"CLINICAL PROFILE OF HOSPITALISED PATIENTS WITH EPISODE OF HYPOGLYCEMIA"

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CERTIFICATE

This is to certify that the dissertation titled "**CLINICAL PROFILE OF HOSPITALISED PATIENTS WITH EPISODE OF HYPOGLYCEMIA"** is the bonafide original work of in partial fulfillment of the requirements for M.D. Branch-I (General Medicine) Examination of the Tamilnadu DR. M.G.R Medical University to be held in APRIL 2015. The Period of study was from April 2015 to September 2015.

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DECLARATION

I, **Dr.R.VASUKI** solemnly declare that dissertation titled **"CLINICAL PROFILE OF HOSPITALISED PATIENTS WITH EPISODE OF HYPOGLYCEMIA"** is a bonafide work done by me at Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-3 during April 2015 to September 2015 under the guidance and supervision of my unit chief Professor of Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai.

This dissertation is submitted to Tamilnadu Dr. M.G.R Medical University, towards partial fulfillment of requirement for the award of **M.D. Degree(BRANCH – I) IN GENERAL MEDICINE**

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INTRODUCTION

Hypoglycaemia is a lab finding which is defined as low levels of plasma glucose which may or may not be related to significant pathology. Hypoglycaemia that is pathological is caused by large spectrum of clinical disorders.

Several studies have revealed that hypoglycaemia is an independent risk factor for mortality and morbidity in hospitalised patients.

Glucose is the major metabolic substrate for brain under physiologic conditions. Brain can neither synthesize glucose nor store glucose supply of more than few minutes. Hence, it needs continuous supply of glucose from systemic circulation.

Traditionally hypoglycaemia has been linked to diabetes as a therapeutic adverse effect. Contrary to popular belief that hypoglycaemia occurs mainly in diabetic patients due to OHA/Insulin-food mismatch, several studies have shown that hypoglycaemia is common in non diabetic patients also. Even in diabetic patients several risk factors predispose the individual to hypoglycaemia.

Glucose is a major fuel source for body tissues and euglycaemia between 70 to 140 mg is maintained between insulin and glucagon from

pancreas and efficient endogenous Hepatic production of glucose by glycogenolysis and neoglucogenesis. When blood sugar level starts falling, body tries to maintain homeostasis by suppressing insulin secretion as first step followed by stimulating counter hormone response, decreasing peripheral glucose uptake and promoting lipolysis and ketogenesis. Any derangement in this homeostasis can lead to hypoglycaemia.

Spontaneous hypoglycaemia is a manifestation of disease process and reflects derangement in glucose homeostasis. It usually presents as sub acute neuroglucopenia. It is essential to recognise different disease process that can precipitate hypoglycaemia in patients and prevent their recurrence.

In our hospital we have patients with different diseases but admitted with hypoglycaemia. This study is aimed to analyse the disease processes and risk factors for hypoglycaemia and to assess whether hypoglycaemia is a predictor of in hospital mortality.

AIMS

AND

OBJECTIVES

AIMS AND OBJECTIVES

AIM OF THE STUDY:

- To identify the clinical pattern of hospitalized patient with at least one episode of documented hypoglycaemia

OBJECTIVE OF THE STUDY:

- To find and analyse the risk factors associated with hypoglycaemia

- To determine the incidence of hypoglycaemia in patients admitted to medical ward

- To identify if hypoglycaemia with associated risk factors predicts increased mortality rate in hospitalized patient

REVIEW

OF

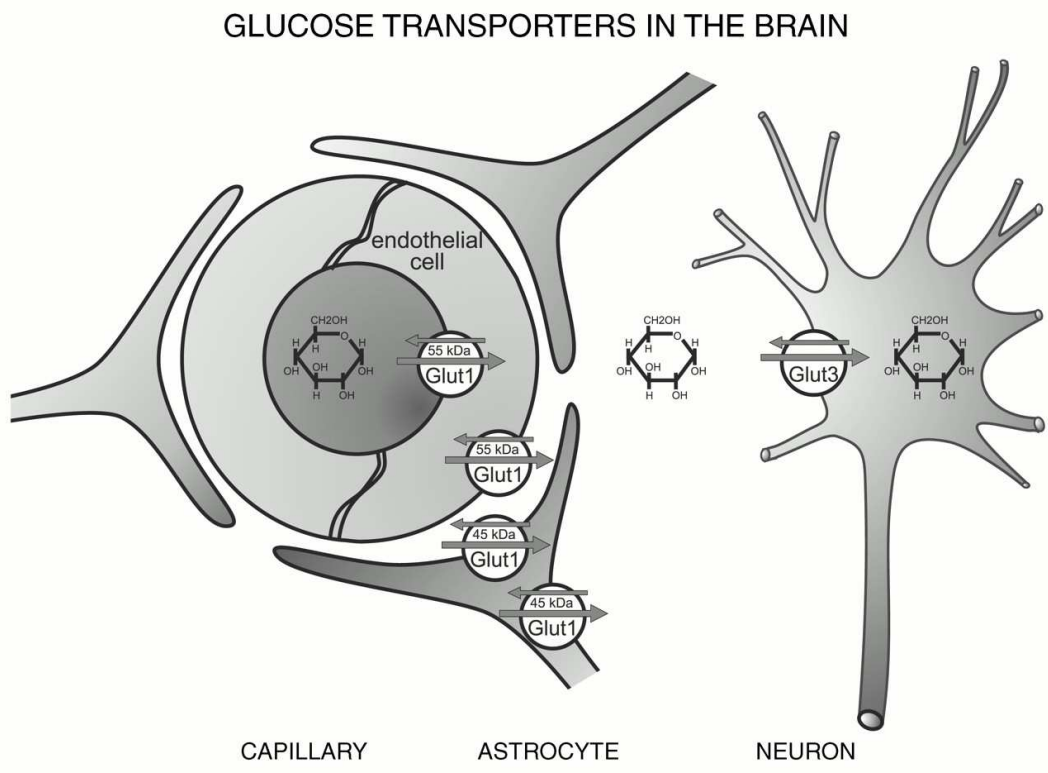
LITERATURE

REVIEW OF THE LITERATURE

BLOOD GLUCOSE REGULATION

Circulating plasma glucose concentration is maintained at a constant range since glucose oxidation is a primary source of energy for central nervous system. The total body glucose is present in extracellular fluid and hepatocytes. This forms the body glucose pool. The glucose pool in man is fifteen to twenty (15 to 20 grams) and turnover of glucose is 120 to 180 mg/min. It corresponds to 170 to 260 grams/day[(1)]. t1/2 of fasting blood glucose is 60 to 80 minutes. Turnover of glucose decreases during fasting and increases during fed state. Lack of adequate supply of glucose results in neuroglucopenia and irreversible damage to brain if hypoglycaemia is prolonged. Death may also occur. Glucose requirements of brain of healthy people are about one mg/kg/min.It corresponds to 100 grams of glucose per day.

Glucose transport in CNS is by GLUT1 AND GLUT3 transporters. Both are independent of insulin. However in fasting state brain can utilise ketone bodies as energy source.



Glucose levels in blood are determined by balance between glucose absorption, production and utilisation. In fasting state glucose production is based on glycogenolysis and substrate availability for neoglucogenesis. Glucose utilisation is based on glucose uptake by peripheral tissues mainly adipose tissue and muscle.[(2)]

The following mechanisms are responsible for prevention of hypoglycaemia**. Glucose levels in blood in post absorptive state is constant due to inflow of glucose into the pool balances outflow.**

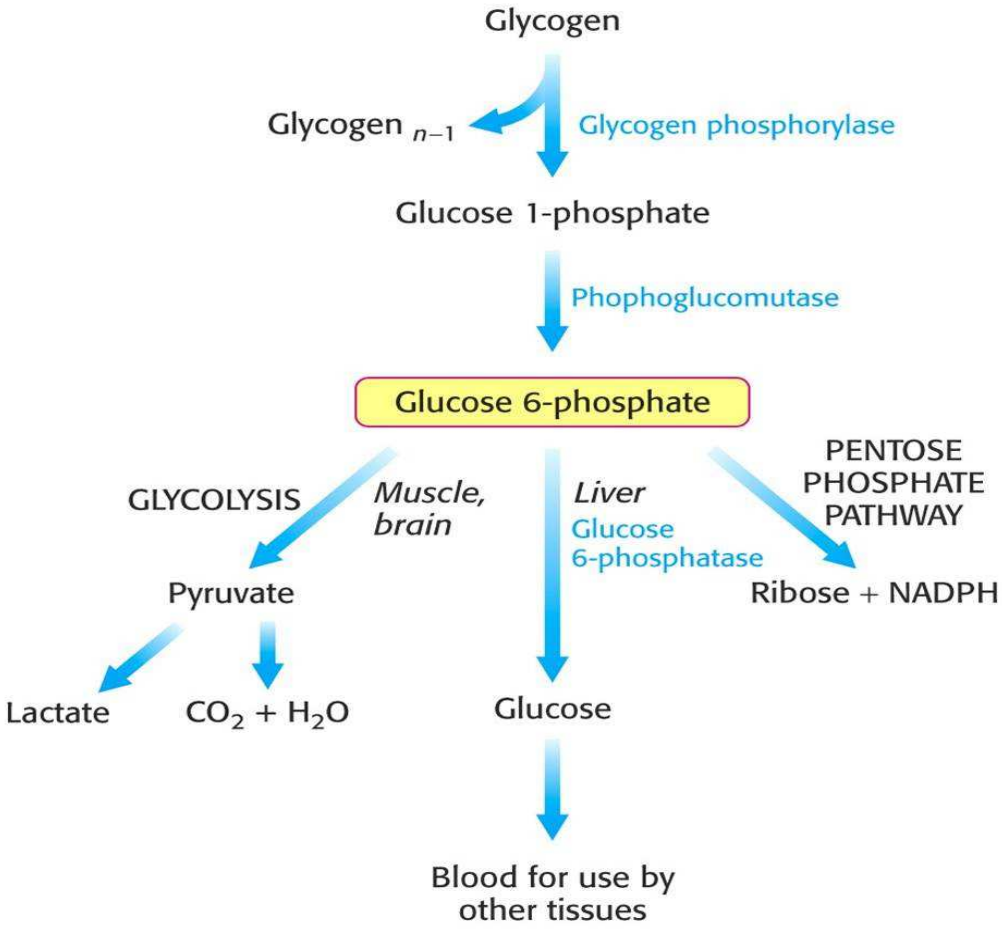
Glucose outflow:

The drain on glucose pool is glucose assimilation by tissues. The cells that are freely permeable to glucose are brain, kidney, islets of pancreas, liver, intestinal mucosa and erythrocytes. Striated muscles and adipose tissue are mainly responsible for post prandial blood glucose disposal and GLUT 4 transporters in muscle and adipose tissue are strictly insulin dependent.

Glucose following entry into the cell is incorporated into the metabolic pool. Glucose is first converted to glucose6 posphate by hexokinase.

Glucose 6 posphate is the starting point for the following pathways :

1) Glycolysis
2) Glycogen synthesis
3) HMP shunt
4) Production of hexosamine and mucopolysaccharid
5) Glucoronic acid



The pathway which the glucose molecule chooses depends on

1) Type of tissue

2) Redox state

3) Other substrate availability

Glucose inflow:

Fed state

The source of inflow is starch from food. Starch is hydrolysed into maltose and isomaltose and finally to monosaccharides before absorption into circulation. Glucose is the monosaccharide that circulates in blood. Galactose and fructose undergo high first pass metabolism in liver.

Glucose after absorption undergoes three changes

1) converted to glycogen
2) converted to fat and others
3) oxidised to provide energy.

Fasting state

Though all tissues remove glucose from blood, liver is the only organ that is capable of adding glucose back to blood. The kidneys to a lesser extent also does this. Three unique properties of liver that makes it a pivotal organ in sugar production is as follows:

1) Glucose is freely permeable between hepatocytes and ECF through GLUT2
2) Presence of glucose 6 posphatase enzyme that liberates free glucose.

3) Presence of neoglucogenic enzymes

Both the processes of glucose uptake and release occurs simultaneously in liver. Net result of glucose uptake or release is determined by the differential rates of the above said processes.[3]

Factors determining the processes in liver are :

1) Insulin concentration in portal vein

2) concentration of blood glucose

- In the post absorptive state insulin levels fall resulting in reduced glucose uptake by muscle, fat and liver. Following suppression of insulin, glycogenolysis, neoglucogenesis and lipolysis are free to occur.
- In the fasting state **glycogenolysis** provides much of the glucose needs in the initial 12 to 24 hours[4]. The amount of liver glycogen is determined by preceding diet.After overnight fast, liver glycogen is 44 grams(15 to 80 grams). In prolonged fasting, hepatic glycogen stores are depleted.36 hours after fasting, glycogen stores is four to eight grams(4 to 8 g) and further contribution to glucose production by glycogenolysis is diminished[5,6]. Lipolysis and protein breakdown take place with supply of glycerol, free fatty acids and amino acids. Amino acids and glycerol are substrates for **neoglucogenesis.**

Neoglucogenesis takes place in liver and kidney. Fatty acids released by lipolysis are used as energy source by the skeletal muscle. Liver uses fatty acids to produce ketone bodies. Ketone bodies are used as source of energy by various tissues.

Basal glucose production from neoglucogenesis accounts for 41% after 12 hours. It increases to 92% following forty hours of prolonged fasting. Kidney accounts for 25% of basal glucose production during extended fasting.

Important enzymes involved in neoglucogenesis are :

- Glucose 6 posphatase
- Fruct ose 1-6 Bisposphatase
- Pyruvate carboxylase
- Posphoenol pyruvate carboxylase.

These enzymes make liver and kidney bye pass otherwise vital irreversible steps of glycolysis.

Important substrates for neoglucogenesis are as follows:

- Lactate
- Alanine
- Pyruvate
- Glycerol
- Glutamate
- Other amino acids

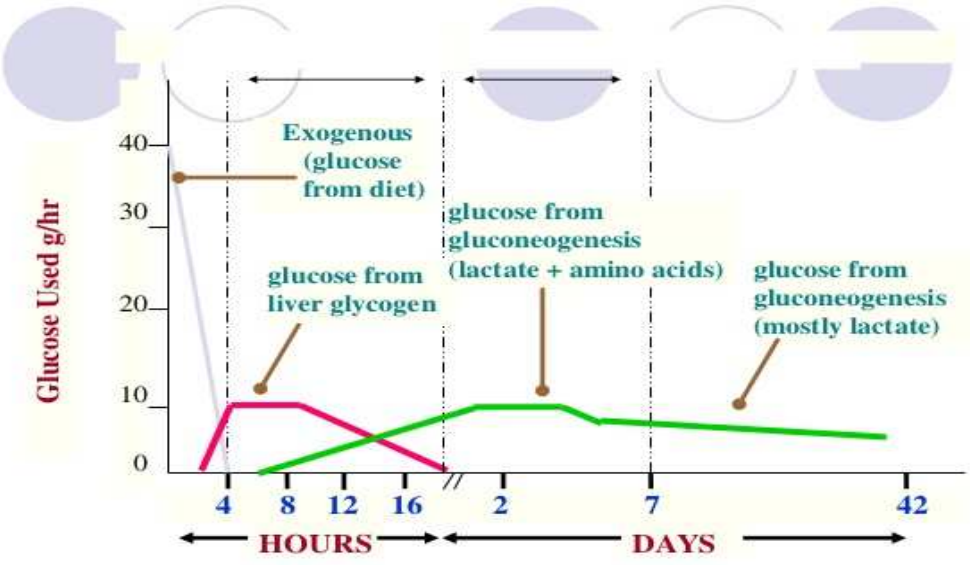
Eating reduces neoglucogenesis while fasting enhances it.

Phases of Glucose Homeostasis

Nutritional Status	Well-Fed	Post-absorptive	Gluconeogenic (early)	Prolonged
Origin of Blood Glucose	Exogenous	Hepatic glycogen, Gluconeogenesis	Hepatic glycogen, Gluconeogenesis	Gluconeo-genesis
Tissues Using Glucose	All	All except liver. Muscle, adipose diminished rates	Brain & RBC's; Small amount by Muscle	Brain Slow rate; RBCs normal
Major Fuel of the Brain	Glucose	Glucose	Glucose	Ketone bodies

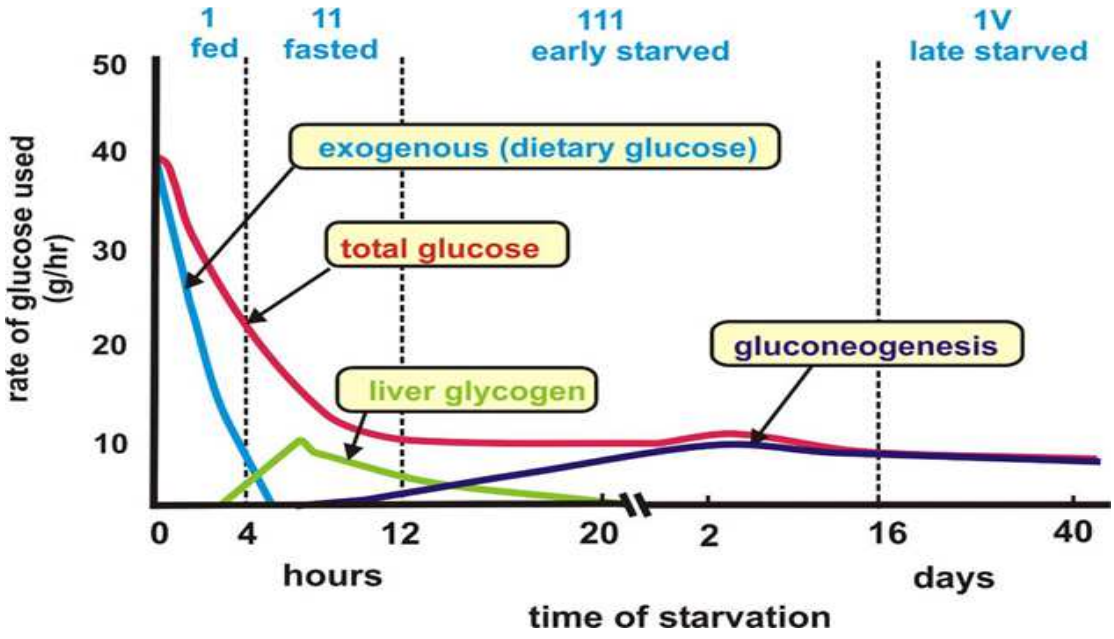
In fed state glucose is the major fuel source to the brain. In the post absorptive state and in early fasting, hepatic breakdown of glycogen occurs and supplies glucose to brain. In prolonged fasting fat break down occurs and ketone bodies form main fuel source for brain.

