcohol dependence and were grouped as cases. Rest 54 patients were non alcoholic primary seizure patients and were grouped as controls. Among 72 excluded patients , 51 satisfied CAGE criteria. **Of the population screened in our emergency department ,58.791% of patients were alcohol dependent and 41.208% of patients were non alcoholics** . **Thus , nearly half of the**

patients admitting with seizures in our hospital are either alcohol related seizures or seizure disorder patient with habit of alcohol abuse.

The prevalence of hypocalcemia among the case was 26.8% and among the control was 14.8%. Though there was no statistical significance in hypocalcemia among cases and controls, the prevalence of hypocalcemia in alcoholic seizures were found to be high. **Nearly one fourth of the alcohol related seizures had hypocalcemia in our study.** The prevalence of hypocalcemia among the total study population is found to be 20.909%.

The prevalence of hypomagnesemia in hypocalcemic patients among cases was found to be 40% and among controls was 25%. In the alcohol related seizures the prevalence of hypomagnesemia in hypocalcemic group was statistically significant. **Thus, the measurement of serum magnesium level along with serum calcium level is of added significance.** It is known that the correction of hypocalcemia alone is not enough without correcting the serum magnesium levels. Hypomagnesemia itself is an independent risk factor for seizures.

Among the excluded patients, the most common cause of alcohol related seizures were found to be metabolic, more specifically hypoglycaemia. The common cause among non alcoholics were found to be previous cerebrovascular accident.

Thus, this study had proven the increased prevalence of hypocalcemia among alcohol related seizures and also an increased prevalence of hypomagnesemia in this population. Further studies are needed to check the correlation of hypocalcemia with other electrolyte abnormalities.

LIMITATIONS

- This study was conducted in a very small population. Further studies in a larger population is recommended.
- Ionised calcium levels which indicates the functional form of calcium were not measured, only the serum calcium levels were measured.
- Correlation of the calcium level with parathormone level was not measured.

CONCLUSION

- The burden of alcohol related health problems are often underestimated in developing countries .This study emphasizes the **high incidence of alcohol related admissions to the emergency department presenting as seizures**.
- Several aetiologies for alcohol related seizures has been postulated. Most common among them are the electrolyte abnormalities. This study was done in view of identifying the common electrolyte disturbance , Hypocalcemia as a cause of seizures in these group of patients.
- A **high prevalence of Hypocalcemia** among alcohol related seizures were identified in this study ,though a statistical significance against primary seizures could not be proven.
- **The prevalence of Hypomagnesemia was statistically significant in the Hypocalcemic alcoholic patients**. Thus, hypomagnesemia as a cause of seizures in these patients needs further studies.
- If Hypocalcemia and Hypomagnesemia as a cause of Alcohol related seizures could be proved on further studies , **inclusion of**

Calcium and Magnesium as a treatment modality for alcohol related seizures could be considered.

DISCLOSURE

The investigator has not received any form of grants or support from any institution or pharmacological company.

REFERENCES

1. Messing RO, Simon RP. Seizures as a manifestation of systemic disease. Neurol Clin 1986;4:563-584.
2. Tohme JF, Bilezikian JP. Hypocalcemic emergencies. Endocrinol Metab Clin North Am 1993;22:363-375.
3. Fonseca OA, Calverley JR. Neurological manifestations of hypoparathyroidism. Arch Intern Med 1967;120:202-206.
4. Gupta MM. Medical emergencies associated with disorders of calcium homeostasis. J Assoc Physicians India 1989;37:629-631.
5. Lloyd G . Hippocratic Writings . Middlesex, UK : Penguin Books , 1978 ; p. 222
6. Rathlev NK, Ulrich AS, Fish SS, D'Onofrio G. Clinical characteristics as predictors of recurrent alcohol-related seizures. Acad Emerg Med 2000;7:886 –91.
7. Reynolds EH. The ILAE/IBE/WHO Global Campaign against Epilepsy: Bringing Epilepsy "Out of the Shadows" Epilepsy Behav. 2000;1:S3–S8.
8. 2. Epigraph WHO. The newsletter of the International League against Epilepsy. Geneva. 1999;1:5–6.

