CLINICAL PROFILE AND OUTCOME OF PATIENTS WITH DIABETIC KETOACIDOSIS IN A TERTIARY CARE HOSPITAL IN WESTERN RAJASTHAN

THESIS

Submitted to

All India Institute of Medical Sciences, Jodhpur

In partial fulfilment of the requirement for the degree of

DOCTOR OF MEDICINE (MD)

(GENERAL MEDICINE)

JUNE, 2022 **DR. KARTIKEY SAINI**

AIIMS JODHPUR

CLINICAL PROFILE AND OUTCOME OF PATIENTS WITH DIABETIC KETOACIDOSIS IN A TERTIARY CARE HOSPITAL IN WESTERN RAJASTHAN

THESIS

Submitted to

All India Institute of Medical Sciences, Jodhpur

In partial fulfilment of the requirement for the degree of

DOCTOR OF MEDICINE (MD)

(GENERAL MEDICINE)

JUNE, 2022 **DR. KARTIKEY SAINI**

AIIMS JODHPUR

All India Institute of Medical Sciences, Jodhpur

DECLARATION

I hereby declare that the thesis titled "***CLINICAL PROFILE AND OUTCOME OF PATIENTS WITH DIABETIC KETOACIDOSIS IN A TERTIARY CARE HOSPITAL IN WESTERN RAJASTHAN***" embodies the original work carried out by the undersigned in All India Institute of Medical Sciences, Jodhpur.

Dr Kartikey Saini
Department of General Medicine
All India Institute of Medical Sciences
Jodhpur

All India Institute of Medical Sciences, Jodhpur

CERTIFICATE

This is to certify that the thesis titled "***CLINICAL PROFILE AND OUTCOME OF PATIENTS WITH DIABETIC KETOACIDOSIS IN A TERTIARY CARE HOSPITAL IN WESTERN RAJASTHAN***" is the bonafide work of Dr Kartikey Saini carried out under our guidance and supervision, in the Department of General Medicine, All India Institute of Medical Sciences, Jodhpur.

Supervisor

Dr Mahendra Kumar Garg
Professor and HOD Department of General Medicine
AIIMS, Jodhpur

Co-Supervisor

Dr Maya Gopalakrishnan
Assistant Professor Department of General Medicine
AIIMS, Jodhpur

All India Institute of Medical Sciences, Jodhpur

CERTIFICATE

This is to certify that the thesis titled "***CLINICAL PROFILE AND OUTCOME OF PATIENTS WITH DIABETIC KETOACIDOSIS IN A TERTIARY CARE HOSPITAL IN WESTERN RAJASTHAN***" is the bonafide work of Dr Kartikey Saini carried out under our guidance and supervision, in the Department of General Medicine, All India Institute of Medical Sciences, Jodhpur.

Dr Mahendra Kumar Garg

Professor and Head

Department of General Medicine & Endocrinology

AIIMS, Jodhpur

Acknowledgement

"Alone we can do so little; together we can do so much" -Helen Keller

Nothing worth achieving has ever been achieved without the guidance of our teachers and the support of family and friends. The immortal words of Helen Keller could not be more undeniable as I stand at the cusp of one of the most prestigious achievements of my life.

I would not be at this landmark moment without the trust and patient patronage of Dr Mahendra Kumar Garg, my MD thesis Guide and Head of Department of General Medicine, All India institute of Medical Sciences, Jodhpur. I am truly honoured and grateful for the opportunity to learn under his tutelage. I am also indebted to my Co-guide Dr Maya Gopalakrishnan, Assistant Professor, Department of General Medicine. Their step by step support and guidance has been instrumental in creating the environment of success and excellence needed for a dissertation from our esteemed institute. I extend my sincere gratitude to all faculty members of our beloved department, Dr. Gopal Krishna Bohra (Associate Professor), Dr. Bharat Kumar, Dr. Naresh Kumar Midha, Dr. Deepak Sharma, Dr. Satyendra Khichar, Dr. Amit Rohila, Dr. Durga Shankar Meena, for their guidance. Family is the backbone which has prevented me from ever faltering in the quest for excellence and knowledge. I cannot express in words my appreciation and love for my parents, Dr Ved Prakash Saini and Mrs Santosh Saini for their immense support and understanding even when I was not worthy of it. I acknowledge the nurturance I have received from my seniors -Dr Karthikeyan Thangaraju, Dr Kamlesh Ahari, Dr. Parag Vijayvergia, Dr. Sonu Pandit, Dr. Saurabh Kumar and Dr. Akhilesh Kumar PH, Dr Neeraja Vijayan, Dr Swapnil Tripathi, Dr S Veena, Dr Prakriti Yadav of the Department of General Medicine. Without their help and reprimands, I would have been clueless as to how to proceed with the work involved in this dissertation. I also thank my esteemed colleagues –Dr Tejaswee Banavathu, Dr Vishwanath Jha for keeping me motivated. I would extend my gratitude to my beloved juniors Dr Nakka Vihari, Dr Naveen, Dr Arjun, Dr Bharti Gindlani, Dr. Isha Stutee Dr. Shilpi Goyal, Dr. Naja K, Dr. Pranav S Kumar , Dr. Pankaj Sukhadiya, Dr. Ramanand S, Dr Ninad Chitnis, Dr Sanjay, Dr Sachin, Dr Mayur, Dr Venkat, Dr Bijit, Dr Divya, Dr Manika, Dr Naveen, Dr Shubham, Dr Lochan who have stepped up in times of need to help balance the duties of a junior resident of our beloved department and the commitments to my thesis. All the faculties

of the Department of General Medicine, All India institute of Medical Sciences, Jodhpur have been pillars of support and understanding and this would not have been possible without them. Last but by far not the least, I express thanks to all my patients without whom this milestone was not possible.

Dedicated to my family

LIST OF ABBREVIATIONS

DM	**Diabetes Mellitus**
GDM	Gestational Diabetes Mellitus
MODY	Maturity Onset Diabetes of Young
HIV	Human Immunodeficiency Virus
AIDS	Acquired immunodeficiency syndrome
DKA	Diabetic Ketoacidosis
HHS	Hyperosmolar Hyperglycaemic Syndrome
ASCVD	Atherosclerotic Cardiovascular Disease
DNA	Deoxyribonucleic acid
E.coli	Escherichia Coli
DALY	Disability and years of life lost
GDM	Gestational Diabetes Mellitus
IR	Insulin Resistance
HNF	Hepatocyte nuclear factor
GADA	Glutamic acid decarboxylase
IA2A	Insulinoma-associated autoantigen2
ZnT8A	Zinc transporter 6
IDDM	Insulin dependant diabetes mellitus
VNTR	Variable number of Tandem repeats
FFA	Free fatty acid
GLP	Glucagon like peptide
NDM	Neonatal diabetes mellitus
LADA	Latent autoimmune diabetes of adults

SPIDDM	Slowly progressive insulin dependent type 1 diabetes mellitus
ADA	American diabetes association
IDS	The immunology for Diabetes society
HBA1c	Glycated haemoglobin
HDL	High density lipoprotein
ACE	Angiotensin Converting enzyme
ARB	Angiotensin receptor blocker
GFR	Glomerular filtration rate
NCV	Nerve conduction velocity
SGLT2	Sodium glucose transporter protein
CoA	Coenzyme A
CPT1-L	carnitine O-palmitoyl transferase 1, liver isoform
Na	Sodium
K	Potassium
Ca	Calcium
PO4	Phosphorous
Mg	Magnesium

INDEX

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

Diabetes is a group of metabolic diseases characterized by hyperglycaemia which can be due to defect in insulin secretion, insulin action, or both.

The classic symptoms of diabetes such as polyuria, polydipsia and polyphagia occur commonly in type 1 diabetes (T1DM), which has a rapid development of severe hyperglycaemia and also in type 2 diabetes (T2DM) with very high levels of hyperglycaemia. Severe weight loss is common only in T1DM or if T2DM remains undetected for a long period. Unexplained weight loss, fatigue and restlessness and body pain are also common signs of undetected diabetes. Symptoms that are mild or have gradual development could also remain unnoticed[(3)].

The most acute complication of DM is diabetic ketoacidosis (DKA), which typically presents in T1DM but can also be seen in cases of Type 2 DM. This condition can be either due to inadequate dosing, missed doses, or ongoing infection. In this condition, the lack of insulin means that tissues are unable to obtain glucose from the bloodstream and the lipids are metabolised into ketones as a substitute energy source, which causes systemic acidosis, and can be calculated as a high anion-gap metabolic acidosis. The combination of hyperglycaemia and ketosis causes diuresis, acidaemia, and vomiting leading to dehydration and electrolyte abnormalities, which can be life-threatening. In T2DM, hyperosmolar hyperglycaemic syndrome (HHS) is an emergent concern. It presents similarly to DKA with excessive thirst, elevated blood glucose, dry mouth, polyuria, tachypnea, and tachycardia (5). The most common precipitating factor in the development of DKA and HHS is infection. Other precipitating factors include discontinuation of or inadequate insulin therapy, pancreatitis, myocardial infarction, cerebrovascular accident, and drugs. In addition, new-onset T1DM or discontinuation of insulin in established T1DM commonly leads to the development of DKA. In young patients with T1DM, psychological problems complicated by eating disorders may be a contributing factor in 20% of recurrent ketoacidosis. The various factors that may lead to insulin omission in younger patients include fear of weight gain with improved metabolic control, fear of hypoglycemia, rebellion against authority, and stress of chronic disease[(6)].

REVIEW OF LITERATURE

History of Diabetes

Diabetes is one of the most extensively studied disease in the history of medicine with descriptions of clinical features similar to diabetes mellitus were described 3000 years ago by the ancient Egyptians they called it “great emptying of urine”. The term "diabetes" was first coined by Araetus of Cappodocia (81-133AD) he stated “no essential part of the drink is absorbed by the body while great masses of the flesh are liquefied into urine”. Avicenna (980–1037 A.D.), the great Persian physician, in The Canon of Medicine not only referred to abnormal appetite and observed diabetic gangrene but also concocted a mixture of seeds (lupin, fenugreek, zedoary) as a panacea.

GALEN (ca A. D. 129-199), ARETAEUS' contemporary, used the terms, Hyderoseisamida which translates as ‘chamber-pot craving’, or Diarrhoiaeisoura, which translates into ‘polyuria’, which soon found its place in the whole medical literature. Indian physicians called the disease madhumeha (honey urine)) or ‘Iksumeha’ (urinarysugar flux) occur.‘Hastimeha’, with ‘hasti’ referring to elephant and ‘meha’ referring to watering with reference to disease to human body, refers to a condition of passing urinelike an intoxicated elephant and remarks found with insects and ants would be attracted to such urine were few evidences which shown that we are dealing with disease of diabetes, later the same phenomena was rediscovered by Thomas Willis (Britain) in 1675 who gave it the term Mellitus he described the disease as “pissing evil”. In 1776 Dobson (Britain) firstly confirmed the presence of excess sugar in urine and blood as a cause of their sweetness. In modern time, the history of diabetes coincided with the emergence of experimental medicine. An important milestone in the history of diabetes is the establishment of the role of the liver in glycogenesis, and the concept that diabetes is due to excess glucose production Claude Bernard (France) in 1857. The role of the pancreas in pathogenesis of diabetes was discovered by Mering and Minkowski (Austria) 1889.(7) In 1884 that the French Louis Vaillard (1850–1935) and Charles Louis Xavier Arnozan (1852–1928) discovered that pancreatic duct occlusion caused pancreatic atrophy without hyperglycaemia. In 1869, Paul Langerhans, then aged 22 and working on his medical doctorate, identified the cells that came to be known as the ‘islets of Langerhans’. However, the name insulin for the secretions of the islets (Latin, insula = island), which could bring down blood glucose levels, was coined only in 1909 and 1910, individually by de Mayer and Schaefer, respectively. In 1889, von Mering

and Minkowski, when experimenting on dogs, found that removal of the pancreas led to diabetes. The Italian endocrinologist and pathologist Giulio Vassale (1862–1913) described (24) that the ligation of Wirsung's duct resulted in atrophy of the esophageal pancreas, sparing the Langerhans islands and, as such, not causing glycosuria. He concluded that the islands had a specific and different function from the rest of the pancreas.

In 1906, the American pathologist and anatomist Lydia Maria Adams DeWitt, after ligating the pancreatic ducts of some cats, observed an exocrine pancreas atrophy and, from the Langerhans islands, obtained a beneficial extract for diabetes, which, despite the fact of not being optimal, maintained a discrete glycolytic power. In 1908, the German physician George Ludwig Zuelzer (1870–1949) found favourable results with the administration of pancreatic alcohol extracts in diabetic patients. Eugène Gley was inspired by the hypothesis formulated by the French histologist Gustave-Édouard Laguesse (1861–1927) (29, 30) according to which the Langerhans islands secrete a substance capable of preventing the elimination of glucose through the urine. He decided to test this hypothesis with an aqueous extract of pancreas, which was administered to diabetic, pancreatectomized dogs. Gley noted that glycosuria was reduced and the symptoms of diabetes significantly improved.

Difficulty encountered by all scholars was to separate the extract of the Langerhans islands from the rest of the pancreatic exocrine tissue. Banting assisted by Best and Noble closed the pancreatic ducts with a technique designed by Banting to get the degeneration of the pancreatic exocrine tissue and to obtain a pancreatic islet from the pure state. With this liquid extract, for the first time, in the history of medicine, Banting and Best found the way to control glucose in a diabetic animal. Leonard Thompson, a 14-year-old, serious diabetic patient at the Toronto General Hospital, was the first patient to be treated. However, the initial clinical experimentation was a failure the administration of 15 ml of pancreatic extract had no impact on ketoacidosis, only slightly reducing glycemia and glycosuria, and resulted in the formation of a sterile abscess. On January 23rd Leonard underwent another series of injections and this time he experienced a normalization of glycaemia, glycosuria, and ketonuria. More in details, glycaemia decreased from 520 mg/dl to 120 mg/dl. Glycosuria dropped from 71 to 9 g; ketonuria disappeared. The merit was also of the clinical biochemist James Bertram Collip (1892–1965), who developed a new extraction and concentration protocol. Collip, from the alcoholic acid extract of oxen and pork pancreas, showed that these preparations were more effective than those obtained by the binding of the ducts and subsequent degeneration of the oesophagus pancreas.

In 1975, fully synthetic insulin (CGP 12 831) was synthesized in the laboratories of Ciba-Geigy in Basel. Genentech rDNA human insulin obtained on 24th August, 1978 from combination of A and B chains individually expressed in E. coli. In 1980, recombinant DNA human insulin was first tested in a sample of 17 non diabetic volunteers, in England. The first diabetic patient treated was Sandy Atherton, 37-year-old, from Wichita, Kansas (USA). In 1982 other synthetic insulins, much less allergenic than animal insulins, became widely available to diabetic patients, such as Humilin, manufactured by Eli Lilly. On 10th April 1986 the approval to market BHI derived from human proinsulin was signed. In the 1980-90s analog insulins were produced, that is to say a genetically modified form of insulin where the amino acid sequence has been altered in order to optimize insulin absorption, distribution, metabolism and excretion. In 1996, Eli Lilly introduced the first type of analog insulin lispro under the brand name of Humalog. Aspart was approved and released in 2000, while glulisine in 2004

Before the invention of insulin, the management of diabetes paved way for some bizarre pharmacological methods such as use of opium or dietary interventions with the diabetic patients being advised to eat extra portion for compensating for their endocrinological and metabolic impairment while some physicians asking their patients to eat hypercaloric diets for counteracting the urinary loss of calories.

