DISSERTATION

ON

STUDY ON PERIOPERATIVE GLYCEMIC CONTROL AND POSTOPERATIVE INFECTIONS

Dissertation submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfilment of the regulations

for the award of the degree of

M.S.-GENERAL SURGERY- BRANCH – I

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THANJAVUR - 613 004.

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

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APRIL – 2015

CERTIFICATE

This is to certify that this dissertation entitled "**DISSERTATION ON STUDY ON PERIOPERATIVE GLYCEMIC CONTROL AND POSTOPERATIVE INFECTIONS"** is the bonafide original work of **Dr. S.ARAVINTH** in partial fulfillment of the requirements for M.S. Branch -I (General surgery) Examination of the Tamilnadu Dr. M.G.R. Medical University to be held in APRIL - 2015. The period of study was from jan 2014 to june 2014.

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DECLARATION

I, **Dr. S.ARAVINTH,** solemnly declare that the dissertation titled "**DISSERTATION ON STUDY ON PERIOPERATIVE GLYCEMIC CONTROL AND POSTOPERATIVE INFECTIONS"** is a bonafide work done by me at Thanjavur Medical College, Thanjavur during jan 2014 to june 2014 under the guidance and supervision of **Prof.Dr. V.BALAKRISHNAN M.S,** Thanjavur Medical College, Thanjavur.

This dissertation is submitted to Tamilnadu Dr. M.G.R Medical University towards partial fulfilment of requirement for the award of **M.S. degree (Branch -I) in General surgery.**

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CONTENTS

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ABSTRACT

OBJECTIVE: To study the effects of perioperative glycemic control and their impact on postoperative infections in various general surgical procedures in patients with diabetes mellitus.

BACKGROUND: Patients with diabetes are more likely to undergo various surgical procedures than non-diabetics. Perioperative glycaemic control in diabetics is challenging and leads to lesser postoperative infectious complications. This study helps to establish the significance of strict glycaemic control in these patients.

METHODS: A prospective study of 50 diabetic patients undergoing various surgical procedures was done for the association of perioperative glycaemic control and the incidence of postoperative infections for a 30-day period during the period, from 1.1.2014 to 30.06.2014 in Thanjavur Medical College. The stastical significance and the overall incidence of postoperative infections were analysed with the amount of glycaemic control achieved.

RESULTS: Of the 50 patients, 28 were males and 22 females. The mean age of the study is 54 years. 35 patients of elective surgery and 15 patients of emergency surgery were included. Mean plasma glucose concentration in the perioperative period calculated and patients were divided into four quartiles (I-120-180 mg/dl; II-181 to 220 mg/dl; III-221 to 260 mg/dl; IV-261 to 350 mg/dl) accordingly. The incidence of SSIs in each quartile (I-IV) was 16.7%, 54.5%, 66.7% & 100% respectively. 13.3%, 18.2% 33.3% & 66.7% incidence of pneumonia and 6.7%, 9.1%, 16.7% & 33.3% incidence of UTI occurred in quartile I to quartile IV respectively. Similarly the rate of occurrence of sepsis is 18.2% in II, 33.3% in III and 66.7% in IV quartile with no sepsis in I quartile patients. The overall incidence of postoperative infectious complications in each quartile from I to IV is 36.7%, 72.7%, 83.3% and 100% respectively. SSI accounted for the most common and sepsis for the least common complication in these patients. Insulin therapy proved to be a better way to achieve glycaemic control in these patients. The optimal glycaemic range desired is between 120 to 180 mg/dl.

CONCLUSION: Good perioperative glycaemic control is associated with a decrease in postoperative infectious complications in diabetic patients undergoing various surgical procedures.

INTRODUCTION

The primary goal of a surgeon is to provide the patient a quick, painless and safe recovery from surgery as possible. Infections following surgical procedures result in pain, poor wound healing, need for additional treatment including antibiotics, extended hospital stays, and increased health care expenditures.

Postoperative infections may cause several problems, which include failure of the surgical procedure, other surgical complications, sepsis, organ failure, and even death.

Diabetes mellitus is an increasing challenge to the surgeons, since these patients are at greater risk of developing postoperative infections when compared to the non-diabetic patients.Alarmingly, diabetes mellitus is being diagnosed more often in younger patients. Strict glycaemic control in the postoperative period has significantly reduced the morbidity in these patients and has increased overall survival rates.

Identifying the factors that play an increased role in the patient with diabetes mellitus can help to alleviate postoperative infection through education, controlling hyperglycaemia, administering appropriate antibiotics whenever needed, and ensuring that the patient is in adequate nutritional status.

This prospective study on perioperative glycaemic control and postoperative infections will give us better understanding about the importance of glycaemic control in diabetes mellitus and helps lessen the burden of postoperative morbidity in these patients.

AIMS AND OBJECTIVES

- To study about the preoperative glycaemic control and postoperative infections.
- To study about the postoperative glycaemic status and postoperative infections.
- To study the range of the blood sugar to be maintained.

MATERIALS AND METHODS

SELECTION OF STUDY SUBJECTS:

All patients with diabetes mellitus who satisfy the inclusion criteria are studied with perioperative blood sugar values and postoperative wound infections, urinary tract infections, lower respiratory tract infections and sepsis.

INCLUSION CRITERIA:

- Patients presenting with diabetes mellitus undergoing general surgical procedures.

EXCLUSION CRITERIA:

- Patients without diabetes mellitus.
- Patients with major comorbid illness.
- Patients presenting with postoperative infections within 36 hours of surgery.
- Patients who were not given consent for surgery.

INVESTIGATIONS DONE:

- Blood sugar values
- Hb A1C

DATA COLLECTION METHODS:

- Clinical
- Blood reports
- Culture & sensitivity reports

STUDY DESIGN : Prospective study

STUDY PERIOD : 1.1.2014 – 30.06.2014

STUDY PLACE : THANJAVUR MEDICAL COLLEGE AND HOSPITAL

REVIEW OF LITERATURE

Diabetes mellitus is one of the diseases of the modern era and it approximately affects 230 million people worldwide.The term is derived from the Greek words dia (=through),bainein (=to go) and diabetes literally means pass through.The disease causes loss of weight as if the body mass is passed through the urine. The Greek word, mellitus, means sweet, as it is known to early workers, that the urine of the patient contains sugar. Diabetes mellitus is a disease known from very ancient times. Charaka in his treatise (circa 400BC) gives a very elaborate clinical description of *madhumeha*(= sweet urine). He had the vision that carbohydrate and fat metabolisms are altered in this disease. In Western literature,Thomas Willis in 1670 noticed the sweet taste of diabetic urine. In 1838, Bouchardt and Peligot proved that the sugarof diabetic urine is the same as that present in grape sugar.Diabetes mellitus is a metabolic disease due to absolute or relative insulin deficiency. Diabetes mellitus is a common clinical condition. It is a major cause for morbidity and mortality. Insulin deficiency leads to increased blood glucose level.In spite of this high blood glucose, the entry of glucose into the cell is inefficient. Hence, all cells are starved of glucose.

There is an expanding incidence and prevalence of diabetes mellitus. About 10% of the total population, and about 1/5th of persons above the age of 50, suffer from this disease.About 50% of people suffering from diabetes mellitus are ignorant of their condition. Approximately 25% of patients with diabetes who undergo surgery are undiagnosed on admission to hospital. Patients with diabetes have a greater risk of certain diseases like cardiovascular disease, etc. Patients with diabetes have a greater perioperative risk for developing infections. This is more likely because of their disease to need surgery and those who undergo surgery are likely to be less well-controlled and to have complications from their diabetes according to their glycaemic control.

Diabetic patients with tight long-term glucose control as measured by the percentage of haemoglobin A1c (HbA1c) has reduced incidence and severity of most of the chronic complications associated with diabetes, such as nephropathy, neuropathy, andretinopathy.It has not been well established whether long term glycaemic control also helps mitigate acute infectious complications in the perioperative period. Therefore this study has been chosen to determine whether good perioperative glycaemic control is associated with decreased incidence of postoperative infections in patients with type 2 diabetes undergoing a various surgical procedures.

Hyperglycemia has the potential to affect multiple pathways of the immune system.It may cause decreased phagocytic and chemotactic functions in neutrophils and monocytes, increased rates of apoptosis of the neutrophils and decreased ability of the monocytes to present antigen. Hyperglycemia primarily affects the cellular immune system. It stimulates inflammatory cytokines and affects the microcirculation, thereby increasing the risk for infection and preventing the phenomena of normal wound healing. Hyperglycemia is a common occurrence in patients undergoing surgery, and undiagnosed insulin resistance identified on the day of surgery is increasingly common. Perioperative hyperglycemia has been associated with postoperative complications in vascular surgery, mastectomies, neurosurgery, spine surgery, transplant surgery, colorectal surgery, hepato-biliary-pancreatic surgery, cholecystectomy, etc. There are evidences that suggest that hyperglycemia is modifiable, independent predictor and possibly a casual factor of adverse outcomes in diabetic patients.

Intensive diabetic therapy with improved blood glucose control has been shown to delay the long term detrimental effects of microvascular complications and to prevent impairment of the white blood cell's ability to phagocytose and effectively kill bacteria. Several studies had showed a significant positive correlation between the mean plasma glucose levels and the frequency of acute infections. The diminution of intracellular bactericidal

activity of leukocytes to both Staphylococcus aureus and Escherichia coli was shown to have a direct relation to glucose control. Similarly short term hyperglycaemia is also associated with detrimental effect on the ability of immunoglobulin G to fix complement. Further, extracellular glycosylation of proteins in diabetics has been shown to impair wound healing and is associated with increased collagenase activity and decreased wound collagen content.

DIABETES MELLITUS

Diabetes mellitus is a common disease in man. A predisposition to the disease is probably inherited as an autosomal recessive trait. About 25 per cent of relatives of diabetics show abnormal glucose tolerance curves as compared to 1 per cent in the general population.

Definition:

A chronic disease primarily due to a disorder of carbohydrate metabolism, cause of which is deficiency or diminished effectiveness of insulin, resulting in hyperglycaemia and glycosuria. Secondary changes may occur in the metabolism of proteins, fats, water and electrolytes and in tissues/organs sometimes with grave consequences.

STAGES OF DIABETES MELLITUS

Since "overt" diabetes is not usually seen till after the age of 40, there must be a stage of Pre-diabetes which dates from the time of conception.American DiabetesAssociation has divided into four stages. The four stages and findings are shown below in tabular form in the box.

Stages	**GTT**	**FBS**	**Plasma insulin**	**Symptoms**	**Angiopathies**
Pre-diabetes	Normal	Normal	Normal	None	+
Suspected diabetes	Abnormal	May be normal	Normal	Symptoms after stress	+
Chemical/Latent Diabetes	Abnormal	Normal or raised	Normal or raised	Unusual	++
Overt Diabetes	Abnormal	Raised	Normal or low	Usual	+++ to ++++

CLINICAL TYPES AND CAUSES

These are two main groups:

(a) Primary (Idiopathic): It constitutes the major group. Exact cause is not known; metabolic defect is insufficient insulin which may be absolute or relative.

(b) Secondary: Constitutes minor group where it can be secondary to some disease process.

(a) Primary (Idiopathic)

Two clinical types:

- "Juvenile"-onset diabetes: Now called as Type-I-(Insulin dependent)—IDDM.
- "Maturity" onset diabetes: Type-II NIDDM— (Non-Insulin Dependent).

Other Factors

1. Heredity: In both types, familial tendency noted.Genetic factors are more important in those who develop after 40. In younger, "Juvenile" type, susceptibility is associated with particular HLA phenotype. Risk is two to three times more in those who are HLA phenotype B8 or BW15.

2. Autoimmunity: Insulin-dependent juvenile type maybe an autoimmune disorder and has been found to co-exist with other autoimmune disorders.

Evidences in favour of autoimmunity:

- Lymphocytic and plasma cells infiltrations in pancreas
- Detection of auto antibodies by immunofluorescence.

3. Infections: Certain viral infections may precipitate Juvenile type. Experimentally it has been shown that certain viruses can induce diabetes. Incidence is high after mumps. Antibodies to coxsackie B4 virus have been found in young Juvenile type.

4. Obesity: Majority of middle aged maturity-onset diabetics are obese, "stress" like pregnancy may precipitate.

5. Diet: Over-eating and under activity are also predisposing factors in elderly middle aged maturity onset diabetes.

6. Insulin antagonism: In "maturity onset" diabetes, the deficiency of insulin is relative and glucose induced insulin secretion may be greater and more prolonged than normal. This relative deficiency may be due to insulin antagonism, exact cause for the same is not known but various factors have been incriminated from time to time. They are:

• Synalbumin of Vallence-Owen in plasma,dialyzable, thermostable substance.

• β1-lipoprotein factor: Another similar factor foundin β1-lipoprotein fraction of plasma in diabetics.

• Insulin “antibodies”.

• Secretion of abnormal and less active insulin or‘altered’ insulin.

• A “tissue barrier” to the transport of insulin to the cells, probably “receptor” deficiency.

• Lack of cellular response to insulin.

(b)Secondary:

This forms a minor group. Diabetes issecondary to some other diseases.

1. Pancreatic diabetes:

• Pancreatitis

• Haemochromatosis

• Malignancy of Pancreas.

2. Abnormal concentrations of antagonistic hormones:

• Hyperthyroidism

• Hypercorticism: like Cushing’s disease andSyndrome

• Hyperpituitarism: Like acromegaly

• Increased glucagon activity.

3. Iatrogenic: In genetically susceptibles, may be precipitated by therapy like corticosteroids, thiazidediuretics.

Recent Advances In Diabetes Mellitus

1. Immune “markers” in type IDM (IDDM): The recent area of interest is the role of “glutamic acid decarboxylase” (GAD) as antigen of potential significance.Recently anti-GAD antibodies have been deomonstrated in most newly diagnosed IDDM (Type I) patients and in predictable first degree relatives.In adults presence of GAD antibody is a “marker” for slow onset Type I DM (IDDM) and helps to differentiate IDDM with age of onset > greater than 35 years and TypeII (NIDDM). The term “Latent Autoimmune DM” inadults or “LADA” is now being used for such patients.

2. Genes of DM discovered: As seen above, some people may be genetically susceptible to Non-insulin dependent (NIDDM) or adult onset diabetes. Recently researchers have discovered 2 (two) genes, called MODY 1 and MODY 3, that appear to contribute to the 2 to 5 per cent of Diabetes cases that are clearly inheritable.MODY 3 gene, located on chromosome 12, produces hepatocyte nuclear factor-1α (HNF-1α), a protein found in the Liver and in the β-cells of the pancreas. Pancreaticβ-cells produce insulin, the hormone that regulates bloodsugar levels.“MODY 1 gene”, located on chromosome 20, makes hepatocyte nuclear factor 4α (HNF 4α), a cell receptor that plays a role in HNF-1α production.The biological effects of mutant forms of HNF-1α and HNF-4α are still not known clearly.

Presentation

The disease has a varied presentation.

• Glycosuria may be detected during routine examination of urine like annual check-up or when doing routine examination due to some other diseases. There may not be any symptoms/signs.

• Some may present with all classical symptoms like thirst, polydypsia, Polyuria, Polyphagia, loss of weight etc. ("Overt" diabetics).

• Some women present during pregnancy (stress)

• A few specially Type-1 cases may present as fulminant ketoacidosis and a few with complications.

Clinical Features & Biochemical Correlation:

• Large amounts of glucose may be excreted in urine(may be 90 to 100 G/day in some cases). Loss of solute produces osmotic diuresis thus large volume of urine(polyuria).

• Loss of fluid leads to thirst and polydypsia.

• Polyphagia: Eats more frequently. More fond of sweets. The above symptoms may persist for many months in maturity-onset diabetes. In juvenile onset type-1, further symptoms develop if treatment is not started.

• Tissues including muscles received liberal supply of glucose but cannot use glucose due to absolute or relative deficiency of insulin/ or transport defect to cells. This causes weakness and tiredness.

• As glucose cannot be used for fuel, fat is mobilised leading to increase FFA- in blood and liver.

• Increased acetyl-CoA is diverted for cholesterol synthesis—Hypercholesterolaemia and atherosclerosis. Xanthomas may develop. Increased ketone bodies leads to acidosis, which leads to hyperventilation (“air-hunger”).

• If ketosis is severe, acetone will be breathed out, giving characteristic “fruity” smell in breath (due to acetone).

• Along with above, there may be excessive breakdown of tissue proteins. Deaminated amino acids are catabolised to provide energy, which accounts for loss of weight.

• Due to ketosis, develops anorexia, nausea, and vomiting.Continued loss of water and electrolytes increases dehydration.

• Ketoacidosis produces increasing drowsiness, leading to diabetic coma in untreated cases.

Metabolic Changes In Diabetes Mellitus

1. **Hyperglycaemia** occurs as a result of:

• Decreased and impaired transport and uptake ofglucose into muscles and adipose tissues.

• Repression of key glycolytic enzymes like Glucokinase, phospho fructokinase and pyruvate kinase takes place.

• Derepression of key gluconeogenic enzymes like Pyruvate carboxylase, phosphoenol pyruvate carboxykinase, fructose biphosphatase andglucose-6-phosphatase occur, promoting gluconeogenesis in Liver. This further contributes to hyperglycaemia.