9. WHO,Factsheet999,epilepsy, www.who.int/mediacentre/factsheets/fs999/en/index.html accessed 1 June 2010
10. Ministry of Health & Family Welfare,Government of India, integrated disease surveillance project (idsp) non-communicable disease risk factors survey 2007-08 Tamil Nadu
11. Feuerlein, W., Alkoholismus — Mißbrauch und Abhaengigkeit, Thieme, Stuttgart, 1989.
12. Victor, M., The effects of alcohol on the nervous system, Medical Diagnosis and Treatment of Alcoholism, Mendelson, J.H. and Mello, N.K., Eds., McGraw-Hill, New York, 1992, 201.
13. Victor, M. and Laureno, R., The neurologic complications of alcohol abuse: Epidemiologic aspects,Advances in Neurology, Vol. 19. Neurological Epidemiology: Principles and Clinical Applications,Schoenberg, B.S., Ed., Raven, New York, 1978, 603.
14. Juvela, S., Alcohol consumption as a risk factor for poor outcome after aneurysmal subarachnoidal hemorrhage, Br. Med. J., 304, 1663, 1992.
15. Klatzky, A.L., Friedmann, G.D., Siegelaub, A.N., and Gerard, M.J., Alcohol consumption and blood pressure. Kaiser-Permanente multiphase health examination data, N. Engl. J. Med., 296, 1194, 1977.

16. Calandre, L., Arenal, C., Fernandez Ortega, J., and Vallejo A., Risk factors for spontaneous cerebral hematomas. Case control study, Stroke, 17, 1226, 1986
17. Sacco, R.L., Elkind, M., and Boden-Albala, B., The protective effect of moderate alcohol consumption on ischemic stroke, JAMA, 281, 53, 1999.
18. Verfaellie, M. and Cermak, L.S., Wernicke-Korsakoff and related nutritional disorders of the nervous system, Behavioural Neurology and Neuropsychology, Feinberg, T.E. and Farah, M.J., Eds., McGraw-Hill, New York, 1997, 606.
19. Sullivan, Edith V.; Fama, Rosemary (2012). "Wernicke's Encephalopathy and Korsakoff's Syndrome Revisited". Neuropsy chology Review 22 (2): 69–71
20. Charness, M.E. and DeLaPaz, R.L., Mammillary body atrophy in Wernicke encephalopathy: antemortem identification using MRI, Ann. Neurol., 22, 595, 1987.
21. Reuler, J.B., Girard, D.E., and Cooney, T.G., Wernickes's encephalopathy, N. Engl. J. Med., 312, 1035,1985.
22. Grant, B. F., Alcohol consumption, alcohol abuse and alcohol dependence: the United States as an example, Addiction, 89, 1357, 1994.
23. Stuppaeck, C.H., Pycha, R., Miller, C., Whitworth, A.B., Oberbauer, H., and Fleischhacker, W.W.,Carbamazepine versus oxazepam in the

treatment of alcohol withdrawal: a double-blind study, Alcohol Alcohol., 27, 153, 1992.

24. Stuppaeck, C.H., Barnas, C., Hackenberg, K., Miller, C., and Fleischhacker, W.W., Carbamazepine monotherapy in the treatment of alcohol withdrawal, Int. Clin. Psychopharmacol., 5, 273, 1990.
25. Ballenger, J.C. and Post, R.M., Kindling as a model for alcohol withdrawal syndromes, Br. J.Psychiatry, 133, 1, 1978.
26. Sullivan, J.T., Sykora, K., Schneiderman, J., Naranjo, C.A., and Sellers, E.M., Assessment of alcohol withdrawal: the revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar), Br. J. Addict., 84, 1353, 1989.
27. Saitz, R. and O'Malley, S.S., Pharmacotherapies for alcohol abuse. Withdrawal and treatment, Alcohol and Other Substance Abuse, 81, 881, 1997.
28. Mayo-Smith, M.F., Pharmacological management of alcohol withdrawal. A meta-analysis and evidence-based practice guide, JAMA, 278, 144, 1997.
29. Kaim, S.C., Klett, C.J., and Rothfeld, B., Treatment of the acute withdrawal state: a comparison of four drugs, Am. J. Psychiatry, 125, 1640, 1969.
30. Mayo-Smith, M.F. and Bernard, D., Late-onset seizures in alcohol withdrawal, Alcohol Clin. Exp.Res., 19, 656, 1995.