DIAGRAM - A



Sources of blood glucose in the various nutritional states

DIAGRAM - B


1
fed
11
fasted
111
early starved
1V
late starved
rate of glucose used (g/hr)
50
40
30
20
10
exogenous (dietary glucose)
total glucose
liver glycogen
gluconeogenesis
0
4
12
20
2
16
40
hours
days
time of starvation

COUNTER HORMONE REGULATORY MECHANISM- DEFENCE MECHANISM AGAINST HYPOGLYCEMIA

Counter regulatory hormones are released when blood glucose levels decrease below thresehold. This threshold has been estimated at 67 mg/dl[7].

Ventromedial hypothalamus is vital in starting counter hormone response[8]. Activation of glucose sensitive neurons in ventro medial hypothalamus of the brain is one of the main physiological response to hypoglycemia. Activation of this region causes :

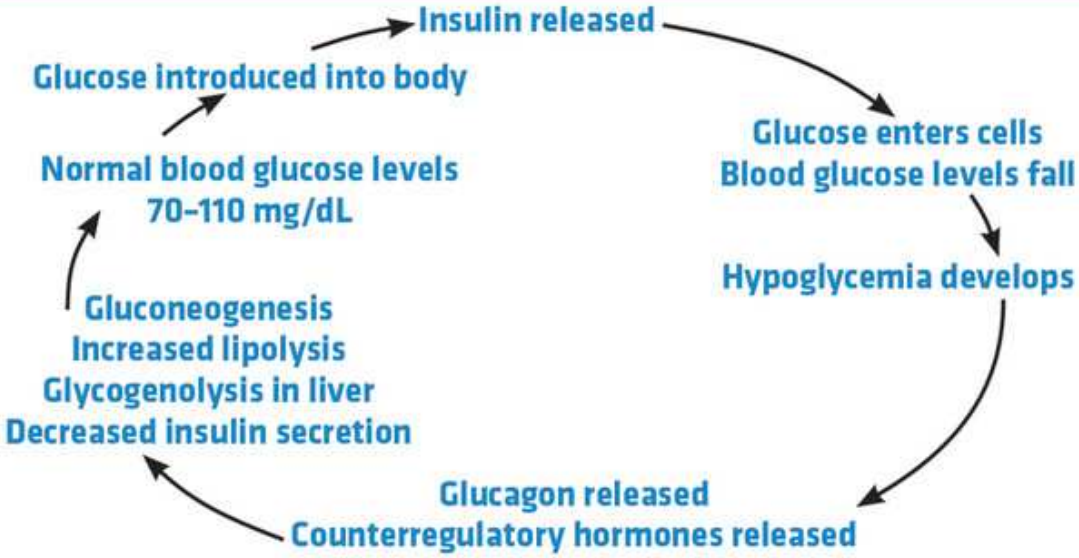
1. Stimulation of autonomic nervous system
2. Release of counterhormones[9-14]

Counter hormones belong to two groups

Rapidly acting hormones - Glucagon , Catecholamine

Slowly acting Hormones - Growth hormone , Cortisol.

Figure 1: Regulation of Blood Glucose Levels



Secretion of insulin is suppressed at glucose levels of 80-75 mg/dl. Counter hormones are released at glycaemic levels of 70 to 65 mg/dl. **Thus, the first defence mechanism against hypoglycaemia is suppression of endogenous insulin secretion.**

Glucagon is the second defence mechanism against hypoglycaemia and the first counter regulatory hormone to rise. The primary action of glucagon is increase in glucose production by liver by stimulating glycogenolysis and neoglucogenesis. It has little effect on peripheral utilisation of glucose and glucose production by kidneys.

Though glucagon stimulates lipolysis and ketogenesis,it has minimal net effect on mobilisation of neoglucogenic precursors from adipose tissue.

Catecholamines have several effects on glucose homeostasis. It causes

- Suppression of insulin secretion
- Stimulation of neoglucogenesis-Hepatic and renal
- Stimulation of glycogenolysis
- Stimulation of lipolysis
- Stimulation of lipolysis provides glycerol for neoglucogenesis and free fatty acids for ketone bodies production.

The slow acting counter regulatory hormones namely Growth hormone and cortisol have a limited role in acute hypoglycaemia. They play a significant role in periods of prolonged fasting. Their levels usually rise about three hours after fasting. The major glucoregulatory effects of these hormones are on hepatic neoglucogenesis and lipolysis. There is increased level in production of free fatty acids and glycerol. They also peripheral utilisation of glucose is also suppressed. The production of free fatty acids and ketone bodies are greatly glucose sparing since they are used as alternate fuel by several tissues including skeletal muscles. Patients with low fat reserve, who cannot adequately augment lipolysis, in period of fasting, are prone for severe hypoglycaemia as they lack these alternate fuels.

DIAGRAM - A

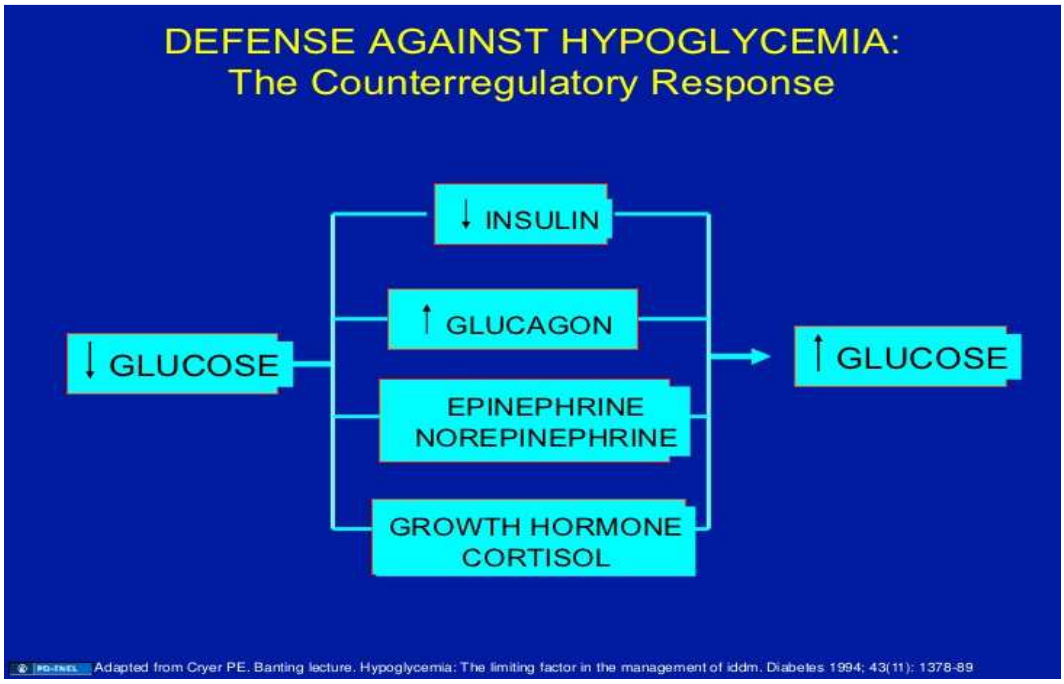
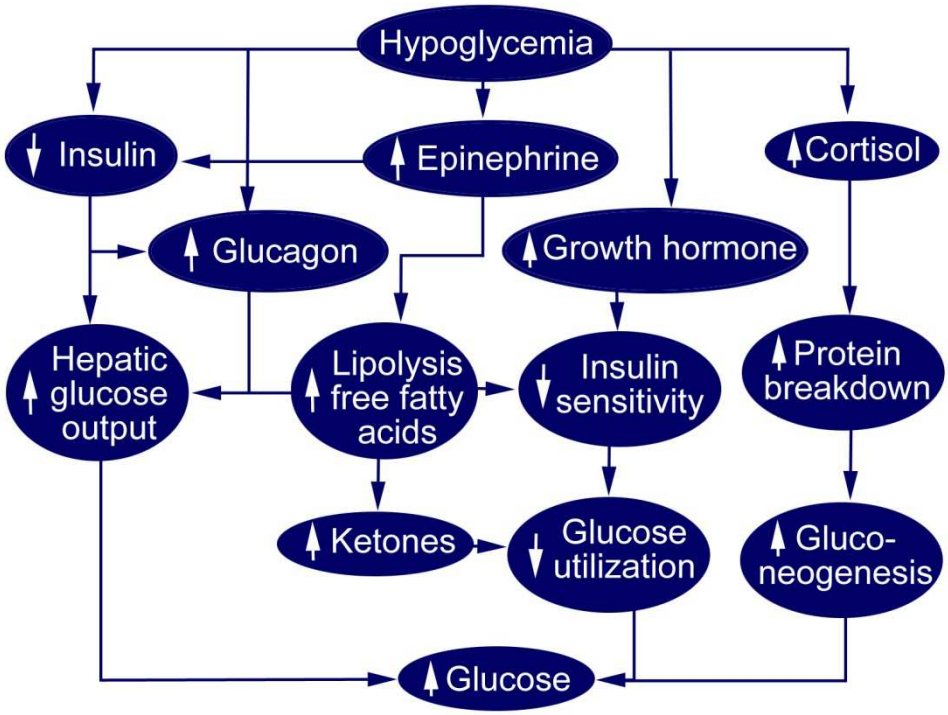
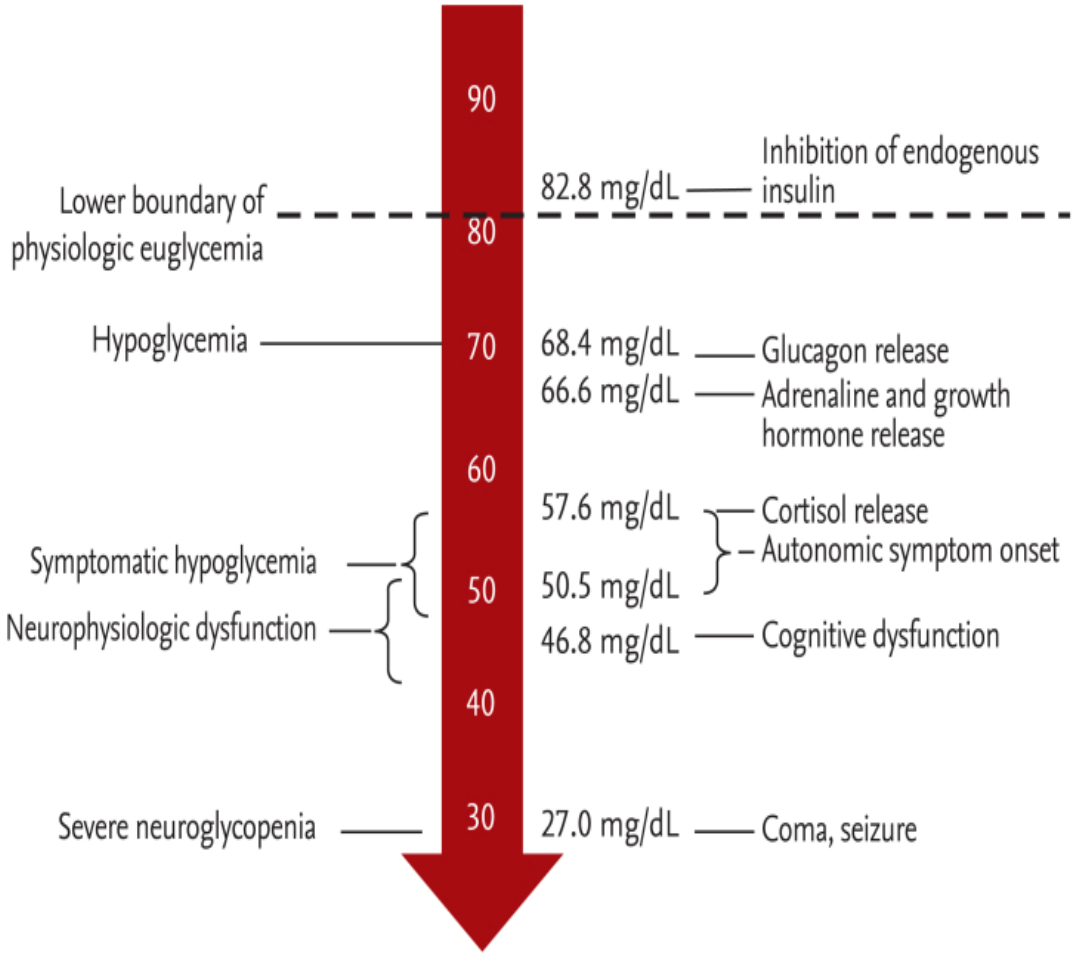

DEFENSE AGAINST HYPOGLYCEMIA:
The Counterregulatory Response
↓ INSULIN
↑ GLUCAGON
↓ GLUCOSE
↑ GLUCOSE
EPINEPHRINE
NOREPINEPHRINE
GROWTH HORMONE
CORTISOL
Adapted from Cryer PE. Banting lecture. Hypoglycemia: The limiting factor in the management of iddm. Diabetes 1994; 43(11): 1378-89

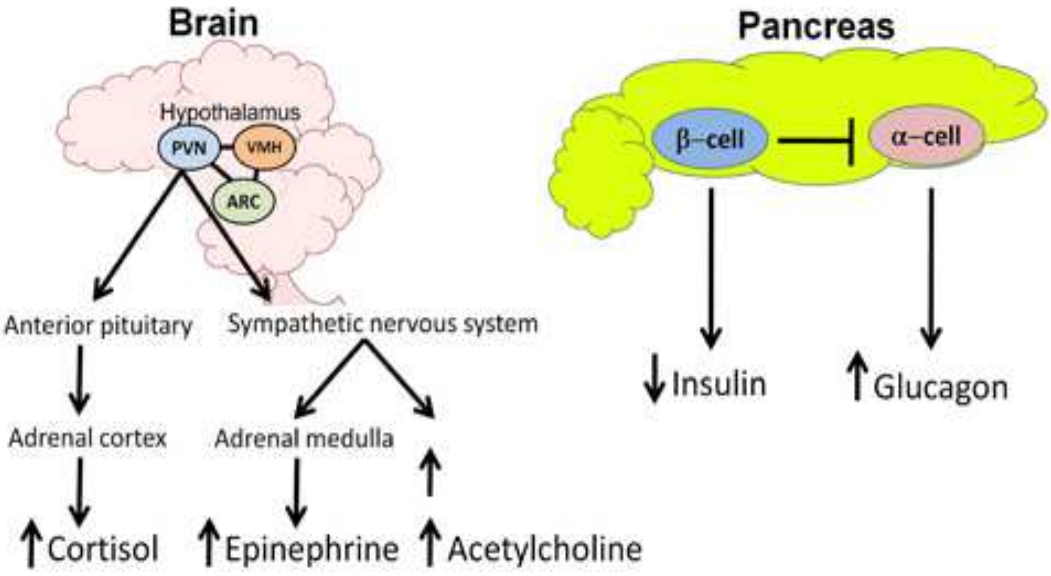
DIAGRAM - B

DEFENCE AGAINST HYPOGLYCEMIA





Thus, when glucose levels start falling, there is pancreatic switch off of beta cells that automatically inhibits Insulin secretion. This occurs at lower limits of physiological levels of blood glucose. The paracrine effect of beta on alpha cells helps to increase glucagon levels.



Normally Brain responds to hypoglycaemia. Several regions of hypothalamus initiate a stress response to bring back euglycemia. The regions of Hypothalamus that are vital in sensing and responding to low blood sugar levels are ventromedial hypothalamus, paraventricular nucleus and arcuate nucleus.

Definition of hypoglycaemia

The diagnosis of hypoglycaemia is based on Whipple's triad[15]

- Symptoms consistent with hypoglycaemia
- Low blood glucose concentration
- Relief of symptoms when blood glucose level is raised to normal by exogenous administration of glucose

As per A DA recommendations plasma glucose level below 70 mg/dl is taken as hypoglycaemia.

SIGNS AND SYMPTOMS OF HYPOGLYCAEMIA

Hypoglycemic symptoms are due to :

1.adrenergic 2.cholinergic 3.neuro glucopenic

Early adrenergic symptoms	Neuroglycopenic signs
Pallor	Confusion
Diaphoresis	Slurred speech
Shakiness	Irrational or uncontrolled behavior
Hunger	Disorientation
Anxiety	Loss of consciousness
Irritability	Seizures
Headache	Pupillary sluggishness
Dizziness	Decreased response to noxious stimuli

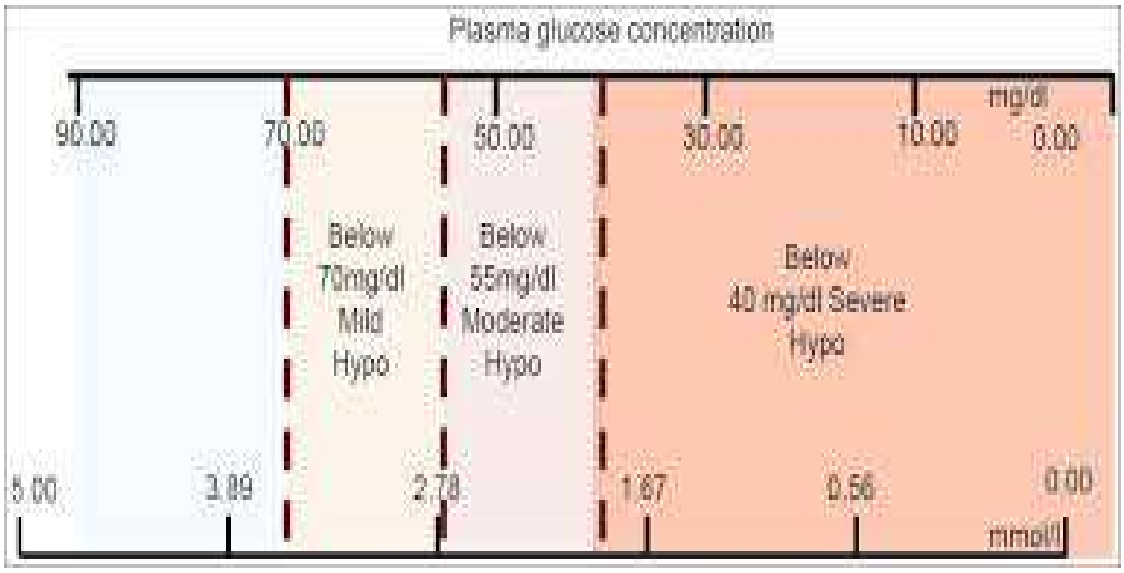
- Cholinergic symptoms are mainly hunger, sweating and paresthesia.