• Elevated amino acid level in the blood particularly alanine provides fuel for gluconeogenesis in Liver.

2. Amino Acids Level

• Transport and uptake of amino acids in peripheral tissues is also depressed causing an elevated circulating level of amino acids, particularly alanine. Gluco corticoid activity predominates having catabolic action on peripheral tissue proteins, releasing more amino acids in blood.

• Amino acids breakdown in Liver results in increased production of urea N ↑.

3. Protein synthesis: Protein synthesis is decreased in all tissues due to:

• Decreased production of ATP↓

• Absolute or relative deficiency of Insulin.

4. Fat Metabolism

• Decrease extra mitochondrial de Novo synthesis of FA and also TG synthesis due to decrease in acetyl-CoA from carbohydrates, ATP, NADPH and α-glycero-(p) in all tissues.

• Stored lipids are hydrolysed by increased Lipolysis liberating free fatty acids (FFA)↑.Increased FFA interferes at several steps of carbohydrate phosphorylation in muscles, further contributing to hyperglycaemia. Effects of Increased FFA Level

• FFA reaching the Liver in high concentration inhibits further FA synthesis by a feedback inhibition at the acetyl-CoA carboxylase step.

• Fats are mobilised for energy; increased fatty acid oxidation increases acetyl-CoA level, which in turn activates Pyruvate carboxylase, stimulating the gluconeogenic pathway required for conversion of amino acids C-skeletons to glucose.

• FA also stimulates gluconeogenesis by entering TCA cycle and increasing production of citrates↑. Citrate in turn inhibits glycolysis at phosphofructokinase level.

• Eventually FA inhibits TCA cycle at the level of citrate synthase and possibly pyruvate dehydrogenase complex and Isocitrate dehydrogenase level.

- Acetyl-CoA which no longer can be channelized to TCA cycle or be used for FA synthesis are diverted to:
    - Cholesterol synthesis
    - Ketone bodies formation. Excessive production of ketone bodies increases the concentration of ketone bodies in blood (ketonaemia) and excretion of ketone bodies in urine (ketonuria) and leads to acidosis.

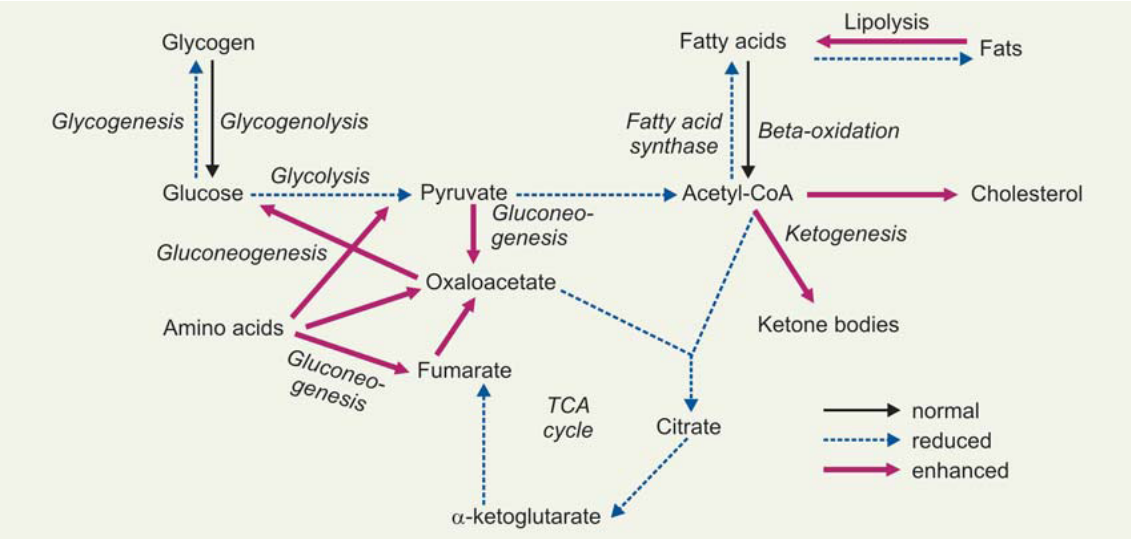
5. Effect on glycogen synthesis: Glycogen synthesis is depressed as a result of:

• Decreased glycogen synthase activity due to deficiency of insulin.

• By activation of phosphorylase producing glycogenolysis through the action of epinephrine and/or glucagon (antagonistic) hormones.

• By increased ADP: ATP ratio.

The insulin-deficient person is in a state of hormonal imbalance favouring the action (Preponderance) of glucocorticoids, growth hormone and glucagon, all of which add to the stimulation of gluconeogenesis, lipolysis and decreased intracellular metabolism.



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6. Other Effects of Hyperglycaemia

(a) *Glycosylation of Hb and formation of glycosylated Hb (HbA1C)*: Glycosylated haemoglobins particularly HbA1C rises in prolonged and uncontrolled diabetes 3 to 4 times than the normal level.

(b) *Non-enzymatic glycosylation of other proteins as plasma albumin, collagenous tissues and the lens protein α-crystallin*: Such glycosylations of collagenous tissues bring about thickening and morphologicalchanges of vessel walls and also glomerular basement membrane thickening. Glycosylation of lens protein may also account for diabetic cataract. Diabetic cataract biochemically may be due to:

- Glycosylation of Lens Proteins, i.e. α-crystallin.
- Accumulation of 'sorbitol' which produces osmotic damage.

7. Sorbitol (polyol) pathway and phosphoinositide metabolism: Over the past few years, quest to discrete pathogenetic mechanisms for the long-term complications of Diabetes has gradually focussed on three promising targets for specific therapeutic intervention:

- Non-enzymatic glycosylation of Proteins
- Altered 'microvascular' haemodynamics, and
- Abnormal sorbitol (polyol)—inositol metabolism.

1. Striking structural similarity between glucose and Myoinositol (MI) results in competition for high affinity myoinositol transporters which explains the selective tissue depletion of myoinositol that accompanies hyperglycaemia. Glucose interferes with“carrier-mediated” myoinositol transport in various tissues specially intestine, renal brush border membranes, peripheral nerves and renal glomerulus. Thus hyperglycaemia may selectively deplete myoinositol from tissues.

2. When tissues that exhibit diabetic complications are exposed to hyperglycaemia, sorbitol (Polyol—alcohol), accumulates because of an increase in the conversion of intracellular glucose to sorbitol by the high Km, i.e. low affinity enzyme aldose reductase and myoinositol level falls.

3. High milli-molar levels of sorbitol that accumulate in Lens of eye cause osmotic damage, which has been linked to the development of Diabetic cataract.

4. Inositol-1,4,5-triphosphate is thought to mobilise intracellular Ca++sequestered in the endoplasmic reticulum. Due to decrease in Inositol Polyphosphaterelease, Ca++ mobilisation is decreased.

5. Due to decreased availability of Diacylglycerol and lower Ca++ mobilisation proteinkinase C activity is decreased, resulting in lowered Na+-K+ ATPase activity, resulting to Na accumulation in tissues.

Clinical Aspect: Several inhibitors like Sorbinil, an aldosereductase inhibitor, the first enzyme in the metabolic cascade shown above can prevent or reverse early diabetic complications in laboratory animals and are being extensively undergoing clinical trials in patients with Diabetes mellitus.

Complications Of Diabetes

I. Immediate: Diabetic ketoacidosis and coma is one ofthe most important and dreaded complication specially in Type-I.

II. Late complications: Other complications are late to appear and are due to changes in blood vessels. These are two types:

- Involvement of large vessels
- Involvement of small vessels.

(a) Large vessels involvement: Atherosclerosis and its effects:

- Involvement of coronary vessels can produce myocardial infarction.
- Involvement of cerebral vessels can produce“stroke”.

(b) Small vessels changes involve:

- Thickening of basement membrane
- Microvascular changes.

1. *Diabetic retinopathy* (70%): Tiny haemorrhages,punctate or flame-shaped, exudates. Haemorrhage in vitreous humour can cause sudden blindness.

2. *Diabetic cataract*: Is due to:

- Non-enzymatic glycosylation of lens protein,α-crystallin;
- Osmotic damage to lens protein due to accumulation of sorbitol.

3. *Diabetic nephropathy* (50% cases): Characterised by

(a) Proteinuria

(b) Hypertension

(c) Oedema.

The triad is called as Kimmelsteil-Wilson syndrome.Microscopic lesions are called as 'Kimmelsteil-Wilsonlesions/disease'. Lesions are often present when syndrome is not developed. Sometimes kidney lesions may be shown as:

- Papillary necrosis: A dangerous complication.
- Pyelonephritis: When secondary infections occur.

4. *Peripheral neuritis (neuropathy)*: Manifestated by loss of sensation and tingling. Biochemically probably the cause is myoinositol deficiency. Sometimes there maybe associated myopathies, weakness of muscles.

5. *Diabetic gangrene*: Cause is due to diminished blood supply due to atherosclerotic changes in blood vessels.Also associated tissue hypoxia due to formation ofHbA1C (glycosylated Hb), less oxygen carrying capacity.

6. *Skin lesions*: Prone to infections: boils/ulcers and carbuncles. There may be

- Necrosis of skin
- Necrobiosis diabetic orum
- Punctate depigmented atrophy
- Wound healing is delayed

7. *Pulmonary tuberculosis*: Susceptible to pulmonary tuberculosis.

POSTOPERATIVE OUTCOMES MEASURED:

The outcomes that were primarily measured were postoperative infections and its complications which include surgical site infections, pneumonia, urinary tract infection, and or sepsis developed on postoperative day 2 or later (i.e., $\geq$ 36 hours following surgery)

Urinary Tract Infections

Urinary tract infection was defined by the Centers for Disease Control and Prevention. It is based on a combination of symptoms, such as

- Urgency
- Frequency
- Dysuria
- Urine culture with greater than 10^5 colonies/mL and no more than 2 species of organisms.

The most common causative organisms causing urinary tract infections in hospitalised patients are as follows:

1. Escherichia coli
2. Klebsiella
3. Enterobacter
4. Serratia
5. Proteus

6. Providentia
7. Pseudomonas aeruginosa
8. Alcaligenes
9. Acinetobacter
10. Moraxella
11. Streptococcus fecalis
12. Staphylococcus pyogenes
13. Streptococcus pyogenes
14. Salmonella
15. Neisseria gonorrheae
16. Mycobacterium tuberculosis
17. Candida albicans.

Surgical Site Infections

Wound infections were defined by the Centers for Disease Control and Prevention as infections occurring at the site of incision within 30 days following surgery with purulent drainage, dehiscence, or cellulitis. Depending upon the severity of these infections they were classified as superficial or deep.

The most common organisms causing surgical site infections are:

Aerobes:

- Staphylococcus aureus
- Streptococcus pyogenes
- B. proteus
- Pseudomonas
- Coliform bacilli.

Anaerobes:

- Streptococci
- Bacteroides—Nonspore former
- Clostridium perfringens
- Clostridium tetani—Spore former
- Clostridium septicum
- Clostridium edematiens

Fungi:

- Candida.
- Aspergillus.

Source of infection may be exogenous(from environment) or endogenous (from commensal of body). Open wound may be infected with multiple organisms where as closed un drained wound is usually infected with single organism like *Staphylococcus aureus, Streptococcus pyogenes* and so on.

Pneumonia

Pneumonia was defined as inflammation of the lungs, based on clinical examination criteria, an organism isolate from sputum culture and sensitivity and/or newly occurring radiographic changes following surgery. Pneumonia was included in the outcome measure only if the patient develops pneumonia postoperatively and was documented no pneumonia in the preoperative period.

Overall, any respiratory infection in diabetic patients is associated with increased mortality. Diabetic persons are four times more likely to die from pneumonia than non-diabetic patients. Specific infections, such as those caused by Staphylococcus aureus and gram negative organisms, are more frequent in diabetes. According to one study, up to 30% of diabetics are nasal carriers of S. aureus as compared with 11% of healthy individuals. On the basis of their high nasal carriage rate, diabetic persons are thought to be at an increased risk for S.aureus pneumonia. More common organisms, such as Streptococcus pneumonia, Legionella, and influenza are associated with increased morbidity and mortality. It is yet to be proved that whether Legionella and influenza causes pneumonia in diabetic patients with increased frequency or causes a severe form of pneumonia in these persons.

More frequently both gram-negative microorganisms and fungi cause pneumonia in patients with diabetes. The management is similar for both diabetics and non-diabetics for bacterial pneumonia.For pneumonia caused by influenza antiviral agents are usually prescribed for these persons.

Several studies has also documented increased incidence and high prevalence of tuberculosis among diabetic patients. Diabetes acts as an independent risk factor for respiratory tract infections. Hence strict glycaemic control is needed in all diabetic patients especially those who undergo surgeries.

Sepsis

Sepsis was characterized by fever, elevated leucocyte count and sometimes with hypotension, shock, and/or bacteraemia requiring management with broad-spectrum antibiotics and other supportive measures for a longer duration.

Severe bacterial infections or septicaemia induce septic shock. It may be the result of Gram negative septicaemia (endotoxic shock) which is morecommon or Gram-positive septicaemia (exotoxic shock). The most common organisms causing sepsis in diabetic patients undergoing various surgical procedures are:

Gram-negative septicaemia (endotoxic shock) e.g. Infection with

- E. coli
- Proteus
- Klebsiella
- Pseudomonas
- Bacteroides

Gram-positive septicaemia (exotoxic shock) e.g. Infection with

- Streptococci
- pneumococci

Septic shock results most often from Gram-negative bacteria entering the body from genitourinary tract, alimentary tract, respiratory tract or skin, and less often from Gram-positive bacteria. In septicshock, there is immune system activation and severe systemic inflammatory response to infection as follows:

i) Activation of macrophage-monocytes: Lysis of Gram negative bacteria release endotoxin, a lipopolysaccharide, into circulation where it binds to lipopolysaccharide-bindingprotein (LBP). The complex of LPS-LBP binds to CD14 molecule on the surface of the monocyte/macrophages whichare stimulated to elaborate cytokines, the most important ones being TNF-α and IL-1. The effects of these cytokines are as under:

a) By altering endothelial cell adhesiveness: This result in recruitment of more neutrophils which liberate free radicals that cause vascular injury.

b) Promoting nitric oxide synthase: This stimulates increased synthesis of nitric oxide which is responsible for vasodilatation and hypotension.

ii) Activation of other inflammatory responses: Microbial infection activates other inflammatory cascades which have profound effects in triggering septic shock. These are as under:

a) Activation of complement pathway: End-products C5a and C3a induce micro emboli and endothelial damage.

b) Activation of mast cells: Histamine is released which increases capillary permeability.

c) Activation of coagulation system: Enhances development of thrombi.

d) Activation of kinin system:Released bradykinin cause vasodilatation and increased capillary permeability.

The net result of above mechanisms is vasodilatation and increased vascular permeability in septic shock. Profound peripheral vasodilatation and pooling of blood causes hyperdynamic circulation in septic shock, in contrast to hypovolaemic and cardiogenic shock. Increased vascular permeability causes development of inflammatory oedema.Disseminated intravascular coagulation (DIC) is prone to develop in septic shock due to endothelial cell injury by toxins. Reduced blood flow produces hypotension, inadequate perfusion of cells and tissues, finally leading to organ dysfunction.

Septic shock is a grave complication in any person particularly it is very difficult to manage in diabetic patients. Since patients undergoing surgery are more prone to develop hyperglycaemia by various metabolic responses, diabetic patients undergoing surgery should be metabolically well controlled to avoid this dangerous complication.

DIAGNOSTIC CRITERIA:

- As per WHO, normal fasting plasma glucose in an adult is 70 to 110 mg/dl.
- American Diabetic Association (ADA) recommends the upper limit as 100 mg/dl, above which the patient has to be tested periodically.
- HbA1C $\geq$6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.
- Fasting plasma glucose $\geq$ 126mg/dl. Fasting is defined as no caloric intake for at least 8 hours.
- 2 hour plasma glucose $\geq$ 200 mg/dl during an OGTT. The test should be performed as described by the World Health Organisation, using a glucose load containing the equivalent of 75g anhydrous glucose dissolved in water.
- In a patient with classic symptoms of hyperglycaemia or hyperglycaemic crisis, a random plasma glucose $\geq$ 200 mg/dl.

	NORMAL PERSONS	CRITERIA FOR DIAGNOSING DIABETES	CRITERIA FOR DIAGNOSING IGT
Fasting	<110 mg/dl <6.1 mmol/L	>126 mg/dl > 7.0 mmol/L	110 to 126 mg/dl
1 hr after glucose	<160 mg/dl <9 mmol/L	Not defined	Not defined
2 hrs after glucose	<140 mg/dl < 7.8 mmol/L	>200 mg/dl > 11.1 mmol /L	140 to 199 mg/dl

METABOLIC RESPONSE TO ANAESTHESIA AND SURGERY:

Surgery induces a considerable stress response in the perioperative period mediated by the neuroendocrine system. This results in the increased release of catecholamines, glucagon, and cortisol in the blood. The principal mechanism by which it acts is by stimulating the sympathetic system which results in the release of cortisol and catecholamines during surgery. In diabetic patients this is affected because of either relative or absolute insulin deficiency, necessitating supplemental insulin in the perioperative period. Hence, type 1 DM patients, who are at increased risk for end-organ complications, usually need intravenous insulin therapy in the perioperative period. Type 2 diabetes patients may be continued on their oral hypoglycaemic agents if they have well controlled glycaemic range.