31. Pycha, R., Miller, C., Barnas, C., Hummer, M., Stuppaeck, C., Whitworth, A., and Fleischhacker,W.W., Intravenous flunitrazepam in the treatment of alcohol withdrawal delirium, Alcohol Clin. Exp.Res., 17, 753, 1993.
32. Kuhn, R., The psychotropic effect of carbamazepine in non-epileptic adults with particular reference to the drug mechanism of action, Epileptic Seizures, Behaviour and Pain, Birkmayer, W., Ed.,University Park Press, Baltimore, 1976.
33. Vamvakas S, Teschner M, Bahner U, Heidland A: Alcohol abuse: Potential role in electrolyte disturbances and kidney diseases. Clin Nephrol 1998;49:205–213.
34. Wrenn KD, Slovis CM, Minion GE, Rutkowski R: The syndrome of alcoholic ketoacidosis.Am J Med 1991;91:119–128.
35. De Marchi S, Cecchin E, Basile A, Bertotti A,Nardini R, Bartoli E: Renal tubular dysfunction in chronic alcoholic abuse – Effects of abstinence. N Engl J Med 1993;329:1927–1934.
36. Shils ME: Magnesium, calcium and parathyroid interaction. Ann NY Acad Sci 1980;355:165–178
37. Parenti P, Giorbana B, Hanozet GM: In vitro effect of ethanol on sodium and glucose transport in rabbit renal brush border membrane vesicles. Biochim Biophys Acta 1991;1070:92–98.

38. Laitinen K, Lamberg-Allardt C, Tunninen R,Karonen SL, Tähtelä R, Ylikahri R, Välimäki M: Transient hypoparathyroidism during acute alcohol intoxication. N Engl J Med 1991;324:721–727.
39. Krapf R, Jaeger P, Hulter HN: Chronic respiratory alkalosis induces renal PTH resistance,hyperphosphatemia and hypocalcemia in humans.Kidney Int 1992;42:727–734.
40. Gascon-Barre M: Interrelationships between vitamin D3 and 25-hydroxyvitamin D3 during chronic ethanol administration in the rat. Metabolism 1982;31:67–72.
41. Ewing, J.A., Detecting alcoholism: the CAGE questionnaire, JAMA, 252, 1905, 1984.
42. Babor, T.F., Hofman, M., Delboca, F.K, Hesselbrock, V., Meyer, R.E., Dolinsky, Z.S., and Rounsaville,B., The Alcohol Use Disorder Test: Guidelines for Use in Primary Health Care. WHO Publication No. 89.4, World Health Organization, Geneva, 1989.
43. Saunders, J.B., Aasland, O.G., Babor, T.F., de la Fuente, J.R., and Grant, M., Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption. II, Addiction, 88, 791, 1993.
44. Aertgeerts B , Buntinx F , Ansoms S , Fevery J . Questionnaires are better than laboratory tests to screen for current alcohol abuse or dependence in a male inpatient population . Acta Clin Belg 2002 ; 57 : 241 – 9 .

45. Bernadt MW , Mumford J , Taylor C , Smith B , Murray RM .Comparison of questionnaire and laboratory tests in the detection of excessive drinking and alcoholism . Lancet 1982 ; i : 325 – 8 .

46. Bråthen G , Bjerve K , Brodtkorb B , Bovim G . Validity of carbohydrate - defi cient transferrin and other markers as diagnostic aids in the detection of alcohol - related seizures .J Neurol Neurosurg Psychiatry 2000 ; 68 : 342 – 8 .

47. Martin MJ , Heyermann C , Neumann T , et al . Preoperative evaluation of chronic alcoholics assessed for surgery of the upper digestive tract . Alcohol Clin Exp Res 2002 ;26 : 836 – 40 .

48. Sorvajarvi, K., Blake, J.E., Israel, Y., and Niemela, O., Sensitivity and specificity of carbohydrate deficient transferrin as a marker of alcohol abuse are significantly influenced by alterations in serum transferrin: comparison of two methods, Alcohol Clin. Exp. Res., 20, 449, 1996.