However some physicians began to notice that it was fasting and not an excess of calories to improve the clinical symptoms of diabetes. In 1706, John Rollo, Surgeon-General to the Royal Artillery, successfully treated a patient by dietary restriction. The French pharmacist and hygienist Apollinaire Bouchardat (1809–1886), considered the modern father of diabetology, observed an improvement of diabetic patients during the German siege of Paris in 1870. His school, which included the physician Bernhard Naunyin (1839–1925), became famous for advising sugar-free diets, known as the “Bouchardat's treatment”. Other nutritional interventions became extremely popular, such as the Allen diet, introduced by the American physician Frederick Madison Allen (1879–1964). It was a carbohydrate-restricted low-calorie diet, described in a book entitled “Studies concerning glycosuria and diabetes” and published in 1913. The American physician Elliott Proctor Joslin (1869–1962), founder of the Joslin Diabetes Centre, one of first structures offering specialized service to diabetic patients, was a fervent advocate of a severe, prolonged fasting and of under-nutrition or under-nourishment as a cure for diabetes, the so-called “starvation diet” [(8)]

Prevalence and Incidence of Diabetes and DKA

The global diabetes prevalence in 2019 was estimated to be a 9.3% (463 million people), with prevalence rising to 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045. The prevalence is higher in urban (10.8%) than rural (7.2%) areas, and in high-income (10.4%) than low-income countries (4.0%). One in two (50.1%) people living with diabetes do not know that they have diabetes. The global prevalence of impaired glucose tolerance is estimated to be 7.5% (374 million) in 2019 and projected to reach 8.0% (454 million) by 2030 and 8.6% (548 million) by 2045[8].

Between 2000 and 2016, there was a 5% increase in premature mortality from diabetes. In 2019, diabetes was the ninth leading cause of death with an estimated 1.5 million deaths directly caused by diabetes.

The incidence of T1DM in Asia is 15 per 100 000 population and the prevalence of T1DM is 6.9 per 10 000 people.

Whereas the incidence of T1DM in world is 15 per 100 000 population, and the prevalence of T1DM is 9.5 per 10 000 people [9].

The prevalence of T2DM shows a distribution pattern that matches socio-economic development. Males show a slightly higher prevalence than females (6219 compared with 5898 cases per 100,000), although this difference is within the margin of uncertainty. The age of onset of new diagnosis is also somewhat earlier among males and shows expected patterns of rising prevalence with increasing age, whereas the incidence peaks at 55–59 years .There appears to be no major shift in the age distribution from 1990 to 2017.

Even though it afflicts individuals later in life, T2DM ranks seventh among the leading causes of disability and years of life lost (DALYs). It has jumped ranks from nineteenth position in 1990, indicating a global transition in disease patterns toward noncommunicable diseases.

Statistical forecasting suggests diabetes prevalence could increase to 7079 per 100,000 by 2030 and 7862 by 2040. This estimate for 2040 is flanked by an upper confidence limit of 9904 and a lower limit of 5821 per 100,000[10].

The incidence of DKA is 46 to 80 per 10,000 person-years among patients with diabetes, and the estimated mortality rate of DKA is 4% to 10%. Only 20% of DKA episodes occur in

patients with new-onset diabetes. Furthermore, 20% of patients with DKA have multiple annual episodes[11].

The incidence of DKA per 10,000 admissions was higher in males (71.2) than females (54.1). However, a higher incidence per 10,000 admissions was noted in patients of ages 1–17 years. The mean age of patients with DKA was 38.4 years.

There is a trend of decreasing DKA prevalence with increasing age. Young adults (aged 18 years to 25 years) had the highest prevalence of DKA (100–120 cases per 1000 in studies with 12-month recall and 40–80 cases per 1000 in studies with 3-month recall), while the elderly (aged ≥65 years) had the lower prevalence of DKA[12].

Description and Definition

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Several pathogenic processes are involved in the development of diabetes and can range from autoimmune destruction of the pancreatic β-cells with consequent insulin deficiency to abnormalities that result in resistance to insulin action. The basis of the abnormalities in carbohydrate, fat, and protein metabolism in diabetes is deficient action of insulin on target tissues. Deficient insulin action results from inadequate insulin secretion and/or diminished tissue responses to insulin at one or more points in the complex pathways of hormone action. Impairment of insulin secretion and defects in insulin action can frequently coexist in the same patient[1].

Hyperglycaemia, which is associated with uncontrolled DM, elicits abnormal metabolism such that the enzymes involved in the metabolic events leading to diabetic complications are expressed and amplified[13]. Diabetes can be classified into the following general categories

Type 1 diabetes (due to autoimmune β-cell destruction, usually leading to absolute insulin deficiency)

Type 2 diabetes (due to a progressive loss of β-cell insulin secretion frequently on the background of insulin resistance)

Gestational diabetes mellitus (GDM) (diabetes diagnosed in the second or third trimester of pregnancy)Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young [MODY]), diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), and drug- or

chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation[2].

T1DM and T2DM are heterogeneous diseases in which clinical presentation and disease progression may vary considerably. Classification is important for determining therapy, but some individuals cannot be clearly classified as having T1DM or T2DM at the time of diagnosis. The traditional paradigms of T2DM occurring only in adults and T1DM only in children are no longer accurate, as both diseases occur in both age-groups. Children with T1DM typically present with the hallmark symptoms of polyuria/polydipsia, and approximately one-third present with diabetic ketoacidosis (DKA)[12].

Occasionally, patients with T2DMmay present with DKA, particularly ethnic minorities. It is important for the provider to realize that classification of diabetes type is not always straightforward at presentation and that misdiagnosis is common (e.g., adults with T1DM misdiagnosed as having T2DM; individuals with maturity-onset diabetes of the young [MODY] misdiagnosed as having T1DM, etc.). Although difficulties in distinguishing diabetes type may occur in all age-groups at onset, the diagnosis becomes more obvious over time[14].

In both T1DM and T2DM, various genetic and environmental factors can result in the progressive loss of β-cell mass and/or function that manifests clinically as hyperglycemia. Once hyperglycemia occurs, patients with all forms of diabetes are at risk for developing the same chronic complications, although rates of progression may differ. The identification of individualized therapies for diabetes in the future will require better characterization of the many paths to β-cell demise or dysfunction[14].

Characterization of the underlying pathophysiology is more developed in T1DM than in T2DM. It is now clear from studies of first-degree relatives of patients with T1DM that the persistent presence of two or more islet autoantibodies is an almost certain predictor of clinical hyperglycemia and diabetes. The rate of progression is dependent on the age at first detection of autoantibody, number of autoantibodies, autoantibody specificity, and autoantibody titer. Glucose and A1C levels rise well before the clinical onset of diabetes, making diagnosis feasible well before the onset of DKA[15].

The β-cell–centric classification of DM is a new approach that obviates the inherent and unintended confusions of the current system. The β-cell–centric model presupposes that all

DM originates from a final common denominator—the abnormal pancreatic β-cell. It recognizes that interactions between genetically predisposed β-cells with a number of factors, including insulin resistance (IR), susceptibility to environmental influences, and immune dysregulation/inflammation, lead to the range of hyperglycemic phenotypes within the spectrum of DM. Individually or in concert, and often self-perpetuating, these factors contribute to β-cell stress, dysfunction

1 Etiologic Classification of Diabetes Mellitus

I. Type 1 diabetes (beta-cell destruction, usually leading to absolute insulin deficiency) Immune mediated Idiopathic
II. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly insulin secretory defect with insulin resistance)
III. Gestational Diabetes mellitus (GDM)
IV. Other specific types **Genetic defects of beta -cell function** Chromosome 20q, HNF-4 alpha (MODY1) Chromosome 7p, glucokinase (MODY2) Chromosome 12q, HNF-1 alpha (MODY3) Chromosome 13q, insulin promoter factor-1 (MODY4) Chromosome 17q, HNF-1 beta (MODY5) Chromosome 2q, Neurogenic differentiation1 (MODY 6) Chromosome 9, carboxyl ester lipase (MODY 7) Transient Neonatal Diabetes (Chromosome 6p22 or 6p24, ZAC encoding zinc finger protein) Permanent Neonatal Diabetes (Chromosome 11p15, usually KCNJ11 encoding for KIR6.2 subunit of the beta-cell KATP channel) Mitochondrial DNA Others **Genetic defects in insulin action** Type A insulin resistance Leprechaunism Rabson-Mendenhall syndrome Lipoatrophic diabetes Others **Diseases of the exocrine pancreas** Pancreatitis Trauma/pancreatectomy Neoplasia Cystic fibrosis Hemochromatosis Fibrocalculouspancreatopathy Others **Endocrinopathies** Acromegaly Cushing's syndrome

Glucagonoma
Pheochromocytoma
Hyperthyroidism
Somatostatinoma
Aldosteronoma
Others
Drug- or chemical-induced
Vacor
Pentamidine
Nicotinic acid
Glucocorticoids
Thyroid hormone
Diazoxide
beta-adrenergic agonists
Thiazides
Dilantin(phenytoin)
alpha-interferon. Others
Infections
Congenital rubella
Cytomegalovirus
Others
Uncommon forms of immune-mediated diabetes
"Stiff-man" syndrome
Anti-insulin receptor antibodies
Others
Other genetic syndromes sometimes associated with diabetes
Down's syndrome
Klinefelter's syndrome
Turner's syndrome
Wolfram's syndrome
Friedreich's ataxia
Huntington's chorea
Laurence-Moon-Bieldel syndrome
Myotonic dystrophy
Porphyria
Prader-Willi syndrome
Others
Post-transplant

TYPE 1 DM

Type 1 diabetes is generally thought to be precipitated by an immune-associated, if not directly immune-mediated, destruction of insulin-producing pancreatic β cells[16].

Historically, T1DM was largely considered a disorder in children and adolescents, but this opinion has changed over the past decade, so that age at symptomatic onset is no longer a restricting factor. Polydipsia, polyphagia, and polyuria (the classic trio of symptoms

associated with disease onset) along with overt hyperglycaemia remain diagnostic hallmarks in children and adolescents, and to a lesser extent in adults. An immediate need for exogenous insulin replacement is also a hallmark of T1DM, for which lifetime treatment is needed[17].

There are two pathophysiological processes proposed for the development of T1DM
1. Autoimmune destruction of insulin-secreting pancreatic β cells. The presence of a chronic inflammatory infiltrate that affects pancreatic islets at symptomatic onset of T1DM is the basis of this observation

2. In patients with longstanding disease, the pancreas is devoid of insulin-producing cells and the remaining β cells are incapable of regeneration[18].

A key distinguishing feature between T1DM and T2DM is the presence of autoantibodies against β-cell autoantigens. More than 90% of individuals with newly diagnosed T1DM have one or more of the following autoantibodies at disease onset insulin (IAA)
Glutamic acid decarboxylase (GADA)
Insulinoma-associated autoantigen 2 (IA2A)
Zinc transporter 8 (ZnT8A)[19].

T1DM is a polygenic disorder, with 40 loci known to affect disease susceptibility.72 The HLA region on chromosome 6 (ie, the IDDM1 locus) provides one-half of the genetic susceptibility that leads to risk of T1DM. Of the many HLA types, HLA class II show the strongest association with T1DM, where haplotypes DRB1*0401-DQB1*0302 and DRB1*0301-DQB1*0201 confer the greatest susceptibility, and DRB1*1501 and DQA1*0102-DQB1*0602 provide disease resistance. Class I MHCs also influence risk for T1DM, independent of class II molecules. Of the remaining loci, only those for the insulin VNTR, PTPN22, CTLA4, and IL2RA are associated with odds ratios greater than 1·1[20].

TYPE 2 DM

T2DM takes up around 90% of all cases of diabetes. T2DM is characterized by diminished response to insulin, and this is defined as insulin resistance. Initially the insulin is ineffective which is countered by an increase in insulin production to maintain glucose homeostasis, but eventually the insulin production decreases which results in T2DM. T2DM is most commonly disease of the elderly seen in persons older than 45 years. But it is increasingly

seen in children, adolescents, and younger adults owing to the increasing levels of obesity, physical inactivity, and energy-dense diets.

Most of the patients with T2DM are commonly obese or have a higher body fat percentage which is distributed predominantly in the abdominal region. This adipose tissue itself drives the insulin resistance anchoring various inflammatory mechanisms, including increased FFA release and adipokine dysregulation. Other risk factors include lack of physical activity, prior GDM in those with hypertension or dyslipidemia. Recent studies suggest a role for adipokine dysregulation, inflammation, abnormal incretin biology with decreased incretins such as glucagon-like peptide-1 (GLP-I) or incretin resistance, hyperglucagonemia, increased renal glucose reabsorption, and abnormalities in gut microbiota[21].

LADA

Latent autoimmune diabetes of adults (LADA) is a form of DM with overlapping features T1DM and T2DM and has therefore been termed Type 1.5 DM. In Japan, the synonym used is slowly progressive insulin-dependent type 1 diabetes mellitus (SPIDDM). The American Diabetes Association (ADA) lists LADA as T1DM that evolves more slowly than the classic disease and does not recognize it as a specific type of DM. The World Health Organization's term for LADA is 'slowly evolving'

Insulin independence for at least the initial 6 months g immune-related diabetes.'

LADA is, by definition, a disease of adults. The Immunology for Diabetes Society (IDS) enlists three criteria for LADA diagnosis

1. Age greater than 35 years
2. Positive autoantibodies to islet beta cells after initial diagnosis
3. Absence of insulin requirement for at atleast 6 months after diagnosis

Diagnosis of Diabetes

Prediabetes and T2DM is detected by measuring fasting plasma glucose or HbA1c level, or with an oral glucose tolerance test. Fasting plasma glucose level of 126 mg/dL (6.99 mmol/L) or greater, an HbA1c level of 6.5% or greater, or a 2-hour postload glucose level of 200 mg/dL (11.1 mmol/L) or greater are consistent with the diagnosis of T2DM. A fasting plasma glucose level of 100 to 125 mg/dL (5.55-6.94 mmol/L), an HbA1c level of 5.7% to 6.4%, or a 2-hour postload glucose level of 140 to 199 mg/dL (7.77-11.04 mmol/L) are consistent with prediabetes[23].

HbA1c is a measure of long-term blood glucose concentration and is not affected by acute changes in glucose levels caused by stress or illness. Because HbA1c measurements do not require fasting, they are more convenient than using a fasting plasma glucose level or an oral glucose tolerance test. Both fasting plasma glucose and HbA1c levels are simpler to measure than performing an oral glucose tolerance test. The oral glucose tolerance test is done in the morning in a fasting state; blood glucose concentration is measured 2 hours after ingestion of a 75-g oral glucose load. The diagnosis of T2DM should be confirmed with repeat testing.

Screening Intervals

There are limited evidenced backed guidelines for re-screening of individuals with normal blood glucose on initial assessment. Cohort and modelling studies suggest that screening every 3 years may be a reasonable approach for adults with normal blood glucose levels[(4)].