Table 1

SIGNS AND SYMPTOMS OF HYPOGLYCEMIA	
Stage	**Signs and Symptoms**
Mild Hypoglycemia	Feeling of shakiness, trembling Perspiration Blurred vision Dizziness Difficulty concentrating Feeling nervous or anxious Feeling of weakness Numbness or tingling around mouth and lips Fatigue Headache Sudden hunger Nausea Rapid heart rate, palpitations
Moderate Hypoglycemia	Irritability Agitation Confusion Lack of coordination Difficulty speaking or slurred speech
Severe Hypoglycemia	Confusion Fainting/loss of consciousness Seizures Inability to swallow

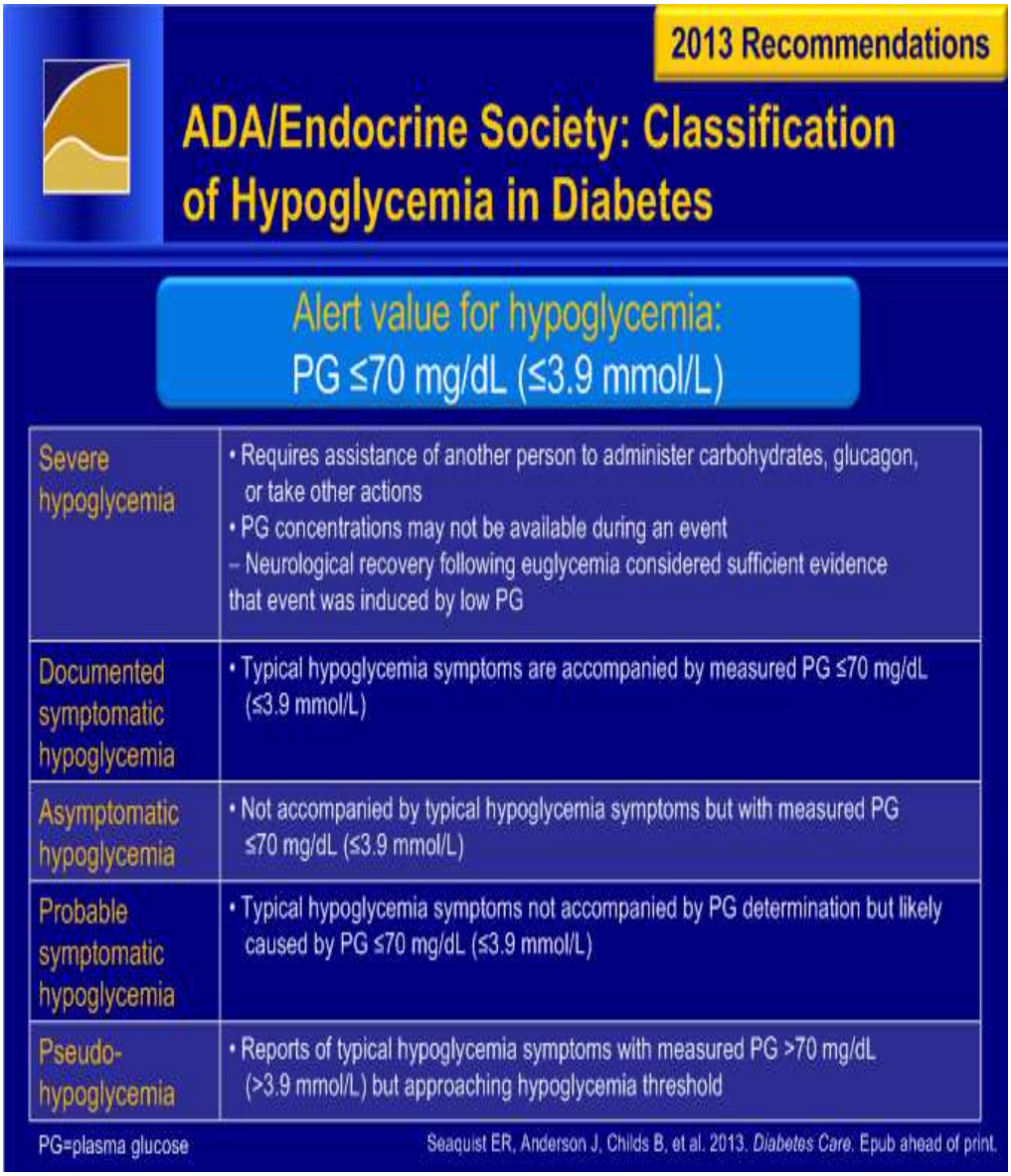
Adapted from references 1, 2, 4, and 5.

Mild, moderate and severe hypoglycaemia are based on prevailing blood sugar levels and the promptness of counterhormone response.



In mild hypoglycaemia patient has increased hunger, tiredness, exhaustion. When sugar levels fall further down patient experiences increased sweating, tremors, palpitations. Neuroglycopenic symptoms also occur simaultaneously like dizziness, lack of concentration, irritability and altered mental behaviour. In severe hypo when blood glucose falls below40 mg % the patient presents with altered sensorium, seizures leading on to coma and death.

CLASSIFICATION OF HYPOGLYCAEMIA



Pseudo hypoglycaemia is also called relative hypoglycaemia.

Hypoglycaemia commonly occurs due to drugs taken for treating diabetes mellitus in outpatient setup but in case of hospitalised patients hypoglycaemia is caused by numerous entities which should be identified and treated accordingly.

The subject of hypoglycaemia in adult hospitalised patient is not dealt in detail in many of the textbooks though it is mainly presented in the context of diabetes mellitus management. But in reality we come across many hypoglycaemic episodes in hospitalised patients not suffering from diabetes mellitus.

The present study is aimed at determining the spectrum of disorders and associated risk factors in causing hypoglycaemia in hospitalised patient in a tertiary care setup.

ADULT HYPOGLYCEMIA - CAUSES

A. Internal causes

1.INSULIN MEDIATED

- Reactive hypoglycemia
- Insulinoma
- Insulin antibody
- nesidioblastosis

2. INSULIN INDEPENDENT

- Congestive cardiac failure
- Liver disorders
- Kidney failure
- Sepsis
- Endocrine abnormalities
- Antibody to insulin receptor
- Neoplasia

B.External causes

1) Medications

i) Direct effect

- sulfonylureas
- insulin
- pentamidine
- anti malarials
- diisopyramide
- $Beta_2$ adrenoreceptor agonist

Drug interaction

- Biguanides
- PPRγ agonists
- Beta blockers
- ACE inhibitors

2) Ethanol

3) Factitious

4) Toxins

Drug induced hypoglycaemia

Various drugs are found to be associated with hypoglycaemia. But, the direct cause effect relationship is not elucidated in many cases. Predisposing factors include :

- Very young age
- Very old age
- Impaired liver function
- Impaired renal function
- Poor nutrition

Mechanism of drug induced Hypoglycaemia

- Augmenting insulin release due to stimulation of insulin secretion mechanism
- Direct toxicity to pancreatic islets causing non regulated insulin release
- Increased peripheral uptake of glucose
- Decreased glucose production by liver
- Potentiate effects of insulin and sulfonylureas

Drugs that increase insulin release:

1.Quinine

Quinine and its derivatives cause hyperinsulinemic hypoglycaemia.

2.Diisopyramide

Diisopyramide increases insulin secretion from Beta cells of pancreas. It closes k^+ATP channel of Beta cell, binding to a site different from site of sulfonylurea.

3.Ritordine

Ritordine therapy to prevent premature labour can cause increased insulin secretion.

4.Pentamidine

Pentamidine used for treating PCP pneumonia and trypanosomiasis and leishmaniasis is toxic to Beta cell of pancreas.

Drugs that increase insulin sensitivity

1.Biguanides and PPRγ agonists

Biguanides and PPRγ agonists usually is not associated with hypoglycaemia when consumed alone.But, they increase the risk of hypoglycaemia caused by insulin and sulfonylureas by augmenting

glucose uptake and utilisation.Metformin also reduces hepatic glucose production and reduces intestinal glucose absorption.

2.ACE inhibitors

ACE inhibitors indirectly augment insulin sensitivity. They increase circulating kinins causing vasodilatation and increase glucose uptake by muscles. However, they are safe and hypoglycaemic risk is low.

3.Beta blockers

Beta blockers oppose the catecholamine effect on uptake of glucose and lipolysis. They enhance uptake of glucose in skeletal muscle. Lipolysis suppression and consequent reduction in NEFA augments insulin sensitivity. They indirectly reduce neoglucogenesis. However they decrease insulin secretion from Beta cells of pancreas. Hence, insulin treated patients are prone for hypoglycaemia and type 2 DM patients are prone for hyperglycaemia. Adrenergic response to hypoglycaemia is blunted by Beta blockers and thus predisposing patients for Hypoglycaemic unawareness.

Alcohol

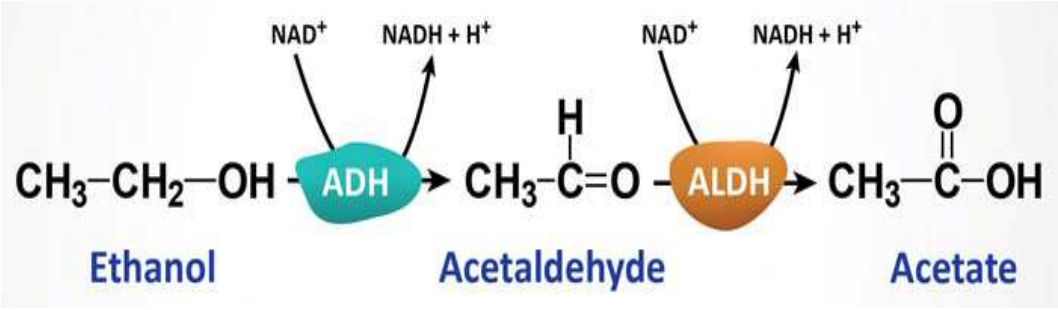
Hypoglycaemia due to alcohol ingestion occurs in all age groups and different classes of society. It is more severe in extremes of age, men, malnourished persons. Consuming alcohol accidentally by young children may cause hypoglycaemia[16].Alcohol is implicated in 18-56% of people admitted due to severe hypoglycaemia[17].

Mortality rate in hospatilised patient due to alcohol related hypoglycaemia is almost 10%[17].

- **The main mechanism of alcohol induced hypoglycaemia is inhibition of neoglucogenesis.**

Cytoplasmic enzyme Alcohol dehydrogenase oxidizes ethanol to aldehyde which is a NAD dependent.

Acetaldehyde is oxidized to acetate by aldehyde dehydrogenase that is a mitochondrial enzyme . It also utilises NAD^+.




Metabolism of Alcohol
Alcohol
Alcohol dehydrogenase
Acetaldehyde
Acetaldehyde dehydrogenase
Acetic acid
Oxygen
Carbon dioxide
+
Water and energy

There is a shift in redox status of the cell with **high NADH/NAD^+ ratio** due to oxidation of ethanol.

Several metabolic changes occur which have dangerous effects in alcoholics. They include :

- **LACTIC ACIDOSIS :**
  - High level of NADH helps in conversion of pyruvate to lactate.

This leads to accumulation of lactate causing lactic acidosis.

- **HYPOGLYCAEMIA:**
  - There is lack of pyruvate for oxaloacetete production along with malfunctioning of malate shuttle depressing neoglucogenesis .This causes hypoglycaemia[18].

- **KETOGENESIS :**
  - TCA cycle slows down due to accumulation of NADH causing increased availability of acetyl coA. This causes ketogenesis.

- **FATTY LIVER :**
    - Synthesis of fatty acid is favoured but there is deficient mobilisation. Lipoproteins are not effectively synthesised. This leads to accumulation of fat in the liver.

- **Ethanol inhibits gluconeogenesis but not glycogenolysis.**

- Ethanol suppresses release of, growth hormone, corticotrophin, cortisol. Epinephrine and glucagon responses to severe hypoglycaemia are delayed. All these contribute to fasting hypoglycaemia[19].

- **Alcohol also causes reactive hypoglycaemia**. Consumption of moderate amount of alcohol increases secretion of insulin following glucose stimulation. Person taking alcohol and sucrose may experience hypoglycaemia due to excess of insulin[20].

Clinical characteristics

Generally patient is an alcoholic with moderate to large consumption of alcohol but no carbohydrate or protein intake in previous 12-24 hours. Patient may be comatose or suffer from seizures. Most of the patients do not have adrenergic responses to low blood sugar levels and directly result in neuroglucopenia.

INTERNAL CAUSES OF HYPOGLYCAEMIA

Hospitalised patients with organ failure are more prone for hypoglycaemia.

CARDIAC FAILURE

Hypoglycaemia occurs in people with severe congestive cardiac failure. causes may be due to cachexia and Liver dysfunction due to congestion and hypoxia and lack of substrates for gluconeogenesis

Patients with severe heart failure in icu may develop ischemic hepatitis and hypoglycaemia[21-23].

Several studies have shown that hypoglycaemia is common in cardiac failure secondary to coronary heart disease, RHD, Cardiomyopathy and even COPD.

Reasons thought are low calorie intake, malabsorption, increase utilization of glucose by cardiac tissues that are ischemic. Hepatic congestion and liver dysfunction are also discussed as one of the mechanisms. Studies recommend checking of blood sugar in people with congestive cardiac failure presenting with altered sensorium or confusion[24].

RENAL FAILURE

End stage kidney disease is associated with hypoglycemia[25].The common pathologies associated are

- Drug induced
- Malnutrition
- Sepsis

There is also high rate of mortality. Haemodialysis can *c*ause spontaneous hypoglycaemia in both diabetic and non diabetic patients during or after dialysis[26].

Response to hypoglycaemia is blunted and unawareness is commonly seen[27].The pathogenesis includes the following

- decreased gluconeogenic substrates In patients with severe cachexia, low carbohydrate intake and malnutrition.

- increased circulating levels of insulin due to decreased clearance
- increased resistance to glucagon
- suppression of renal gluconeogenesis[28,29]

Kidney glucose production and output accounts for 25% of serum blood glucose level in post absorbtive states in normal people. It increases to 40% during hypoglycemic states in healthy individuals. As this is hampered in chronic renal disease, these people are prone for hypoglycaemia[29,30]

LIVER DISORDERS

As we have already seen, neoglucogenesis and glycogenolysis are important for maintaining the post absorptive glucose state.Both the processes occur almost exclusively in the liver and hence hypoglycaemia occurs in liver dysfunction.

Hypoglycaemia occurs in severe hepatic failure due to fulminant viral, toxic hepatitis. It is also common in alcoholic hepatitis and fatty liver. Hypoglycaemia occurs in last stages of cirrhosis with liver cell failure[31].

SEPSIS

In hospitalized patients hypoglycaemia is commonly seen in sepsis. There are generally two metabolically different phases associated with sepsis. In its early phase there is hyperglycaemia and this is followed by phase of hypoglycaemia in which there is reduction in glucose output in liver. There is

- Rapid depletion of glycogen content in liver
- Impaired glycogenolysis
- Depressed neoglucogenesis
- Enhanced peripheral utilization of glucose[32]

There is alteration in transcriptional regulation of beta 2 adrenergic receptor gene expression. This is responsible for altered glucose metabolism in liver in sepsis[33].

There is increased utilisation of glucose by macrophage rich tissues like spleen, liver and lung.This causes increased utilization[34].

Muscle and fat cells make less contribution to the enhanced glucose utilization. Cytokines produce insulin resistance and also increase insulin secretion. The imbalance between glucose utilization and glucose production contribute to prevailing glycaemic status[35,36].

In cases of endotoxemic shock, in experimental animals, hypoglycaemia has been documented due to inhibition of neoglucogenesis[37].

Hypoglycaemia in sepsis and mortality:

Several studies have revealed that overwhelming sepsis is associated hypoglycaemia, which indicates grave prognosis. The risk of hypoglycaemia in sepsis increases with prolonged starvation, malnutrition and presence of organ failures[38].