These oral hypoglycaemics may be discontinued preoperatively and the patient may be started on intravenous insulin therapy depending on the nature of surgery and taking into account other associated risk factors.

Hyperglycaemia may occur even in nondiabetic patients, because of the considerable stress response induced by the surgery in the perioperative period. It has been shown by multiple randomized controlled studies that achieving a strict glycaemic control in all surgical patients has a greater impact on the outcome of these patients particularly those who are critically ill.

By affecting the sympathetic tone several anaesthetic agents will also affect the glucose metabolism. Several studies suggested that inhalational agents have shown to suppress insulin secretion. This resulting insulin insufficiency or relative deficiency often results in dysregulation of the glucose metabolism and hyperglycemia. This deficiency along with insulin resistance in diabetic patients raises the risk of ketoacidosis in this group. To mitigate these concerns, the use of regional anaesthesia or peripheral nerve blocks has been advocated. But there is a lacking evidence to support that these forms of anaesthesia are associated with improved postoperative survival in patients with DM.

As there is a rising need for surgical procedures in the diabetes patients so is the increasing postoperative morbidity and mortality in these patients. The incidence of perioperative ketoacidosis and/or hyperosmolar syndrome is increased in these patients in response to the stress of the surgery and its resultant complications such as hyperglycaemia, osmotic diuresis and hypo insulinemia. Hyperglycemia results in the impairment of leukocyte function and normal wound healing. Our primary goal in the perioperative period is to achieve an optimized glycaemic control by serial monitoring, adequate hydration, sufficient caloric replacement and judicious utilisation of insulin administration.

The need for various surgical procedures is higher in patients with diabetes when compared with the non-diabetic people. Oral hypoglycaemic agents cannot be used during the period of fasting required preoperatively in major surgical procedures. Metabolic perturbations resulting from the stress of surgery result in the alteration of glucose homeostasis with resultant persistent hyperglycaemia.These changes ultimately result in endothelial dysfunction, impaired wound healing,sepsis in the postoperative period, and end organ damage including cerebral ischemia. Diabetic crises such as diabetic ketoacidosis, hyperglycaemic hyperosmolar syndrome may be precipitated by the stress response induce by the surgery either during the procedure or

perioperatively with negative prognostic consequences. Several studies have documented hyperglycaemic hyperosmolar syndrome as a most noted complication after some surgical procedures such as cardiac bypass surgery with a mortality rate of 42%.

Additionally, gastrointestinal instability triggered by anaesthesia, medications, and stress-related vagal overlay may result in nausea, vomiting, and dehydration. This in addition to the volume contraction that is already present from osmotic diuresis provoked by hyperglycaemia may add additional complications by increasing the risk for ischemic events and acute renal shutdown. There is also an increased risk for arrhythmias in these patients because of the deficits in electrolytes, principally potassium and to a little extent magnesium also. These deficits are added to the burden of the risks of coronary artery disease in elderly and also in middle ages patients suffering from diabetes.

It therefore becomes essential in people with diabetes who undergo surgical procedures to pay careful attention to their metabolic status. It is imperative that whenever elective surgical procedures are planned in people with uncontrolled glycaemic status, it should be deferred until acceptable glycaemic control is achieved. Admitting these patients prior i.e. one or two days before the planned procedure to achieve the desired glycaemic control is advisable.Whenever possible, even emergency surgical procedures can be

delayed for better stabilisation of these patients perioperatively and also to avoid diabetic crises in such patients.

Based on the individual's diabetes class, their regular diabetes regimen, current glycaemic state, nature of the undergoing surgical procedure & its extent, it is advisable to make the treatment recommendations individualised. Whenever feasible some generalised recommendations can be applied however. It is imperative to look for electrolytes deficits, hyperosmolar state and diabetic ketoacidosis preoperatively and should be corrected whenever possible before the surgery and the procedure should be delayed taking into consideration of the various factors causing diabetic crises.

STRESS RESPONSE AND GLUCOREGULATION

Anaesthesia and surgery induced metabolic stress response cause hyperglycaemia even in non-diabetics. In patients with diabetes who already have abnormalities in glucose metabolism this stress response will compound to the complications that are already affecting their homeostatic mechanisms. The invariant features of the metabolic stress response include release of the catabolic hormones epinephrine, norepinephrine, cortisol, glucagons, and growth hormone and inhibition of insulin secretion and action.

Surgical Stress & Its Anti Insulin Effects

The circulating stress hormones induced by the surgical stress causes insulin resistance and also have a deleterious effect on the normally functioning β-cell of the pancreas. During surgery the plasma insulin levels decreases and in addition the insulin secretory responses to glucose also become impaired. It has not been well established how surgery causes impairment of β-cell responsiveness since this defect has not a clear correlation with the circulating catecholamine levels during surgery.However it has been documented that there is an inverse correlation between the insulin secretory response and the plasma epinephrine levels in the postoperative period.

The physiological anabolic and anti-catabolic actions of insulin are altered by the metabolic stress response induced by surgery and its anti-insulin effects. The following important anabolic actions of insulin are either reversed or attenuated by the surgery induced metabolic stress response.

- stimulation of glucose uptake and glycogen storage
- stimulation of amino acid uptake and protein synthesis by skeletal muscle
- stimulation of fatty acid synthesis in the liver and storage in adipocytes
- Renal sodium reabsorption and intravascular volume preservation.

The anti-catabolic effects of insulin that are altered include:

- inhibition of hepatic glycogen breakdown
- inhibition of gluconeogenesis
- inhibition of lipolysis
- inhibition of fatty acid oxidation and ketone body formation
- Inhibition of proteolysis and amino acid oxidation.

Therefore through a wide variety of physiological mechanisms the perioperative milieu is being shifted towards hyper catabolic state by reduced insulin secretory response and by affecting the normal physiological actions of insulin.

Stress Hormones & Its Catabolic Effects

Anaesthesia and surgery induced neuroendocrine response to the metabolic stress will cause activation of counter-regulatory hormones. The catecholamines are released and their circulating levels increase in the perioperative period. It is interestingly noted that during surgery it is the norephinerphrine that is augmented and in the postoperative period it is the ephinephrine. Some of the hyperglycemic hormones that are released in the circulation which have anti-insulin effects are:

- Glucagon
- Ephinephrine or Adrenaline
- Glucocorticoids
- ACTH
- Growth Hormone
- Thyroxine

The metabolic effects of these hormones include:

- Stimulation of gluconeogenesis and glycogenolysis
- Inhibition of glucose utilization by peripheral tissues
- Inhibition of insulin secretion.
- Activation of phosphoproteins by cAMP-dependent protein kinases on liver and muscle glycogen breakdown.
- Phosphorylation of glycogen synthase resulting in decreased glycogen synthesis.
- Increases adipocyte cAMP levels, leading to phosphorylation and activation of hormone-sensitive lipase, which in turn promotes lipolysis and release of free fatty acids in the circulation.
- Causes ketogenesis

These effects in addition to the stimulatory effects of catecholamines on glucagon secretion predispose to severe hyperglycemia.

Similar to the catabolic actions of catecholamines, glucagon whose plasma level is increased by the metabolic stress also exhibits catabolic effects such as:

- Stimulation of hepatic glucose production
- Ketogenesis
- Inhibition of insulin action in peripheral tissues.

The catabolic actions of glucagon and catecholamines are exacerbated by the glucocorticoids and growth hormone.Glucocorticoids cause:

- Increase in hepatic glucose production
- Induce lipolysis
- Causes negative nitrogen balance by stimulating proteolysis.
- Free fatty acids, glycerol, glutamine, alanine, etc. which are the products of lipolysis and proteolysis acts as substrates for gluconeogenesis thereby increasing plasma glucose level.

METABOLISM	INSULIN	GLUCAG-ON	GLUCOCOR -TICOIDS	GROWTH HORMONE
Glycolysis	Stimulation			Inhibition
Gluconeogenesis	Inhibition	Stimulation	Stimulation	Stimulation
Glycogen synthesis	Activation	Inhibition		
Glycogenolysis	Inactivation	Activation		
Lipolysis	Inhibition	Stimulation	Stimulation	Stimulation
Ketogenesis	Inhibition	Stimulation		Stimulation
Protein Breakdown	Inhibition		Stimulation	
Protein synthesis	Anabolism		Catabolism	Anabolism
Blood glucose level	Decreases	Increases	Increases	Increases

The blend of relative hypo insulinism, insulin resistance and catabolic effects of counter-regulatory hormone is a genuine risk to the diabetic patients with resultant disastrous effect in their glucose homeostatic mechanism, especially in those with poorly controlled glycaemic status in the perioperative period.It is therefore practical that vast majority of diabetic patients undergoing surgery will require insulin therapy in the perioperative period for better glycaemic control.

INSULIN

The word "insulin" is derived from Latin, insula, meaning island(islet). In 1869, Langerhans identified the alpha and beta cellsin islets of pancreas. In 1889, von Mering and Minkowski produced experimental diabetes by pancreatectomy. In 1922,Banting and Best extracted insulin from pancreas. Insulin was the first hormone to be isolated in a pure form. In 1927, Abel crystallized the insulin. In 1954, Sanger studied the amino acid sequence of insulin; it was the first protein in which complete amino acid sequencing was done. For this workSanger got Nobel Prize in 1958. Insulin is the first protein produced by recombinant DNA technology (1982).

Mechanisms of Action of Insulin

1. Insulin Receptors

Insulin acts by binding to a plasma membrane receptor on the target cells. In obesity, the number of receptors is decreased and target tissue becomes less sensitive to insulin(diabetes mellitus Type 2). Insulin receptor is a glycoprotein with 4 subunits; 2 alpha and 2 beta subunits. The alpha units(135 kD) are located on the extracellular side, to which insulin binds. The beta subunits (95 kD) traverse the membrane and are exposed on the cytoplasmic side. Beta subunit has tyrosine kinase activity.

2. Signal Transduction

Insulin binds to the alpha subunit. This binding activates the tyrosine kinase activity of the beta subunit, leading to auto phosphorylation of the beta subunit. This event, inturn, phosphorylates insulin receptor substrates (IRS). The message is later transmitted into a series of serine/threonine kinases, such as IRS → Ras → Raf → MAPK, etc. which causes cellular responses.

3. Gene Transcription (new enzyme synthesis)

Insulin acts at the transcriptional level to regulate synthesis of more than 100 proteins.

3-A. Insulin induces the following enzymes:

i. Glucokinase

ii. Pyruvate kinase

iii. Phosphofructo kinase

iv. Acetyl CoA carboxylase

3-B. Insulin represses the following enzymes:

i. Glucose-6-phosphatase

ii. Phosphoenol pyruvate carboxy kinase

iii. Fructose-1,6-bisphosphatase

4. Activation of Enzymes

Insulin activates the existing molecules of enzymes by covalent modification (phosphorylation or dephosphorylation). There are more than 50 enzymes activated by this mechanism. Insulin activates protein phosphatase I (PPI) which dephosphorylates enzyme proteins.

5. DNA Synthesis

Through the IRS-1 pathway, insulin increases DNA synthesis, cell growth and anabolism. In all the above mentioned pathways, intracellular mediators have been implicated in insulin action. These are Ca++ and cyclic AMP. Insulin activates phosphodiesterase and thereby decreases cAMP. So, reactions dependent on cAMP are inhibited, e.g. glycogen phosphorylase.

6. Glucose Uptake

Insulin increases the recruitment of GluT4 in cells.

Metabolic actions of Insulin:

Insulin plays a central role in regulation of the metabolism of carbohydrates, lipids and proteins.

1. Uptake of Glucose by Tissues

Insulin facilitates the membrane transport of glucose. Facilitated diffusion of glucose in muscleis enhanced by insulin. In diabetes mellitus, the transporter, GIuT4 is reduced. However, glucose uptake in liver (by GluT2) is independent of insulin.

2. Utilization of Glucose

i. Glycolysis is stimulated by insulin**.** The activity and amount of key glycolytic enzymes (glucokinase, phosphofructokinase and pyruvate kinase) are increased.

ii. Glycogen synthase enzyme is activated, and so insulin favours glucose storage as glycogen.

iii. Insulin favours synthesis of fatty acid from glucose and so glucose utilization is increased.

3. Hypoglycemic Effect

i. Insulin lowers the blood glucose level by promoting utilization and storage.

ii. Gluconeogenesis is inhibited by insulin by repressing the key enzymes, pyruvatecarboxylase (PC) phosphoenol pyruvate carboxykinase (PEPCK) and glucose-6-phosphatase.

iii. Insulin inhibits glycogenolysis by favouring the inactivation of glycogen phosphorylase and inhibiting glucose-6-phosphatase. The net effect of all these three mechanisms, blood glucose level is lowered.

4. Lipogenesis

i. Lipogenesis is favoured by providing more acetylCoA by pyruvate dehydrogenase reaction.

ii. Insulin increases the activity of acetyl CoA carboxylase and provides glycerol for esterification of fatty acids to TAG.

iii. Insulin also provides NADPH by increasing theGPD activity of the HMP shunt pathway.

5. Anti-lipolytic Effect

i. Insulin inhibits lipolysis in adipose tissue due to inhibition of hormone sensitive lipase.

ii. The increased level of FFA in plasma in diabetes is due to the loss of this inhibitory effect on lipolysis.

6. Anti-ketogenic Effect

i. Insulin depresses HMG CoA synthase and so ketogenesis is decreased.

GLYCATED HEMOGLOBIN

Glycated haemoglobin (HbA1c) was formerly known as an "unusual" haemoglobin in diabetic patients above 40 years of age. Numerous studies had been conducted since then and its correlation with plasma glucose levels was established. This resulted in using HbA1c as an objective measure of long term glycaemic control in diabetic patients. The widely known A1C-Derived Average Glucose (ADAG) study involved 643 members expressing a wide range of A1C levels. This study proved the strong correlation between A1C level and plasma glucose levels among the population studied. After this HbA1c was introduced in the 1980s in clinical practice and consequently has remained a cornerstone in the management of diabetic patients.

HbA1c levels correlates with long term glycaemic status of an individual as it reflects mean plasma glucose levels over the past eight to twelve weeks. It can be done at any period of the day and does not need any special preparation

like fasting. These qualities have made HbA1c as the favourite test for assessing glycaemic control in diabetic patients. In recent times, there has been an increasing interest in utilising it as a screening test for high risk patients prone to diabetes and also as a diagnostic test in patients with diabetes.

The practical difficulties that have been encountered in measuring fasting blood glucose levels, in performing oral glucose tolerance test, and the daily variability in plasma glucose in diagnosing diabetes had led us to the search for an alternative. HbA1c overcomes these problems in the clinical practice making it practically plausible. ADA now recommends HbA1c as a means in diagnose diabetes.Even though the sensitivity and specificity is almost equal to the plasma glucose measurement in predicting chronic complications of diabetes such as diabetic retinopathy, it is still not available in most of the parts of the world.It has also been seen that patients diagnosed as having diabetes on the basis of HbA1c may not have diabetes by plasma glucose measurements.

If stringent quality assurance tests and assays are standardised to the international reference values, HbA1c can be used as a diagnostic test for diabetes.

The cut off for diagnosing diabetes on the basis of HbA1C is 6.5%. HbA1C values less than 6.5% does not exclude diabetes already identified on the basis of plasma glucose measurements.

The advantages of using HbA1c are:

- Avoids the difficulty faced by day to day plasma glucose variability.
- Evades the need for the patient to fast and/or to have special dietary preparations preceding the test.

These benefits have made it an ideal tool for early diagnosis and treatment which have been strongly advocated in recent years.

Nevertheless, HbA1c may be affected by a variety of factors such as hereditary, haematological, other existing comorbid illnesses. Some of the most common variables affecting the HbA1c levels worldwide are:

- Haemoglobinopathies
- Anaemias, and
- Accelerated red cell turnover (e.g. malaria)

Presently it is necessary to weigh the benefits and convenience of utilising HbA1c in diagnosing diabetes against the plasma glucose measurement, as it is not available currently in most parts of the world, even though it has been acknowledged as an ideal test in the management of diabetes. And also it needs further standardisation to recommend its use universally. It is

not a distant dream as many countries have already optimized its use in the clinical practice in diabetes management.

It is the global consistency that remains as a problem, even though HbA1c and plasma glucose measurement is similar in most laboratories. Whatever is used i.e. either plasma glucose or HbA1c, international standardisation is required to achieve consistent and comparable values. Despite it started happening in most of the countries, it has not become a standard all over the world.

The following programs have attempted for international standardisation and improved harmonization in measuring HbA1c levels across various manufacturers:

- The National Glycohaemoglobin Standardization Program (NGSP) being established on accomplishment of Diabetes Complications and Control Trial has remained as a basis for improved harmonisation.
- International Federation of Clinical Chemists (IFCC) has recently established a working group to introduce an international standardization program.

Because of these efforts, reference method procedures are being established for HbA1c assays. At present NGSP and IFCC, to enhance the standardisation and harmonisation, base their findings on reference method procedures for HbA1c levels.

Apart from standardisation, the cost and availability across many countries across the world is another important concern. In addition the prevalence of factors affecting HbA1c levels such as haemoglobinopathies in several countries also affect its measurement as already mentioned.