49. Bråthen G , Bjerve K , Brodtkorb B , Bovim G . Validity of carbohydrate - defi cient transferrin and other markers as diagnostic aids in the detection of alcohol - related seizures .J Neurol Neurosurg Psychiatry 2000 ; 68 : 342 – 8 .

50. Hietala J , Koivisto H , Anttila P , Niemelä O . Comparison of the combined marker GGT - CDT and the conventional laboratory markers of alcohol abuse in heavy drinkers,moderate drinkers and abstainers . Alcohol Alcohol 2006 ; 41 : 528 – 33 .

51. Bentele M , Kriston L , Clement HW , Härter M , Mundle G ,Berner MM . The validity of the laboratory marker combinations DOVER and QUVER to detect physician ’ s diagnosis of at- risk drinking . Addict Biol 2007 ; 12 : 85 – 92

52. Sillanaukee P , Olsson U . Improved diagnostic classification of alcohol abusers by combining carbohydrate – deficient transferrin and G-glutamyltransferase. Clin Chem 2001 ;47 : 681 – 5

53. Savola O , Niemel ä O , Hillbom M . Blood alcohol is the best indicator of hazardous alcohol drinking in young adults and working aged patients with trauma . Alcohol Alcohol 2004 ; 39 : 340 – 5 .

54. 74. Sullivan JT , Sykora K , Schneiderman J , Naranjo CA , Sellers EM . Assessment of alcohol withdrawal: the revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA -AR) . Br J Addict 1989 ; 84 : 1353 – 7 .

55. Earnest MP , Feldman H , Marx JA , Harris BS , Biletch M ,Sullivan LP . Intracranial lesions shown by CT in 259 cases of fi rst alcohol related seizure . Neurology 1988 ; 38 : 1561 .

56. Schoenenberger RA , Heim SM . Indication for computed tomography of the brain in patients with fi rst uncomplicated generalised seizure . BMJ 1994 ; 309 : 986 – 9

57. Hillbom ME , Hjelm - Jaeger M . Should alcohol withdrawal seizures be treated with anti - epileptic drugs? Acta Neurol Scand 1984 ; 69 : 39 – 2 .

58. Holzbach E . Thiamine absorption in alcoholic delirium patients . J Studies Alcohol 1996 ; 57 : 581 – 4 .

59. Day E , Bentham P , Callaghan R , Kuruvilla T , George S . Thiamine for Wernicke - Korsakoff Syndrome in people at risk from alcohol abuse. Cochrane Database of Systematic Reviews 2004 ;(1):Art. No.: CD004033. DOI: 10.1002/14651858.CD004033.pub2.

60. Mochizuki H , Masaki T , Miyakawa T , et al . Benign type of central pontine myelinolysis in alcoholism: clinical, neuroradiological and electrophysiological fi ndings . J Neurol 2003 ; 250 : 1077 – 83 .

61. Kelly J , Wassif W , Mitchard J , Gardner WN . Severe hyponatremia secondary to beer potomania complicated by central pontine myelinolysis . Int J Clin Pract 1998 ; 52 : 585 – 7 .

62. Saeed BO , Beaumont D , Handley GH , Weaver JU . Severe hyponatremia: investigation and management in a district general hospital . J Clin Pathol 2002 ; 55 : 893 – 6 .

63. Lampl C , Yazdi K . Central pontine myelinolysis. Eur Neurol 2002 ; 47 (1): 3 – 10 .

64. Victor M . The role of hypomagnesemia and respiratory alkalosis in the genesis of alcohol withdrawal symptoms .Ann NY Acad Sci 1973 ; 215 : 235 – 48 .

65. Traviesa DC . Magnesium defi ciency: a possible cause of thiamine refractoriness in Wernicke - Korsakoff encephalopathy . J Neurol Neurosurg Psychiatry 1974 ; 37 : 959 – 62 .

66. Hillbom M , Pieninkeroinen I , Leone M . Seizures in alcoholdependent patients. Epidemiology, pathophysiology and management. CNS Drugs 2003 ; 17 : 1013 – 30 .