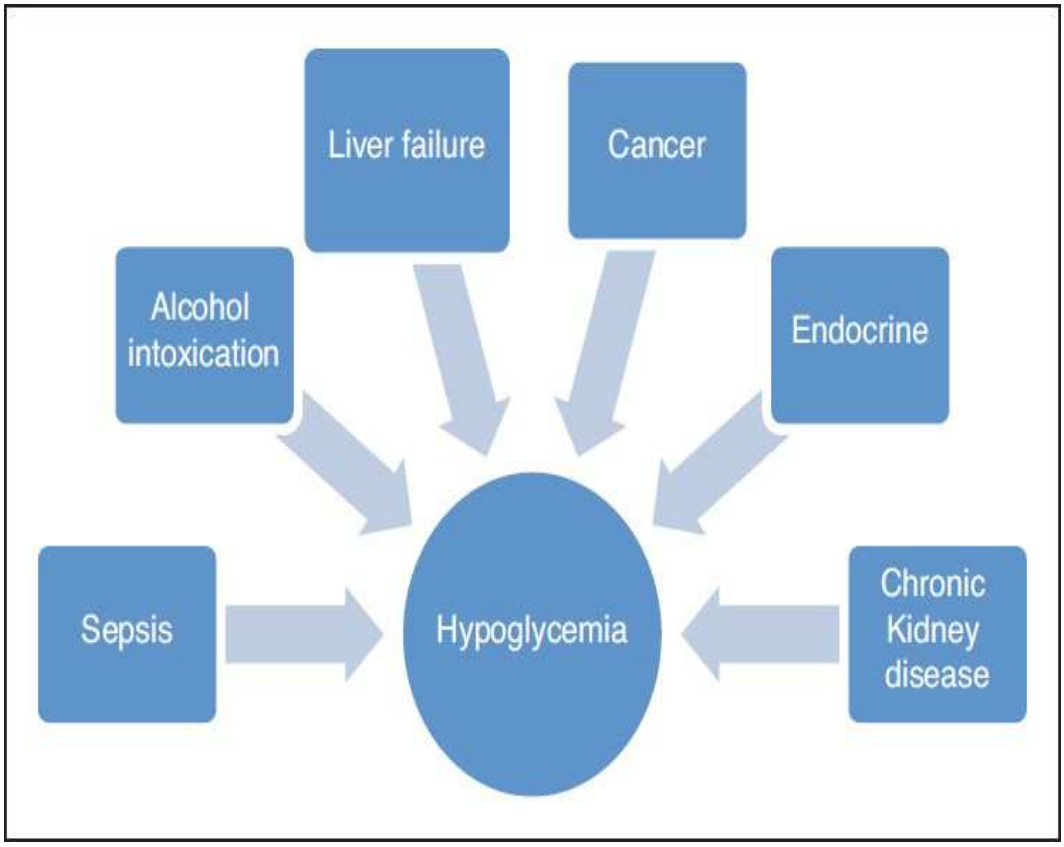
One study showed that about 8.6% of patients with severe pneumococcal sepsis had episodes of hypoglycaemia that correlated with increased mortality. Hence, the study recommends frequent blood sugar measurements even in non diabetic patients with sepsis to avoid deleterious effects of hypoglycaemia[39].

Endocrine Deficiencies :

Deficiency of glucagon is generally rare in clinical practice. Similarly deficiency of epinephrine alone rarely ever causes hypoglycemia in the absence of hyperinsulism.

- Patients with hypopituitarism can have low blood sugar when glucose utilization is enhanced as during exercise. In patients with primary adrenal insufficiency fasting glucose levels are usually normal[(40)].

CAUSE OF HYPOGLYCEMIA



Immune hypoglycemia :

Due to:

- antibodies against insulin
- antibodies against insulin receptor
- Insulin antibodies

Predisposition

- Japanese
- New onset type I DM
- Autoimmune diseases
- Relatives of type I DM
- Patient taking insulin injection
- Medications having –SH group

Post insulin injection/Post meals leads to large amount of insulin in blood which is mainly bound to antibodies. This leads to hyperglycaemia followed few hours later in the release of bound insulin leading to late hypoglycaemia.

Remedial measures to be taken are

- Avoid inciting drugs
- Frequent low carbohydrate diet
- Drugs which delays glucose absorption
- Insulin receptor antibodies

Predisposing causes

i) Women

ii) Autoimmune disorders

iii) Hodgkin's lymphoma

Antibodies are of polyclonal origin with multiple sub classes of immunoglobulins. Some Ig stimulates the insulin receptor while others inhibit it. Titer of these subclasses of immunoglobulin varies at various point of time. This leads to the occurrence of hyperglycaemia and hypoglycaemia at varied intervals in the same patient[(41)].

Lab findings

i) Hypoglycaemia and hyperglycaemia

ii) Insulin receptor antibodies in varying titer

iii) Low C peptide levels

iv) High insulin levels

Postulated mechanisms

1) Diminished clearance of circulating insulin

2) Stimulation of pancreatic beta cells receptor by antibodies.

Management

- Plasmapheresis
- Cytotoxic drugs

Poor prognosis due to :

- Severe hypoglycaemia
- Associated malignancy
- Associated auto immune diseases

Reactive hypoglycaemia

It is a direct but delayed consequence to a rise in blood sugar following glucose load. It may be symptomatic or asymptomatic.

Mechanism

Ingestion of oral glucose is followed by rise in blood sugar concentrations. Peak is reached in thirty to sixty minutes. This time also corresponds to peripheral uptake of glucose maximally. Generally glucose levels start falling after this time. However, second and third peaks of glucose and insulin levels have been documented[42,43,44].

- Concentration of blood glucose falls at a rate that is slower and with considerable variations than the rise. Generally, plasma glucose levels reach nadir three to five hours following ingestion of glucose drink[43,45].

The size of oral glucose load ,presence of other nutrients and the rate of gastric emptying determine the time of glucose nadir. Following ingestion of one hundred grams of glucose, it takes two hundred and forty minutes(four hours) to achieve this nadir[43,45]. However, it may occur between one hundred and twenty to three hundred and sixty minutes. (2 to 6 hours). The nadir is below the fasting blood sugar levels.

Larger quantity of glucose used for loading test result in occurrence of reactive hypoglycaemia more frequently. Consuming large quantity during loading test leads to prolonged duration of hyperglycaemia. But, the peak value is not increased to the same extent[46-50].It is followed by hypoglycaemia.

Mechanism postulated for above phenomenon are

1) Absorption of glucose is rate limited

2) Increased insulin secretion on account of large glucose load and stimulation by other enteric hormones.

Reactive hypoglycaemia represents short period in absorptive and post absorptive phase, when glucose uptake by peripheral tissues and the liver exceeds glucose input from both GIT and liver. It occurs due to :

- Continuous glucose uptake by skeletal muscle and adipose tissue following preceding hyperinsulinemia.
- Enhanced tissue sensitivity, eventhough the insulin levels are returned to baseline.
- Input from GIT stops abruptly during a brief period when liver is predominantly in the process of glycogen storage.

The severity of reactive hypoglycaemia is increased by :

- Intake of very large glucose loads and insulinotropic carbohydrates which include galactose, maltose, sucrose but not fructose.
- Ingestion of carbohydrate with alcohol
- Ingestion of sugars following carbohydrate deprivation[51-53].

The rate of gastric emptying plays a major role in reactive hypoglycaemia.

Types of reactive hypoglycemia :

- i) Alimentary
- ii) Early diabetes
- iii) Idiopathic

Alimentary:

Occurs after gastrectomy surgery[54] due to rapid transit of food in the GIT leading to fast absorption of glucose which in turn stimulates insulin secretion. The effect of secreted insulin lasts long leading to hypoglycaemia.

Early diabetes:

Reactive hypoglycaemia is considered to be a harbinger of early Diabetes Mellitus in the person[55]. This manifestation, however, is not seen frequently in Diabetes mellitus. Post meals, these people have minimal hyperglycaemia and hypoglycaemia after 3 to 5 hours.

Idiopathic

Autonomic symptoms occurring after meals in few individuals fall under this category. Many a times the blood sugar measured during the period of symptoms were found to be normal.

HYPOGLYCEMIC EPISODES IN DIABETES :

Hypoglycemic episodes are significant limiting factor in the treatment of Diabetes[56,57]. it causes severe morbidity in patients with

- T1DM and in advanced T2DM.

- Hypoglycemia may sometimes prove fatal in diabetes. Several papers have reported death in bed where hypoglycemia has been cited as an important risk factor[58,59]. It can cause death due to cerebral damage also[60].

- Hypoglycemia in both T1DM and T2DM are the net result of :

1.therapeuic hyperinsulinemia that is absolute or relative

2.reduced defence mechanisms against hypoglycemia[61,62].

- Hypoglycemia is more common in T1DM patients with absolute insulin deficiency than T2DM patients with OHA . however incidence of hypoglycemia in patients with advanced long standing duration of T2DM is also increased.

- Hypoglycemia in diabetics is a complex process. It is not a mere therapeutic side effect. The endogenous defense mechanism

against hypoglycemia are blunted starting early in T1DM and in advanced T2DM.The impairment of defense mechanism is profound in long standing T1DM patients and mild in T2DM patients.

Hypoglycemia in T1DM :

In T1DM mechanism of hypoglycaemia is very complex because it is due to:

- Complete exogenous administration of insulin
- The first defence mechanism to hypoglycaemia of inhibiting endogenous insulin secretion from beta cells is not there. Hence, sugar level drops down.
- The response of glucagon to low blood sugar levels begins to fail within two years of T1DM and after five years, an impaired response is universal[63].This is because of disruption in the paracrine effect of beta cells on alpha cells as endogenous insulin production is negligible.
- There is also decreased sympathoadrenal responses to hypoglycaemia in long standing diabetes[64].

- The above mechanisms make T1DM patient more sucesptible to severe and fatal hypoglycaemic episodes.Recent reports reveal that 6 to10% of patients with T1DM die of hypoglycaemia[65].

Hypoglycaemia in T2DM

Hypoglycaemia in type 2 diabetes occurs due to the following reasons.

- Long acting sulfonylureas
- Missing if meals/delayed meals.
- Insulin/OHA- food mismatch
- Sternuous/unaccustomed exercise
- Elderly patients
- Gastroparesis
- Drugs that either enhance sulfonylurea action or improve insulin sensitivity
- Organ failure
- Endocrine disturbance like hypopituitarism, hypothyroidism

Hypoglycaemia associated autonomic failure

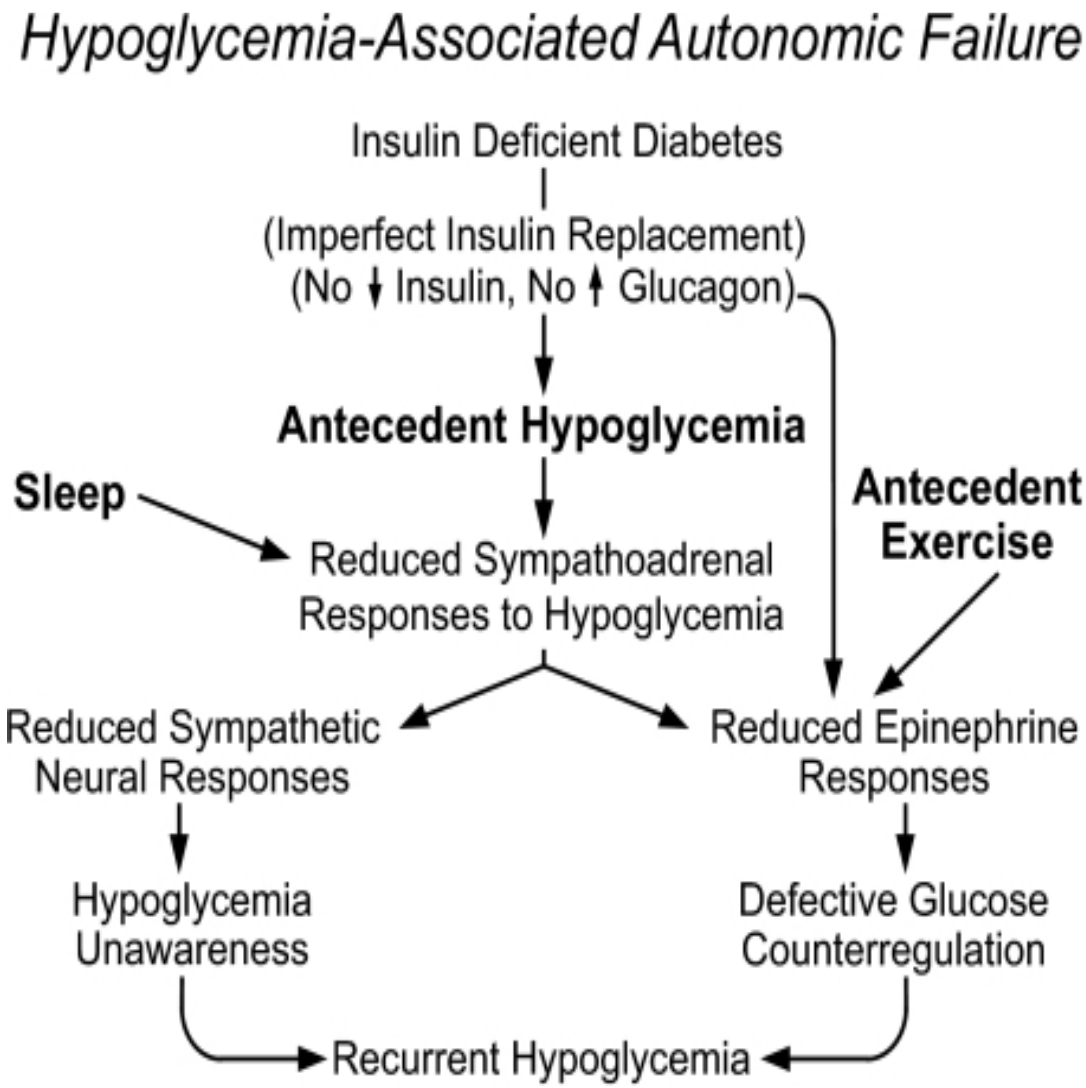
- HAAF is functional disorder of dynamic nature which is associated with defective glucose counter regulation and hypoglycaemia unawareness. Dysregulated counter hormone response includes failure of inhibition of insulin secretion and failure of increase in glucagon secretion following hypoglycaemia.

- This is accompanied by reduction of epinephrine responses to further episodes of hypoglycaemia. The reduced sympatho - adrenal responses results in attenuation of symptoms.

Three main predisposing factors are

- Nocturnal hypoglycaemia
- Prior exercise
- Antecedent hypoglycaemia[66-69].

HAFF is more characteristic of T2DM than T1DM.


Hypoglycemia-Associated Autonomic Failure
Insulin Deficient Diabetes
(Imperfect Insulin Replacement)
(No ↓ Insulin, No ↑ Glucagon)
Antecedent Hypoglycemia
Sleep
Antecedent Exercise
Reduced Sympathoadrenal Responses to Hypoglycemia
Reduced Sympathetic Neural Responses
Reduced Epinephrine Responses
Hypoglycemia Unawareness
Defective Glucose Counterregulation
Recurrent Hypoglycemia

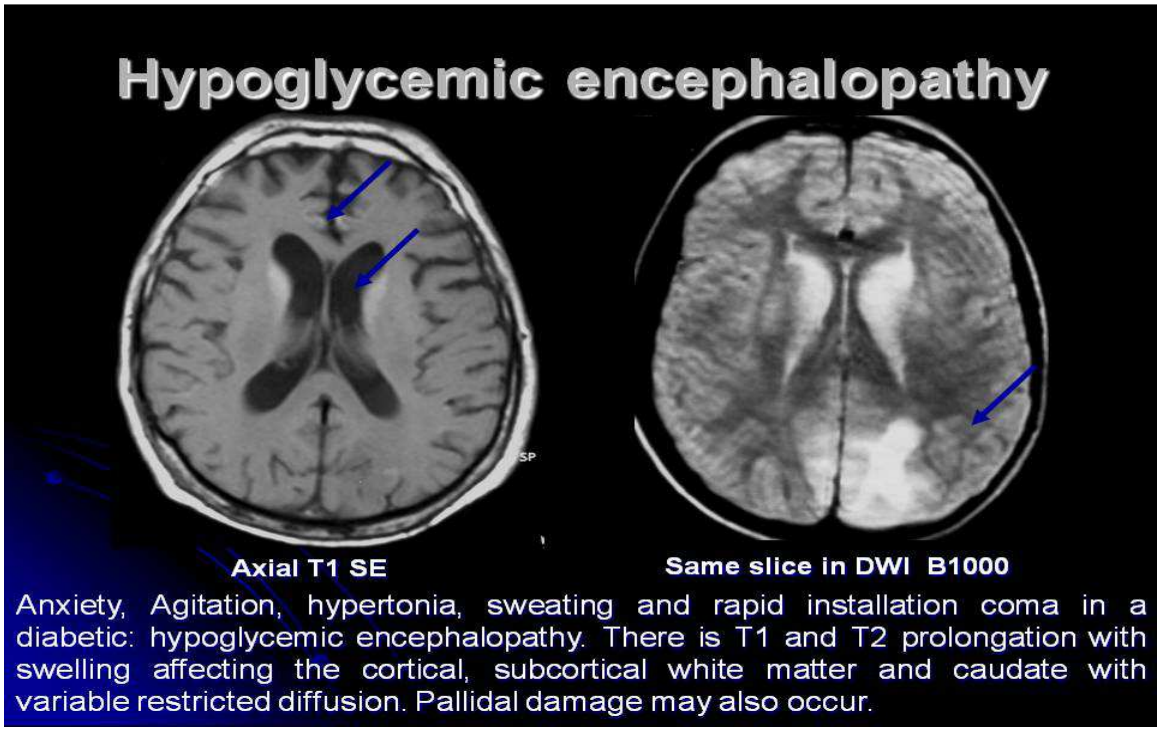
HYPOGLYCEMIA AND BRAIN

Activation of glucose sensitive neurons in ventro medial hypothalamus of the brain is one of the main physiological response to acute hypoglycemia. Activation of this region causes :

1. Stimulation of autonomic nervous system

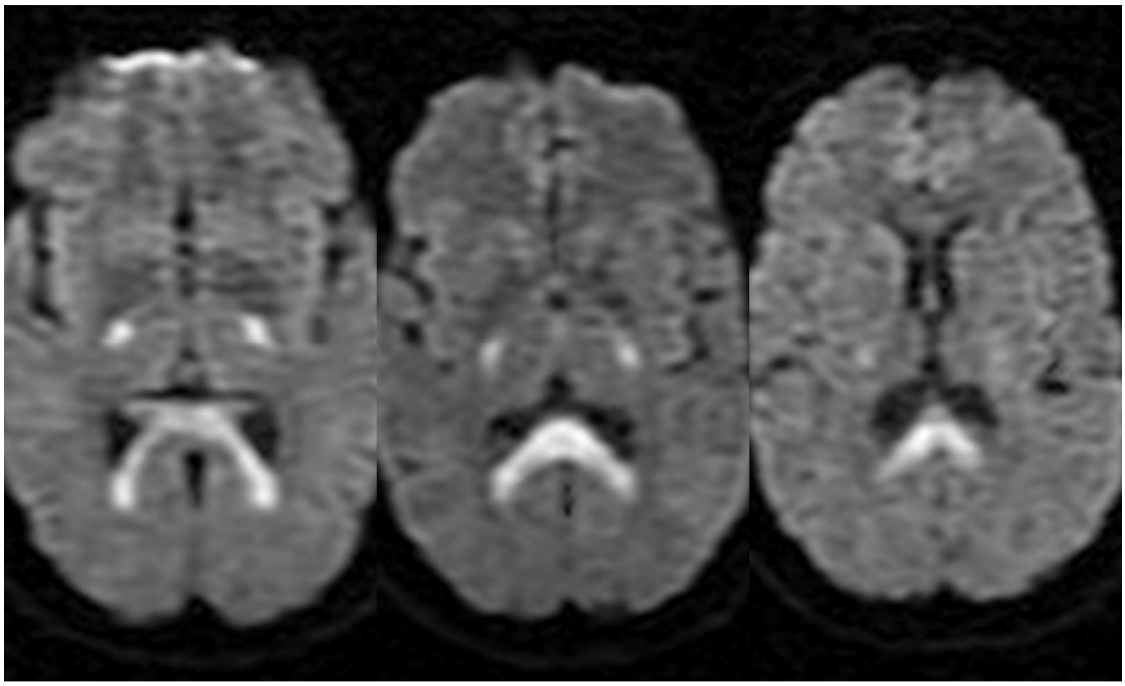
2. Release of counterhormones[70]

In patients with severe and profound hypoglycemia hypoglycaemic encephalopathy occurs.