Screening Recommendations

Summary of Screening Recommendations for Type 2 Diabetes Mellitus

American Association of Clinical Endocrinologists
Screen asymptomatic individuals if risk factors present
Acanthosis nigricans
Age ≥ 45 years
Antipsychotic therapy for schizophrenia and/or severe bipolar disease
Cardiovascular disease or family history of type 2 diabetes
Chronic glucocorticoid exposure
HDL cholesterol level < 35 mg per dL (0.91 mmol per L) and/or a triglyceride level > 250 mg per dL (2.8 mmol per L)
History of gestational diabetes mellitus or delivery of a baby weighing > 9 lb (4.1 kg)
Hypertension (blood pressure > 140/90 mm Hg or taking medication for hypertension)
Impaired glucose tolerance, impaired fasting glucose, and/or metabolic syndrome
Member of an at-risk racial or ethnic group Asian, black, Hispanic, Native American (Alaska Native or American Indian), or Pacific Islander
Nonalcoholic fatty liver disease
Overweight or obese
Polycystic ovary syndrome
Sedentary lifestyle
Sleep disorders in the presence of glucose intolerance (A1C > 5.7%, impaired glucose tolerance, or impaired fasting glucose on previous testing), including obstructive sleep apnea, chronic sleep deprivation, and night-shift occupation) every three years
Screen persons with two or more risk factors annually
American Diabetes Association(2)
Screen asymptomatic adults with a body mass index ≥ 25 kg per m2, and one or more additional risk factors
A1C > 5.7%, impaired glucose tolerance, or impaired fasting glucose on previous testing
Acanthosis nigricans
Cardiovascular disease
First-degree relative with type 2 diabetes

	HDL cholesterol level < 35 mg per dL and/or a triglyceride level > 250 mg per dL
	High-risk ethnicity black, Native American/Alaska Native, Hispanic/Latino, Asian American, and Native Hawaiian/Pacific Islander
	Hypertension (blood pressure > 140/90 mm Hg or taking medication for hypertension)
	Physical inactivity
	Polycystic ovary syndrome
	Women who had gestational diabetes or who delivered a baby weighing > 9 lb
In persons without risk factors, testing should begin at 45 years of age	
If test results are normal, repeat testing should be performed at least every three years.	

Complications of Diabetes

The complications of diabetes develop secondary to the direct and indirect effects on the human vascular tree and is the major source of morbidity and mortality in both T1DM and T2DM. The complications of hyperglycemia can be separated into macrovascular complications (coronary artery disease, peripheral arterial disease, and stroke) and microvascular complications (diabetic nephropathy, neuropathy, and retinopathy).

Diabetic retinopathy

Diabetic retinopathy is the most common microvascular complication of diabetes. Development of diabetic retinopathy in patients with T2DM is related to both severity of hyperglycemia and presence of hypertension in the U.K. Most patients with T1DM develop evidence of retinopathy within 20 years of diagnosis. diabetic retinopathy is generally classified as either background or proliferative.

Background retinopathy includes such features as small haemorrhages in the middle layers of the retina called as “dot haemorrhages.” Hard exudates caused by lipid deposition that typically occurs at the margins of haemorrhages. Microaneurysms are small vascular dilatations that occur in the retina and are the first sign of retinopathy. They clinically appear as red dots during retinal examination. Retinal edema may result from microvascular leakage and is indicative of compromise of the blood-retinal barrier and appears as one of greyish retinal areas. Retinal edema is interventional emergency because it is sometimes associated with visual deterioration.

Proliferative retinopathy is the formation of new blood vessels on the surface of the retina and is associated with a component of vitreous haemorrhage. White areas on the retina (“cotton wool spots”) are a sign of impending proliferative retinopathy. If proliferation continues, blindness can occur through vitreous haemorrhage and traction retinal detachment. With no intervention, visual loss occurs. Laser photocoagulation can prevent proliferative

retinopathy from progressing to blindness and therefore, close surveillance for the existence or progression of retinopathy in patients with diabetes is crucial[25].

Diabetic nephropathy

Diabetic Nephropathy is as defined by proteinuria > 500 mg in 24 hours but its preceded by lower degrees of proteinuria, or "microalbuminuria." Microalbuminuria is defined as albumin excretion of 30-299 mg/24 hours. Diabetic patients with microalbuminuria progress to proteinuria and overt diabetic nephropathy. This progression is seen in both T1DM and T2DM.

Around 7% of patients with T2DM have microalbuminuria at the time of diagnosis of Diabetes(26). The incidence of microalbuminuria is 2% per year in patients with T2DM, and the 10-year prevalence after diagnosis is 25%.

The pathological changes to the kidney include increased glomerular basement membrane thickness, microaneurysm formation, mesangial nodule formation (Kimmelsteil-Wilson bodies), and other changes (27).Screening for diabetic nephropathy or microalbuminuria is done by a 24-hour urine collection or a spot urine measurement of microalbumin. Measurement of the microalbumin-to-creatinine ratio may help account for concentration or dilution of urine, and spot measurements are more convenient for patients than 24-hour urine collections.

Initial treatment of diabetic nephropathy, as of other complications of diabetes, is prevention. There is a strong association between glucose control (as measured by hemoglobin A1c [A1C]) and the risk of developing diabetic nephropathy. Patients should be targeted to the lowest safe glucose level that can be obtained to prevent or control diabetic nephropathy. Treatment with angiotensin-converting enzyme (ACE) inhibitors does not prevent the development of microalbuminuria in patients with type 1 diabetes but it decreases the risk of developing nephropathy and cardiovascular events in patients with T2DM[28].

ACE inhibitors and angiotensin receptor blockers (ARBs)decrease the intraglomerular pressure and have been shown to decrease the risk of progression to macroalbuminuria in patients with microalbuminuria. These drugs are recommended as the first-line pharmacological treatment of microalbuminuria, even in patients without hypertension.

Patients with macroalbuminuria benefit from control of hypertension. Hypertension control in patients with macroalbuminuria from diabetic kidney disease slows decline in glomerular filtration rate (GFR). Treatment with ACE inhibitors or ARBs has been shown to further decrease the risk of progression of kidney disease, also independent of the blood pressure-lowering effect.

Combination treatment with an ACE inhibitor and an ARB has been shown to have additional Reno protective effects. Some patients on combination drugs may experience an initial increase in creatinine and hyperkalemia should be screened for hyperkalemia. Considerable increase in creatinine after initiation of these agents should call for an evaluation for renal artery stenosis[29].

Diabetic neuropathy

Diabetic neuropathy is defined according to the American Diabetes Association (ADA) as "the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other cause" (30). The risk of developing diabetic neuropathy is proportional to both the magnitude and duration of hyperglycemia, and some individuals may possess genetic attributes that affect their predisposition to developing such complications.

The precise nature of injury to the peripheral nerves from hyperglycemia is not known but likely is related to mechanisms such as polyol accumulation, injury from AGEs, and oxidative stress. Peripheral neuropathy in diabetes can manifest as sensory, focal/multifocal, and autonomic neuropathies.(30) About 80% of amputations occur after foot ulceration or injury, as a consequence of diabetic neuropathy.

Chronic sensorimotor distal symmetric polyneuropathy is the most common form of neuropathy in diabetes. Patient complains of burning, tingling, and "electrical" pain, but can experience simple numbness. Patient often report worsening of symptoms at night. Physical examination reveals sensory loss to light touch, vibration, and temperature. Abnormalities in more than one test of peripheral sensation are > 87% sensitive in detecting the presence of neuropathy. Patients also typically experience loss of ankle reflex. Patients with loss of 10-g monofilament sensation are at increased risk for developing foot ulceration.

Pure sensory neuropathy is relatively rare and associated with fluctuating levels of inadequate blood glucose control[31].

Mononeuropathies typically have a sudden onset and can involve any nerve, but the median, ulnar, and radial nerves are most frequently affected. Cranial nerve involvement can also occur but is rare. Nerve involvement in the form of nerve entrapment also occurs frequently in the setting of diabetes. NCV demonstrates decreases in both amplitude of nerve impulse and conduction but may be useful in identifying the location of nerve entrapment. Diabetic amyotrophy can be a manifestation of diabetic mononeuropathy and manifests as severe pain and muscle weakness and atrophy, most frequently in a large thigh muscles.

Chronic inflammatory polyneuropathy, vitamin B12 deficiency, hypothyroidism, and uremia are important differentials of Diabetic Neuropathy.

Diabetic autonomic neuropathy is another cause of morbidity and mortality in diabetes. Neurological dysfunction may occur in most organ systems and manifests as gastroparesis, constipation, diarrhoea, anhidrosis, bladder dysfunction, erectile dysfunction, exercise intolerance, resting tachycardia, silent ischemia and sudden cardiac death. Cardiovascular autonomic dysfunction is associated with increased risk of silent myocardial ischemia and mortality[31].

Macrovascular complications

The various macrovascular complications include coronary artery disease, cerebrovascular disease (stroke, transient ischemic attack, carotid artery stenting, and carotid endarterectomy), peripheral artery disease (history of peripheral artery disease including revascularization procedures, diabetic foot, and amputation), heart failure, and implant cardioverter defibrillator use.[32]

Acute Complications of Diabetes

Diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state (HHS) are the two most common life-threatening acute metabolic complications of DM.[6].

HHS is also a medical emergency, but typically occurs in the elderly and sometimes in young adults and teenagers as an initial presentation of T2DM. HHS has a higher mortality rate of up to 15% — that is significantly higher than mortality for DKA. The most serious complications of both HHS and DKA are cerebral edema and acute respiratory distress syndrome[33].

The hyperosmolar hyperglycemic state (HHS) is the most serious acute hyperglycemic emergency in patients with T2DM. Initial cases were reported as “unusual diabetic coma” characterized by severe hyperglycemia and glycosuria in the absence of Kussmaul breathing, with a fruity breath odour or positive acetone test in the urine. The incidence of HHS is estimated to be <1% of hospital admissions of patients with diabetes with mortality range between 10 and 20%, which is around 10 times higher than the mortality rate in patients with diabetic ketoacidosis (DKA)[34].

HHS is characterized by extreme elevations in serum glucose concentrations and hyperosmolality without significant ketosis. These metabolic derangements result from insulin deficiency with increased levels of counterregulatory hormones (glucagon, catecholamines, cortisol, and growth hormone). Hyperglycemia develops secondary to increased gluconeogenesis and accelerated conversion of glycogen to glucose (glycogenolysis) and by inadequate use of glucose by peripheral tissues, primarily muscle. Hepatic glucose production represents the major pathogenic disturbance responsible for hyperglycemia. As the glucose concentration and osmolality of extracellular fluid increase, an osmolar gradient is created that draws water out of the cells. Glomerular filtration increases leading to glucosuria and osmotic diuresis which prevents the development of severe hyperglycemia as long as the glomerular filtration rate is normal. With continued osmotic diuresis, hypovolemia eventually develops culminating in progressive decline in glomerular filtration rate and worsening hyperglycemia.

Higher hepatic and circulating insulin concentration as well as lower glucagon are present in HHS compared with patients with ketoacidosis the higher circulating ratio of insulin/glucagon in patients with HHS prevents ketogenesis and the development of ketoacidosis. hyperosmolarity is also believed to inhibit lipolysis and free fatty acid release from adipose tissue[35].

Diagnostic criteria of HHS as recommended by the American Diabetes Association (ADA) and international guidelines include a plasma glucose level >600 mg/dL, plasma effective osmolarity >320 mOsm/L, and an absence of significant ketoacidosis. Many patients present without significant decline in the level of consciousness (less than one-third of patients present with coma) and some patients can present with mild to moderate degrees of ketosis. Up to 20% of patients presenting with severe hyperglycemia and hyperosmolarity are reported to have combined features of HHS and DKA according to some studies[36].

DKA

Diabetic ketoacidosis (DKA) is a serious acute metabolic complication of diabetes mellitus. Although DKA most often occurs in patients of T1DM, patients with T2DM may also present with DKA. From the time of the original description of DKA by Dreshfeld in 1866 until the discovery of insulin in 1922 the mortality rate was almost 100%. By 1932 however the mortality rate was down to 29% and to 5 % by 1960. The mortality rate reported by National Institutes of Health was 10% before 1983[23].

The actual incidence rate for DKA is difficult to establish, but population based studies have reported ranges from 4.6 to 8 cases per 1000 patient with diabetes, DKA rates may be between 5 to 7% in individuals aged <18 years . The Global incidence of DKA is influenced by various factors and is reflective of the prevalence of diabetes in the population[37].

The symptoms and physical signs of DKA usually develop over 24 hour and generally include nausea, vomiting, thirst, polyurea, abdominal pain and shortness of breath a physical finding include tachycardia, dehydration, hypotension, tachypnea, Kassaumaul breathing with Respiratory distress, abdominal tenderness, acute pancreatitis, lethargy, obtundation, cerebral edema and possibly coma.

DKA consists of the biochemical triad of hyperglycemia, ketonemia and metabolic acidosis resulting from absolute or relative insulin deficiency in the presence of an increase in counter regulatory hormones (glucagon, catecholamines, cortisol, and growth hormone). Although DKA is typically characterized by hyperglycemia, euglycemic DKA can be seen in patients with T1DM who were vomiting, fasting or had been treated with insulin prior to presentation, pregnancy and in patient taking (SGLT2) inhibitors. Hyperglycemia develops due to three main mechanisms enhanced gluconeogenesis, increased glycogenolysis and impaired glucose utilization by peripheral tissues. The combination of insulin deficiency and increased hormones results in increased lipolysis, i.e. release of free fatty acids into the circulation and to hepatic fatty acid oxidation to ketone bodies (β-hydroxybutyrate and acetoacetate), leading to ketonemia and metabolic acidosis[38].

Common precipitating factors for DKA are omission/ improper dose of insulin, acute medical, surgical and obstetrical emergencies. Younger age at diabetic onset, poor baseline glycaemic control, elevated HbA1c, substance abuse, omission/error of insulin administration, acute illness, alcohol excess are all risk factor for recurrent admissions with DKA..

DKA remains an important life threatening complication in DM contributing to significant mortality and morbidity. A recent study from Italy in 2019 concluded that DKA is still prevalent had increased in incidence despite increased awareness levels[39].

In a Study the frequency of newly diagnosed T1DM Patients with presentation at diagnosis of DKA was 29 %, in comparison to the 38% rates 15 years ago. DKA is characterised by the triad of hyperglycemia (blood glucose >250 mg/dl), metabolic acidosis (arterial pH <7.3 and serum bicarbonate <18 mEq/L) and ketosis[39].

Pathophysiological mechanisms in DKA

Glucose metabolism in DKA shifts towards glycogenolysis and gluconeogenesis from glucose utilization. The mechanism involves insulin deficiency with glucagon excess which reduces the hepatic fructose 2,6 bisphosphate in turn reducing the activity of phosphofructokinase and fructose 1,6-bisphosphonate. Glucagon excess also decreases the activity of pyruvate kinase, while insulin deficiency increases the activity of phospheonal pyruvate carboxykinase. This shifts the pyruvate towards glucose synthesis and away from the glycolysis. The increased levels of glucagon and catecholamine in the face of low insulin levels promote glycogenolysis. Insulin deficiency also impairs GLUT 4 glucose transporter, responsible for skeletal muscle glucose uptake.