67. D ' Onofrio G , Rathlev NK , Ulrich AS , Fish SS , Freedland ES .Lorazepam for the prevention of recurrent seizures related to alcohol . N Engl J Med 1999 ; 340 : 915 – 9 .

68. Hillbom ME , Hjelm - Jaeger M . Should alcohol withdrawal seizures be treated with anti - epileptic drugs? Acta Neurol Scand 1984 ; 69 : 39 – 2 .

69. Malcolm R , Myrick H , Brady KT , Ballenger JC . Update on anticonvulsants for the treatment of alcohol withdrawal . Am J Addict 2001 ; 10 (Suppl.): 16 – 23.

70. Mueller TI , Stout RL , Rudden S , et al . A double- blind,placebo - controlled pilot study of carbamazepine for the treatment of alcohol dependence . Alcohol Clin Exp Res 1997 ; 21 (1): 86 – 92 .

71. Brower KJ , Myra Kim H , Strobbe S , Karam - Hage MA ,Consens F , Zucker RA . A randomized double- blind pilot trial of gabapentin versus placebo to treat alcohol dependence and comorbid insomnia . Alcohol Clin Exp Res 2008 ; 32 (8): 1429 – 38 .

72. Salloum IM , Cornelius JR , Daley DC , Kirisci L , Himmelhoch JM , Thase ME . Effi cacy of valproate maintenance inpatients with bipolar disorder and alcoholism: a double -blind placebo - controlled study . Arch Gen Psychiatry 2005 ;62 (1): 37 – 45 .

73. Martinotti G , Di Nicola M , Tedeschi D , Mazza M , Janiri L ,Bria P . Effi cacy and safety of pregabalin in alcohol dependence. Adv Ther 2008 ; 25 (6): 608 – 18 .

74. Johnson BA , Rosenthal N , Capece JA , et al . Topiramate for Alcoholism Advisory Board; Topiramate for Alcoholism Study Group. Topiramate for treating alcohol dependence:a randomized controlled trial . JAMA 2007 ; 298 (14):1641 – 51 .

75. Wasserman RH, Chandler JS, Meyer SA, et al. Intestinal calcium transport and calcium extrusion process at the basolateral membrane. J Nutr. 1992;122:662-671.

76. Wasserman RH, Fullmer CS. Vitamin D and intestinal calcium transport: Facts, speculations and hypotheses. J Nutr. 1995;125: 1971S-1979S.

77. Kinyamu HK, Gallagher C, Prahl JM, et al. Association between intestinal vitamin D receptor, calcium absorption, and serum 1,25 dihydroxyvitamin D in normal young and elderly women. J Bone Miner Res.1997;12:922-928.

78. Martin T, Gooi JH, Sims NA. Molecular mechanisms in coupling of bone formation to resorption. Crit Rev Eukaryot Gene Expr. 2009;19:73-88.

PROFORMA

NAME: AGE: SEX:

ADDRESS:

PRESENT HISTORY:

CAGE QUESTION:

Cut down : Y/N
Annoyed : Y/N
Guilty : Y/N
Eye opener : Y/N

PAST HISTORY:

TREATMENT HISTORY:

PERSONAL HISTORY:

CLINICAL EXAMINATION:

CVS : RS:

ABDOMEN: CNS:

INVESTIGATION

1. random blood sugar :
2. Serum Na+, K+ :
3. Serum amylase :
4. serum bilirubin :
5. serum calcium :
6. serum magnesium :
7. serum albumin :
8. EEG :
9. CT- brain :

SIGNATURE OF INVESTIGATOR SIGNATURE OF GUIDE

PATIENT CONSENT FORM

STUDY DETAIL :

STUDY CENTRE :

PATIENT'S NAME :

PATIENT'S AGE :

IDENTIFICATION NUMBER :

I confirm that I have understood the purpose and procedure of the above study. I have the opportunity to ask questions and all my questions and doubts have been answered to my complete satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

I understand that the sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However I understand that my identity would not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

I hereby consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic tests including haematological, biochemical, radiological tests.