MRI Bran in patients with hypoglycaemic encephalopathy reveals increased vulnerability of basal ganglia, substantia nigra, cerebral cortex and hippocampal regions . The lesions are usually non haemorragic[71].

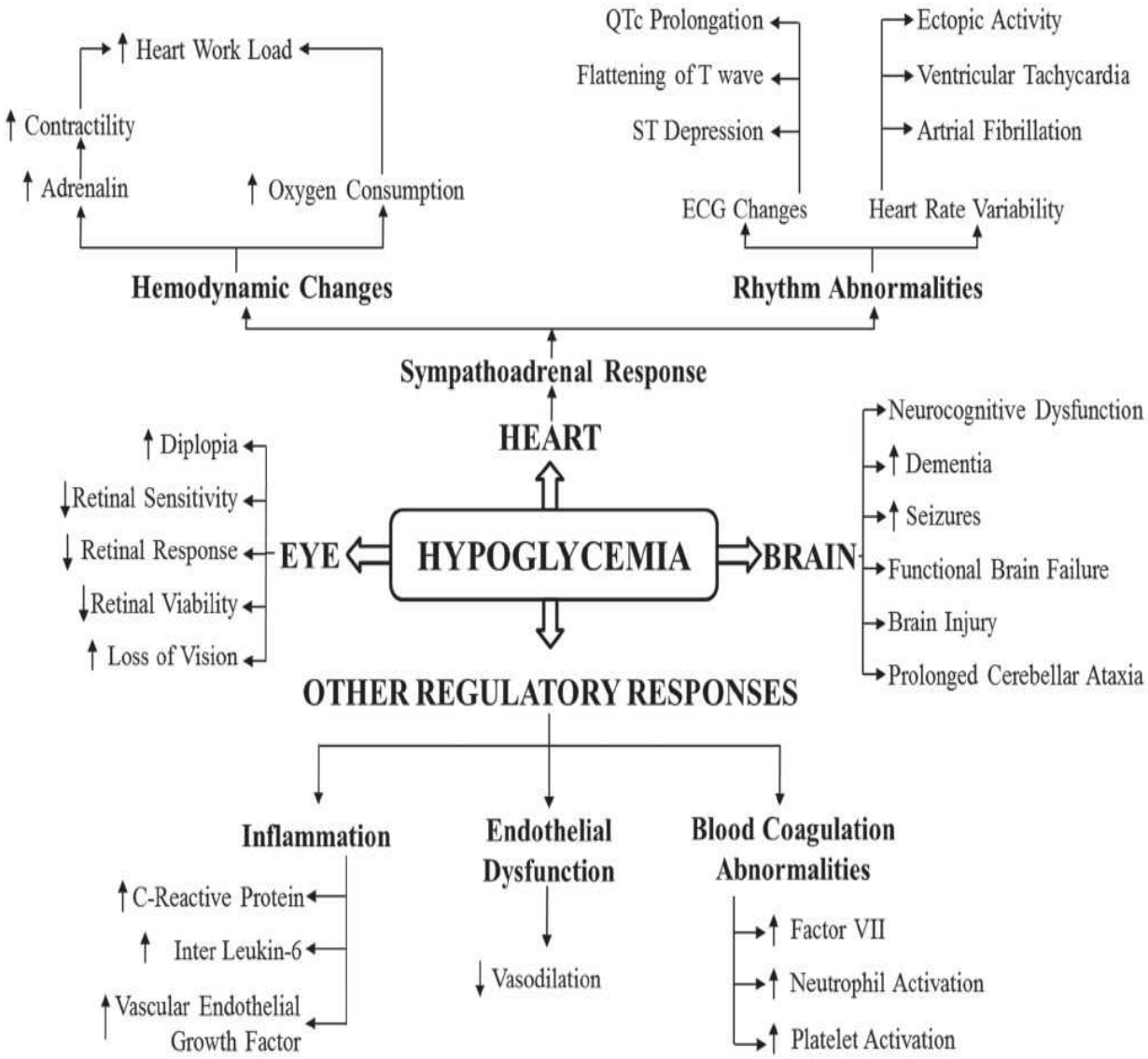
- Repeated hypoglycaemic episodes may lead to cognitive impairement due to neuronal cell death in the hippocampus[72].



Diffusion restricted MRI in a patient with hypoglyemic coma reveals diffusion restriction in bilateral internal capsules along the post. Limb and splenium of corpus callosum.

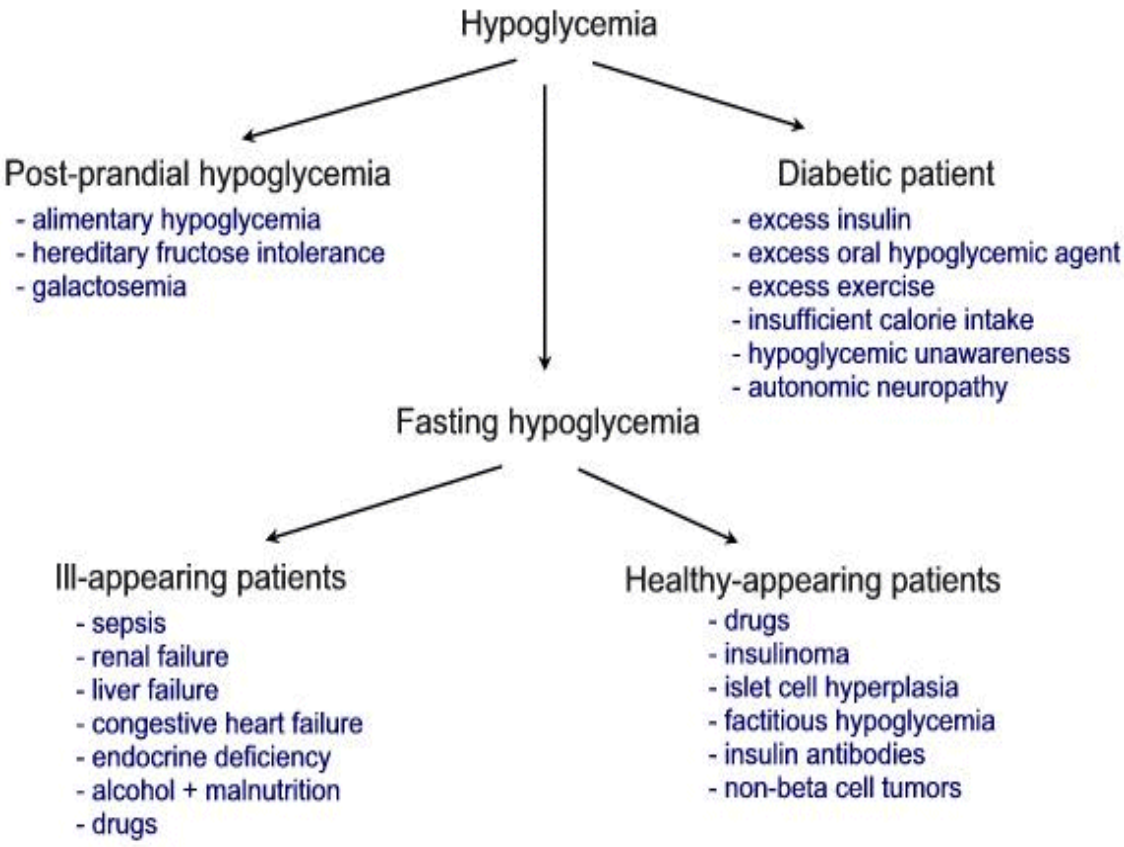
HYPOGLYCEMIA AND HEART

Hypoglycaemia produces significant prolongation of QT c interval. Increased levels of catecholamines during hypoglycaemic episodes may be responsible for QTc lengthening leading onto ventricular arrhythmias and sudden cardiac death.They may also lead to hypokalemia that may cause cardiac repolarisation abnormalities[73,74,75].



Hypoglycaemic episodes are associated with the relase of inflammatory cytokines which include IL-8,IL-6,CRP,TNFα and endothelin-1.These cytokines produce injury to endothelium and cause coagulation abnormalities.Stiffness of vessel wall increases during hypoglycaemia. Thus, endothelial dysfunction and inflammation can potentiate cardiovascular risk in hypoglycaemia[75,76,77]

APPROACH TO HYPOGLYCEMIA



MANAGEMENT OF HYPOGLYCEMIA

Oral carbohydrates	Liquid, for example, dextrose drink, fruit juice
Simple sugars	Buccal Absorption, for example, honey, chewable toffees/candy
	Oral absorption, for example, chocolates
Complex carbohydrates	Liquid, for example, meal substitutes
	Solid, for example, biscuits, bread
Parenteral drugs, approved drugs	IV dextrose 50%, 25%, 10%, 5%
	Glucagon SC/IM
Improvised drugs	IV hydrocortisone
	SC adrenaline
	SC terbutaline

MATERIALS

AND

METHODS

MATERIALS AND METHODS

Study Population:

All patients admitted in medical ward with hypoglycemia in Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai.

Inclusion Criteria:

1. Patients admitted in medical ward who have at least one episode of documented hypoglycaemia i.e less than 70mg/dl.
2. Age > =18 years

Exclusion Criteria:

1. Pregnant woman
2. Paients less than 18 years of age
3. Patients not willing to participate in the study

Study Centre:

Institute of Internal Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai.

Study Design:

Prospective, Observational study

Sample Size:

119 cases

Duration of the study:

6 months : April 2015-September 2015.

Ethical committee approval :

Ethical committee approval was obtained from institution ethical committee before starting the study.

Data collection and Methods:

Patients who present with symptoms of hypoglycemia at the time of admission or during the hospital stay are taken up for the study. Symptoms of hypoglycemia may vary from mild to severe.

Patient presenting with sudden onset of seizure, altered behavior or altered sensorium either in the emergency department or in the medical wards are checked immediately for blood sugar with capillary blood glucose measurement. Any documented blood sugar value less than 70 mg/dl is taken as hypoglycaemia and the patient is taken up for study after obtaining consent from the patient or the relatives ,if the patient is in altered sensorium. Even those patients whose routine blood sugar shows

hypoglycaemia (<70 mg/dl) are included in the study, even if they are asymptomatic.

Only pregnant patients and patients less than 18 years of age are excluded from the study. Detailed informed consent is obtained from the patient or from his close relatives, if the patient is in altered sensorium. All patients who qualify for the study and had given consent are evaluated by means of a questionnaire which contains details of

1. Clinical history which includes includes relevant symptoms

2. Detailed past medical history that includes the presence or absence of diabetes, duration of diabetes and other known clinical illness like RHD,CAD, CKD, DCLD, Pulmonary Tuberculosis, Bronchial Asthma, Seizure disorder etc.

3. Personal habits which include diet sleep pattern, Alcohol/tobacco/cannabis/ cocaine and other drug abuse.

4. Previous drug and treatment including insulin injection,oral hypoglycaemic drugs and other medications.

5. History of recent poisoning, native drug abuse, tattooing, blood transfusion.

6. Sexual behavior and promiscuity

7. Detailed Physical examination

- General examination including vital signs
- Anthropometry
- Cardio vascular system
- Respiratory system
- Abdomen
- Central nervous system

8. Laboratory investigations

- Complete Blood Count, ESR
- CRP
- Urine routine
- Renal function test
- Liver function test
- Serum Electrolytes
- Thyroid function test
- Urine culture and sensitivity
- Blood culture and sensitivity.
- Electrocardiogram

9. Relavent imaging

- Chest Xray
- Ultrasonogram abdomen
- CT scan Brain
- MRI Brain

Data thus collected was subjected to detailed statistical analysis including chi square test.

OBSERVATION

AND

RESULTS

OBSERVATION AND RESULTS

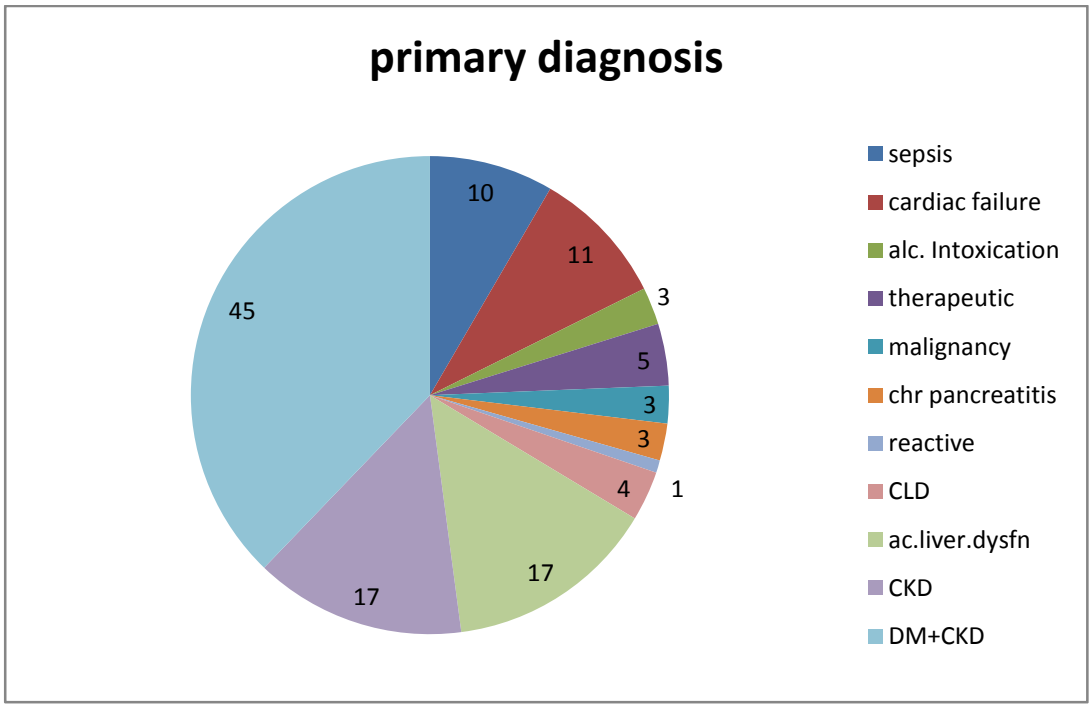
In the six months study period around 119 patients admitted in medical wards of Madras medical college hospital were found to have atleast one episode of documented hypoglycaemia. Patients were further investigated and data obtained analysed statistically.

The primary diagnoses of the patients are as follows:

- Diabetes with Chronic kidney disease : 45 (37.81%)
- Chronic kidney disease : 17 (14.28%)
- Acute liver dysfunction : 17 (14.28%)
- Chronic liver disease : 4 (3.36%)
- Sepsis : 10 (8.4%)
- Congestive cardiac failure : 11 (9.24%)
- Alcohol intoxication : 3 (2.52%)
- Malignancy : 3 (2.52%)
- Chronic Pancreatitis : 3 (2.52%)
- Diabetes Therapy related : 5 (4.20%)
- Reactive : 1 (0.84%)

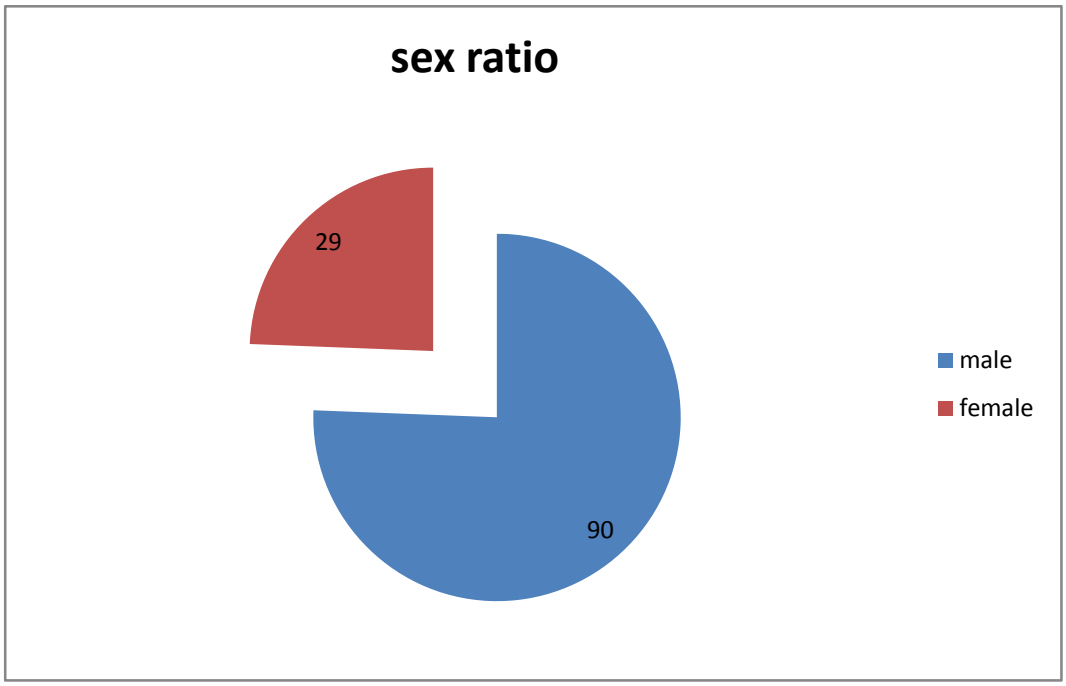
The aim of the study is to analyse the clinical pattern of patients admitted with hypoglycaemia. This is done by analyzing the

- Primary Diagnosis
- Sex pattern
- Age pattern



Diabetes with Chronic Kidney Disease was found to be the most common primary diagnosis .There were totally 45 patients in this category which accounts for 37.81%. Non Diabetic CKD and Acute Liver Dysfunction account for 14.28% each. Sepsis and Congestive cardiac failure Constituted 8.4% and 9.24% respectively. Contrary to the popular belief, Diabetes therapy related cases account for 4.2% only.