Severe insulin deficiency correlates with increased activity of the hormone-sensitive lipase in the adipose tissue, which breakdown triglycerides into glycerol and free fatty acids. Free fatty acids are oxidized to ketone bodies stimulated by glucagon in the liver. Increased glucagon lowers hepatic levels of malonyl coenzyme A (CoA), the first rate-limiting enzyme in de novo fatty acid synthesis. Decreased levels of malonyl-CoA stimulates the rate-limiting enzyme of ketogenesis (carnitine O-palmitoyltransferase 1, liver isoform - CPT1-L), which promotes transesterification of fatty acyl carnitine and oxidation of free fatty acids to ketone bodies (acetoacetate and β-hydroxybutyrate).

Thus, production of ketone bodies is accelerated as a result of increased fatty acyl CoA and CPT1-L activity The metabolism and the clearance of the ketones is also impaired in DKA. Ketone bodies are strong acids causing metabolic acidosis. Both hyperglycaemia and high levels of ketone bodies cause osmotic diuresis, leading to hypovolaemia and decreased glomerular filtration rate, further aggravating hyperglycemia[27].

1 Diagnostic criteria and typical total body deficits of water and electrolytes in diabetic ketoacidosis.

Particulars	Mild	Moderate	Severe
Diagnostic criteria and classification			
Plasma glucose (mg/dl)	> 250	> 250	> 250
Arterial Ph	7.25–7.30	7.00- < 7.24	< 7.00
Serum bicarbonate (mEq/L)	15–18	10- < 15	< 10
Urine ketone	Positive	Positive	Positive
Serum ketone	Positive	Positive	Positive
Effective Serum Osmolality	Variable	Variable	Variable
Anion Gap	> 10	> 12	> 12
Mental Status	Alert	Alert/Drowsy	Stupor/Coma
Typical deficits			
Total Water (L)	6		
Water (ml/kg)δ	100		
Na + (mEq/kg)	7–10		
Cl- (mEq/kg)	3–5		
K + (mEq/kg)	3–5		
PO4 (mmol/kg)	5–7		
Mg ++ (mEq/kg)	1–2		
Ca ++ (mEq/kg)	1–2		

Investigations for the precipitating condition are imperative in DKA, as mortality is usually related to the associated co-morbidity. Omission or inadequate dosing of insulin and infection are the most common precipitants of DKA. Intercurrent illnesses such as cerebrovascular accident, pancreatitis, myocardial infarction, trauma, and drugs are also known to trigger DKA. Drugs that affect carbohydrate metabolism - corticosteroids, thiazides, and sympathomimetic agents e.g. terbutaline, amphetamines and atypical antipsychotic agents also precipitate DKA in susceptible individuals (40). Emerging data suggests Sodium-Glucose Co-transporter 2 (SGLT2) inhibition may increase the risk of DKA, prompting the FDA to issue a warning in this regard in May 2015(41). The exact mechanism of DKA in subjects treated with SGLT2 is not known with certainty; proposed mechanisms include reduced insulin, glucagon secretion and decreased excretion of ketone bodies. In young patients with T1DM, psychological problems complicated by eating disorders may be a contributing factor in upto 20% of recurrent ketoacidosis. Other factors explored in younger patients include fear of weight gain, rebellion against authority and the stress of chronic disease. Cocaine use was reported as an independent risk factor for recurrent DKA in a retrospective study of over 200 cases of DKA from the United States (42). Another study of a large cohort of DKA patients observed that substance abuse including alcohol and cannabis were associated with recurrent episodes[(43)]. Additionally, mechanical problems with

continuous subcutaneous insulin infusion devices (CSII) has also been associated with DKA (30). Finally, DKA has also been reported as the initial manifestation of previously undiagnosed endocrine conditions like acromegaly and pheochromocytoma[38].

A study of DKA admissions at a tertiary centre at Chandigarh, India concluded that the severity, complications, morbidity and mortality associated with DKA is far higher than that reported in the West. The root causes analysis of which revealed that parental ignorance, lower socioeconomic status, missed or late diagnosis due to lack of clinical experience and lack of facilities at peripheral healthcare setup were important factors.

Another study evaluating the outcomes and severity in 1527 patients of diabetes of which 63 had DKA, concluded that the ADA classification of severity correlated well with the duration of stay, cost of care, ICU admission and mortality. They suggested that the classification system could be valuable tool in predicting the outcome. The researchers also observed that the infections were the most common precipitating factors accounting for 58% among those with DKA[44].

A retrospective study from a tertiary care centre of northern India investigated the precipitating and prognostic factors, concluded that noncompliance was a major precipitating factor followed by infections. Mean duration of stay at the hospital being 8.2 days and low hemoglobin and high pulse rates were independent predictors of longer stay[45].

Brandstaetter et al studied recurrent DKA and found younger age at diabetic onset, poor baseline glycaemic control, elevated HbA1c, substance abuse were associated with recurrent admissions. Other factors were omission /error of insulin administration, acute illness, alcohol excess[46].

Bradford et al defined six potential risk factors for DKA readmissions in the United states age <35, history of depressions, HbA1c >10.5%, substance or alcohol abuse history, ethnic minority status and self-pay and publically funded insurance[47]. Randal et al concluded that insulin discontinuation was most common in first time (56%) as well as recurrent admissions (78%), next most common cause being medical illness. They also found that the patients with multiple admissions had longer stay, had developed diabetes at a younger age, were leaner and had a higher rate of receiving insulin education. However there was no significant increase in the knowledge the meaning of HbA1c or its control as the number of admissions increased[48].

A retrospective study of DKA from Thailand observed no difference in the type of diabetes, duration of diabetes and severity of DKA when compared between the patient with first episodes and those with recurrent episodes. They concluded that omission of insulin most common risk factor in T1DMwhile sepsis was more common in T2DM. Mean length of stay was 3 days, 76.3% patients discharged were within 5 days.

A study from Lucknow India, published in 2016 indicated that significant predictors for outcome included male sex, total leukocyte count, Acute Physiology and Chronic Health Evaluation II (APACHE II) score[49].

A study in 2017, found that appropriate education and counselling diminished impact of diabetes, improves quality of life and help to achieve desired HbA1c level in poorly controlled T1DM patients[50].

Treatment of DKA

Once the patient arrives in the emergency the patient should be initiated on fluids with saline 0.9% is started at 15 to 20 mL per kg per hour, or 1 L per hour initially. Fluid status, cardiac status, urine output, blood pressure, and electrolyte level should be monitored. After patient stabilizes, fluids are lowered to 4 to 14 mL per kg per hour, or 250 to 500 mL per hour. Once the corrected sodium concentration is normal or high (greater than 135 mEq per L [135 mmol per L]), the solution should be changed to saline 0.45%. Dextrose is added when the glucose level decreases to 200 mg per dL[6].

Insulin should be added to intravenous fluids one to two hours after fluid initiation. An initial bolus of 0.1 units per kg should be given with an infusion of 0.1 units per kg per hour. Some studies suggest bolus dose is unnecessary as long as an adequate infusion of insulin is maintained.[51] An infusion of 0.14 units per kg per hour is recommended in the absence of a bolus. Glucose level should decrease by about 50 to 70 mg per dL (2.77 to 3.89 mmol per L) per hour, and the insulin infusion should be adjusted to achieve this goal. Once glucose level decreases to 200 mg per dL, the insulin infusion rate is decreased to 0.05 to 0.1 units per kg per hour, and dextrose should be added to the intravenous fluids to maintain a glucose level between 150 and 200 mg per dL (8.32 and 11.10 mmol per L). In uncomplicated DKA subcutaneous Insulin can be used(52). A study reported a randomized trial of 45 persons, 15 received insulin aspart (Novolog) hourly, 15 received insulin aspart every two hours, and 15 received standard intravenous infusion of regular insulin and similar physiologic and clinical

outcomes were seen all three groups.[53] Subcutaneous administration of rapid-acting insulin analogues, such as lispro (Humalog), every hour (bolus of 0.3 units per kg, then 0.1 units per kg) or two hours (bolus of 0.3 units per kg, then 0.2 units per kg) as a reasonable alternative to intravenous regular insulin for treating uncomplicated DKA.

DKA is resolved when the glucose level is less than 200 mg per dL, the pH is greater than 7.3, and the bicarbonate level is 18 mEq per L or higher[6].

Once these levels are achieved and oral fluids are tolerated, the patient can be started on an insulin regimen that includes an intermediate- or long-acting insulin and a short- or rapid-acting insulin. When intravenous insulin is used, it should remain in place for one to two hours after subcutaneous insulin is initiated. Persons known to have diabetes can be started on their outpatient dose, with adjustments to improve control. Those new to insulin should receive 0.5 to 0.8 mg per kg per day in divided doses.

Potassium

Potassium is depleted in patients with DKA and is expected to further fall with the onset of treatment and should be closely monitored. If the potassium level is between 3.3 and 5.2 mEq per L (3.3 and 5.2 mmol per L) with normal urine output, the replacement should be started at 10 mEq per hour but the replacement can be increased to 20 to 30 mEq potassium per hour. If the potassium level is lower than 3.3 mEq per L, insulin should be withheld and the potassium should be repleted first. With potassium level is greater than 5.2 mEq per L, insulin therapy without potassium replacement can be initiated, and serum potassium levels should be checked every two hours. Some guidelines recommend potassium replacement with potassium chloride, whereas others recommend combining it with potassium phosphate or potassium acetate although there is a lack of concrete clinical trials supporting the recommendations.

Bicarbonate

Current American Diabetes Association guidelines recommend bicarbonate replacement in persons with a pH lower than 6.9 using 100 mEq of sodium bicarbonate in 400 mL of sterile water with 20 mEq of potassium chloride at a rate of 200 mL per hour for two hours. This should be repeated every two hours until the patient's pH is 6.9 or greater. Studies fail to support the use of bicarbonates in patients with pH >6.9 although theoretical benefit of avoidance of neurological and cardiac complications exist[54].

Phosphate deficiency develops with treatment of DKA and can manifests as muscle fatigue, rhabdomyolysis, hemolysis, respiratory failure, and cardiac arrhythmia, replacement is recommended when the phosphate level falls below 1.0 mg per dL (0.32 mmol per L) Replacement is done by adding 20 to 30 mEq of potassium phosphate to the intravenous fluid.

DKA can cause a drop in magnesium, which can result in paraesthesia, tremor, muscle spasm, seizures, and cardiac arrhythmia and it should be replaced if it falls below 1.2 mg per dL or once symptoms of hypomagnesemia develops[(54)].

MATERIALS AND METHODS

PRIMARY OBJECTIVES

1. To determine the clinical, biochemical and severity profile of adult patients presenting with DKA to AIIMS, Jodhpur
2. To determine the common precipitating factors, risk factors, and outcome for DKA in patients presenting to AIIMS Jodhpur

STUDY SETTING: Patients attending the Emergency and patients admitted in the Department of Internal Medicine and Endocrinology at all India Institute of Medical Sciences, Jodhpur.

STUDY DURATION: From January 2020 to July 2021

STUDY DESIGN: The study was conducted after seeking written informed consent from the study participants. Patients were labelled to have DKA if they satisfied the criteria proposed by the ADA of hyperglycemia (blood glucose >250 mg/dl), metabolic acidosis (arterial pH <7.3 and serum bicarbonate <18 m Eq/L) and ketosis. And the patients were further subclassified as Severe DKA if the pH at presentation was <7.0 with Bicarbonates <10; Moderate if pH was between 7.0-7.24 with bicarbonate between 10-15 and Mild if the pH at presentation was >7.25. On the patient visit hospital baseline assessment of various variables were done which includes:

1. **Socio-demographic:** Name, age and gender, residence, socio-economic status, education of patient/parents.

2. **Clinical:** Duration of diabetes, details and duration of treatment, previous hospitalizations with DKA, symptoms at presentation, general physical examination, and systemic examination.

3. **Investigations:** All patients underwent the following investigations:

a. All patients underwent ABGs, Urinary ketones and Blood glucose testing as required for standard clinical care.

b. Baseline hematological and biochemical assessment as per routine clinical care including Complete Blood count, serum electrolytes, blood glucose, Erythrocyte sedimentation rate.

Kidney Function Test, Chest X-ray, Urine routine/microscopy, Urine culture, HbA1c, ABG, Serum electrolytes, ECG, Blood cultures. 24hour urinary protein was done after the resolution of DKA.

For the assessment of complications Fundoscopy was performed by the ophthalmology department and were screened in our department. Diabetic neuropathy was assessed clinically and for selected patients NCS was preformed.

STUDY PARTICIPANTS

Inclusion Criteria: Patient's age 18 and above having DKA defined as i.e., Blood glucose greater than 250 mg /dl, Arterial pH < 7.3, serum bicarbonate < 15 mmol/dl with positive urinary ketones the criteria were not kept robust as many patients were referred from outside hospital and had values not fulfilling the proposed diagnostic criteria.

Exclusion Criteria: All patients with DKA less than 18 years were not included in the study

Sampling and Sample Size: Using alpha value (probability of type I error) of 5% and prevalence of DKA 4.5% in patients getting admitted with DM from previous hospital-based studies, a sample size of 63 was calculated.(37)

STATISTICAL ANALYSIS

Statistical analysis was performed using software SPSS 25.0 (Check). Descriptive statistics are being presented as mean with standard deviation in case of continuous variables and number with number% in case of categorical variables. Risk factors for mortality, ICU admissions, prolonged hospital stay, severity, readmissions were determined by univariable logistic regression analysis followed by multivariable logistic regression with the desired outcome as the dependent variable and other risk factors as independent variables. The results of the multivariable analysis are being reported as adjusted Odds Ratio with 95% Confidence Intervals. A two tailed p value less than 0.05 is considered significant.

RESULTS

Gender Distribution

Out of the total 84 patients 43 were female and 41 were males with females accounting for 51.2 % of patients and males 48.8% (Table 1 & Fig.1).