A report published in 2009 by an International Expert Committee on the role of HbA1c in the diagnosis of diabetes recommended the following:

- HbA1c level $\geq$ 6.5% to diagnose diabetes.
- Diagnosis should be confirmed with a repeat HbA1c test, unless clinical symptoms and plasma glucose levels >11.1mmol/l (200 mg/dl) are present in which case further testing is not required.
- Levels of HbA1c just below 6.5% may indicate the presence of intermediate hyperglycaemia.
- The precise lower cut-off point for this has yet to be defined, although the ADA has suggested 5.7 – 6.4% as the high risk range.
- Persons with HbA1c level between 6.0 and 6.5% were at particularly high risk and might be considered for diabetes prevention interventions.

To establish the predictive value of plasma glucose and HbA1c level in diagnosing micro and macrovascular complications of diabetes further studies are needed. It is required to establish a working group to observe various factors affecting HbA1c and plasma glucose measurement among all major ethnicities.

A single abnormal value of either plasma glucose measurement or HbA1c is not enough to make the diagnosis of type 2 diabetes in an asymptomatic person. The diagnosis is confirmed with either one more abnormal plasma glucose or HbA1c measurement at least from a random sample, or from fasting sample or from abnormal oral glucose tolerance test which should be in the diabetic range.

Either one test is enough to make the diagnosis, but if both plasma glucose and HbA1c are available and both are in the diabetic range, then the diagnosis is confirmed. It is not advisable to confirm the diagnosis on the basis of only one abnormal result. It is mandatory for another abnormal test value to diagnose a patient with diabetes.

The diagnostic certainty is vital because of the increasing screening programmes by which many more asymptomatic persons are being identified to have diabetes. In such individuals if the screening tests do not confirm the diagnosis, continued surveillance through periodic screening is essential to

include or exclude the patient in the diabetes group as defined earlier for appropriate management.

Association of HbA1c Levels and Mean Plasma Glucose Levels	
HbA1c Level, %	Mean Plasma Glucose Level, mg/dl (mmol/L)
6	135 (7.5)
7	170 (9.5)
8	205 (11.5)
9	240 (13.5)
10	275 (15.5)
11	310 (17.5)
12	345 (19.5)

PREOPERATIVE BLOOD GLUCOSE EFFECTS ON INTRAOPERATIVE CARE

The major factors which play an important role in the intraoperative glycaemic control are the oral hypoglycaemic agents, insulin therapy and the HbA1c levels. At present there are no defined standard guidelines for preoperative plasma glucose range; however few important inferences are made from various research studies.All patients with diabetes should always have a preoperative fasting blood glucose value even if they have well controlled glycaemic status and when glucose level is above 180 mg/dl, it is ideal to start insulin therapy for a better glycaemic control in the perioperative period.

The better long term glycaemic control is being established by HbA1c value less than 7%. With good glycaemic control the postoperative infections and its complications are less. In patients with poorly controlled blood glucose as indicated by HbA1c levels ≥7% need gradual reduction of blood glucose with careful surveillance. Oral hypoglycaemic agents such as sulfonylureas, biguanides, thiazolidinediones are not routinely used in the perioperative period for glycaemic control since they have the propensity to induce hypoglycaemia.With the knowledge of the metabolic stress induced by anaesthesia and surgery, diabetes patients are advised to stop the oral hypoglycaemics one day prior to the surgical procedures. For emergency

surgical procedures, diabetic patients on oral hypoglycaemics are prone to more complications, since they are ill prepared. Some examples for these are:

- Biguanides cause lactic acidosis, hepatic and renal failure in hypoperfused condition and hence it is imperative to stop it 48 hours prior to surgery.

- Sulfonylureas with a potassium-channel-blocking effect impede the myocardial ischemia pre conditioning. Patients on sulfonylureas who undergo coronary angioplasty have been proved to have a higher mortality rate than those who receive insulin preoperatively. Similarly greater mortality rate has been established among diabetes patients on sulfonylureas during the time of myocardial infarction.

With recent advances in the improved glucose monitoring and the availability of different types of insulin, the recommendations of preoperative insulin therapy have been changed. The rational thinking now is that the originally advised one half of the insulin dose required in the morning of day of surgery will not be appropriate in the current settings. When the patient is in nil per oral, the blood glucose should be monitored and treated with short-acting insulin preoperatively. Diabetic patients undergoing surgery who are on basal insulin regimen should be continued on their dose until the day of surgery. In

patients on nil oral, it is necessary to supply enough calories by infusing 5% dextrose and hourly plasma glucose monitoring.

The acceptable range of glycaemic control is not clearly yet defined, but it has been clearly established that intraoperative management with intravenous insulin infusion has reduced the unwanted metabolic and infectious complications associated with hyperglycaemia. The micro and macro vascular complications associated with diabetes have been shown to be decreased by long term intensive glycaemic control. The best and least complicated way for blood glucose control in diabetic patients is by dietary carbohydrate restriction as it is associated with less chance of hypoglycaemic crises.As insulin activity depends on GLUT4 glucose transporter, dietary restriction is the advisable efficient way in maintaining glycaemic control.

Nowadays many advanced anaesthetic and surgical techniques have been introduced that minimises the metabolic stress response, thereby mitigating the hyperglycaemic response.For example minimally invasive surgical techniques and neuro axial anaesthesia alleviates the metabolic stress response. The duration and the technique of the surgical procedure have a strong direct correlation with reduced insulin sensitivity induced by the surgery. Thorell and co workers compared conventional open cholecystectomy with that of laparoscopically performed cholecystectomy and demonstrated that laparoscopic procedure which is minimally invasive showed less reduction in

insulin sensitivity. General anaesthesia produced higher concentration of circulating stress hormones when compared with either local and/or epidural anaesthesia. Moreover, volatile anaesthetics utilised in induction and maintenance of general anaesthesia increase glucose synthesis in liver and inhibit insulin secretory response thereby causing hyperglycaemia.Preoperative glycaemic control is mandatory for an optimal intraoperative management of diabetic patients. In uncontrolled diabetes i.e. in patients with plasma glucose levels above 300 mg/dl it is difficult to achieve normo glycaemia preoperatively and requires stringent monitoring to avoid complications.

POSTOPERATIVE INFECTIONS IN DIABETICS:

Hyperglycaemia is strongly associated with poor postoperative outcomes in hospitalised patients in both diabetic and non-diabetic patients. Recent studies suggested that vigorous control of blood glucose level to maintain in euglycaemic range is related to decreased perioperative morbidity and mortality.

Pomposellie et al established the correlation between perioperative glycaemic control and postoperative infection by an extensive study in 100 patients with diabetes undergoing surgical procedures electively. The important conclusions obtained from their research were:

- Single blood glucose value more than 220 mg/dl on the first postoperative day was a sensitive (87.5%) predictor of postoperative infection.

- Patients with blood glucose values >220 mg/dl had infection rates that were 2.7 times higher than the rate for patients with lower blood glucose values.
- When minor infections were excluded, the relative risk for serious postoperative infection, including sepsis, pneumonia, and wound infections, was 5.7 times higher than those with glucose levels less than 220 mg/dl.

Particularly in diabetic patients who undergo coronary artery bypass graft, diabetes poses a considerable independent risk factor. Perioperative hyperglycaemia is related with a greater risk of deep sternal wound infections and increased mortality. Strict glycaemic control in patient undergoing coronary artery bypass graft resulted in better postoperative outcomes. Furnary et al stated that maintaining the glycaemic range within 150 to 200 mg/dl by perioperative insulin infusion regimen is associated with a substantial (59%) reduction in risks associated with deep sternal wound infections when compared with the standardized control group.

Several mechanisms have been stated for poor clinical outcomes in diabetic patients with hyperglycaemia in the perioperative period. Neverthless, the exact reasons are not yet clearly established. More interest has been laid

upon the poor wound healing rate and increasing infection rates. Hyperglycaemia has certain potential impacts on the body's immune system and affects normal physiological wound healing by various modes such as:

- Impaired leukocyte function
- Decreased phagocytosis
- Impaired bacterial killing
- Defective chemotaxis
- Inhibition of polymorphonuclear leukocyte respiratory burst
- Diminished superoxide generation
- Inhibition of phospholipase D activity
- Altered complement function
- Impaired collagen synthesis
- Reduced wound tensile strength
- Reduced neovascularisation at the wound site
- Reduced capillary volume at the site of injury

Many randomised controlled trials and various research studies have established the direct relationship between the incidence postoperative infections with perioperative glycaemic control. Postoperative blood glucose values more than 200 mg/dl have a 17 to 86% increased risk for infectious complications. Leucocyte functions are known to be improved by achieving a normal glycaemic range by insulin therapy thereby decreasing the risk for systemic and local infections. In diabetes it is the advanced glycosylation end products that accumulate which adversely affect the cellular function, formation of extracellular matrix, synthesis of cytokines and thereby preventing normal wound healing.

GLYCAEMIC GOAL DURING THE PERIOPERATIVE PERIOD

The recommendations made by American Diabetes Association and American Association of Clinical Endocrinologists are:

- Critical care patients should be maintained on glycaemic range within 80-110 mg/dl.
- Pre-prandial blood glucose $\leq$ 110 mg/dl and random blood glucose $\leq$ 180 mg/dl were recommended for non-critically ill patients.

METHODS OF ACHIEVING GLYCAEMIC CONTROL

As many perioperative complications have been documented in diabetic patients with poorly controlled glycaemic status, it is imperative to vigorously monitor the plasma glucose level and maintain it in the desirable range while at the same time avoiding hypoglycaemia.Patients on oral diabetic agents prior to surgery may resume their earlier regimen in the postoperative period after careful assessment.However the risk-benefit ratio of oral hypo glycaemics should be thoroughly weighed before because of the possible unwanted complications. The most easily titratablility and flexibility made intravenous insulin therapy as the perfect modality for glycaemic control in the perioperative period.

Ideally all diabetic patients undergoing various surgical procedures should be on intensive management of diabetes perioperatively. Patients undergoing surgery are operationally managed by combined insulin, dextrose and potassium therapy. Any surgery which requires general anaesthesia more than one hour is defined as major surgery. Management of patients with type 2 diabetes is usually based on their regular diabetes regimen, glycaemic status, the nature and the duration of the procedure and also the expertise available.

Dietary Management

Dietary carbohydrate restriction and regular physical exercises alone is sufficient for diabetic patients with good glycaemic control. On the day of

surgery, fasting blood sample should be measured. Intraoperative monitoring of plasma glucose is required for any surgery extending more than one hour.For minor surgical procedures their regular regimen will be appropriate and may not need any special intervention. For major surgeries and patients with poorly controlled diabetes i.e. plasma glucose level more than 200 mg/dl, intravenous insulin therapy combined with dextrose is required with periodic intraoperative glucose monitoring.

Managements with Oral Hypoglycaemic Agents

There are some special considerations for patients managed with oral anti-diabetic agents. Sulfonylureas are discontinued one day prior to surgery except chlorpropramide. Chlorpropramide is discontinued at least 2 to 3 days before surgery. Despite metformin having short half-life i.e. 6 hours, it is advisable to stop it 1 to 2 days prior to surgery, especially in patients with hypo perfused state as there is an increased risk for lactic acidosis, tissue hypoxia and renal failure. Other oral hypoglycaemics may be continued till the day of surgery.

It is ideal to monitor the blood glucose levels at least before and immediately after the procedure in every diabetic patient. Hourly monitoring is mandatory for patients undergoing major surgical procedures followed by immediate postoperative value. Capillary blood glucose measurements available by bedside glucose meters are sufficient for postoperative monitoring

and management. Only in cases reported to have high variability either in the form of hyper or hypoglycaemia require blood glucose measurement by a standard laboratory before starting specific therapeutic management.

Class of Oral Agent	**Example**	**Considerations**
Alpha-glucosidase inhibitors	Acarbose	Inhibit enzymes that metabolize carbohydrates; no benefit if NPO
Secretagogues (eg, sulfonylureas, meglitinides)	Glyburide, glimepiride	Hypoglycemia, prolonged action, may be unpredictable, difficult to titrate
Biguanides	Metformin	Increased risk for lactic acidosis; Cautious use in hepatic and renal failure, congestive heart failure; available in combination therapy

Thiazolidinediones	Rosiglitazone	Increased intravascular volume (CHF), slow onset of effect, difficult to titrate
Dipeptidyl peptidase-4 (DPP-4) inhibitor	Sitagliptin	Slows inactivation of incretin hormones to enhance physiologic glucose control; dosage reduction required for renal insufficiency

Perioperative blood glucose values more than 200 mg/dl is usually managed with small doses of subcutaneous short-acting insulin with careful watch for hypoglycaemia. Oral anti diabetic agents can be resumed following minor surgeries immediately following oral intake usually without any complications. Patients on metformin are restarted only after 72 hours after surgery or any iodinated radio contrast procedures performed. It is ideal to resume metformin therapy after properly establishing normal renal function and in the absence of nephropathy caused by contrast studies.The optimal recommendations for managing patients with poorly controlled blood glucose levels and who underwent major surgical procedures is by intravenous insulin therapy with dextrose usually following either of the two standard regimens as mentioned later in this text.

Insulin Therapy

Minor surgery

Ideally patients on long-acting insulin therapy such as ultra lente, glargine, protamine zinc insulin is substituted with intermediate-acting insulin 1 to 2 days prior to elective surgical procedures. Vigilant monitoring of perioperative glucose levels is vital to prevent extremes of glycaemia.Intravenous insulin/glucose/potassium should be started prior to surgery. Blood glucose monitoring should be done hourly during the procedure and one immediately following surgery. Intravenous insulin infusion should ideally be stopped once oral intake is resumed and the regular regimen should be reinitiated.It is ideal to have an hour overlap in between stopping insulin infusion and restarting subcutaneous insulin.

Major surgery

Ideally patients treated with insulin who undergo major surgical procedures should be admitted 2 to 3 days prior to surgery, if glycaemic status is not in the desirable range i.e. HbA1c more than 8%. If the patient could not be admitted, self monitoring of blood glucose should be taught to the patient to optimize the blood glucose value to the euglycaemic range in the preoperative period. Self monitoring is advisable before every meal and before sleep. The

recommended pre prandial range is between 80 to 120 mg/dl and bedtime range is between 100 to 140 mg/dl.

The preoperative evaluation of the diabetic patient should include the following:

- Physical examination particularly focusing on cardiac evaluation and autonomic neuropathy.
- Serum blood glucose levels
- Serum electrolytes
- Serum creatinine
- Urinary ketones

Increased surveillance is mandatory in patients with autonomic neuropathy because of its propensity to cause hypotension, respiratory depression and hemodynamic instability. Metabolic and electrolyte imbalance such as acidosis, hyponatremia, dyskalemia should be corrected prior to surgery.

Intravenous Insulin, Glucose, Potassium, and Fluids

Intravenous infusion of insulin, glucose, and potassium is the recommended therapy and has substituted subcutaneous insulin therapy for the

perioperative management of diabetes. Many studies have stressed the benefits of insulin infusion therapy against subcutaneous insulin.

As once thought it is not needed to supplement albumin with insulin infusion in order to prevent nonspecific adsorption to the infusion apparatus. The same thing can be achieved by flushing 50 ml of insulin infusion mixture via the tubing.

Intravascular volume should be maintained with adequate fluid administration. Osmotic diuresis in poorly controlled diabetes may result in fluid deficit and should be managed properly for a better perioperative management. The preferred intravenous fluids for replacement are normal saline and dextrose solutions. Solutions containing lactate such as Ringer's lactate, Hartmann's solution etc. will exacerbate hyperglycaemia.

Insulin

There are two methods of insulin infusion that is used currently:

- Insulin infusion in combination with glucose and potassium in the same solution i.e. GIK regimen.
- Administering insulin separately via an infusion pump.

Of the above the GIK infusion is the preferred one because it is more effective, safe and efficient in most of the patients. The only drawback is that it is not possible to do selective adjustment of insulin dosage. The glucose

solution usually used in this regimen is 5% dextrose or 10% dextrose. 10% dextrose provides more calories.

Irrespective of whatever means insulin is administered i.e. either by combined or separate infusions, continued surveillance of blood glucose level is imperative to avoid extremes of glycaemia. The recommendations of insulin therapy should be individualised and should be flexible to adjust the patient factors and the nature of the surgical procedure. The usual universally recommended glycaemic range based on evidence based studies is between 120 to 180 mg/dl.

The rate of initial insulin infusion is estimated as between one-half and three-fourths of the total daily insulin requirement expressed in units/h. In most of the type 1 diabetes patient it is ideal to start with 0.5 to 1 unit/h regular insulin. Patients on oral hypoglycaemics requiring perioperative insulin and type 2 diabetes patients on insulin therapy can be started with an infusion rate of 1 to 2 units/h.

Insulin infusion rate of one unit/h achieved either by:

- 25 units of regular insulin mixed in 250 ml of normal saline resulting in a solution containing 0.1 unit/ml. This is infused at the rate of 10ml/h.
- Regular insulin 50 units with normal saline is made to a 50 ml solution. This is then administered via an infusion pump at the rate of 1ml/h.

The rate of insulin infusion is so adjusted to maintain the blood glucose level in the range of 120-180 mg/dl.