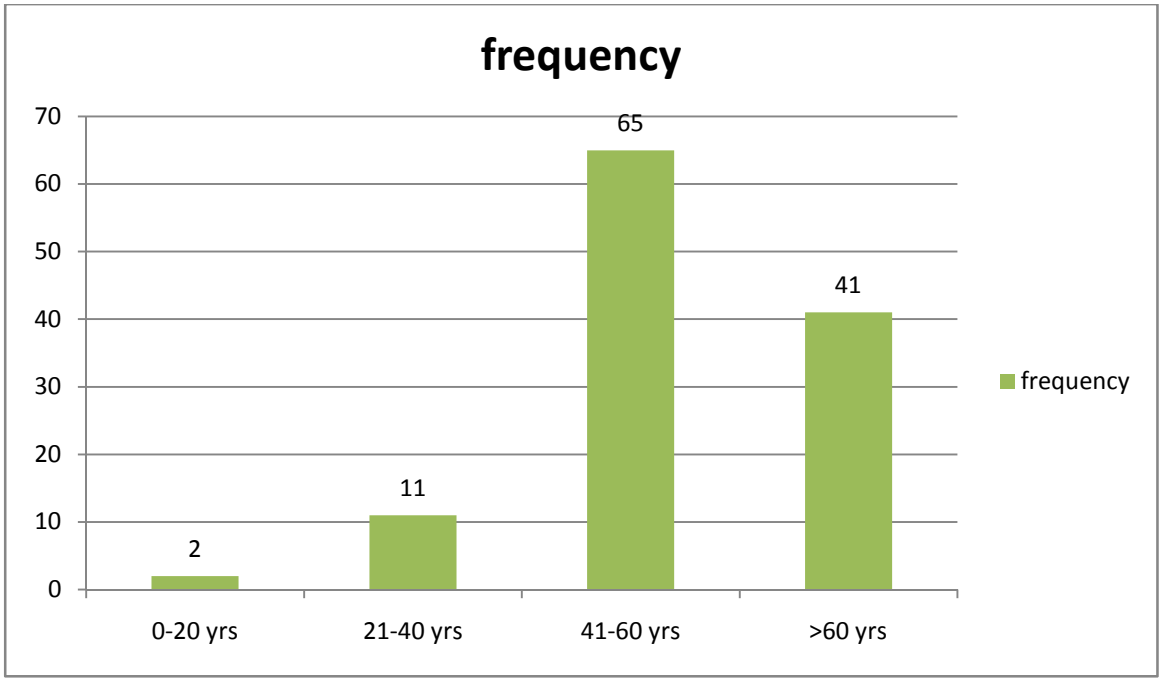
Sex distribution of the study sample



male	90
female	29
total	119

In the present study male population accounted for 75.63% and females accounted for 24.36%.Thus in the present study male gender constituted for significant 3/4th of the study sample.

Age distribution of the study sample



Age	Frequency	Percentage
0-20	2	1.7
21-40	11	9.2
41-60	65	54.6
61-80	41	34.5

In the present study patients in the age group of 41 to 60 years accounted for 54.6% followed by 61 to 80 years age group which constituted 34.5%.

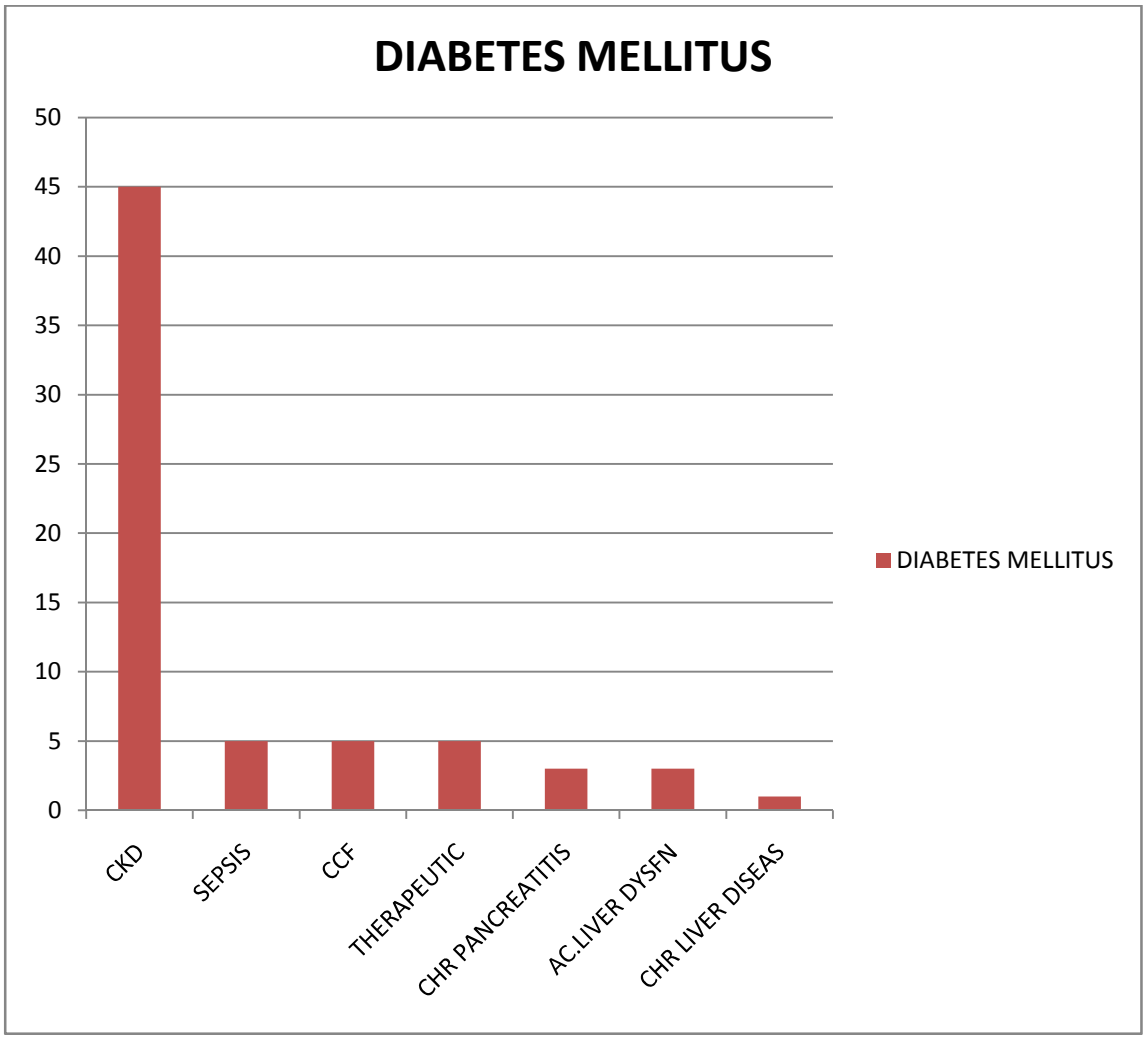
INCIDENCE OF HYPOGLYCAEMIA DURING THE STUDY PERIOD

Total number patients with documented hypoglycaemia is 119.

Total number of Patients admitted in medical wards during the period 11276

Incidence of hypoglycemia in the present study is about **1.05%.** Incidence of hypoglycaemia was calculated by taking into account the patients admitted in medical wards alone during the study period .

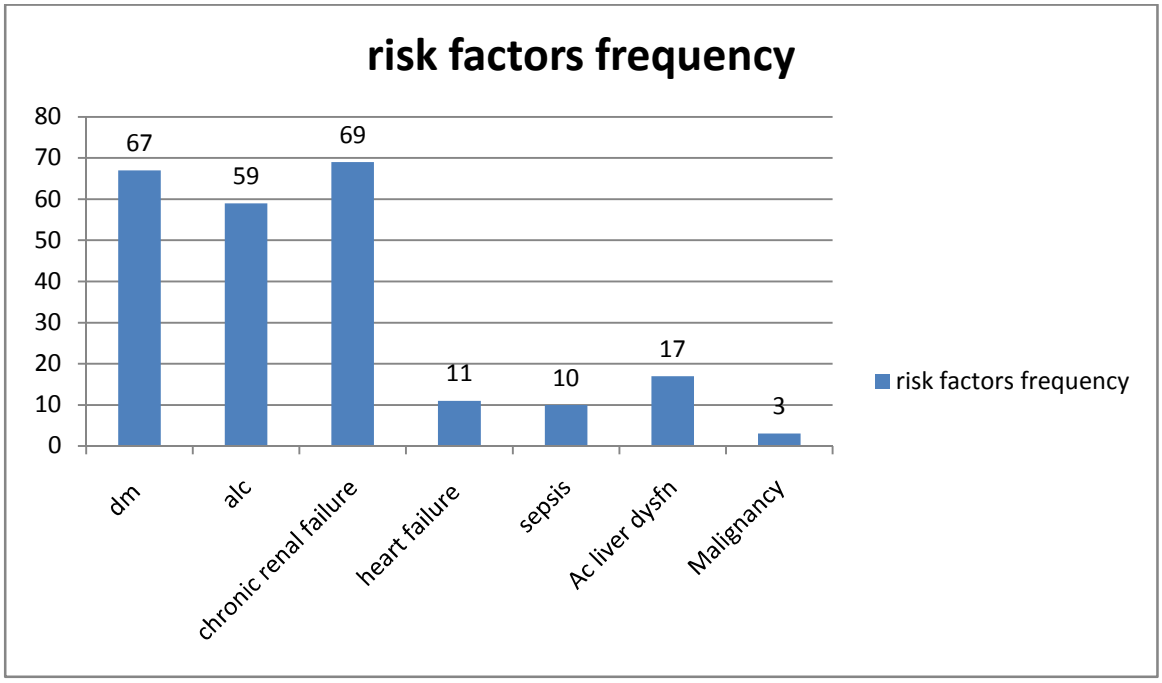
Hypoglycaemia in diabetic patients



DM ASSOCIATION	FREQUENCY	PERCENTAGE (%)
CKD	45	67.1
SEPSIS	5	7.46
THERAPY RELATED	5	7.46
CCF	5	7.46
ALD	3	4.47
CH.PANCREATITIS	3	4.47
CLD	1	1.49
TOTAL	67	100%

In diabetic patients Kidney disease accounts for major cause of hypoglycemia accounting for 67.1%. Therapy related hypoglycemia accounts for only 7.46% in the present study. Sepsis and CCF accounts for 7.46% each.

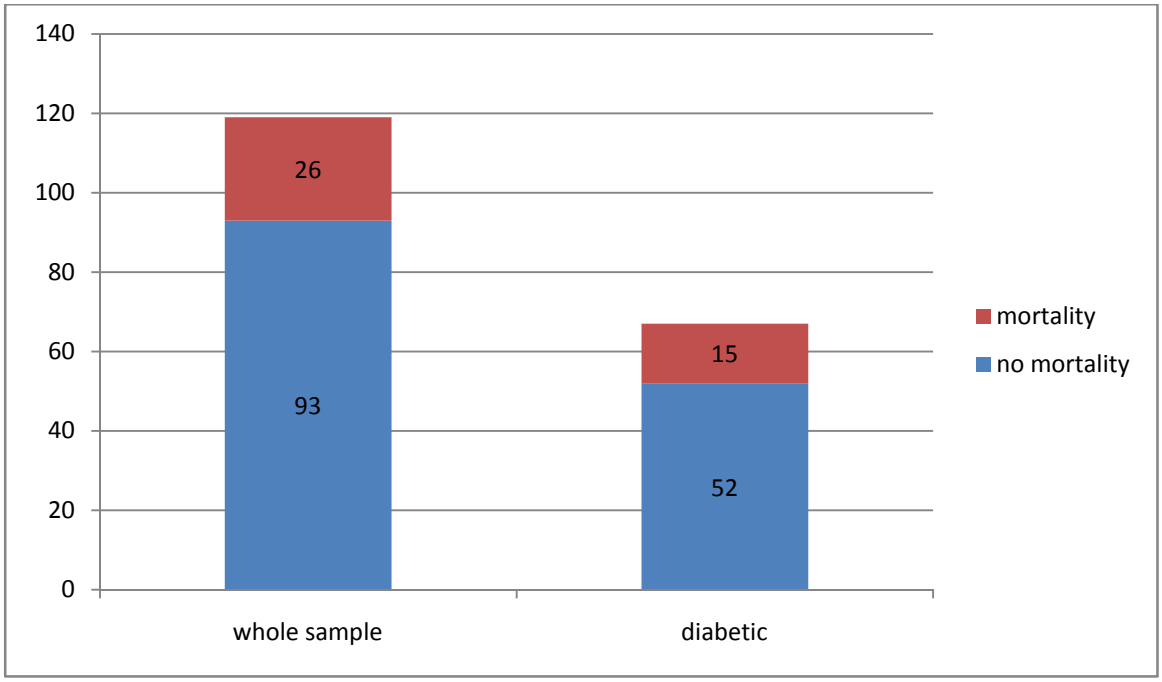
Various risk factors frequency



Risk Factor	Frequency	Percentage (%)
Renal Failure	69	57.98
Diabetes Mellitus	67	56.3
Alcoholism	59	49.57

In the present study, Chronic Renal Failure and Diabetes Mellitus ranks close first and second risk factors associated with occurrence of Hypoglycemia in hospitalized patient. Out of 119 patients, 69 patients had chronic renal failure and 67 patients had diabetes mellitus. Alcoholism was also found in 59 patients.

Mortality Pattern in Diabetes Mellitus



Chi square table for DM as a predictor of mortality

Risk factor	mortality	No mortality	total
Diabetes present	15	52	67
Diabetes absent	11	41	52
total	26	93	119

p value significance level 0.05

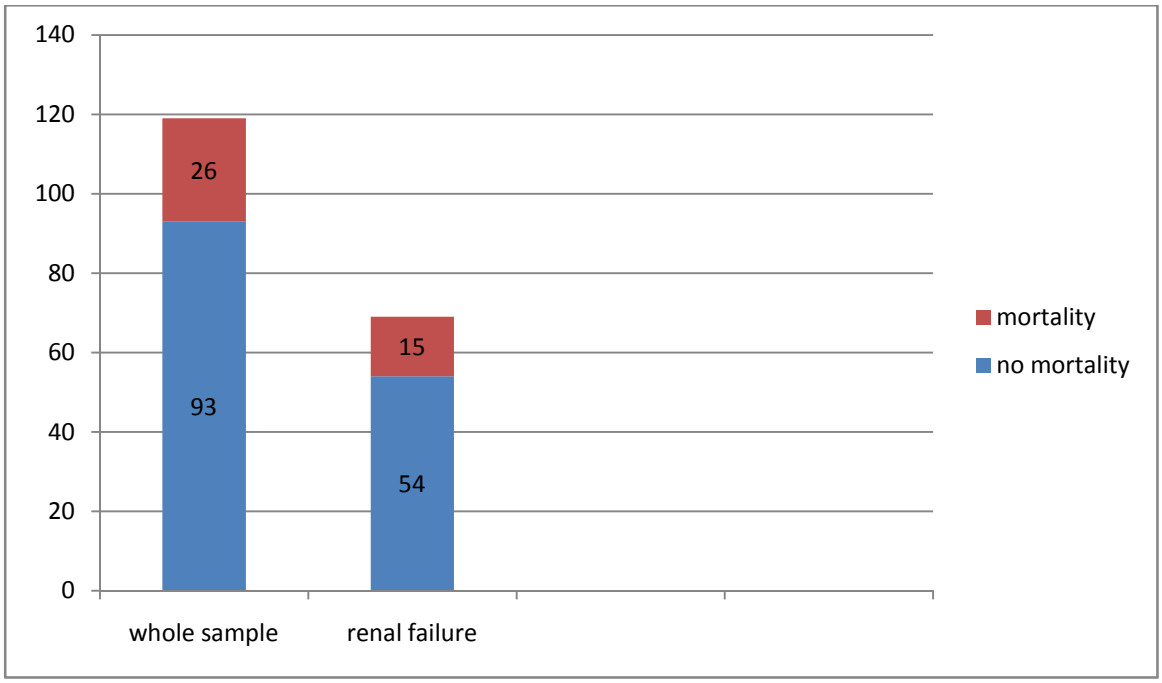
Chi Square Value : 0.0261

P value : 0.8716

As the p value for the given data is greater than 0.05 ,it is not significant. Thus, diabetes mellitus, though is common association of hypoglycaemia, it is not a predictor of mortality.

In the present study, there were 67 patients (56.3%) who had diabetes mellitus. Number of deaths among the diabetic patients were fifteen (15) while it was twenty six 26 for the whole study sample. Thus, diabetes mellitus accounted for 56.3% of cases and57.9% of the cases of death. In order to find out if diabetes mellitus is predictor of mortality in hospitalized patients having hypoglycaemia, statistical analysis by using chi square test was done with significant p value at 0.05.