Table 1: Gender distribution of study population (N=84)

Gender	Frequency
Female	43 (51.2%)
Male	41 (48.8%)
Total	84 (100%)

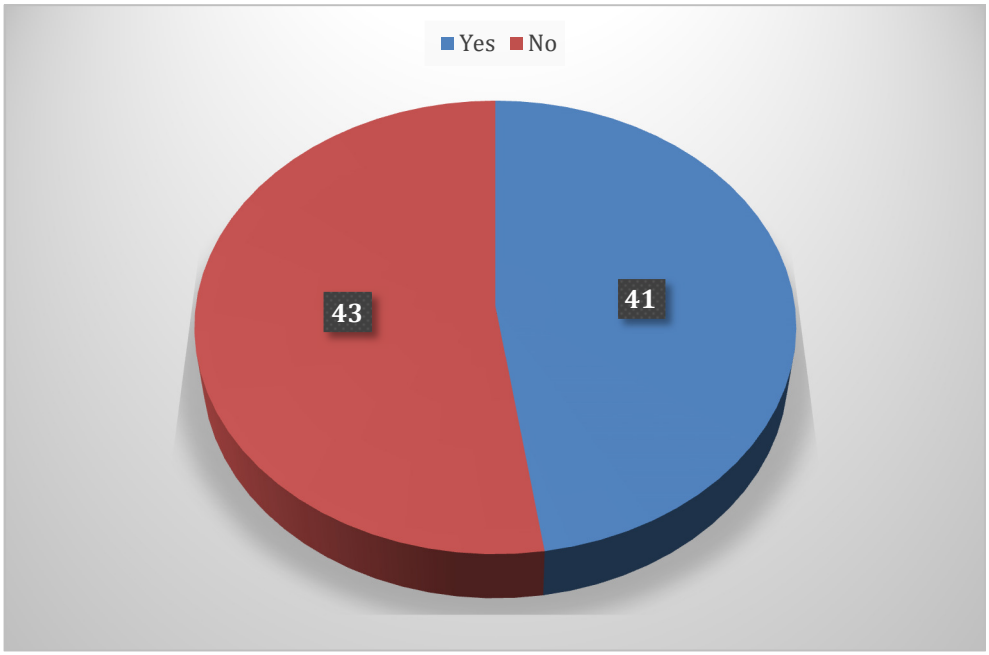

Fig.1: Gender distribution of the study population (N=84)

Age Distribution

The patients were divided into following age groups 18-25 yrs., 26- 35 yrs., 36-45 yrs., 46-55 yrs., 56-65 yrs., > 65 yrs. and most patients belonged to the 18–25-year age group followed by 26- 35 and 46- 55-year age groups. Only 6 patients belonged to the >65 yrs. age group category (Table 2 & Fig. 2).

Table 2 : Age Distribution in the study population (N=84)

Age Group	Frequency
18-25	25 (29.8%)
26-35	14 (16.7%)
36-45	12 (14.3%)
46-55	14 (16.7%)
56-65	13 (15.5%)
>66	6 (7.1%)
Total	84 (100%)

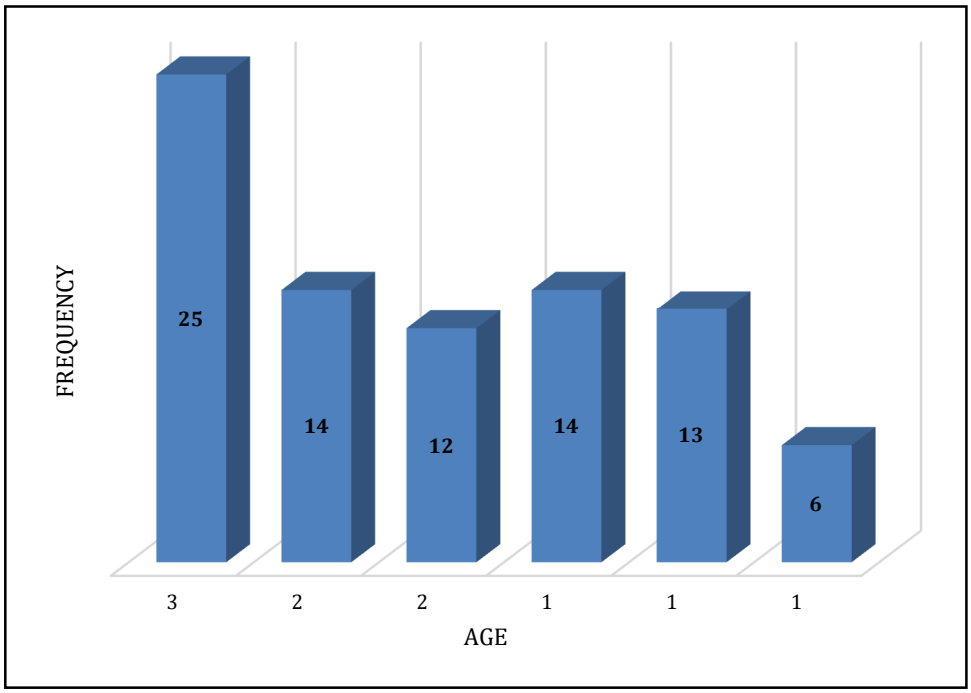

Fig. 2 : Age distribution of our population in Bar chart form (N=84)

Severity of DKA

Out of the 84 patients presenting to the emergency department, 43 patients belonged to the moderate category while 20 patients belonged to the severe category

Table 3 : Severity of DKA(N=84)

	Frequency
Mild	21 (25%)
Moderate	43 (51.2%)
Severe	20 (23.8%)
	84(100%)

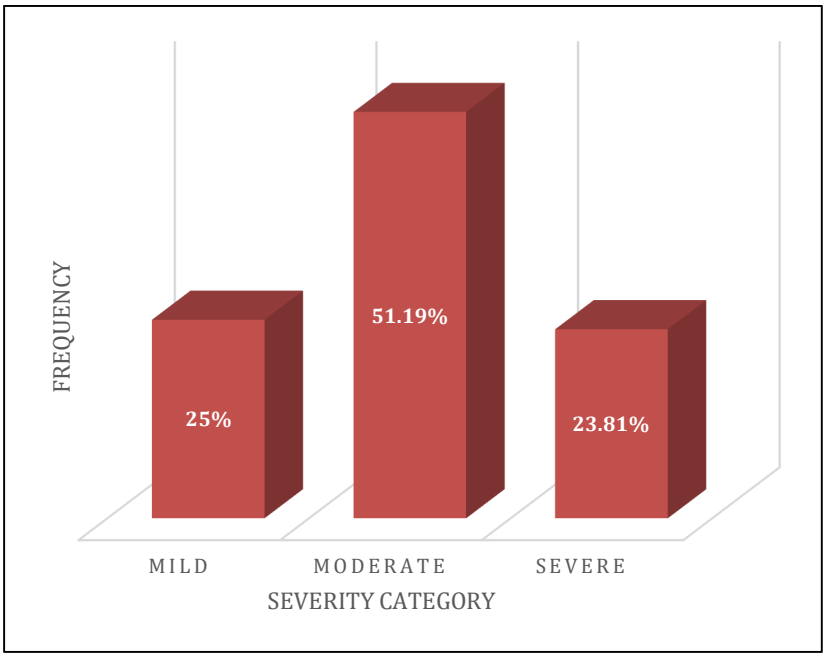

Fig. 3: Bar chart representation of DKA severity at presentation (N=84)

Distribution of type of diabetes in the study population

Forty patients had Type 1 Diabetes while 34 patients had type 2 diabetes. MODY and secondary accounted for 1 patient each. The diagnosis of MODY was established based on clinical history

Table 4 : Type of Diabetes of the patients presenting as DKA (N=84)

	Frequency
Type 1	40 (47.6%)
Type 2	34 (40.5%)
Latent autoimmune diabetes in adults	8 (9.5%)
Possible Maturity onset diabetes of the adults	1 (1.2%)
Secondary	1 (1.2%)
Total	84 (100%)

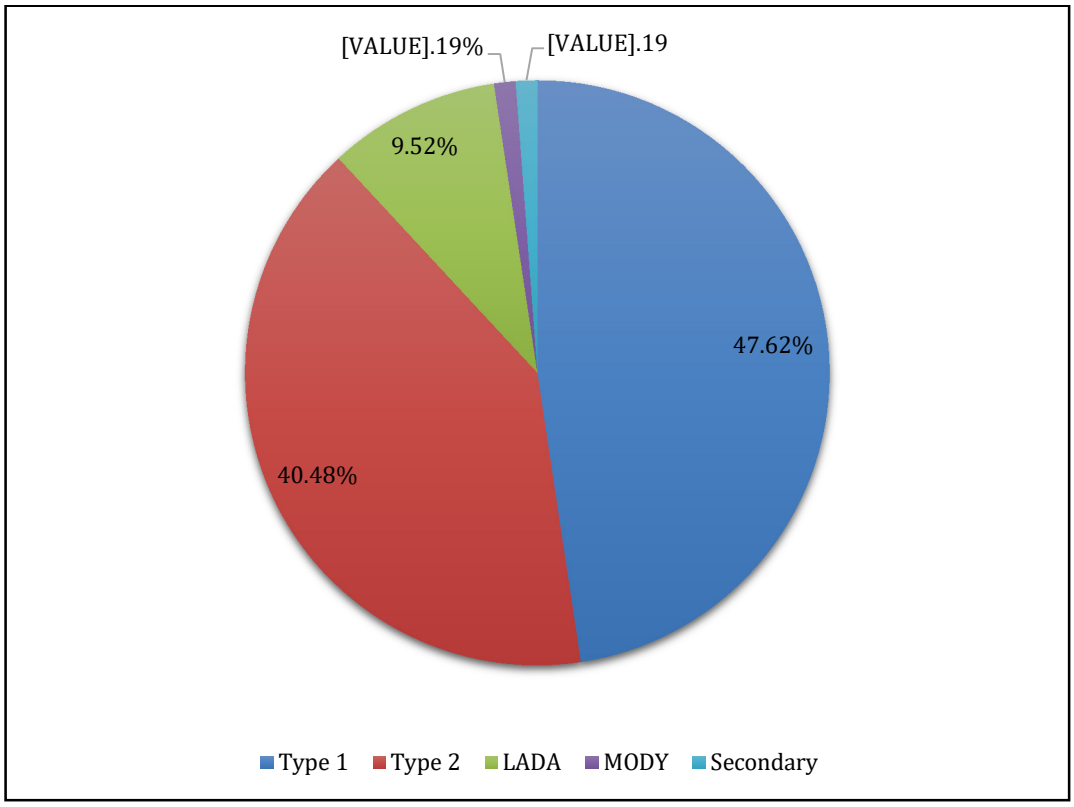

Fig 4: Pie chart representation of Type of Diabetes in our patients (N=84)

Duration of diabetes in the study population

A total of 16 patients were newly diagnosed at the time of presentation with DKA while the maximum patients had antecedent history of diabetes for last 6-10 years while only 4 patients had history of >20 years of diabetes.

Table: 5 Duration of Diabetes(N=84)

	Frequency
Newly Diagnosed	16 (19%)
<1 year	5 (6%)
2-5 year	21 (25%)
6-10 year	22 (26.2%)
11-20 year	16 (19%)
>20 years	4 (4.8%)

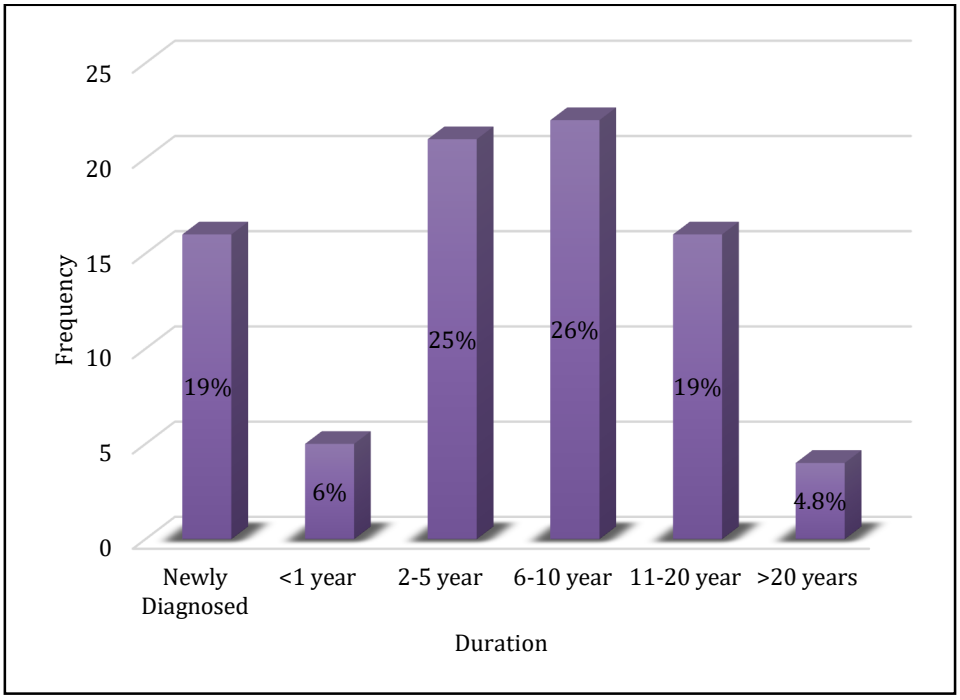

Fig.5: Bar chart representing duration of Diabetes (N=84)

SYMPTOMS AT PRESENTATION

Pain abdomen was the most common symptom at the onset of disease followed by the complaints of fever, shortness of breath and pain abdomen.

Other Symptoms

Other less frequently encountered complaints included-constipation, loose stools, fever, lower limb pain, abdominal swelling, burning micturition, altered mentation, generalised oedema, weakness

Rare encounters were for – Hematemesis, melaena, electrocution, chest pain and facial pain

Table 6: Symptoms at presentation(N=84)

Pain abdomen/Vomiting	17(20.2%)
Fever/Shortness of breath	7(8.3%)
Fever/burning micturition	3(3.5%)
Others	57(67.8%)
Total	84

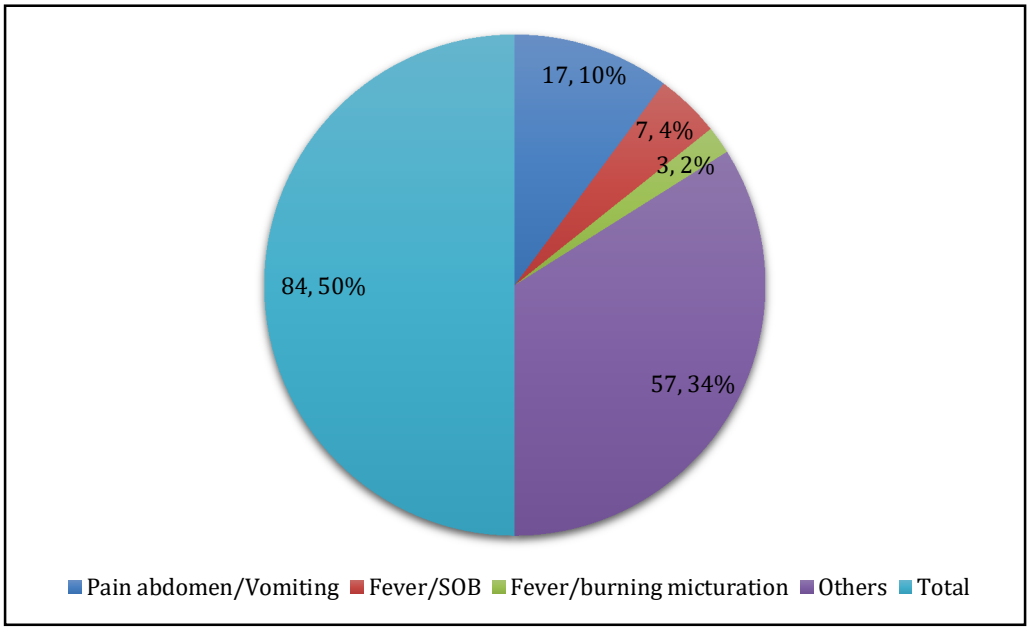

Fig 6: Pie charting demonstrating the symptomatology at presentation(N=84)

Previous history of DKA

43 out of 84 patients had a history of DKA while 41 patients did not have past history of DKA