The duration and nature of the surgery and the degree of glycaemic disturbances determine the dose of insulin to be supplemented. Elective surgeries in type 1 diabetes patient should be scheduled as the initial case to avoid the variability of blood glucose levels and to minimize the need to change their regular regimen. Patients may be administered half of their regular dose of long acting insulin depending upon the nature of their procedure. They are permitted earlier in the preoperative waiting room to have their blood glucose checked to determine the need for dextrose infusion.

Preferably a separate intravenous line is established for insulin infusion during surgery. The rate of insulin infusion is calculated using the following formula:

Insulin (U/hr) = serum glucose (mg/dL)/150

A second intravenous access is required for volume replacement. Another intra-arterial cannulation is required to monitor blood glucose levels hourly during the procedure and in the postoperative period.

Several protocols for insulin therapy are widely available without any standardisation. Recently computer based systems are also available to calculate the required insulin dose based on blood glucose level and its rate of change. Glucommander introduced was one such system. In this the initial factors and the baseline blood glucose value are given. The auto programme then calculates the rate of insulin infusion and also recommends the periodic intervals for further blood glucose monitoring. This can be repeated indefinitely. The amount of insulin required is calculated on the basis of the following equation:

$$\text{Insulin per hour} = \text{multiplier} \times (\text{blood glucose} - 60)$$

The periodic intervals in which the blood glucose to be monitored is detected automatically by the programme. It is monitored as frequently as every twenty minutes or up to maximum interval that is specified. Practically blood glucose levels are monitored every hourly. The frequency is shortened automatically if there is rapid change is blood glucose levels and is lengthened when the glycaemic range is maintained in the desired level. Glucommander

has been proved to very useful in critically ill and also in non-critically ill patients. Studies are still pending to assess the utility of such systems.

Table 1. Regimen for Separate Intravenous Insulin Infusion for Perioperative Diabetes Management

- Prepare a 0.1 unit/ml solution by adding 25 units regular insulin to 250 ml normal saline.
- Flush 50 ml of insulin solution through infusion tubing to saturate nonspecific binding sites.
- Set initial infusion rate (generally, 0.5 unit/h [5 ml/h] for thin women; 1.0 unit/h [10 ml/h] for others)
- Adjust infusion rate according to bedside blood glucose measurement as follows:

Blood Glucose (mg/dl)	Insulin Infusion Rate
<80	Check glucose after 15 min*
80–140	Decrease infusion by 0.4 unit/h (4 ml/h)
141–180	No change
181–220	Increase infusion by 0.4 unit/h (4 ml/h)
221–250	Increase infusion by 0.6 unit/h (6 ml/h)
251–300	Increase infusion by 0.8 unit/h (8 ml/h)
>300	Increase infusion by 1 unit/h (10 ml/h)

*Regimen assumes separate infusion of glucose at ~5–10 g/h and hourly blood glucose monitoring. Extremely high or low glucose values should be confirmed with an immediate repeat measurement. Intravenous boluses of dextrose (50%) or supplemental regular insulin can be used for rapid correction but are rarely necessary.

Table 2. Regimen for Glucose-Insulin-Potassium (GIK) Combined Infusion*

Blood Glucose (mg/dl)	Glucose-Insulin-Potassium Infusion Rate	
	5% Dextrose	10% Dextrose
<80	↓ 5 units	↓ 10 units
<120	↓ 3 units	↓ 5 units
120–180	No change	No change
181–270	↑ 3 units	↑ 5 units
>270	↑ 5 units	↑ 10 units

5% dextrose: 1,000 ml containing 20 mEq KCl + 15 units regular insu
10% dextrose: 1,000 ml containing 20 mEq KCl + 30 units regular insulin
Arrows indicate amount by which insulin in each 1,000-ml bag of infusate is to be decreased or increased.
*Adapted from reference 31.

The clinical status of the diabetic patient determines the duration of insulin-dextrose infusion therapy. Ideally it is continued postoperatively until the patients resumes oral feeds. Once oral intake is established the regular diabetic regimen can be reinitiated. It is necessary to administer first subcutaneous dose of insulin postoperatively half to one hour before discontinuing the intravenous access.

Glucose

Sufficient caloric replacement in the form of glucose should be administered in patients undergoing surgery to avoid catabolic reactions, starvation ketosis and hypoglycaemia. The normal physiological amount of glucose essential to inhibit catabolism in a normal non-diabetic adult is about

120 g/day or 5 g/h. Preoperative fasting, metabolic stress response to anaesthesia and surgery and the required insulin therapy in the preoperative period all increases the caloric requirement in diabetic patients. The caloric requirement in these patients averages between 5 to 10 g/h of glucose. This is either administered by 5% or 10% dextrose solution. In patients requiring fluid restriction, 10% dextrose is recommended. An infusion rate of 100 ml/h with 5% dextrose delivers 5 g/h glucose. Nowadays it is preferred to administer 10% dextrose at an initial infusion rate of 100 ml/h.

The recommended range of blood glucose level in the perioperative period is 120 to 180 mg/dl. Insulin-dextrose infusion therapy are adjusted to maintain in the desired range when there is marked variability. Normally 0.3 units of insulin / gram glucose is given for most of the stable patients. Insulin requirements are increased in

- Sepsis
- Obesity
- Unstable patients with comorbid illness
- Steroid therapy
- Carido pulmonary bypass surgery.

Potassium

Insulin and glucose infusion causes intracellular translocation of potassium thereby increasing the risk of hypokalemia. In normokalemic patients, 10 mEq potassium chloride is routinely added to every 500 ml of dextrose to maintain normal serum potassium, if the renal function is adequate. Existing hyperkalemia as evidenced by laboratory measurement and electrocardiogram and renal failure are contraindication for potassium supplementation.

Emergency Surgery

Nearly around 5 to 10 % of diabetic patients required emergency surgery in their lifetime. Most commonly performed surgeries include laparotomy, cholecystectomy, appendectomy, and similar general surgical procedures. Additionally diabetes complicating surgeries such as incision and drainage of abscesses, ulcer management and amputations are also performed.

When these emergencies occur, is not predictable and immediate surgical intervention should be done without any delay. It is prudent to exclude diabetic ketoacidosis and similar conditions complicating diabetes that mimic surgical emergencies. Patients with DKA present as acute abdomen in the emergency and it has been reported to undergone unnecessary exploratory laparotomies. Diabetic autonomic neuropathy can affect gastrointestinal tract causing

gastroparesis, intractable vomiting, gastro enteropathy. These simulate abdominal surgical emergencies. Diabetic pseudotabes syndrome similarly causes sharp neuropathic pain along thoracolumbar dermatomes which is similar to that of visceral disorders. Therefore it is essential to take a thorough clinical history and physical evaluation in diabetic patients presenting as surgical emergency to exclude such pitfalls.

Most of the diabetic patients requiring emergency surgical intervention will have poorly controlled glycaemic status. This should not contraindicate a timely performed lifesaving procedure. Assessment of blood glucose levels, serum electrolytes and acid base analysis should be done immediately after securing an intravenous catheter. Any gross abnormalities detected should be corrected preoperatively as far as possible to optimise the patient for surgery.

Whenever possible, surgery should be delayed diabetic ketoacidosis until the acid base disorder is corrected. Intravascular volume replacement and improved of metabolic status should be carried out in patients with HHS without undue delay as they are significantly dehydrated. Hourly monitoring of blood glucose should be done at bedside. Insulin-glucose-potassium infusion therapy should be initiated and titrated appropriately to maintain the glycaemic range between 120 to 180 mg/dl. Serum potassium should be monitored every

2^{nd} or 4^{th} hourly and potassium should be supplemented accordingly to maintain the patient in eukalemic state during and after surgery.

Diabetic patients pose specific challenges postoperatively. To reduce the adverse events, methods of achieving glycaemic control in the perioperative period in these patients should be individualised in order to achieve an optimal result.

Perioperative management of patients with diabetes:

I) Minor surgery in DM2 patients not treated with insulin

- Hold oral agents the day of surgery.
- Patients with "fair" metabolic control (fasting blood glucose 180mg/dL)—cover with regular insulin or rapid-acting (lispro, aspart,glulisine) insulin as needed.
- Patients with "poor" metabolic control (fasting blood glucose 180mg/dL)—start continuous insulin infusion.
- Goals: avoid excessive hyperglycemia (blood glucose 180 mg/dL) and hypoglycemia (blood glucose 80 mg/dL).

II) Minor surgery in DM1 and DM2 patients treated with insulin

● Hold oral agents (if treated with combination therapy) the day of surgery.

● Patients in “fair” metabolic control (fasting blood glucose 180 mg/dL):

– Give half of intermediate-acting insulin (NPH) the morning of the surgery.

– While NPO, infuse dextrose 5% saline plus KCl (10-20 mEq/L) at 100 mL/hour.

– Check blood glucose every 4 to 6 hours while NPO and supplement with short-acting insulin.

– Patient treated with basal (glargine) insulin should receive their usual basal insulin dose. Similarly, patients treated with continuous insulin infusion therapy (insulin pump) should receive their usual basal infusion rate.

– Restart preadmission insulin therapy once food intake is tolerated

● Patients in “poor’ control (fasting blood glucose 180 mg/dL)—start continuous insulin infusion.

III) Major surgery in DM1 and DM2 patients treated with insulin

● Hold oral agents the day of surgery

● Start continuous insulin infusion prior to surgery and continue during perioperative period.

● Goals: Maintain blood glucose 180 mg/dL during surgery, and blood glucose between 80 to 120 mg/dL during the perioperative period in the surgical intensive care unit. Start subcutaneous insulintwo hours prior to discontinuation of insulin infusion. In non-ICU settings, avoid excessive hyperglycemia (blood glucose 180 mg/dL)and hypoglycemia (blood glucose 80 mg/dL).

HYPOGLYCAEMIA COMPLICATING GLYCAEMIC CONTROL:

While maintaining the patient in strict glycaemic control it is imperative to avoid hypoglycaemia and its complications. Despite advances in the treatment of diabetes, hypoglycaemic episodes are often the limiting factor in achieving optimal blood sugar control. The risk of severe hypoglycaemia is higher in elderly patients, those having comorbidities such as vascular disease or renal failure, pregnant women. Moreover in type 2 diabetes, progressive insulin deficiency, longer duration of diabetes and tight glycaemic control increase the risk of hypoglycaemia.

Hypoglycaemic manifestations usually occurs when the blood glucose level is abnormally low, usually less than 70 mg/dl (4mmol/L).Hypoglycaemia with decreasing plasma glucose concentration causes a series of signs and symptoms by signalling central nervous system which is mediated via autonomic nervous system and by decreasing metabolism of neurons. Neurogenic symptoms are the result of the perception of physiological changes caused by the activation of the autonomic nervous system triggered by

hypoglycaemia. Although all three efferent components of the autonomic nervous system—adreno medullary, sympathetic neural, and parasympathetic neural—are activated by hypoglycemia, neurogenic symptoms are thought to be caused by sympatho adrenal activation and mediated by norepinephrine released from sympathetic adrenergic postganglionic neurons, the adrenal medullae, or both, by acetylcholine released from cholinergic sympathetic postganglionic neurons and by epinephrine released from the adrenal medullae. Some neurogenic symptoms, such as tremulousness, palpitations, and anxiety/arousal, are adrenergic (catecholamine mediated); whereas others, such as sweating, hunger, and paresthesias, are cholinergic. Awareness of hypoglycemia is largely the result of the perception of neurogenic symptoms and the recognition that they are indicative of hypoglycemia. Clearly, therefore, awareness of hypoglycemia is a function of the knowledge and the experience of the individual, as well as the physiological responses to low glucose concentrations.

Neuroglycopenic symptoms are the result of brain neuronal glucose deprivation. They include sensations of warmth, weakness, and fatigue as well as difficulty thinking, confusion, behavioral changes (not infrequently confused with inebriation by others), and emotional lability. They also include seizures, loss of consciousness, and, if hypoglycemia is severe and prolonged, brain damage and even death.

Physical signs that result from activation of the sympatho adrenal system include pallor and diaphoresis, which are often prominent, and an increased

heart rate and systolic blood pressure, which are often more subtle. Evidence of neuroglycopenia can be the most apparent, or even the only, observable manifestation of hypoglycemia. Indeed, the neuroglycopenic symptoms are often the clues recognized by family and friends of the affected individual. Hypothermia is often present. Transient focal neurological deficits (e.g., diplopia, hemiparesis) occur occasionally. As noted earlier, permanent brain damage is rare.

Hypoglycaemia is a true medical emergency which requires prompt recognition and treatment to prevent organ and brain damage. The short and long term complications include neurologic damage, cardiovascular events and death.

Prevention of hypoglycaemia

The prevention of hypoglycaemia requires some principles consideration. These include:

1. Diabetes self-management supported by education and empowerment.
2. Self-monitoring of blood glucose or continuous glucose sensing.
3. Flexible and appropriate insulin or other drug regimens.
4. Individualised glycaemic goals.
5. Consideration of known risk factors of hypoglycaemia.
6. Professional support and guidance.

Blood glucose monitoring is an important part of management of diabetes patients experiencing hypoglycaemic episodes. Substitution of short-acting (regular) insulin with rapid-acting insulin (e.g. lispro or aspart) reduces frequency of daytime hypoglycaemia. Substitution of long-acting (e.g., glargine or determir) insulin for intermediate-acting insulin (e.g., NPH or premix 70/30) reduces frequency of nocturnal and daytime hypoglycaemia

Continuous subcutaneous insulin infusion with a rapid-acting insulin analog improves the glycaemic control and reduces the rate of hypoglycaemia compared with multiple daily insulin injection.

Glycaemic goals should be individualized based on patient characteristics with some degree of safety. Recognition of hypoglycaemia risk factors, blood glucose monitoring, selection of appropriate regimens, education programs for health care professionals and patients with diabetes are the major issues to maintain good glycaemic control, minimize the risk of hypoglycaemia, and prevent long-term complications.

STUDY METHODOLOGY

This dissertation is based on a prospective analysis of fifty diabetic patients undergoing surgical procedures in Thanjavur Medical College Hospital, Thanjavur, from 1.1.2014 to 30.06.2014.

Non-diabetics, patients with major comorbid illness, patients presenting with postoperative infection within 36 hours of surgery were excluded from this study.

Total numbers of 50 cases were included in this study which includes 22 females and 28 male patients. All patients were above 30 years of age with mean age of study being 54 years.

Both patients undergoing elective and emergency surgical procedures were included in this study. In this study 35 patients undergoing elective procedures and 15 patients undergoing emergency procedures were included.

All patients were followed up for a period of 30 days following surgery.

All patients were treated with insulin to achieve glycaemic control.

Baseline investigations that were utilised in this study were:

- Plasma glucose values
    - At the time of admission
    - Fasting plasma glucose value on the day of surgery
    - Postoperatively 6^{th} hourly for first 36 hours

    - Patient Mean Blood glucose value of the total 7 samples collected as mentioned above.
- HbA1c values
- Total leukocyte count
- Differential white blood cell count
- Wound swab culture and sensitivity
- Urine Complete examination
- Urine culture and sensitivity
- Sputum culture and sensitivity
- Chest X ray
- Blood culture and sensitivity

Depending upon the mean plasma glucose concentration obtained as mentioned above patients were divided into four quartiles as follows:

- Quartile 1 – 120 to 180 mg/dl
- Quartile 2 – 181 to 220 mg/dl
- Quartile 3 – 221 to 260 mg/dl
- Quartile 4 – 261 to 350 mg/dl

All patients were followed up for signs and symptoms of postoperative infections which included

- Surgical site infections
    - Redness and pain around the wound site

    - Purulent discharge
    - Fever
    - Wound dehiscence
- Pneumonia
    - Cough with expectoration
    - Fever
    - Dyspnoea
    - Newly appearing radiological changes in Chest X-ray
- Urinary tract infections
    - Pain or burning with micturition
    - Pain in the lower abdomen or back
    - Fever
    - Cloudy or bloody urine
    - Urgency
    - Frequency
    - Urine culture with greater than 10^5 colonies/mL and no more than 2 species of organisms.
- Sepsis
    - Fever
    - Elevated leukocyte count
    - Positive blood culture
    - Hypotension

- Shock

Patients who underwent the following surgical procedures were included in this study and were observed for signs and symptoms of postoperative infections as mentioned earlier.

- Cholecystectomy
- Appendectomy
- Amputations
- Intestinal resection anastomosis
- Duodenal and gastric perforation closure
- Hernioplasty
- Mastectomy
- Thyroidectomy
- Split skin grafts
- Trendelenberg procedure for varicose veins

OBSERVATIONS

The following observations were made in the prospective analysis of fifty diabetic patients in the perioperative period. All patients were treated with insulin to achieve glycaemic control. The incidence of postoperative infections was evaluated in each of these patients as mentioned earlier and was grouped against their mean plasma glucose concentration in the perioperative period.

All the patients participated in this study were above 30 years of age. The minimum age is 35 years and maximum age is 75 years. The mean age of this study is 54.36 years with standard deviation 11.080.

Item	Min	Max.	Mean	S.D
Age	35	75	54.36	11.080

Age Group

The number of males participated in this study were 28 and females 22. The sex of the patients does not have any influence on this study conducted.