Signature/thumb impression:

INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Ref.No.2318/ME-1/Ethics/2012 Dt:04.04.2013
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "A Study on comparison of serum calcium levels among patients with alcohol related seizures and primary seizures" – For Research work.submitted by Dr.V.Priyadarshini, MD (GM), PG Student, Govt. Royapettah Hospital, Chennai-14.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

GOVT. KILPAUK MEDICAL COLLEGE
29 MAY 2013
Kilpauk, Chennai-10.

29/5/13
CHAIRMAN,
Ethical Committee
Govt.Kilpauk Medical College,Chennai

Name	Age	Sex	I.P.No	Cage	RBS	S.Na+	S.K+	S.Amylase	S.Bilirubin	S.Albumin	S.Ca2+	S.Mg2+	Corrected Ca2+
imran	35	M	7290	1	92	137	4.6	44	0.9	4.2	8.7	1.7	na
elavarasu	42	M	7565	1	101	136	3.7	80	0.4	4.3	8.9	2	na
gandhi	52	M	7592	1	92	142	4.2	44	1	4.3	8.5	2.2	na
angu	39	M	8898	1	101	142	3.5	64	0.4	4.4	8.6	1.4	na
kannan	50	M	9016	1	80	142	4.7	32	0.6	4.2	9.2	1.9	na
ravi	43	M	9030	1	112	138	3.8	80	0.7	4.4	9.3	1.6	na
kanniah	43	M	9241	1	108	140	3.7	39	0.9	4.6	10.3	1.8	na
nagarajan	39	M	9319	1	116	143	4.6	26	0.4	3.9	9.9	2.1	10
venkatesan	30	M	9446	1	92	137	3.7	27	0.9	4.3	8.7	1.7	na
thangaraj	45	M	9941	1	107	144	3.5	54	0.5	4.3	8.5	2	na
saravanan	37	M	10098	1	116	142	3.7	72	0.8	4.6	8.6	2.1	na
rajendran	46	M	10564	1	108	140	4.2	36	0.3	4	10.1	1.3	na
mahesh	37	M	11920	1	114	144	3.7	66	0.7	4.6	9.4	2.1	na
bazeer	46	M	12345	1	92	136	3.5	54	0.8	4.6	8.6	1.7	na
gopalan	30	M	12495	1	113	142	3.7	58	0.9	3.4	10.1	2	10.6
munusamy	48	M	12721	1	122	142	4.2	44	0.4	4.2	8.9	1.5	na
ameer	52	M	12814	1	82	136	3.7	72	1.1	4.2	9.3	2.1	na
ramanan	39	M	12848	1	124	144	3.8	49	1	4.4	8.7	2	na
anbarasu	49	M	13566	1	102	136	4.2	47	0.6	3.6	10	2.1	10.2
chinnathambi	30	M	13696	1	136	139	4.4	58	0.6	4.2	8.6	1.3	na
karthikeyan	44	M	14097	1	105	137	5	24	0.6	4.6	8.7	1.87	na
gopal	29	M	14235	1	82	142	3.6	53	0.4	4.5	9.6	2	na
kesavan	37	M	14369	1	116	`137	4.2	36	0.9	4.6	9.9	1.6	na
gopi	43	M	14401	1	124	142	3.7	24	0.8	3.8	9.4	1.7	9.6
ravi	49	M	14476	1	102	143	3.7	46	0.5	4.2	10.3	1.9	na
munusamy	46	M	15129	1	102	141	3.9	36	0.8	4.6	9.5	2	na
venganna	35	M	15231	1	124	139	4.2	55	0.8	4.6	9.6	2.1	na
raju	52	M	15409	1	109	144	3.6	44	0.6	4.7	8.7	1.7	na
suban	38	M	15584	1	92	138	3.7	58	0.8	4	8.6	1.8	na
satheesh	43	M	15582	1	92	137	4.4	34	0.7	4.5	9.4	1.7	na
anil	43	M	16157	1	112	142	3.6	43	0.7	4.7	8.6	1.8	na
thirunavukarasu	45	M	16707	1	118	145	4.7	62	0.9	4.2	9.7	1.9	na
ramesh	52	M	16740	1	142	136	4.2	32	0.3	4.4	9.5	1.4	na
selvamani	46	M	16763	1	106	142	3.7	69	0.9	4.6	9.7	1.9	na
ganapathy	37	M	17021	1	122	139	4.1	82	0.9	4.7	8.7	1.3	na
angu	53	M	17024	1	101	143	3.6	90	0.5	4.8	8.5	1.2	na
ganesh	45	M	17269	1	150	143	3.5	26	0.7	4.3	8.6	2.2	na
vasudevan	46	M	17405	1	132	136	4.2	78	0.9	4.3	9.6	2.2	na