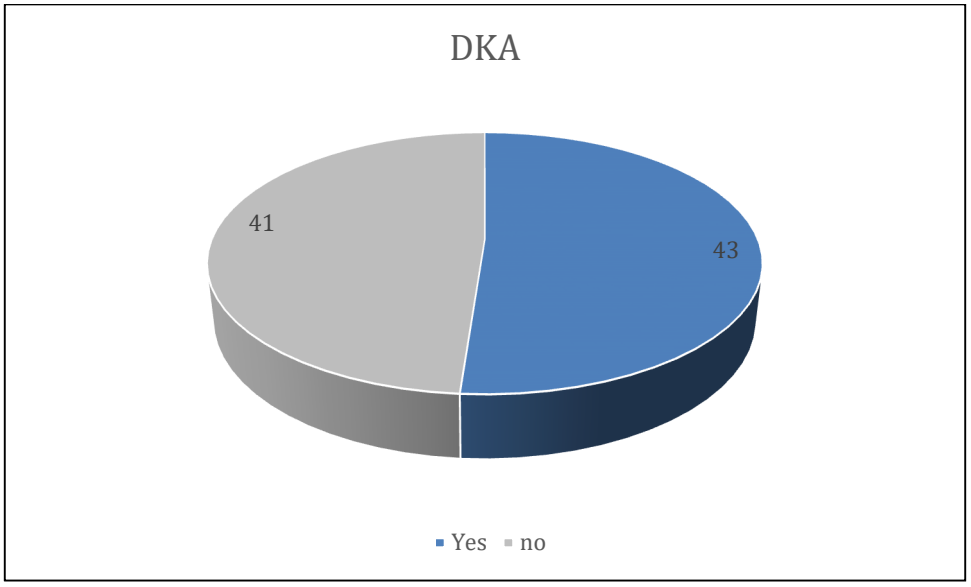

Figure 7: Pie chart illustrating prior DKA history in our patients

Diabetes Education

Forty (40) out of 84 patients had received Diabetic education while 3 patients did not receive any diabetes education despite having prior history of DKA

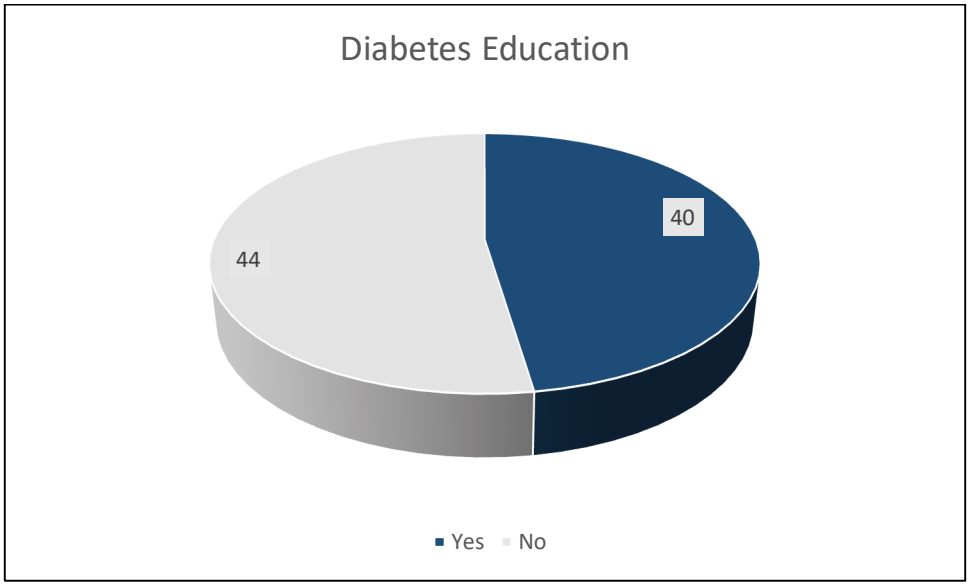

Figure8: Pie chart illustrating prior history of Diabetes Education(N=84)

Blood Glucose Monitoring at Home

Around 26 patients did not perform blood glucose at home during the current episode while 58 patients performed the blood glucose monitoring.

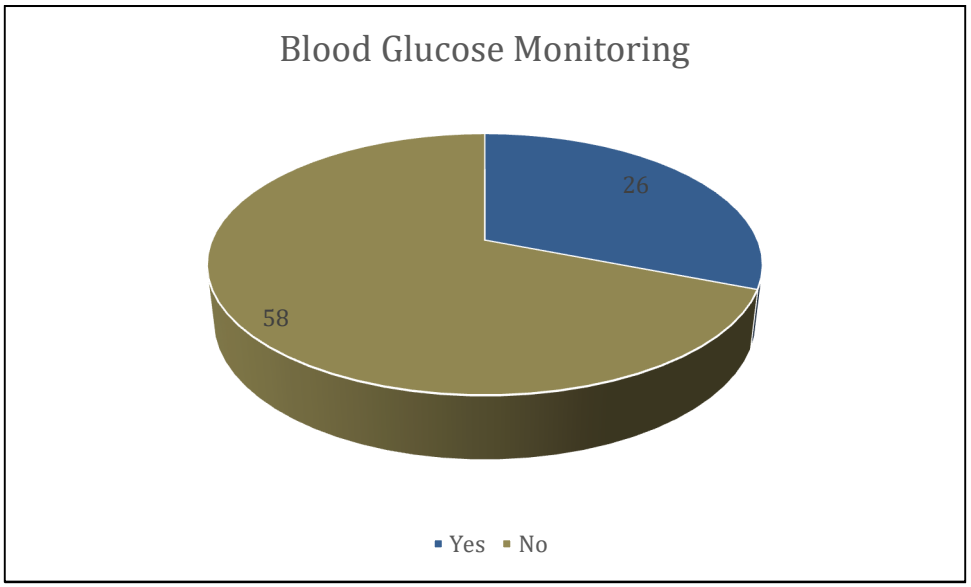

Fig. 9: Pie chart denoting blood glucose charting at home(N=84)

Total 21 out of 47 patients did not take their usual dose of insulin dose prior to the episode of DKA despite already being on insulin, one of the most common reasons given was the poor oral intake of the patient during the episode.

INSULIN DOSE FOR PATIENTS ALREADY ON INSULIN

Out of 47, 27 patients did not take their usual dose of insulin dose prior to the episode of DKA despite already being on insulin, one of the most common reasons given was the poor oral intake of the patient during the episode.

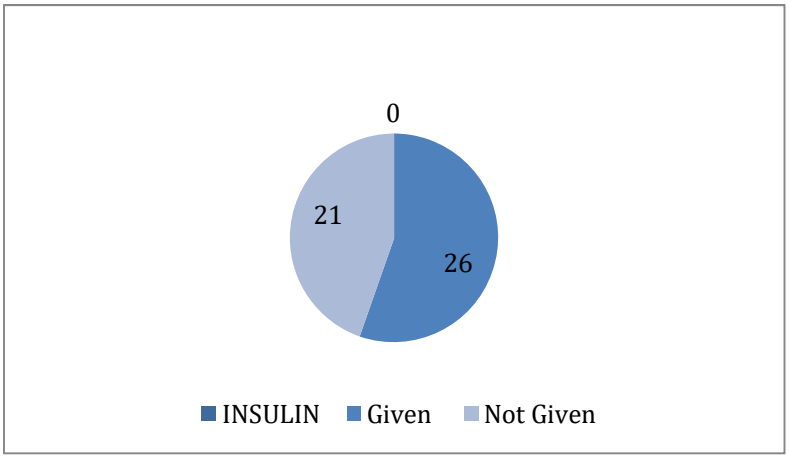

Fig 10: Pie chart illustrating Insulin use in patients already on Insulin(N=47)

OHA USE

Total 25 out of 84 patients were on OHA prior to development of DKA

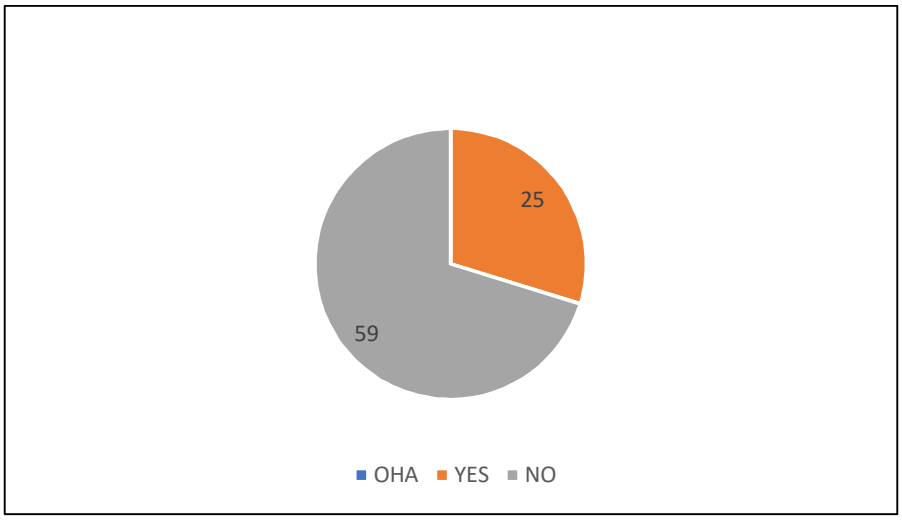

Fig 11: Pie chart illustrating OHA use prior to DKA episode (n=84)

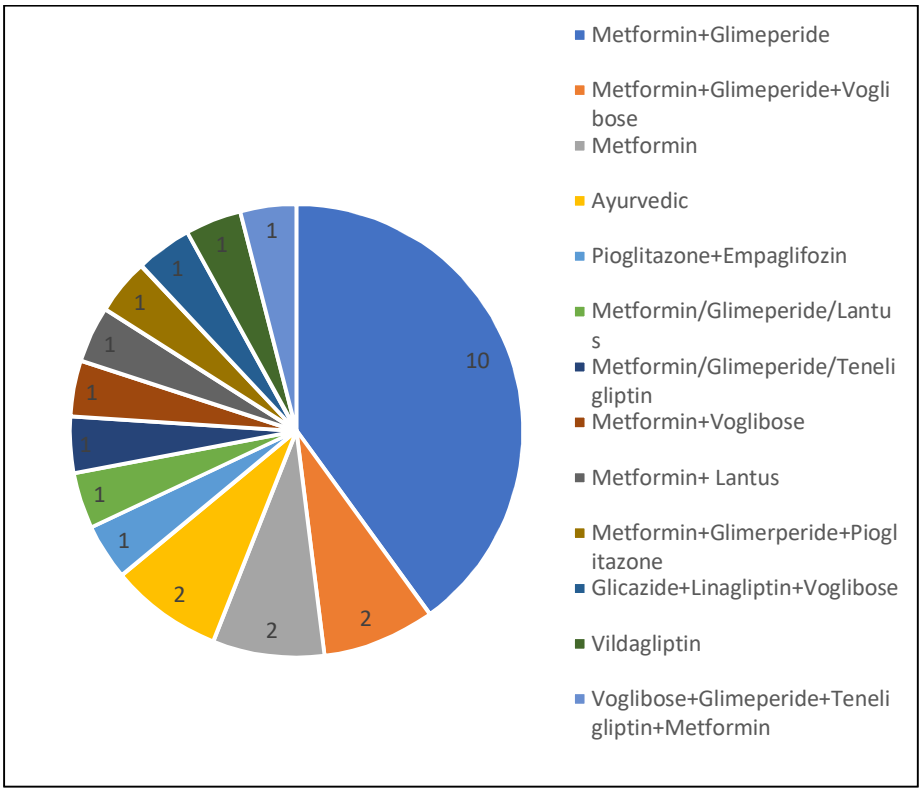

Fig. 12: Pie chart illustrating various OHAs taken at the time of DKA(N=25)

Table 7: OHA used prior to the episode of DKA (N=25)

OHA	
Metformin+Glimeperide	10
Metformin+Glimeperide+Voglibose	2
Metformin	2
Ayurvedic	2
Pioglitazone+Empaglifozin	1
Metformin/Glimeperide/Lantus	1
Metformin/Glimeperide/Teneligliptin	1
Metformin+Voglibose	1
Metformin+ Lantus	1
Metformin+Glimerperide+Pioglitazone	1
Glicazide+Linagliptin+Voglibose	1
Vildagliptin	1
Voglibose+Glimeperide+Teneligliptin+Metformin	1
	25

Comorbidities

A total of 48 patients (57.1%) had comorbities with HTN being the most frequent. HTN present in 15 of the 84 patients (17.8%) other comorbidities included Coronary artery disease, Chronic kidney disease, Hypothyroidism, Hyperthyroidism

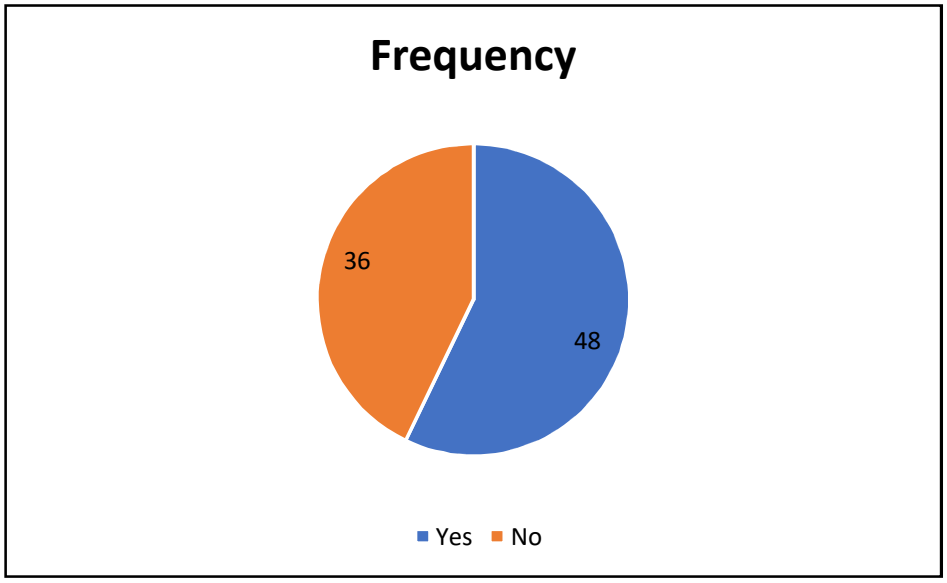

Fig. 13: Pie chart demonstrating Presence of comorbidities in our population(N=84)

Table 8 Comorbidities present in our study population(N=84)

Hypertension	15(57.1%)
Coronary artery disease	14(17.8%)
Chronic kidney disease	8((9.5%)
Hypothyroidism	7(8.3%)

Family history of Diabetes

Eight patients of type 1 DM had family history of diabetes while 5 of type 2 DM patients had family history. 1 patient of MODY gave a classical history of generational diabetes in the family.