Mortality Pattern of Renal Failure



Renal Failure was diagnosed in 69 cases .This form about 57.98% of the study sample. Of the 69 cases 15 patients died .This means 21.73% of the patient afflicted with Chronic Renal Failure died. This amounts to 57.69% of the total deaths.(15/26)

To know if Renal Failure is a mortality predictor in hypoglycaemic patient statistical analysis by utilizing chi square test was carried out.

Chi Square Table for Renal Failure as a predictor of Mortality

Risk factor	mortality	No mortality	total
Renal failure present	15	54	69
Renal failure absent	11	39	50
total	26	93	119

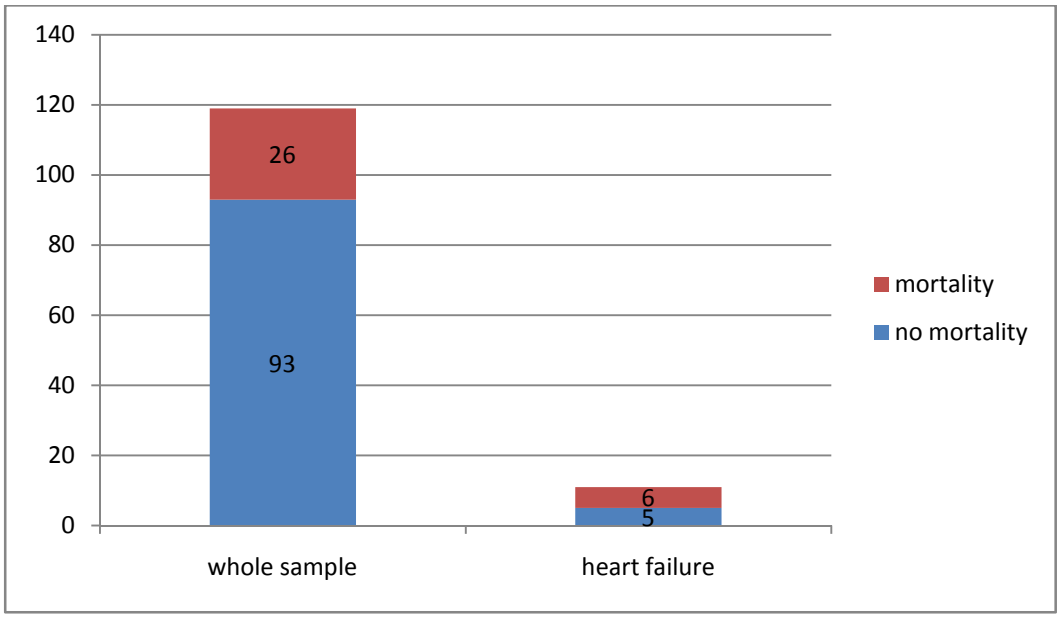
p value significance level 0.05

Chi Square Value : 0.0012

P value : 0.9728

As the p value for the given data is greater than 0.05 ,it is not significant. Thus, Renal failure, though is common in hospitalized hypoglyvaemic patient, it is not a predictor of mortality.

Mortality Pattern of Congestive Cardiac Failure



Of the 119 patients enrolled in the study, Congestive heart Failure was present in eleven(11) cases. This is found to be 9.24% of the study sample. But, the number of cases who died in this sub class were six i.e 6 patients. This is approximately 23% of all deaths.Death rate among this sub category of patients were 6/11*100 which is 54.54%

A Chi Square test analysis was carried out on the above data to find out if the presence of CCF is a significant predictor of mortality.

Chi Square Table for CCF as a predictor of Mortality

Risk factor	mortality	No mortality	total
Heart failure present	6	5	11
Heart failure absent	20	88	108
total	26	93	119

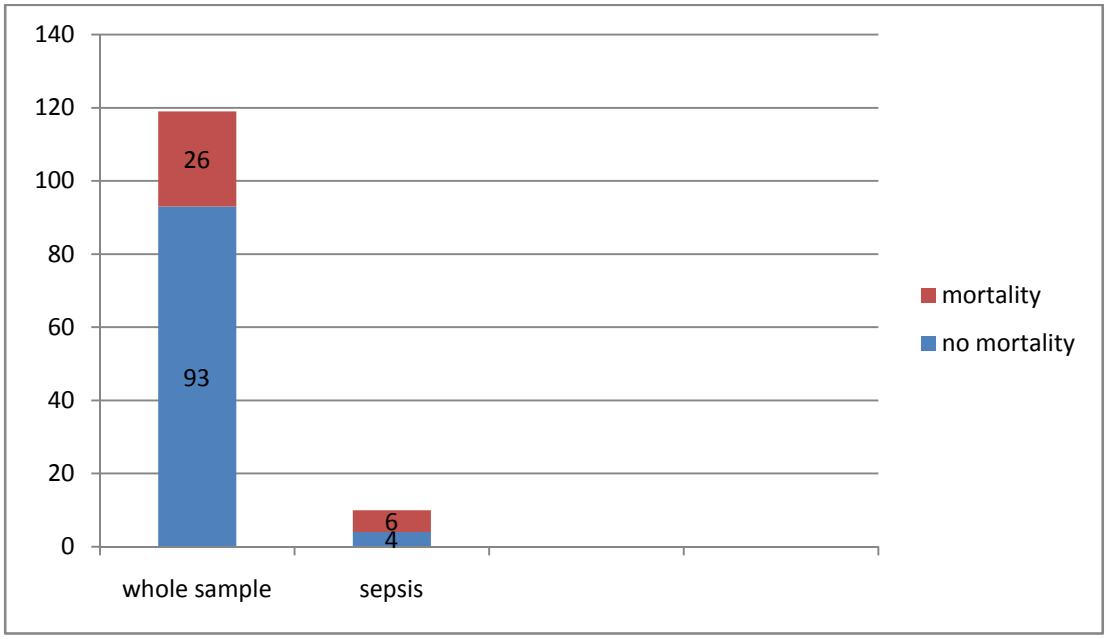
p value significance level 0.05

Chi Square Value : 7.5886

P value : 0.0058

As the p value for the given data is lesser($p<0.05$) than 0.05 ,it is significant. Thus , cardiac failure in hypoglycaemic patient is a significant predictor of mortality.

Mortality Pattern of sepsis



Sepsis was diagnosed in ten cases (10 cases).While this amounts to just 8.4% of the study sample about 60% of the sepsis diagnosed patient that is 6 out of 10 sepsis diagnosed patients succumbed to it.

Statistical analysis by utilizing chi square method with 0.05 significant p value was done.The result is tabulated as follows

Chi Square Table for Sepsis as a predictor of Mortality

Risk factor	mortality	No mortality	total
sepsis present	6	4	10
sepsis absent	20	89	109
total	26	93	119

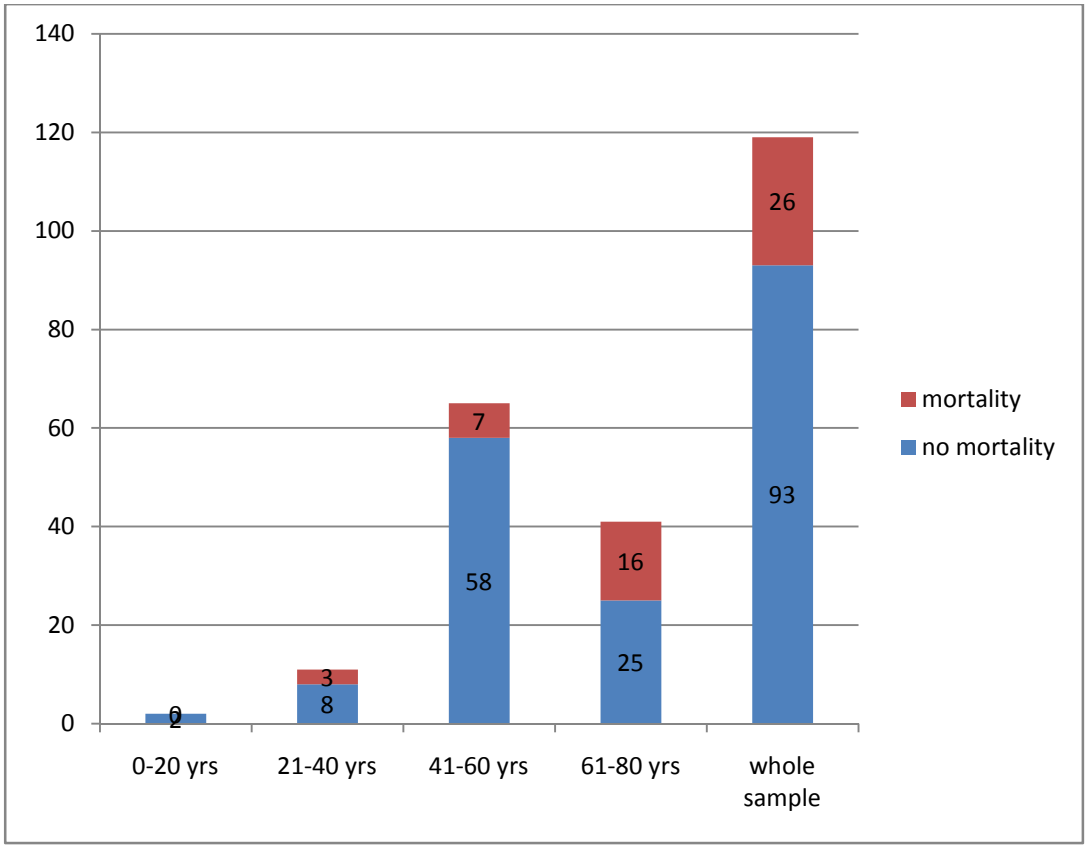
p value significance level 0.05

Chi Square Value : 9.3063

P value : 0.0022

As the p value for the given data is lesser($p<0.05$) than 0.05 ,it is significant. Thus, sepsis in hypoglycaemic patient is a significant predictor of mortality.

Mortality Pattern Based on Age Group



Maximum number of people in the study were in the category of 41-60 years. This category accounted to 54.62% of the sample. Next in order of frequency was 61-80 years category. There were 41 patients (34.45%) in this age group. However, maximum number of deaths belong to this category of patients.

Chi square statistical analysis was done on the age group data of the sample to know if increasing age was an important predictor of mortality in hypoglycaemic patient.

Chi Square Table for Age Group as a predictor of Mortality

Age	Mortality	No Mortality	Total
0-20	0 (0%)	2 (2.2%)	2 (1.7%)
21-40	3 (11.5%)	8 (8.6%)	11 (9.2%)
41-60	7 (26.9%)	58 (62.4%)	65 (54.6%)
61-80	16 (61.5%)	25 (26.9%)	41 (34.5)
Total	26 (100%)	93 (100%)	119 (100%)

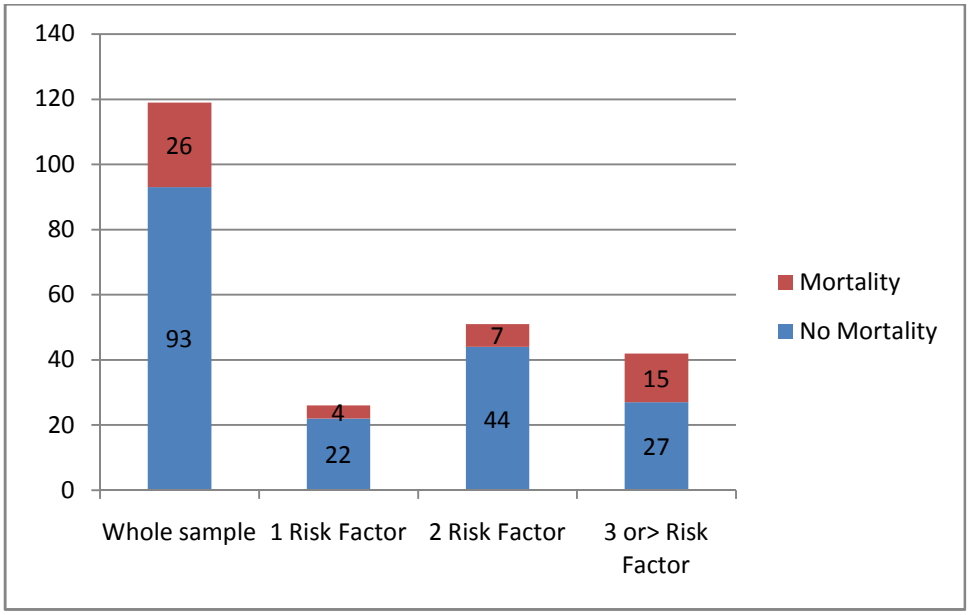
p value significance level 0.05

Chi Square Value : 9.3063

P value : 0.0022

As the p value for the given data is lesser($p<0.05$) than 0.05 ,it is significant. Thus, sepsis in hypoglycaemic patient is a significant predictor of mortality.

Mortality Pattern Based on Number of Risk Factors



As we analyse the presence of risk factors in hospitalized hypoglycaemic patents, it was found that as the number of risk factors in a patient increases, chance of succumbing to them also increases. Number of deaths which occur when there was one risk factor was 4 out of 26 which works out to 15.38%. In the category of patients having 3 or more risk factors death rate was 15 out of 42 which is 35.71%.

Chi square test analysis was done on the data of number of risk factors to know if the number of risk factors could be a predictor of mortality.

Chi Square Table for Number of risk Factors as a predictor of Mortality

Number of Risk Factors	Mortality	No Mortality	Total
1	4	22	26
2	7	44	51
3 or More	15	27	42
Total	26	93	119

p value significance level 0.05

Chi Square Value : 7.3361

P value : 0.0255

As the p value for the given data is lesser($p<0.05$) than 0.05 ,it is significant. Thus, presence of increase number of risk factors in hypoglycaemic patient is a significant predictor of mortality.

DISCUSSION

DISCUSSION

In our study conducted in the medical wards of madras medical college hospital around 119 patients were found to have at least one episode of hypoglycemia in 6 month study period. The incidence is found to be 1.05%. This includes in both diabetic and non diabetic patients. Alexander turchin etal[78] have shown an incidence of 7.7% in patients with diabetes. The lower incidence in our study is probably due to considering hypoglycemia incidence in both diabetic and non diabetic population. More over incidence was calculated for the entire admissions to the medical wards in the entire 6 month period that includes 11276 admissions.

In our study maximum number of patients was in the age group of 41-60 yrs accounting for 54.6% followed by >60 yrs age group accounting for 34.5%. However this age group of >60 yrs constituted 61.5% of total deaths. Hypoglycemia in elderly age group is a significant predictor of mortality.

The commonest risk factors associated with low blood sugar levels in our study are Renal failure (57.98%) , Diabetes on therapy (56.3%) and alcoholism (49.57%).

Within the category of Diabetes Mellitus patients association with renal failure was the commonest cause of hypoglycaemia.

In our study diabetes and chronic kidney disease are the major risk factors for hypoglycemia. This is in accordance with Kathleen.F . Fischer et al[79] in whose study diabetes was present in 45% of patients with hypoglycemia and CKD was the next most common cause of hypoglycemia in non diabetic patients.

The present study highglights the fact that low blood sugar levels can also occur in non diabetic patients.

In diabetic patients also renal failure forms the major risk factor for hypoglycemia. This is in accordance to S.G.Bruderer et al[80] in whose study risk factors for severe hypoglycemia were insulin treatment , renal failure and increasing age.

In Non-diabetic patients renal failure and sepsis form common causes of hypoglycaemia.

Though CKD and diabetes are the major risk factors for hypoglycemia they are not significant predictors of mortality.

In our study hypoglycemia is also seen in congestive cardiac failure. This is in accordance with several previous studies. Benzing G. Scheubert et al[23], Heydati et al[24] and Block M.B et al[81] have shown spontaneous hypoglycemia in CCF.

Hypoglycemia is also common in elderly. This is in accordance with Shilo.S.et al[82] study. In our study hypoglycemia in sepsis and CCF significantly predicts mortality. Similarly, we found that hypoglycemia in old age is also a significant predictor of mortality. The present study also shows that more the number of risk factors the greater chance of mortality. In our study , significant predictors of mortality in hospitalised hypoglycaemic patients are associations with 1.sepsis 2.CCF 3.elderly age 4. Presence of multiple risk factors.

Alcohol intoxication and alcoholic hepatitis are also major risk factors of hypoglycemia in our study. This is in accordance to Heather Hammerstedt et al[83] who have demonstrated hypoglycemia in alcohol intoxication. Though western studies have shown less incidence of

alcohol induced hypoglycemia , in our study acute alcohol intoxication accounts for 2.52% and alcoholic hepatitis accounts for 8.4% in our study. Next to diabetes and CKD alcohol also forms a major risk factor for hypoglycemia. This may be due to higher prevalence of significant alcohol in this part of the country. The higher incidence of hypoglycemia in males in our study may be alcohol related.

Thus, to conclude predisposing factors for hypoglycemia in hospitalised patients in present study are diabetes on treatment, CKD, alcohol dependence, sepsis, CCF and elderly. These risk factors are in accordance with previous studies.

CONCLUSION

CONCLUSION

- Hypoglycaemia reveals dysregulation in glucose metabolism in the body and failure of endogenous defense mechanisms to combat low blood sugar levels.

- Hypoglycaemia should always be taken seriously and investigated properly.

- Apparently hypoglycaemia is common in diabetes but it is clear from this study that even in diabetes serious disease process like renal dysfunction, cardiac failure or sepsis precipitates hypoglycaemia.

- In Non-diabetic patients renal failure, sepsis and alcoholic hepatitis are the common causes of hypoglycaemia.

- In a T2DM patients without organ failure, the low blood sugars experienced due to OHA/Insulin food mismatch is only mild.

- Alcohol is another most important factor for causing hypoglycaemia in our country.

- In our study of 119 patients, we did not find Insulinoma as a cause of hypoglycaemia. Insulinoma is very rare and it is prudent to think of common causes like alcoholism and CKD apart from diabetes as main causes of hypoglycaemia.

- Though mild hypoglcemia is reversible with oral or IV glucose, profound and prolonged hypoglycaemia can cause encephalopathy and prove fatal.

- In patients with sepsis and congestive cardiac failure hypoglycaemia is a predictor of mortality.