suresh kumar	38	M	17905	1	106	136	4.3	64	0.8	4.7	9.7	2	na
martin	47	M	18138	1	135	138	4.4	46	0.7	4	9.5	1.8	na
kannabiran	39	M	18422	1	91	142	3.6	44	0.7	4.6	9.8	1.4	na
ganesan	45	M	18731	1	126	142	3.5	72	0.7	4.8	8.6	1.9	na
kannan	39	M	19054	1	142	140	3.8	24	0.7	4.7	8.5	1.4	na
sampath	51	M	19135	1	126	139	4.4	50	0.8	4	8.7	1.8	na
sivakumar	39	M	19539	1	101	142	3.6	44	0.4	4	9.7	1.5	na
dhayalan	36	M	19776	1	92	140	4	46	0.5	4.2	9.4	2	na
velusamy	42	M	20222	1	136	136	4.1	34	1.1	4.2	8.4	1.4	na
ramakrishnan	41	M	20588	1	102	136	4.4	80	0.5	4.4	8.6	2.1	na
srinivasan	46	M`	21378	1	110	142	3.6	52	0.5	4.6	8.6	1.3	na
john	44	M	21646	1	132	135	4	46	0.9	4.2	9.5	1.9	na
nazeer	35	M	21652	1	92	136	4.1	34	0.8	4.2	9.4	1.6	na
srinivasan	47	M	21685	1	132	142	4.3	54	0.9	4.4	9.5	2.1	na
mani	52	M	21717	1	82	135	4.4	80	0.3	4	9.2	1.5	na
jayakumar	43	M	21847	1	102	137	3.6	45	0.7	4.1	9.6	2	na
elumalai	50	M	21919	1	152	139	4.2	53	0.5	4.3	9.8	1.9	na
venkatesan	49	M	21254	1	131	141	3.8	52	1.1	4.6	9.2	1.8	na

Name	Age	Sex	I.P.No	Cage	RBS	S.Na+	S.K+	S.Amylase	S.Bilirubin	S.Albumin	S.Ca2+	S.Mg2+	Corrected Ca2+
kaboor	36	M	8672	0	102	136	3.6	42	0.5	4.2	9.2	1.9	NA
murugan	30	m	8764	0	132	142	4	42	0.6	4.3	8.9	2.1	NA
veerappan	38	m	8766	0	152	140	4.3	26	1.1	4.3	9.3	1.8	NA
muralidharan	42	m	8711	0	102	136	4.1	47	0.3	4	9.9	1.7	NA
ramanathan	34	m	9120	0	92	144	3.6	52	0.9	4.2	9	1.4	NA
ganesan	44	m	9133	0	82	139	4.5	32	0.7	4.6	9.2	1.8	NA
thirunavukarasu	45	m	9295	0	142	136	4.3	52	0.7	4.3	9.3	2.1	NA
chakkarapani	36	m	9548	0	104	136	3.7	42	0.6	4.3	8.5	1.4	NA
krishnan	46	m	10031	0	102	138	3.9	49	0.9	4.7	9.6	4.7	NA
muthulingam	39	m	10089	0	106	138	4.2	36	0.8	4.3	9.2	1.7	NA
nandakumar	47	m	10157	0	139	137	4.5	54	0.6	4.3	8.6	1.9	NA
balaji	48	m	10212	0	90	137	4.1	35	1	4	9.9	2.2	NA
selvakumar	40	m	10414	0	142	145	3.6	72	0.3	4.1	8.4	2.3	NA
dhanakotti	49	m	10661	0	109	142	3.5	37	0.7	4	8.6	1.8	NA
kumar	38	m	10662	0	82	135	4.3	39	0.6	4.2	9.2	2.2	NA
manoharan	50	m	10707	0	108	137	4.3	44	0.8	4.2	9.1	1.6	NA
jayapal	17	m	10791	0	116	137	4	38	0.5	4.3	8.9	1.4	NA
loganathan	38	m	11125	0	123	143	3.5	45	0.9	4.6	8.9	1.5	NA
sikkander	42	m	11153	0	126	135	4.1	53	0.5	4.6	9.4	2	NA
shankar	48	m	11317	0	90	139	4.9	26	0.3	4.1	9.4	2	NA
bhagavan	37	m	11570	0	82	137	4.3	37	0.9	4.3	9.1	1.7	NA
mohan	55	m	11584	0	101	139	4.5	39	0.5	4.4	9.5	2.1	NA
arunachalam	43	m	11658	0	130	136	3.6	42	0.5	4	9.8	1.5	NA
sarath kumar	37	m	12854	0	80	138	4.2	39	0.7	4	8.8	1.6	NA
subramani	29	m	12732	0	142	131	3.9	46	0.9	4.4	9	1.5	NA
subramani	46	m	12932	0	100	136	4.2	52	1	4	8.6	1.9	NA
umapathy	33	m	14531	0	124	138	3.7	39	0.4	4.4	9.1	1.7	NA
kabali	48	m	14694	0	96	142	4.3	38	0.4	4.2	9	1.8	NA
daniel moses	32	m	14696	0	127	139	4.4	52	0.8	4.3	8.9	1.9	NA
krishnasamy	49	m	14817	0	111	136	4.1	42	0.5	4	8.7	1.8	NA
premkumar	51	m	14859	0	107	136	4	38	0.7	4.1	9.2	2.1	NA