Table 9: Family history in patients with various types of diabetes(N=19)

Type of Diabetes	Frequency
Type1	8
Type2	5
Latent autoimmune diabetes in adults	4
Possible Maturity onset diabetes in young	1
Secondary	1

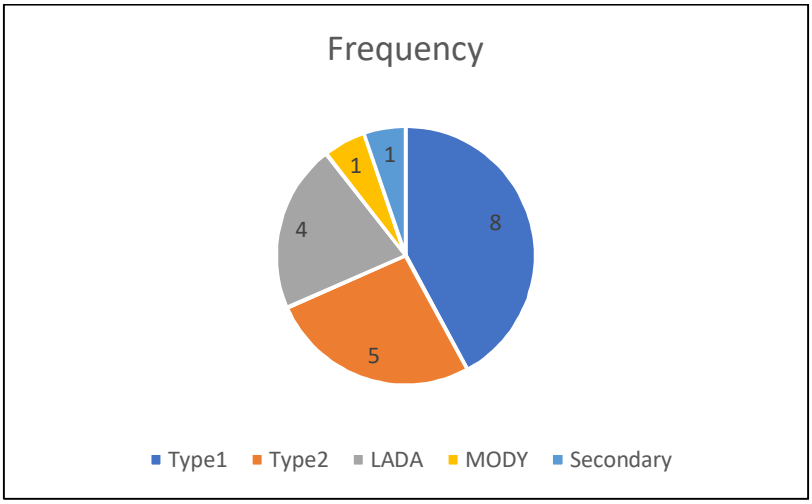

Fig. 14: Family history of diabetes in our population in various diabetes subtypes(N=19)

Symptoms at Onset

In general 29.76% patient gave a history of starvation due to poor oral intake as assessed by 24 hour diet recall method.

Table 10: Symptomatolgy at presentation(N=84)

S.no	Symptoms at presentation	Frequency
1	Starvation	25(29.76%)
2	Fever	30(36.24%)
3	Cough	13(15.48%)
4	Shortness of breath	28(33.33%)
5	Burning micturition	12(14.29%)

PRECIPITATING EVENT

UTI followed by drug noncompliance was the most common precipitating factor. Twelve patients had COVID as precipitating factor with 7 patients had LRTI as precipitating factor. The various precipitating factors included surgery/medicinal/drug intoxication and gynaecological emergency also rarely phenomena such as electrocution precipitating factor for DKA.

Table 11 Precipitating factors for DKA (N=84)

	Frequency
Infections	44(52.3%)
Non compliance	13(15.5%)
Newly diagnosed	5(6.0%)
Acute Pancreatitis	4(34.7%)
Acute coronary Syndrome	3(3.6%)
Acute cholelithiasis	1(1.2%)
Acute decompensated heart failure	1(1.2%)
Covishield vaccination	1(1.2%)
Cerebrovascular accident	1(1.2%)
Electrocution	1(1.2%)
Mucormycosis/Cerebrovascular accident	1(1.2%)
Opioid withdrawal	1(1.2%)
Seizures	1(1.2%)
Surgery	1(1.2%)
Treatment change	1(1.2%)
Drug induced Upper gastrointestinal bleed	1(1.2%)
Not known	3(3.6%)
Total	84

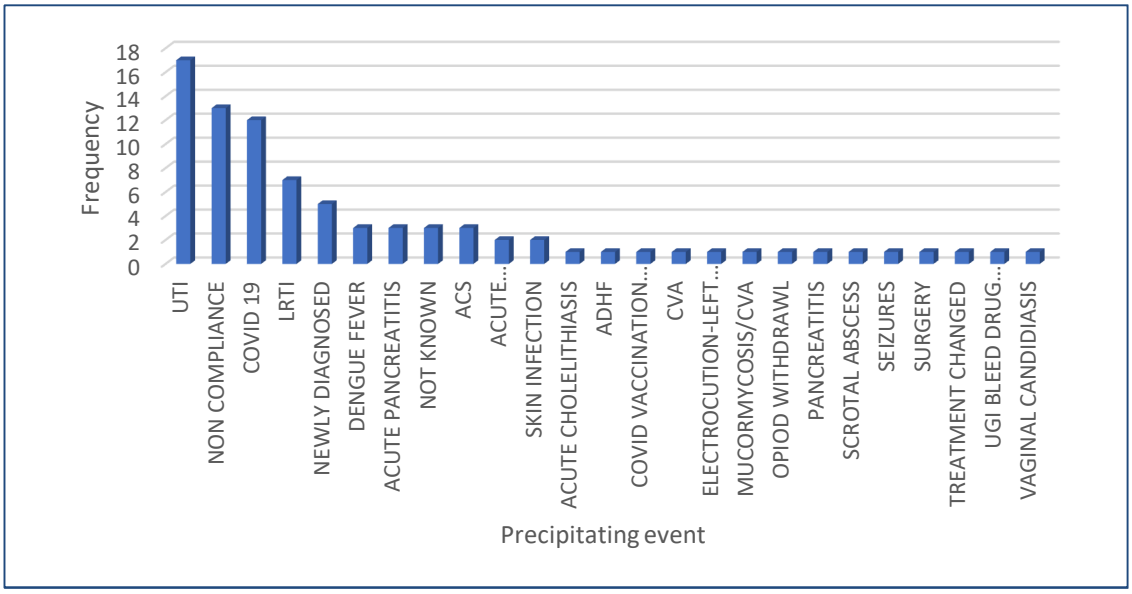

Fig. 15: Bar chart demonstrating the various precipitating factors and their frequency(N=84)

Chronic Complications

Out of the total patients screened 17 of the 77 screened patients had evidence of NPDR while 3 patients had PDR.

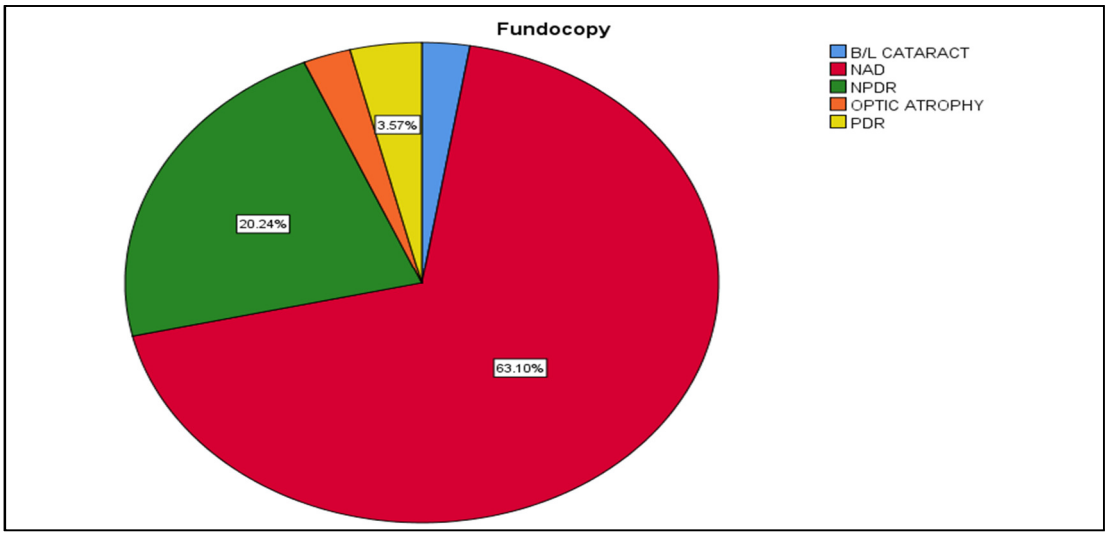

Fig. 16: Pie charting illustrating the frequency of various Fundoscopy findings(N=84)

Table 12 Fundocopy findings(N=84)

	Frequency
NAD	53(63.1%)
Non proliferative diabetic retinopathy	17(20.2%)
NOT DONE	7(8.3%)
Proliferative diabetic retinopathy	3(3.6%)
B/L CATARACT	2(2.4%)
OPTIC ATROPHY	2(2.4%)
Total	84

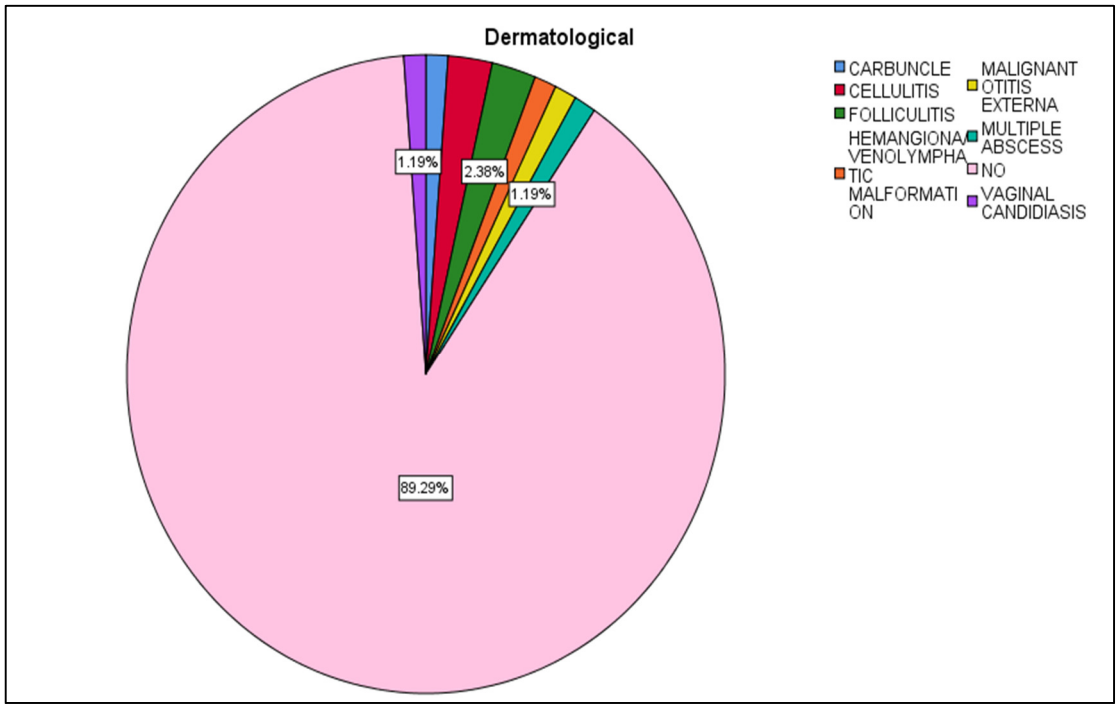

Fig. 17: Pie chart demonstrating Dermatological findings in our patients (N=84)

Table13: Various Dermatological findings in patients with DKA (N=84)

	Frequency
NO	75(89.3%)
CELLULITIS	2(2.4%)
FOLLICULITIS	2(2.4%)
CARBUNCLE	1(1.2%)
HEMANGIONA/VENOLYMPHATIC MALFORMATION	1(1.2%)
MALIGNANT OTITIS EXTERNA	1(1.2%)
MULTIPLE ABSCESS	1(1.2%)
VAGINAL CANDIDIASIS	1(1.2%)
Total	84

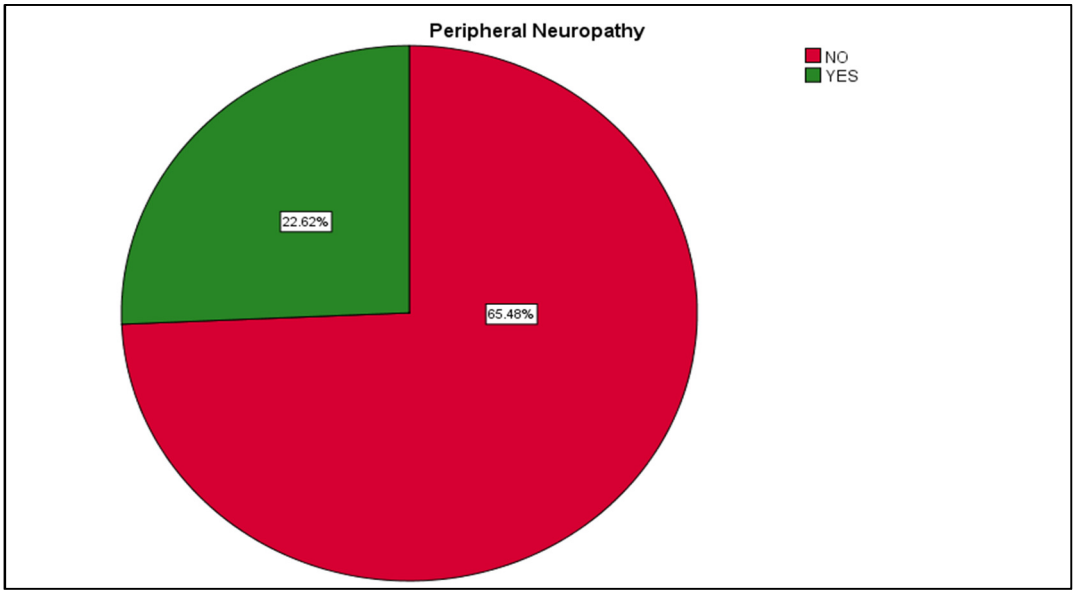

Fig. 18: Pie chart presence of Peripheral neuropathy in our population(N=84)

Table 14 Frequency of peripheral neuropathy in our patients(N=84)

Peripheral Neuropathy	**Frequency**
No	55(11.9%)
Yes	19(65.5%)
	84

Laboratory parameters at Presentation

The mean blood sugars were 442±113mg/dl (range 108-600 mg/dL)

Table 15 Blood Glucose, HbA1c, Urnary ketones at presentation(N=84)

		Blood Glucose (mg/dL)	HbA1c (%)	Urinary ketones
N	Valid	84	77	84
	Missing	0	7	0
Mean ± SD		442±113	12.1 ± 2.7	2.33 ± 1.01

Euglycemic DKA	3(3.5%)

Total of three patients presented with euglycemic DKA(3.5%) and had taken treatment from a outside hospital before being referred to our hospital.