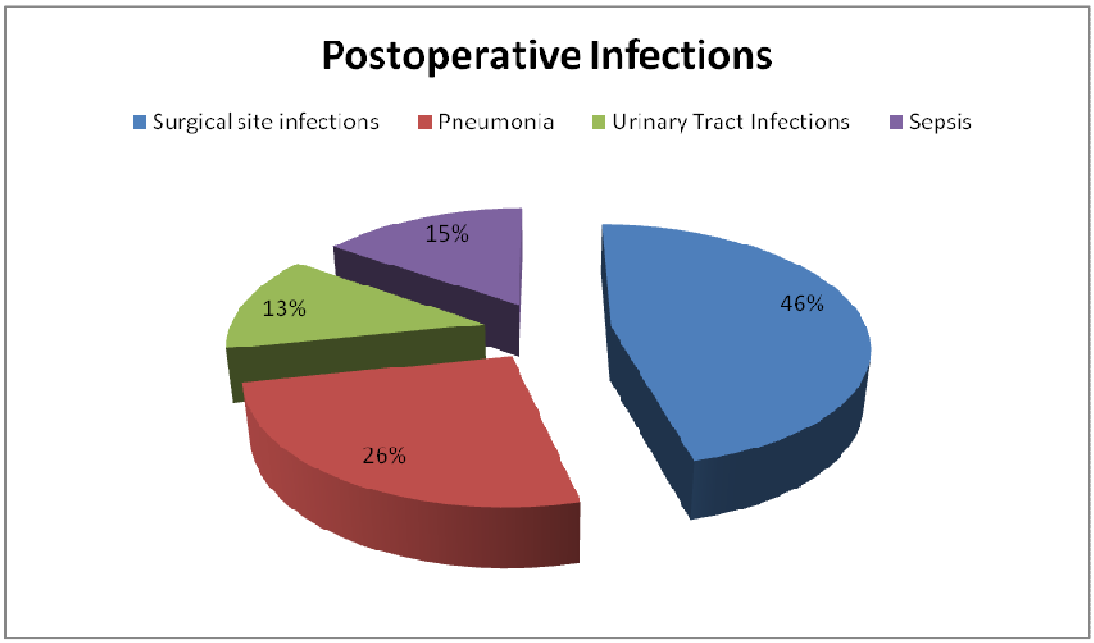
Particulars	No. of respondents (n=50)	Percentage (100%)
Male	28	56.0
Female	22	44.0

The number of patients in each quartile in this study was shown in the following table:

Particulars	No. of respondents (n=50)	Percentage (100%)
120 to 180	30	60.0
181 to 220	11	22.0
221 to 280	6	12.0
281 to 350	3	6.0

The postoperative infections observed in these patients were

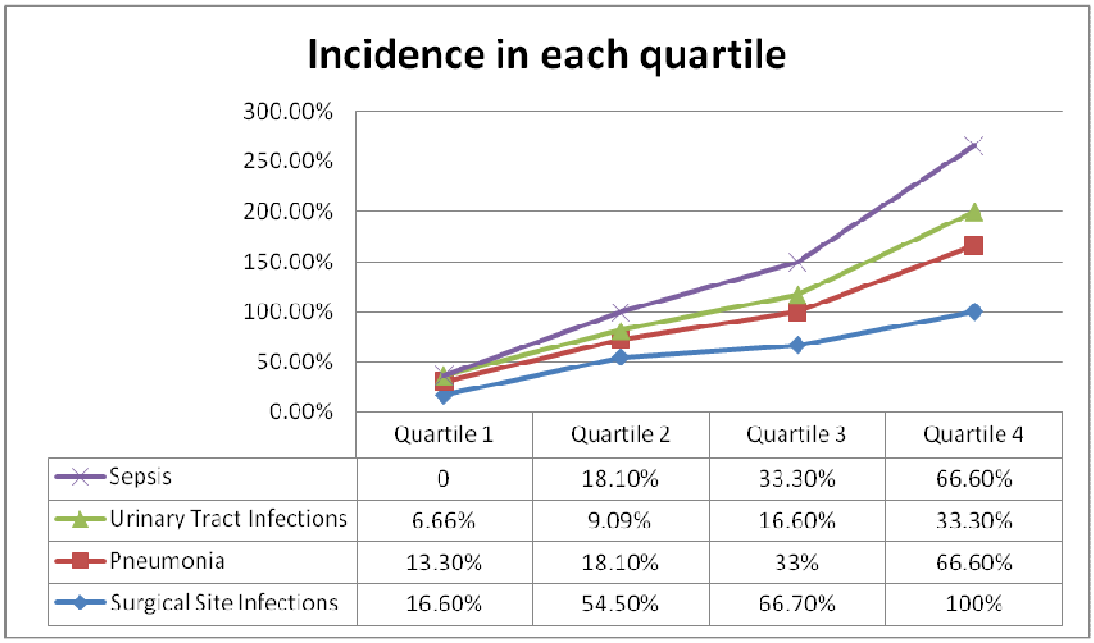
- Surgical Site Infections
- Pneumonia
- Urinary Tract Infections
- Sepsis



Among the postoperative infections observed in the diabetic patients surgical site infections were the most frequent one in each quartile followed by pneumonia, sepsis and finally urinary tract infection irrespective of the glycaemic range.

The overall incidence being as follows:

- Surgical site infections – 46%
- Pneumonia – 26%
- Urinary Tract Infections – 13%
- Sepsis – 15%



	Quartile 1	Quartile 2	Quartile 3	Quartile 4
Sepsis	0	18.10%	33.30%	66.60%
Urinary Tract Infections	6.66%	9.09%	16.60%	33.30%
Pneumonia	13.30%	18.10%	33%	66.60%
Surgical Site Infections	16.60%	54.50%	66.70%	100%

It is noted that the incidence of postoperative infections is directly proportional to the mean plasma glucose concentration. The occurrence being less in the first quartile with glycaemic range 120 to 180 mg/dl.

Patients in the I quartile had 16.6% incidence of surgical site infections, 13.3% incidence of pneumonia, 6.66% incidence of urinary tract infections. Sepsis was observed in none of the patients with glycaemic range 120-180 mg/dl.

Quartile 2 patients whose glycaemic range was 181 to 220 mg/dl had the following incidence:

- Surgical site infections – 54.5%
- Pneumonia – 18.1%
- Urinary Tract Infections – 9.09%
- Sepsis – 18.1%

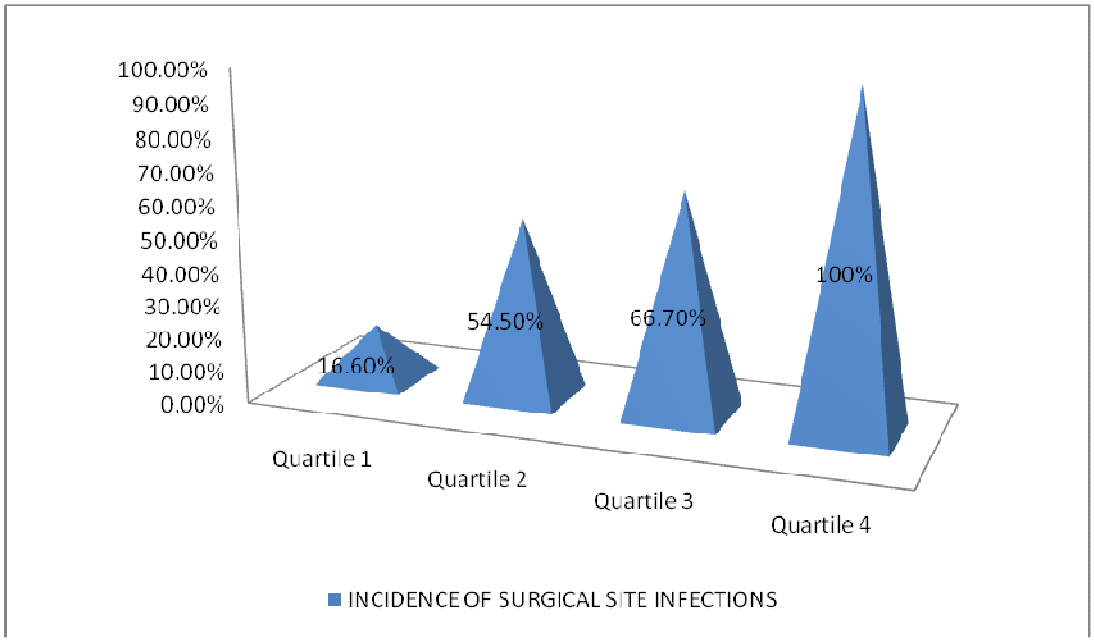
Quartile 3 patients whose glycaemic range was between 221 and 260mg/dl had the following incidence:

- Surgical site infections – 66.7%
- Pneumonia – 33.3%
- Urinary Tract Infections – 16.6%
- Sepsis- 33.3%

The observations made in the fourth quartile patients with glycaemic range 261 to 350 mg/dl were as follows:

- Surgical site infections – 100%
- Pneumonia – 66.6%
- Urinary Tract Infections – 33.3%
- Sepsis – 66.6%

Incidence of surgical site infections:

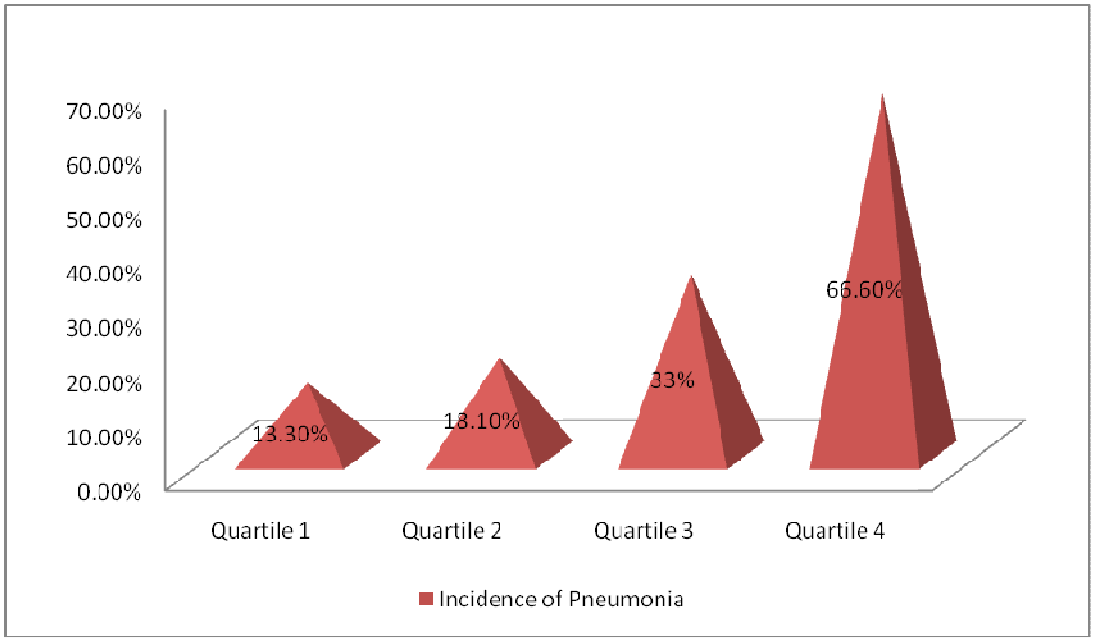


The incidence of surgical site infections in these patients were proportional to the glycaemic control achieved, the highest being in the fourth quartile patients i.e. 100% and the least being in the first quartile patients i.e.16.6%. In the glycaemic range above 260mg/dl almost all patients had surgical site infections invariably stressing the importance of strict glycaemic control in these patients to avoid long hospital stay and the health care expenditure that results.

Blood sugar	Wound infection			Statistical inference
	Negative	Positive	Total	
120 to 180	25(83.3%)	5(16.7%)	30(100%)	X^2=14.291df=3 .003<0.05 Significant
181 to 220	5(45.5%)	6(54.5%)	11(100%)	
221 to 280	2(33.3%)	4(66.7%)	6(100%)	
281 to 350	0	3(100%)	3(100%)	
Total	32(64%)	18(36%)	50(100%)	

The association of surgical site infections with blood glucose level in this study is statistically significant proving the need for good glycaemic control to prevent postoperative wound infections in these patients.

INCIDENCE OF PNEUMONIA:

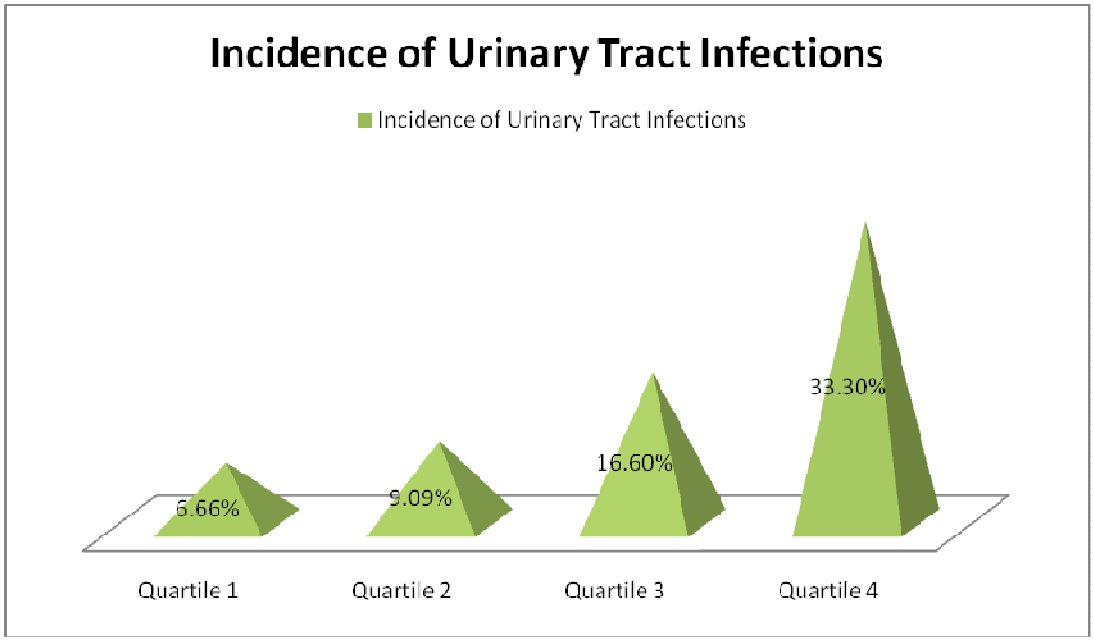


Again the incidence of pneumonia documented clinically and by newly occurring radiographic changes and positive sputum culture was highest in the fourth quartile patients with 66.6% incidence. The incidence is lesser in the third quartile patients with glycaemic range 221 to 260 mg/dl with 33%. Again with strict glycaemic control the incidence of pneumonia is lower in the well-controlled group with mean plasma glucose less than 200 mg/dl; being 18.1% in second quartile and 13.3% in first quartile patients.

Blood sugar	Pneumonia			**Statistical inference**
	Negative	**Positive**	**Total**	
120 to 180	26(86.7%)	4(13.3%)	30(100%)	X^2=5.606 df=3 .132>0.05 Not significant
181 to 220	9(81.8%)	2(18.2%)	11(100%)	
221 to 280	4(66.7%)	2(33.3%)	6(100%)	
281 to 350	1(33.3%)	2(66.7%)	3(100%)	
Total	40(8%)	10(20%)	50(100%)	

According to the statistics, the association of incidence of pneumonia with increasing blood glucose level is statistically not significant in this study. However it is evident that the possibility of pneumonia occurrence is higher in the patients with high blood glucose level when compared with the well-controlled group.

Incidence of Urinary Tract Infections:

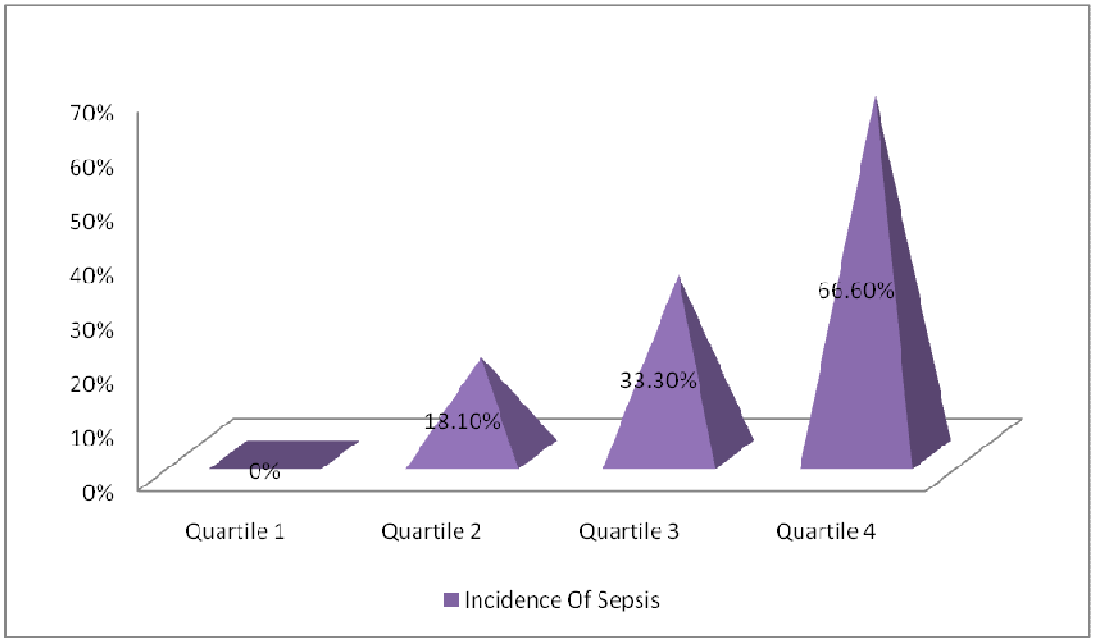


The incidence of urinary tract infections observed in each quartile (I-6.66%, II-9.09%, III-16.6%, IV-33.3%) were similar to the observations made in other postoperative infections. There is a proportionate increase in urinary tract infections and their complications with increasing mean plasma glucose concentrations.