- Similarly as the number of risk factors increase, the mortality rate also increases. Perhaps here multiple risk factors play a role.

- Elderly people are more prone for low blood sugar levels. In them Diabetes treatment should be moderate. Tight glycemic control in the elderly can lead to fatal episodes of hypoglycaemia.

- It is better to prevent hypoglycaemia in diabetes. However it is prudent to investigate any patient presenting with hypoglycaemia.

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ANNEXURES

ABBREVIATIONS

1. OHA	-	Oral hypoglycemic agents
2.CNS	-	Central nervous system
3. HMP	-	Hexose monophosphate shunt
4.GLUT	-	glucose transporters
5.ECF	-	Extracellular fluid
6.PPRγ	-	Peroxisome proliferator activated receptor
7.PCP	-	Pneumocystis carinii pneumonia
8.ACE	-	Angiotensin converting enzyme
9.NEFA	-	Non esterified fatty acids
10. T1DM	-	Type 1 Diabetes mellitus
11.T2DM	-	Type 2 Diabetes mellitus
13.DM	-	Diabetes mellitus
14.NAD	-	Nicotinamide Adenine Dinucleotide coenzyme
15. NADH	-	Nicotinamide Adenine Dinucleotide hydride
16.ICU	-	Intensive care unit
17.RHD	-	Rheumatic Heart disease
18. COPD	-	Chronic obstructive pulmonary disease
19.GIT	-	Gastro intestinal tract
20.HAAF	-	Hypoglycemia associated autonomic failure
21.MRI	-	Magnetic resonance imaging
22.QTc	-	Corrected QT interval
23. IL-8	-	Interleukin 8

24.IL-6	-	Interleukin 6
25.CRP	-	C-Reactive protein
26.TNF α	-	Tumour necrosis factor α
27.SC	-	Subcutaneous
28.IM	-	Intramuscular
29.CCF	-	Congestive cardiac failure
30.i.e	-	that is
31.RHD	-	Rheumatic Heart disease
32.CAD	-	Coronary Heart disease
33.CKD	-	Chronic kidney disease
34.DCLD	-	Decompensated liver disease
35.ESR	-	Erythrocyte sedimentation rate
36.CT scan	-	Computed tomography scan

PROFORMA

PROFILE OF HOSPITALISED PATIENTS WITH EPISODES OF HYPOGLYCEMIA

Name: Age: Sex: IP Number:

Presenting Complaints:

H/O Present Illness :

Past History :

Diabetes :

Hypertension :

CAD / DCM :

RHD :

Cirrhosis :

CKD :

Others :

Personal History :

Alcohol :

Smoking :

Others :

Occupational History :

Nutritional Pattern :

Drug Intake :

O/E :

PR :

BP:

RR:

Temp :

CBG (at time of admission) :

General examination :

CVS :

RS :

ABDOMEN :

CNS :

Investigations:

1. Complete Blood Count:

Hb: TC: DC: P L E M

ESR: PCV: Platelet:

2. Renal Function Tests:

S. Urea: S.Creatinine:

S. Na: S. K:

3. FBS:

4. PPBS

5.RBS

6.Liver Function Tests :

Total Bilirubin

SGOT

SGPT

GGT

Alkaline phosphatise

Sr.Total protein :

Sr.Albumin :

7. Thyroid Function Tests:

8.ECG :

9. USG :

10.ECHO:

11. Others (if any):

INFORMATION SHEET

We are conducting a study on **"CLINICAL PROFILE OF HOSPITALISED PATIENTS WITH EPISODE OF HYPOGLYCEMIA''** among patients in Rajiv Gandhi Government General Hospital, Chennai and for that your specimen may be valuable to us.

The purpose of this study is to identify the incidence, clinical pattern, associated risk factors and mortality rate among hospitalised patients with hypoglycaemic episodes. We are selecting certain cases, and if you are eligible, 2 samples of 3 cc blood will be collected in fasting state in the morning and sent for investigations. These tests do not affect your final report or management.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment

Signature of the Investigator Signature of the Participant

Date:

Place:

ஆராய்ச்சி தகவல் தாள்

சென்னை இராஜிவ் காந்தி அரசு பொது மருத்துவமனையில் தாழ்நிலை சர்க்கரை பற்றிய ஒரு ஆராய்ச்சி நடைபெற்று வருகிறது.

தாழ்நிலை சர்க்கரை காரணமாக மருத்துவமனையில் அனுமதிகப்பட்ட நோயாளிகளின் மருத்துவ விவரங்களை அறிவதே இந்த ஆராய்ச்சியின் நோக்கமாகும்.

நீங்களும் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம். முடிவுகளை அல்லது கருத்துக்களை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம். இந்த ஆராய்ச்சியில் தங்களுக்கு இரத்தபரிசோதனையும் தேவைபட்டால் ஸ்கேன் பரிசோதனையும் செய்யப்படும்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருத்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த சிறப்புப் பரிசோதனைகளின் முடிவுகளை ஆராய்ச்சியின் போது அல்லது ஆராய்ச்சியின் முடிவில் தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

தேதி:

PATIENT CONSENT FORM

Study Title	:	**PROFILE OF HOSPITALISED PATIENTS WITH EPISODE OF HYPOGLYCEMIA**
Study Centre	:	Rajiv Gandhi Government General Hospital, Chennai.
Name	:	
Age/Sex	:	
Identification Number	:	

Patient may check (☑) these boxes

The details of the study have been provided to me in writing and explained to me in my own language ❑

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 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 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 will 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 agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms. ❑

I hereby consent to participate in this study. ❑

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological and biochemical tests. ❑

Signature/thumb impression	Signature of Investigator
Patient's Name and Address:	Study Investigator's Name:
	Dr. R.VASUKI

ஆராய்ச்சி ஒப்புதல் கடிதம்

ஆராய்ச்சி தலைப்பு:

தாழ்நிலை சர்க்கரை காரணமாக மருத்துவமனையில் அனுமதிகப்பட்ட நோயாளிகளின் மருத்துவ விவரங்கள் பற்றிய ஆராய்ச்சி.

பெயர்: **தேதி:**

வயது: **உள்நோயாளி எண்:**

பால்: **ஆராய்ச்சி சேர்க்கை எண்:**

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது. எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்து கொண்டு நான் எனது சம்மதத்தை தெரிவிக்கிறேன்.

இதற்காக மேற்கொள்ள வேண்டிய இரத்தபரிசோதனை மற்றும் ஸ்கேன் பரிசோதனை பற்றியும் விளக்கபெற்று நான் ஆராய்ச்சியில் பங்கேற்கிறேன்.

மேற்கொண்ட பரிசோதனையின் போது ஏற்படக்கூடிய பின்விளைவுகளையும் முழுவதும் உணர்ந்து இந்த பரிசோதனைக்கு மனமார சம்மதிக்கிறேன்.

ஆராய்ச்சியாளர் கையொப்பம் **பங்கேற்பாளர் கையொப்பம்**

தேதி:

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
Dr.Vasuki.R.
Post Graduate in MD (General Medicine)
Madras Medical College
Chennai 600 003

Dear Dr.Vasuki.R.

The Institutional Ethics Committee has considered your request and approved your study titled **" CLINICAL PROFILE OF HOSPITALISED PATIENTS WITH EPISODE OF HYPOGLYCEMIA "** NO.31042015.

The following members of Ethics Committee were present in the meeting hold on 07.04.2015 conducted at Madras Medical College, Chennai 3

1. Prof.C.Rajendran, MD	:Chairperson
2. Prof.R.Vimala,MD.,Dean,MMC,Ch-3	: Deputy Chairperson
3. Prof.B.Kalaiselvi,MD.,Vice Principal,MMC,Ch-3	: Member Secretary
4. Prof.B.Vasanthi,MD.,Prof.of Pharmacology,MMC	: Member
5. Prof.Raghumani,MS.,Prof.of Surgery,MMC	:Member
6. Prof.S.Baby Vasumathi, Director, Inst. of O&G,MMC	: Member
7. Prof.K.Ramadevi,MD., Director ,Inst.of Bio-Chem.MMC	: Member
8. Prof.Saraswathy,MD.,Director,Pathology, MMC	: Member
9.Prof.K.Srinivasagalu,MD.,Director, I.I.M , MMC	: Member
10.Thiru S.Rameshkumar, B.Com., MBA.	: Lay Person
11.Thiru S.Govindasamy, BA., BL.,	: Lawyer
12.Tmt.Arnold Saulina, MA., MSW.,	: Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

27/4/15

Member Secretary – Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

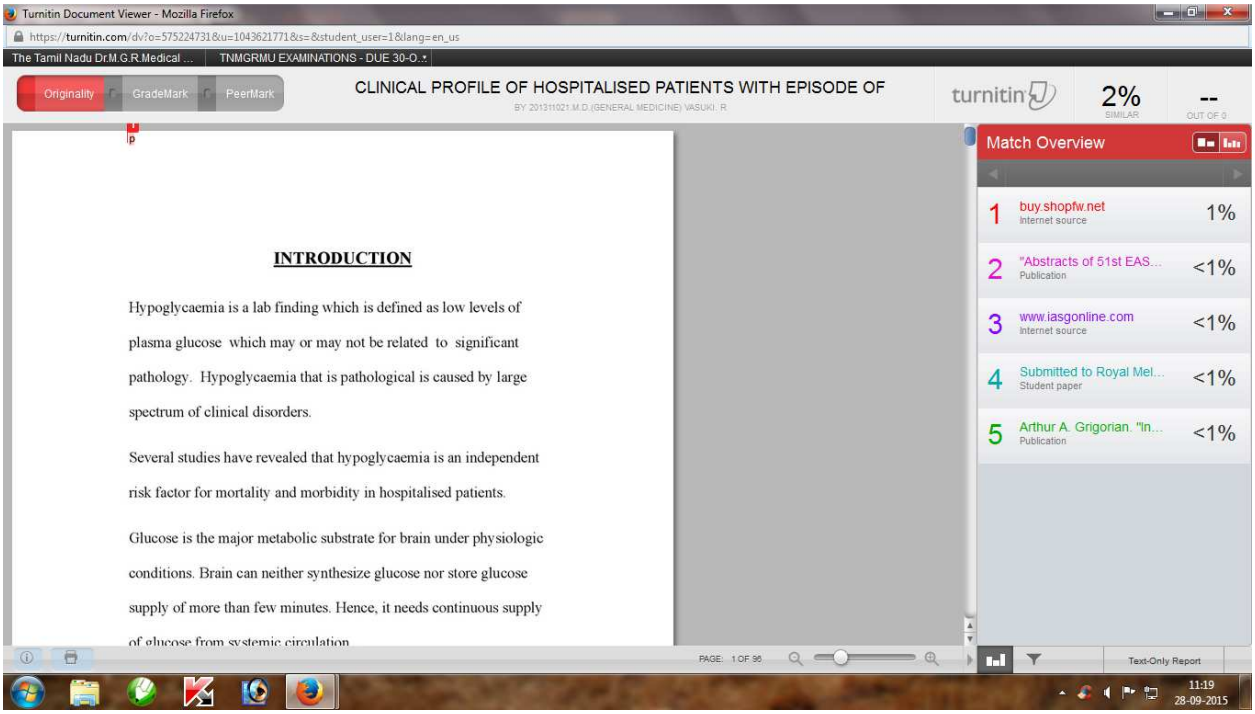
Sys 2

MASTER CHART

S.No	IP No	AGE	SEX	CBG ONADMISSION	HEMOGLOBIN	DM	CHRONIC ALCHOHOLIC	RENAL FAILURE	DCLD	ACUTE HEPATITIS			HEART FAILURE			SEPSIS	CHRONIC PANCREATITS	ALCHOHOL INTOXICATION	MALIGNANCY		THERAPY INDUCED		REACTIVE HYPOGLYCEMIA	MORTALITY
										VIRAL	ALCHOHOL	TOXIC	CAD	RHD	DCM				LIVER	OTHERS	OHA	INSULIN		
1	40653	68	M	62	6.8	N	Y	Y	Y	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	Y
2	46785	66	M	69	6.5	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
3	67584	70	M	45	7	N	N	Y	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	Y
4	56784	69	M	68	5.8	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
5	56784	71	M	45	7.4	N	N	Y	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	Y
6	56743	74	M	57	6.4	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
7	58765	76	M	66	6.5	N	N	Y	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	Y
8	56784	77	M	65	6	N	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
9	52876	74	F	45	7.5	Y	N	Y	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	Y
10	56784	69	F	56	5.6	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
11	56432	75	F	45	5.8	Y	N	Y	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	Y
12	56473	77	M	46	6.7	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
13	47658	71	M	64	5.7	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
14	49876	28	F	56	5.5	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	Y
15	42768	31	M	45	6.7	N	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	Y
16	56721	37	M	56	4.5	N	Y	N	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	Y
17	56487	68	M	67	6.8	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
18	55674	74	M	56	6.7	N	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
19	55342	71	M	45	7	N	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
20	55876	79	M	46	5.7	N	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
21	53452	72	M	67	5.8	N	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
22	57896	68	M	45	6	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
23	53897	48	M	34	7.8	Y	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
24	56786	58	M	56	8.6	N	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
25	56784	44	F	56	6.8	N	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N
26	47896	51	F	45	7.8	Y	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N
27	46537	50	F	45	6.5	Y	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N
28	57863	49	F	56	7.9	Y	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N
29	49399	43	M	56	8	N	Y	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N	Y
30	50221	44	M	67	7.5	N	Y	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N	Y
31	50477	42	M	66	7.5	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N	N	Y
32	50789	71	M	66	5.6	Y	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N	Y
33	50967	69	M	45	6.7	Y	Y	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N	Y
34	51124	70	M	54	6.6	Y	Y	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N	Y
35	51231	68	M	54	5.8	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
36	51179	77	M	45	5.9	N	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

37	52343	74	M	42	7.6	N	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
38	53234	70	M	56	5.8	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
39	53222	47	M	56	6.9	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
40	53127	49	F	55	7.9	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
41	52179	57	M	56	6.9	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
42	52774	51	F	54	7.6	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
43	52144	54	M	67	5.8	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
44	52411	53	M	56	6.8	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
45	52737	56	F	56	7.8	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y
46	52999	51	M	56	5.9	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y
47	53044	59	F	56	7	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y
48	53087	54	M	67	6.5	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y
49	53094	66	F	65	6.6	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
50	53123	77	M	55	6	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
51	53717	51	F	44	6.8	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
52	53786	54	F	45	6.9	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
53	53799	49	F	45	7	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
54	53914	47	M	45	6	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N
55	53977	29	F	45	7	N	NN	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N
56	53988	37	M	57	6.8	N	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N
57	53993	31	M	56	6.9	N	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N
58	53967	57	M	56	6.8	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
59	54110	47	M	56	6.5	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
60	53211	51	M	65	7	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
61	53216	49	M	56	7.5	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
62	54719	56	M	57	5.9	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
63	54747	69	M	68	6.9	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y
64	54788	70	F	56	7	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y
65	54792	76	M	55	7.5	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y
66	54800	78	F	54	6.8	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y
67	54804	74	M	41	6.9	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
68	54807	73	F	45	5.6	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
69	54813	69	F	48	6.6	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
70	54834	78	M	42	5.9	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
71	54867	49	M	56	6.5	N	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N
72	54888	57	M	57	6.9	N	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N
73	54991	51	M	54	7	N	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N
74	54997	76	M	39	6.5	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y
75	54998	71	M	35	7.5	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y
76	55110	54	M	54	5.9	N	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N

77	55117	39	M	34	7.6	Y	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N
78	55222	34	M	45	5.6	Y	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N
79	55234	37	M	56	6.8	Y	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N
80	55267	34	M	46	6.8	N	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N
81	55319	51	M	67	6	N	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N
82	55198	80	M	54	7.8	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N	N
83	55190	49	F	68	6.8	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
84	55343	57	M	67	5.9	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
85	47895	56	F	66	6.8	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
86	43687	51	M	68	6.5	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
87	44786	54	F	68	6	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
88	45891	49	M	66	5.6	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
89	51423	57	M	68	7.8	N	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N
90	51347	58	M	68	6.8	N	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N
91	52673	69	M	67	7	N	N	N	N	N	Y	N	N	N	N	N	N	N	N	Y	N	N	N
92	52874	71	M	54	6.5	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N
93	52789	32	M	54	6.8	N	Y	N	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N
94	53784	51	M	55	7.9	N	Y	N	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N
95	51908	57	M	55	6.9	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
96	54896	50	M	56	5.7	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
97	54872	59	M	68	6.9	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
98	54908	54	M	54	5.8	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
99	56743	51	M	58	6.8	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
100	55478	58	M	56	6.9	Y	Y	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	N
101	55453	56	M	56	6.8	Y	Y	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	N
102	55674	59	M	47	6.9	Y	Y	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	N
103	57812	51	M	54	6.7	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
104	57621	54	M	47	6.9	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
105	49764	53	M	48	5.9	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
106	42903	58	M	56	6.9	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
107	42563	57	M	58	6.6	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
108	46752	19	F	67	6.8	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N
109	47586	19	F	65	5.9	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N
110	41433	54	F	54	5.5	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N
111	478592	47	F	78	6	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N
112	47652	49	F	65	5.9	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N
113	43675	46	M	54	6	Y	Y	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N
114	45987	51	M	44	7	Y	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N	N	N
115	51367	58	M	44	6.5	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N	N
116	47652	54	M	56	5.9	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N	N
117	47659	53	M	57	6.7	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N	N	N
118	53622	51	M	54	6.5	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N
119	53711	56	M	55	6	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N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INTRODUCTION
Hypoglycaemia is a lab finding which is defined as low levels of plasma glucose which may or may not be related to significant pathology. Hypoglycaemia that is pathological is caused by large spectrum of clinical disorders.
Several studies have revealed that hypoglycaemia is an independent risk factor for mortality and morbidity in hospitalised patients.
Glucose is the major metabolic substrate for brain under physiologic conditions. Brain can neither synthesize glucose nor store glucose supply of more than few minutes. Hence, it needs continuous supply of glucose from systemic circulation
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INTRODUCTION