ponnan	45	m	14900	0	138	135	4.2	45	0.5	4.1	9.2	1.6	NA
suryamoorthy	30	m	15214	0	101	139	4.3	33	0.9	3.8	8.8	2.1	8.96
devendran	39	m	17168	0	117	136	4.1	51	0.7	4.7	8.7	1.5	NA
saravanan	46	m	17241	0	82	136	3.7	41	0.7	4..2	9.1	1.8	NA
mohan	31	m	17709	0	112	137	3.8	52	0.6	3.9	8.9	1.5	9
buviraj	48	m	17799	0	132	139	4.1	49	0.7	4.3	8.3	1.3	NA
razool moiden	40	m	17960	0	108	144	3.8	28	0.8	4.4	10.3	1.7	NA
abdul 1	42	m	18014	0	102	138	4.3	59	0.5	4.2	8.9	1.6	NA
rosekumar	47	m	18159	0	83	138	4	38	0.7	4.3	9.3	1.9	NA
naresh	32	m	18218	0	127	139	4.1	46	0.4	4	9	1.6	NA
velu	36	m	18779	0	124	138	3.7	32	0.6	4.2	8.9	1.5	NA
muralidharan	35	m	18886	0	91	144	3.6	42	0.7	4.4	9.1	1.6	NA
ashok	48	m	19774	0	127	141	4.6	56	0.8	4.3	9	2	NA
govindaraj	37	m	20013	0	117	137	3.5	40	0.6	4	10.2	1.6	NA
angu	40	m	20104	0	104	138	3.9	29	0.5	4.3	8.6	1.5	NA
suresh kumar	41	m	20227	0	108	139	4.3	42	0.9	4.4	8.7	1.9	NA
kannan	50	m	20921	0	109	144	4.5	48	0.3	4	9.2	1.6	NA
kuppuraj	39	m	21884	0	94	135	4	39	0.7	4.3	8.9	2	NA
narayanan	22	m	22070	0	82	136	4	39	0.7	4.3	8.9	1.6	NA
murugan	35	m	22248	0	122	135	4.1	32	0.9	3.9	8.8	1.4	NA
anand	52	m	22322	0	101	136	4.7	31	0	4	8.8	1.5	NA
deepan	34	m	22397	0	127	139	4.1	44	0.6	4.2	9.1	1.6	NA
murugesan	55	m	22615	0	108	138	3.9	41	0.7	4.1	8.6	1.6	NA