Blood sugar	UTI			Statistical inference
	Negative	Positive	Total	
120 to 180	28(93.3%)	2(6.7%)	30(100%)	X^2=2.492 df=3 .477>0.05 Not significant
181 to 220	10(90.9%)	1(9.1%)	11(100%)	
221 to 280	5(83.3%)	1(16.7%)	6(100%)	
281 to 350	2(66.7%)	1(33.3%)	3(100%)	
Total	45(90%)	5(10%)	50(50%)	

In this study, even though the rate of genito-urinary infections and its complications is higher in the poorly controlled group; it does not have a statistically significant correlation. Despite good glycaemic control decreased the incidence of these complications in the postoperative period.

Incidence of Sepsis

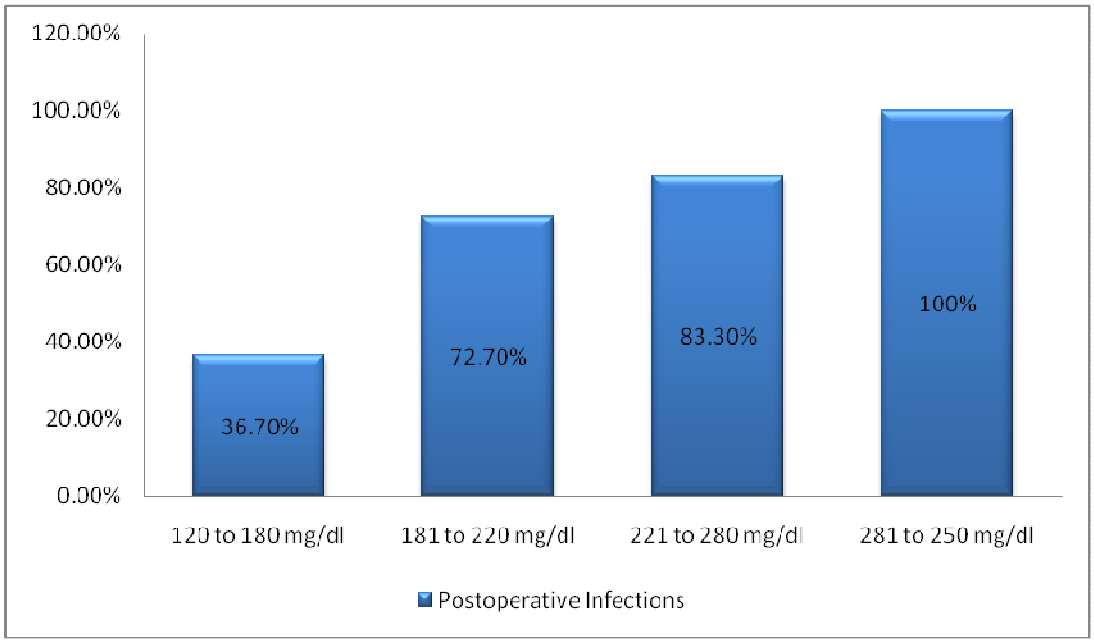


Sepsis was characterised by high peaks of fever, elevated leukocyte count and sometimes hypotension and shock. Patients with mean plasma glucose concentration with 120 to 180 mg/dl did not have this potential complication in this study. Patients with mean plasma glucose concentration above 180 mg/dl are susceptible and at higher risk with higher concentrations. The incidences in 2^{nd}, 3^{rd} and 4^{th} quartile being 18.1%, 33.3% and 66.6% respectively.

Blood sugar	SEPSIS			Statistical inference
	Negative	Positive	Total	
120 to 180	30(100%)	0	30(100%)	X^2=15.565 df=3 .001<0.05 Significant
181 to 220	9(81.8%)	2(18.2%)	11(100%)	
221 to 280	4(66.7%)	2(33.3%)	6(100%)	
281 to 350	1(33.3%)	2(66.7%)	3(100%)	
Total	44 (88%)	6(12%)	50(100%)	

The rate of occurrence of sepsis was proportionate to the mean plasma glucose level, with a statistically significant relation in this study with a 'p' value of .001.

The overall incidence of postoperative infections in patients with diabetes undergoing surgeries is higher with greater mean plasma glucose levels. Even though some infections rate does not show a statistically significant correlation in this study, it is evident from all of the above observations that tight perioperative glycaemic control within the acceptable range prevented unwanted postoperative infectious complications.



Blood sugar	Infected			Statistical inference
	Negative	Positive	Total	
120 to 180	19(63.3%)	11(36.7%)	30(100%)	X^2=9.816 df=3 .020<0.05 Significant
181 to 220	3(27.3%)	8(72.7%)	11(100%)	
221 to 280	1(16.7%)	5(83.3%)	6(100%)	
281 to 350	0	3(100%)	3(100%)	
Total	23(46%)	27(54%)	50(50%)	

All of the above observations made, stressed the importance of strict glycaemic control in the perioperative period for an optimal recovery in the diabetes patients undergoing surgical procedures.

DISCUSSION

For diabetic patients, tight long-term glucose control has significantly reduced the incidence and severity of many chronic complications associated with diabetes, such as nephropathy, neuropathy, and retinopathy. It is yet to be established whether long-term glycaemic control also helps to reduce postoperative infections and its complications, and this has been studied extensively worldwide. This study therefore chose to define whether well controlled perioperative glycaemic status in the acceptable range is associated with lesser incidence of postoperative infectious complications in patients with diabetes undergoing various surgeries.

As already mentioned, that hyperglycaemia plays an important role in the postoperative infectious complications.Several approaches to reduce the postoperative morbidity by perioperative strict glycaemic control have been shown to be promising in both diabetic and non-diabetic patients. Van den Berghe et al demonstrated the effectiveness of strict glycaemic control, i.e. in the range of 80 to 110 mg/dl, against normal standard control, i.e. less than 200 mg/dl, in critically ill patients. He also established a 42% reduction in the postoperative morbidity and mortality rate by strict glycaemic control.

Several studies showed that good preoperative glycemic control is related with a considerably reduced postoperative infectious complication when other factors influencing the outcomes were adjusted. Randomized control trials in medical, cardiac, and neurosurgical populations have also found reduced rates of bacteremia, duration of antibiotic usage, infection rates and incidence of recurrent infections when patients have strict glycaemic control (<150mg/dl).

Bishop et al in 1992, studied the impact of HbA1c levels on postoperative surgical site infections in patients receiving penile prostheses prospectively. Infections occurred only in the diabetic patients. Of these patients it has been documented about 31% were having HbA1C levels above 11.5% and only 5% had HbA1c levels below 11.5%. Based on these observations, surgery was denied for patients with HbA1c levels above 11.5% suggesting, them to have poor outcomes because of poor control of diabetic status. This suggestion was widely accepted and was then "used as the 'standard of care' in several legal cases."

In 1998, Wilson et al disproved the importance of the above findings by a prospective study conducted in 389 patients over a period of 2 years. The authors did not found a reliable association between postoperative wound infections and HbA1c levels more than 11.5%.

Both of the above prospective studies relied their finding based on HbA1c value of 11.5% as the cut off for analysis. Diabetes Control and Complications Trial group showed that an HbA1c level of 11.5% is equivalent to mean blood glucose of more than 310 mg/dl. Using HbA1c level of 11.5% as the break point places patients with 7% to 11.5% HbA1c value in the well-controlled group which is not correct according to the current guidelines.

Another study was conducted by Latham et al based on HbA1c value of 8% as the cut-off point. They prospectively evaluated the relationship between HbA1c levels and postoperative wound infections in1000 patients undergoing cardiac surgery.The observations made in this study were:

- Infection rate was twice higher in the high HbA1c patients with values more than or equal to 8%.
- 78% of poorly controlled patient group developed perioperative hyperglycaemia when compared with the well-controlled group which is only 43%.
- Infection rates were higher in patients with perioperative hyperglycaemia when compared to the euglycaemics.

In our study the patients have been divided into four quartiles based on their mean perioperative plasma glucose concentration. Patients undergoing various surgical procedures were included in this study.

The incidence of postoperative infectious complications such as surgical site infections, pneumonia, urinary tract infections and sepsis were evaluated in the study group. The observations made in our study shows a strong correlation between well-controlled glycaemic status and reduced postoperative infections in various surgical procedures.All patients were treated with insulin therapy though the type of management to achieve glycaemic control has not been shown significant in various studies, because it only reflects the management at the time of surgery and does not influence the long term glycaemic control.

Better perioperative glycaemic control is associated with fewer complications in the postoperative period. It not only includes the postoperative infectious complications but also other metabolic complications associated with hyperglycaemia such as diabetic ketoacidosis, HHS, acute myocardial infarction, cerebral ischemia. Good control of blood glucose in the perioperative period not only associated with better outcomes in diabetic patients but also in the non-diabetics. Several prospective studies have established the relationship between hyperglycaemia and infections in the postoperative period.

As earlier discussed, hyperglycaemia impairs neutrophil activity, intracellular bactericidal property, chemotaxis and phagocytosis. The degree of impairment correlates with the level of hyperglycaemia. Some of these effects are effectively reverted with appropriate insulin therapy. Hyperglycaemia also affects vascular permeability and physiological redox reactions occuring in the body resulting in a state of pseudo hypoxia. This further weakens the body's immune response.

Glucose acts as a pro inflammatory mediator known to have various effects on immune response such as cytokine production, inhibition of endothelial nitric oxide. Even in normal persons hyperglycaemia is associated with increased generation of reactive oxygen species. The association of long term glycaemic control with reduced postoperative infections has also been shown because of general well-being and well controlled metabolic homeostasis in these patients. It is proved by the Diabetes Control and Complications Research Group that intensive therapy with insulin therapy has decreased the risk of retinopathy by 76% in type 1 diabetic patients. Intensive therapy has also been shown to reduce the risk of albuminuria by 56%, micro albuminuria by43%, and neuropathy by 69%. United Kingdom Prospective Diabetes Study Group has established similar effects in the patients with type 2 diabetes. Several epidemiological studies have shown decreased rate of cardiovascular disorders in patients with well-controlled blood glucose levels.

Results from more recent research has triggered national associations to amend their guidelines to more conservative glucose parameters. Currently, the Institute for Healthcare Improvement (IHI, 2011) recommends cardiovascular surgery patients, who are at a high risk for complications from hyperglycaemia, maintain blood glucose levels below 180 mg/dl for the first two postoperative days. The American Diabetes Association (ADA, 2012) recommends initiating insulin therapy for persistent hyperglycaemia starting at a threshold of no greater than 180 mg/dl. Once insulin therapy is initiated, blood glucose levels in critically ill patients should be maintained from 140 to 180 mg/dl. More stringent goals, such as 110 to 140 mg/dl may be appropriate for selected patients, as long as this is achieved without significant hypoglycaemia.

The ideal method of insulin administration in the perioperative period is by intravenous infusion. Lazar et al compared the glycaemic control achieved by insulin-glucose-potassium infusion against standard intermittent subcutaneous insulin therapy. Both of the regimens were started preoperatively and continued postoperatively for 12 hours. The following observations were made in this study: patients on insulin-glucose-potassium infusion had decreased incidence of postoperative infectious complications, atrial fibrillation, ischaemic events and better survival rates following surgery for 2 years.

Studies have proven insulin infusion therapy is associated with better glycaemic control either with separate insulin infusion or with combined insulin-glucose-potassium infusion. Separate insulin infusion has the advantage to adjust the rate of infusion without replacing the bag. Even though GIK infusions are safe and effective, separate infusions are more preferred because of the possibility of easily achieving better glycaemic control.

It is not only the extremes of glycaemia i.e. hypo or hyperglycamia that is detrimental, but the increased variability in the blood glucose also plays a vital role with respect to the postoperative outcomes and complications. The study conducted by EGI and colleagues, which is a retrospective observational study, has established that reduced blood glucose variability is an independent factor affecting the outcome in critically ill patient.

In both diabetes and non-diabetes patients postoperative hyperglycaemia is directly associated with a greater risk of postoperative infections in the 30day period following surgery leading to an extended hospital stay. It is stated that for every 40 mg/dl increase in postoperative blood glucose level there has been a 30% increased risk for postoperative infectious complications. A target of 150 mg/dl of blood glucose has been recommended by the Portland Glucose Control Group in patients with diabetes undergoing cardiac surgery.

Studies established decreased infectious rates in the postoperative period with this blood glucose target. There is still lack of clinical studies to establish the effect of blood glucose control in metabolic stress induced by hyperglycaemia in diabetic and non-diabetic patients. Several studies have prematurely stopped because of the increased incidence of hypoglycaemia and its complications occurring with intensive insulin therapy.

Diabetes patients undergoing surgery requires stringent glycaemic control with pre, intra and postoperative blood glucose monitoring. Blood glucose level more than 180 mg/dl is treated with insulin therapy for perioperative glycaemic management. Intra operatively the ideal range to be maintained is 140 to 180 mg/dl for safe titration of insulin therapy to avoid extremes of glycaemia and blood glucose variability.

There are several limitations to the present study as the study was conducted in a single institution. Thus the results cannot be generalised for a general population. Despite adjusting several factors confounding the results, many risk factors associated with post-operative infections could not be controlled in acute settings such as nutrition, smoking etc. In conclusion the relationship betweenstrict perioperative glycaemic control and a decreased risk of postoperative infections across a spectrum of surgical cases has been established.

If the association is confirmed in other studies, strategies to improve glycaemic control prior to elective surgery can be employed to decrease infections and improve overall outcomes for diabetic surgical patients.

Tight glucose control in the perioperative period awaits further advances in real-time monitoring technology and treatment protocols but promises to benefit hospitalized diabetes and non-diabetes patients.

CONCLUSION

The following were the conclusions made from this study:

- Patients with diabetes undergoing various surgical procedures show a good response in respect to glycaemic status with insulin therapy.
- Metabolic stress induced by surgery and anaesthesia produces hyperglycaemia even in normo-glycaemic patients, requiring the need for insulin therapy in the perioperative period for optimal glycaemic control.
- The optimal glycaemic range to be maintained for lesser postoperative infections is 120 to 180 mg/dl.
- Surgical site infections are the most common postoperative infections occurring in diabetic patients undergoing surgery.
- Urinary tract infection accounted for the least common infectious complication in these patients.
- The incidence of surgical site infections and sepsis showed a statistically significant correlation with glycaemic status; the higher the mean plasma glucose level, the higher the rate of these infections.

- Even though the incidence of pneumonia and urinary tract complications does not have statistically significant correlation, strict glycaemic control had lesser incidence of these infections.
- Patients with higher blood glucose levels are at increased risk for postoperative infectious complications when compared with the well-controlled diabetic patients.

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EVALUATION OF PERIOPERATIVE GLYCEMIC CONTROL AND POSTOPERATIVE INFECTIONS IN PATIENTS WITH DIABETES MELLITUS

PROFORMA

NAME : AGE/SEX :

I.P. NO. : OCCUPATION :

ADDRESS : UNIT :

DATE OF ADMISSION :

DATE OF DISCHARGE :

PRESENTING COMPLAINTS :

HISTORY OF PRESENTING ILLNESS :

DURATION

BURNING MICTURITION YES/NO

FEVER YES/NO

COUGH WITH EXPECTORATION YES/NO

DISCHARGE FROM THE WOUND YES/NO

GIDDINESS YES/NO

PAST HISTORY :

H/O DIABETES MELLITUS YES/NO

H/O PREVIOUS GI SURGERIES YES/NO

H/O HT/BA/TB

PERSONAL HISTORY :

DIET

SMOKING

ALCOHOL

TREATMENT HISTORY:

TAKING INSULIN OR ORAL HYPOGLYCEMIC AGENTS FOR DM

O/E:

GENERAL EXAMINATION :

ANAEMIA +/- FEVER +/-

BP : PULSE :

S/E:

CVS :

RS :CREPTS

P/A :

WOUND INFECTION

WOUND GAPING

BLOOD INVESTIGATION:

PREOPERATIVE BLOOD SUGAR :

POSTOPERATIVELY BLOOD SUGAR EVERY 6^{TH} HOURLY

FOR FIRST 36 HRS :

HbA1C :

COMPLETE BLOOD COUNT:

CULTURE SENSITIVITY:

PUS CULTURE

SPUTUM CULTURE

URINE CULTURE

BLOOD CULTURE

RADIOLOGICAL INVESTIGATION:

X RAY CHEST PA VIEW

INFORMATION SHEET

We are conducting a prospective study on **"PERIOPERATIVE GLYCEMIC CONTROL AND POSTOPERATIVE INFECTIONS"** in the Department of General Surgery , Thanjavur Medical College & Hospital, Thanjavur – 613004.

- At the time of announcing the results and suggestions, name and identity of the patients will be confidential.

- 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 investigator **Signature of participant**

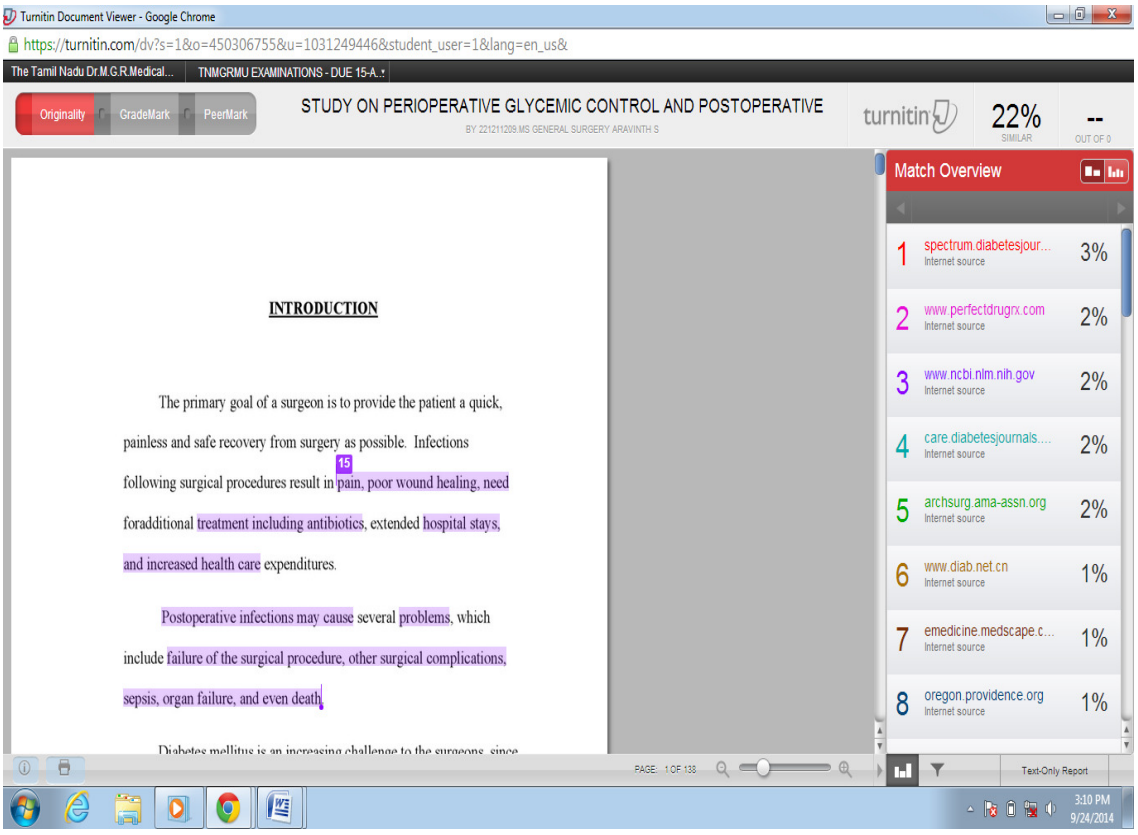
Date:

CONSENT FORM

I _____ hereby give consent to participate in the study conducted by **DR.S.ARAVINTH. ,** Post graduate in the Department of General Surgery ,Thanjavur Medical College & Hospital, Thanjavur – 613004 and to use my personal, clinical data and result of investigation for the purpose of analysis and to study the nature of disease. I also give consent for further investigations

Place :

Date : Signature of participant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The primary goal of a surgeon is to provide the patient a quick, painless and safe recovery from surgery as possible. Infections following surgical procedures result in pain, poor wound healing, need foradditional treatment including antibiotics, extended hospital stays, and increased health care expenditures.
Postoperative infections may cause several problems, which include failure of the surgical procedure, other surgical complications, sepsis, organ failure, and even death.
Diabetes mellitus is an increasing challenge to the surgeons, since
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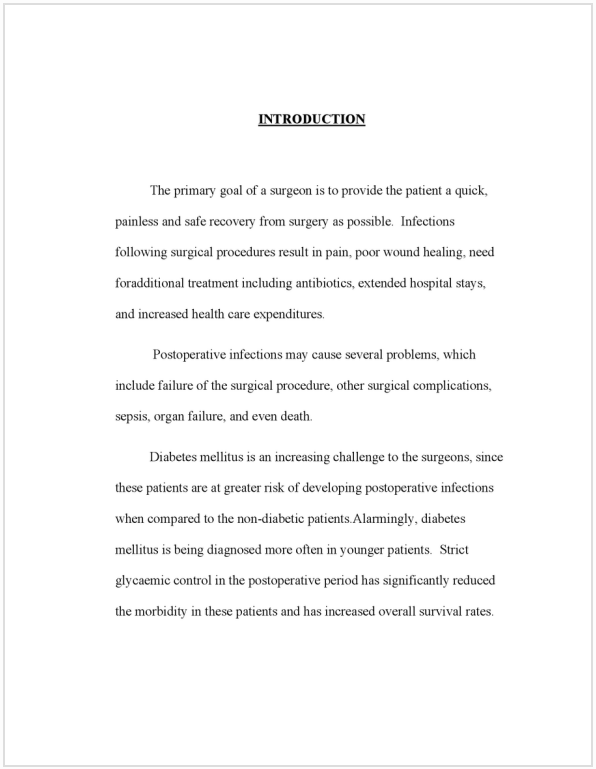


INTRODUCTION

The primary goal of a surgeon is to provide the patient a quick, painless and safe recovery from surgery as possible. Infections following surgical procedures result in pain, poor wound healing, need foradditional treatment including antibiotics, extended hospital stays, and increased health care expenditures.

Postoperative infections may cause several problems, which include failure of the surgical procedure, other surgical complications, sepsis, organ failure, and even death.

Diabetes mellitus is an increasing challenge to the surgeons, since these patients are at greater risk of developing postoperative infections when compared to the non-diabetic patients.Alarmingly, diabetes mellitus is being diagnosed more often in younger patients. Strict glycaemic control in the postoperative period has significantly reduced the morbidity in these patients and has increased overall survival rates.

S.NO	NAME	AGE	SEX	IP NO	BLOOD SUGAR GROUP	WOUND INFECTION	PNEUMONIA	SEPSIS	UTI	INFECTED	Type of surgery
1	Usha	53	F	12945	2	+	-	-	-	+	Eme
2	Kumar	47	M	12623	1	-	-	-	-	-	Ele
3	Stephen	63	M	12652	1	-	-	-	-	-	Ele
4	Chinnasamy	72	M	12676	3	+	+	-	+	+	Eme
5	Rengammal	57	F	12690	1	+	-	-	-	+	Ele
6	Ahemed	64	M	12703	1	-	-	-	-	-	Ele
7	Parameshwari	60	F	12718	2	-	-	-	-	-	Ele
8	Malarkodi	58	F	12737	1	-	+	-	-	+	Ele
9	Ganesan	43	M	12744	1	-	-	-	-	-	Ele
10	Jeya	65	F	12753	3	+	-	-	-	+	Eme
11	Anjammal	49	F	12769	1	-	+	-	-	+	Eme
12	Velu	35	M	12771	1	+	-	-	-	+	Ele
13	Mala	59	F	12783	2	-	+	-	-	+	Eme
14	Seethea	56	F	12786	3	-	-	-	-	-	Ele
15	Perumal	48	M	12792	1	-	-	-	-	-	Ele
16	Kaliyamoorthy	67	M	12799	2	+	-	-	+	+	Eme
17	John	44	M	12839	1	-	-	-	-	-	Ele
18	Selvi	73	F	12845	1	-	-	-	-	-	Ele
19	Abdhul	61	M	12853	4	+	+	+	-	+	Eme
20	Chinnaiyan	45	M	12870	1	-	-	-	-	-	Ele
21	Kathan	70	M	12895	1	-	-	-	-	-	Ele
22	Amutha	45	F	12898	1	+	-	-	-	+	Eme
23	Sundaram	37	M	12917	2	-	-	-	-	-	Ele
24	Vadivelu	48	M	12920	1	-	-	-	+	+	Eme
25	Valarmathy	56	F	12948	2	+	-	-	-	+	Ele
26	Chellammal	74	F	12955	2	-	+	+	-	+	Eme
27	Nagooran	49	M	12963	1	-	-	-	-	-	Ele
28	Shanmugam	66	M	12978	3	+	-	+	-	+	Eme
29	Mookayee	62	F	12979	1	-	-	-	-	-	Ele

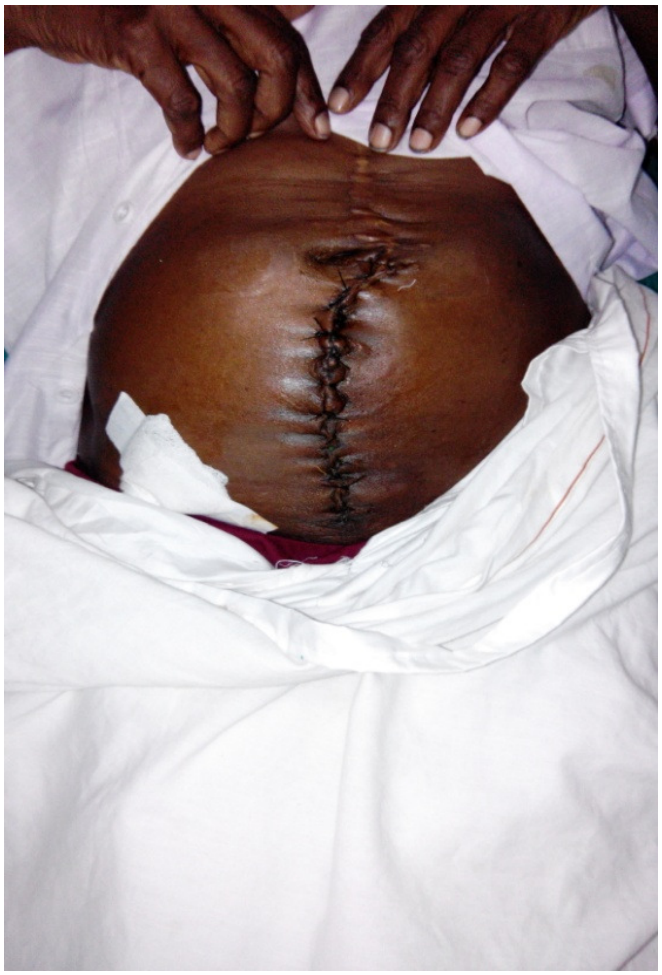
30	Guru	42	M	12986	1	-	-	-	-	-	Ele
31	Pushpam	58	F	12988	1	-	-	-	+	+	Ele
32	Chandran	42	M	12992	1	-	-	-	-	-	Ele
33	Joseph	62	M	12997	2	+	-	+	-	+	Eme
34	Mahendran	45	M	13311	1	+	-	-	-	+	Ele
35	Padmini	36	F	13327	2	+	-	-	-	+	Ele
36	Kaliyan	75	M	13346	3	+	+	-	-	+	Eme
37	Vijaya	41	F	13370	1	-	+	-	-	+	Ele
38	Kathayee	56	F	13396	4	+	-	-	-	+	Ele
39	Manikam	54	M	13402	1	-	-	-	-	-	Ele
40	Sathish	48	M	13430	1	-	-	-	-	-	Ele
41	Periyasamy	73	M	13446	1	-	+	-	-	+	Ele
42	Maniyammal	41	F	13459	3	-	-	+	-	+	Ele
43	Vaniyammal	64	F	13468	1	-	-	-	-	-	Ele
44	Muthukaruppan	58	M	13474	1	+	-	-	-	+	Eme
45	Santha	66	F	13497	2	+	-	-	-	+	Ele
46	Selvam	48	M	13519	1	-	-	-	-	-	Ele
47	Ravi	44	M	13526	2	-	-	-	-	-	Ele
48	Indirani	54	F	13547	4	+	+	+	+	+	Eme
49	Mani	38	M	13563	1	-	-	-	-	-	Ele
50	Banumathi	47	F	13599	1	-	-	-	-	-	Ele

ABBREVIATIONS

- ACTH – Adrenocorticotrophic Hormone
- ADA – American Diabetes Association
- ADP – Adenosine Diphosphate
- ATP – Adenosine Triphosphate
- Ca++ - Calcium
- cAMP – Cyclic Adenosine Monophosphate
- DCCT – Diabetes Complications and Control Trial
- DKA – Diabetic Ketoacidosis
- DM – Diabetes Mellitus
- FA – Fatty acid
- FBS – Fasting Blood Glucose
- FFA – Free Fatty Acid
- GAD – Glutamic Acid Decarboxylase
- GIK – Glucose-Insulin-Potassium
- GluT – Glucose Transporter
- GTT – Glucose Tolerance Test
- HbA1c – GlycatedHemoglobin
- HHS – Hyperosmolar Hyperglycaemic Syndrome
- HLA – Human Leukocyte Antigen
- HMG CoA – Hydroxy Methyl Glutaryl CoA

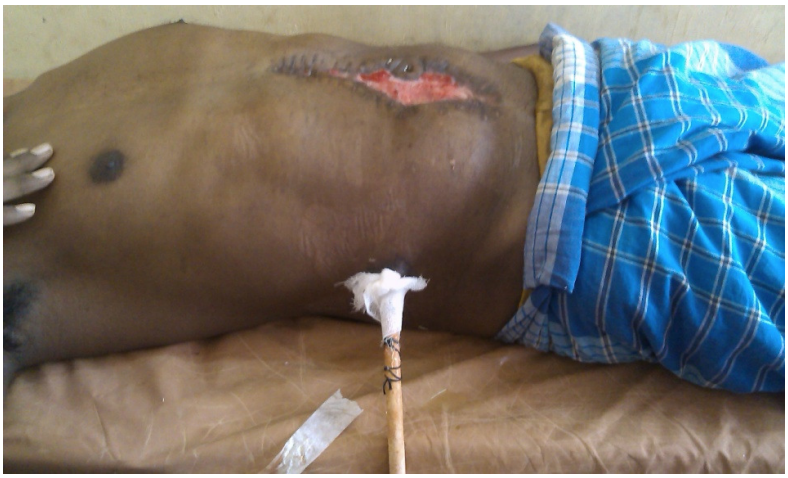
- HNF – Hepatocyte Nuclear Factor
- ICU – Intensive Care Unit
- IDDM – Insulin Dependent Diabetes Mellitus
- IFCC – International Federation of Clinical Chemists
- IGT – Impaired Glucose Tolerance
- IHI – Institute for Healthcare Improvement
- IL – Interleukin
- IRS – Insulin Receptor Substrates
- KCl – Potassium Chloride
- LADA – Latent Autoimmune Diabetes Mellitus
- LBP – Lipopolysaccharide Binding Protein
- LPS – Lipopolysaccharide
- LRI – Lower Respiratory Tract Infection
- mEq/L – milliequivalent/litre
- mg/dl – milligram /decilitre
- mmol/l – millimol/litre
- MODY – Maturity Onset Diabetes of the Young
- NADPH – Nicotinamide adenine dinucleotide phosphate
- NGSP – National Glycohemoglobin Standardisation Program
- NIDM – Non Insulin Diabetes Mellitus
- NPH – Neutral Protamine Hagedorn

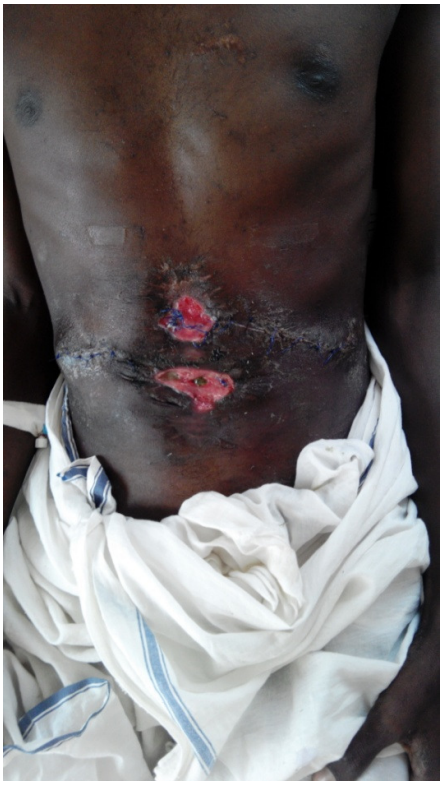
- NPO – Nil Per Oral
- OGTT – Oral Glucose Tolerance Test
- PC – Pyruvate Carboxylase
- PEPCK – Phosphoenol Pyruvate Carboxykinase
- TAG – Triacyl Glycerol
- TCA – Tricarboxylic Acid
- TG – Triglycerides
- TNF – Tumor Necrosis Factor
- UTI – Urinary Tract Infection
- WHO – World Health Organisation
- ELE – Elective
- EME - Emergency



Clean wound

SEPSIS





Infected wound