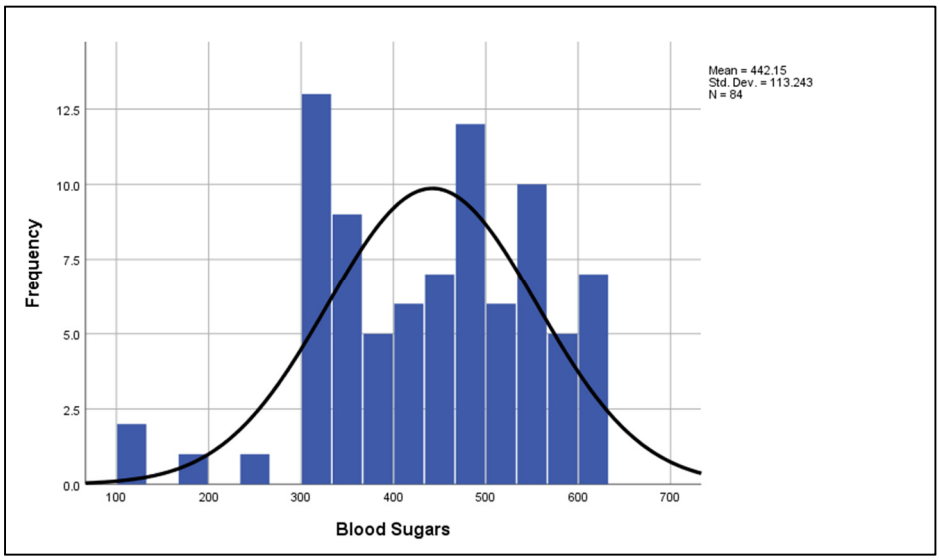

Fig.19: Frequency histogram of Blood sugar levels at presentation(N=84)

The mean HbA1c was 12.12 ± 2.67

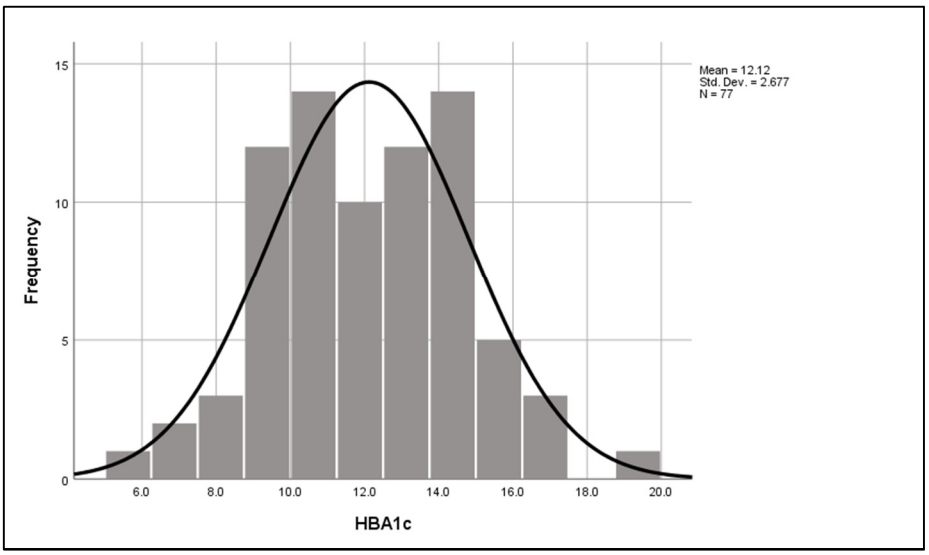

Fig. 20: Frequency histogram of HbA1c levels of patients presenting with DKA (N=84)

Table 16 Anion gap, Total leucocyte count, pH, Bicarbonate values at presentation(N=84)

	Anion Gap	TLC	pH	Bicarbonates
N		81	84	84
Valid	84			
		3	0	0
Missing	0			
Mean	21.3869	14.0809	7.1354	8.9143
Std. Deviation	6.17129	8.38305	.15573	4.59453

The average anion gap was 21.38 ±6.17 and the average pH was 7.12±.155 average bicarbonate value at presentation was 8.91±4.59

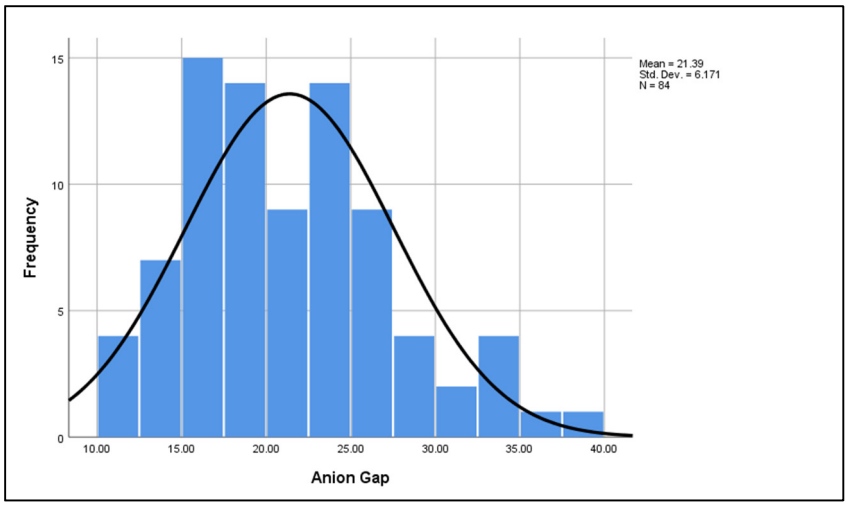

Fig. 21: Frequency histogram of Anion gap at presentation(N=84)

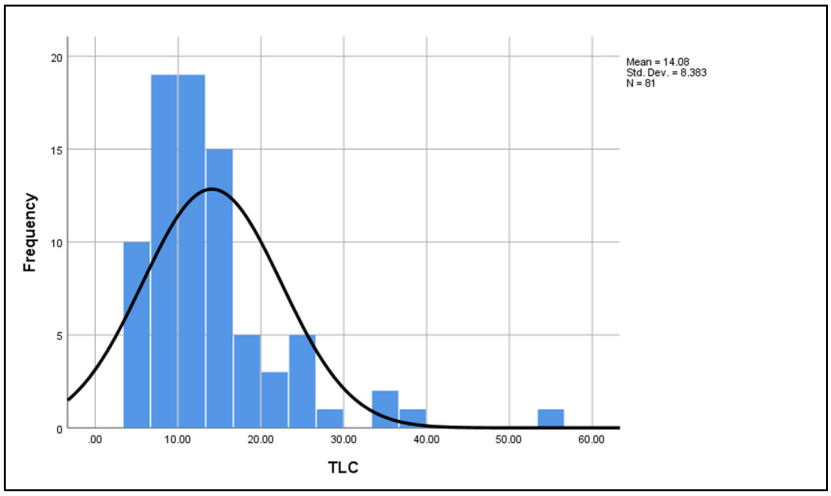

Fig. 22: Frequency histogram of TLC at presentation(N=84)

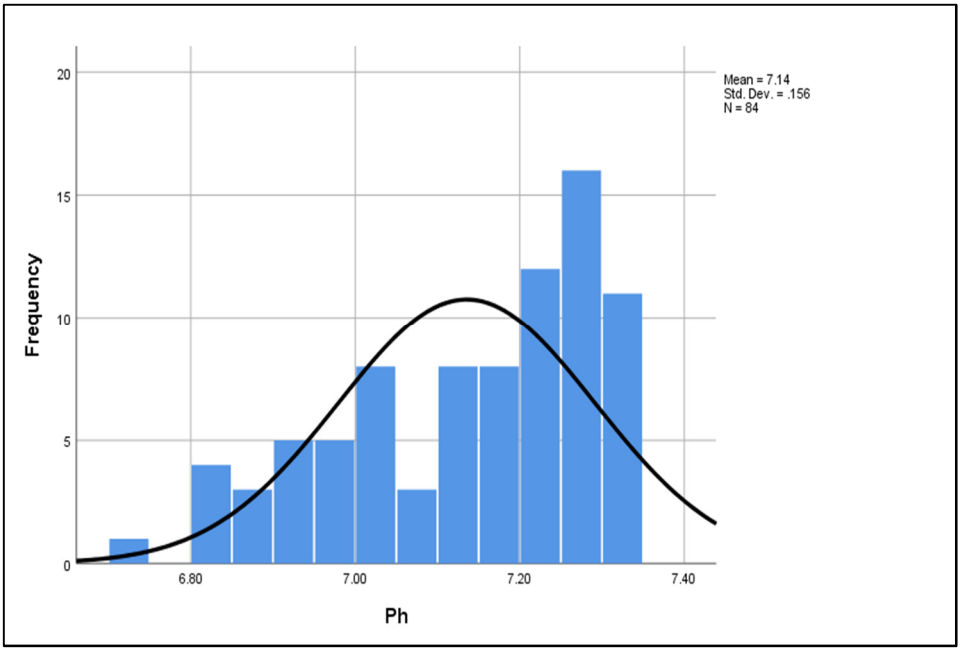

Fig. 23: Frequency histogram of pH at presentation(N=84)

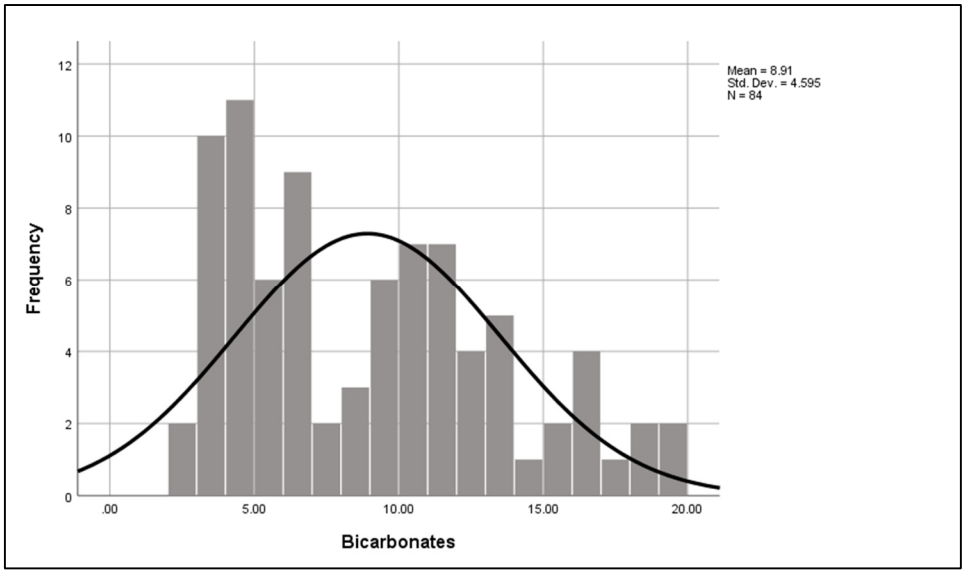

Fig 24: Frequency histogram of Bicarbonate levels at presentation(N=84)

Duration of Hospital Stay

The average hospital stay for the patients diagnosed to have DKA at presentation was 8.4±5.7 days

Table 17 Duration of hospital stay for patients admitted with DKA (N=84)

	N	Minimum	Maximum	Mean
Hospital stay	84	1	31	8.4±5.7

Urine culture and sensitivity

Table 18 Urine culture isolates (N=84)

	Frequency
Budding Yeast	2(2.4%)
Candida/Pseudomonas aeuroginosa	1(1.2%)
Eecherechia coli	6(7.1%)
Enterococcis	2(2.4%)
Klebsiella pneumonia	2(2.4%)
Mixed Growth	1(1.2%)
Pseudomonas aeuroginosa	1(1.2%)
Sterile	69(82.1%)
Total	84

A total 25 patients grew organisms on urine c/s out which the most frequently cultured was *Escherichia .coli*.

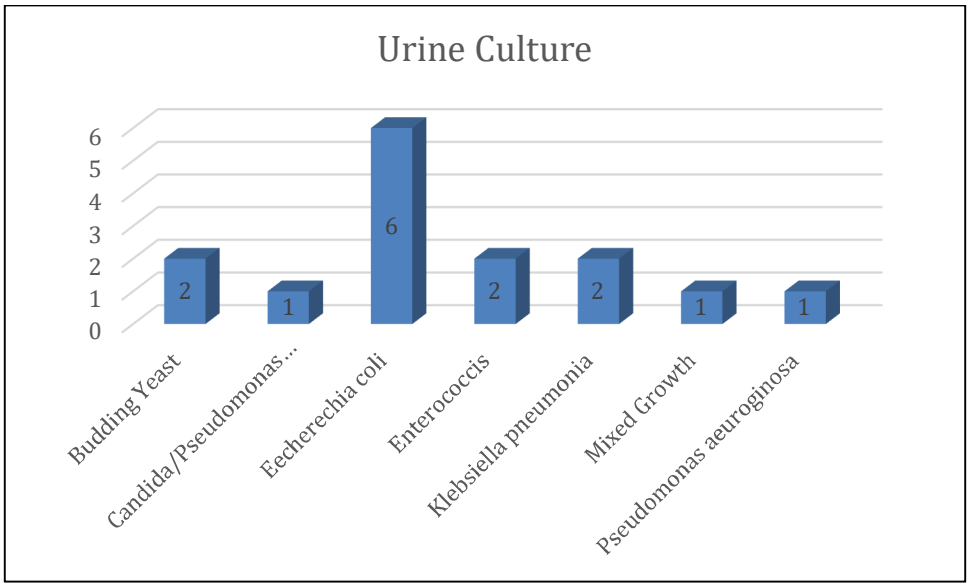

Fig. 25: Bar chart representation of Urine culture isolates(N=84)

Blood C/s

Table 19 Blood culture isolates(N=84)

	Frequency
STERILE	72 (85.7%)
Escherichia coli	2 (2.4%)
Acinetobacter baumannii	1 (1.2%)
Burkholderia cepacian	1 (1.2%)
Cougulase negative staphylococus aureus	1 (1.2%)
Gram negative bacilli	1 (1.2%)
Klebsiella sp.	1 (1.2%)
Staphylococus aureus	1 (1.2%)
Not done	4 (2.4%)
Total	84

From 12 blood cultures isolated for organisms with *E.coli* being the most frequent organism being isolated.

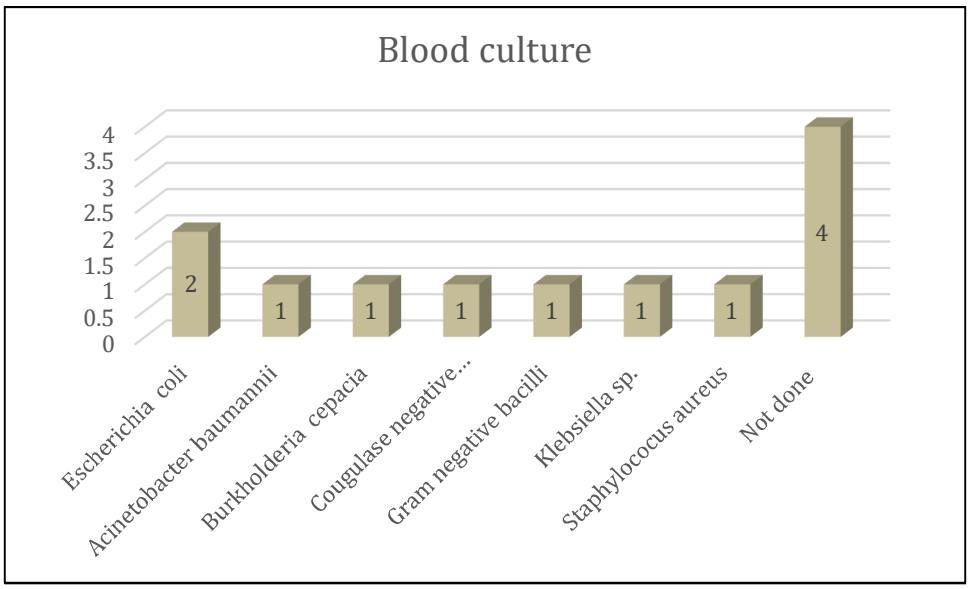

Fig. 26: Bar chart representation of Blood culture isolates(N=84)

ECG

Table 20 Electrocardiogram findings at presentation(N=84)

	Frequency
Sinus Tachycardia	18(21.4%)
Poor R wave progression	7(8.3%)
ST elevation myocardial infarction	4(4.8%)
Generalized ST segment depression	1(1.2%)
Hyperkalemic changes	1(1.2%)
Inverted T waves in V1-V3	1(1.2%)
Low Voltage electrocardiogram	1(1.2%)
Poor R wave progression, multiple ectopic	1(1.2%)
SVT	1(1.2%)
T wave inversion inV1-V6, prolonged QTc	1(1.2%)
T wave inversion V4-V6	1(1.2%)
NA	5(6%)
Total	84

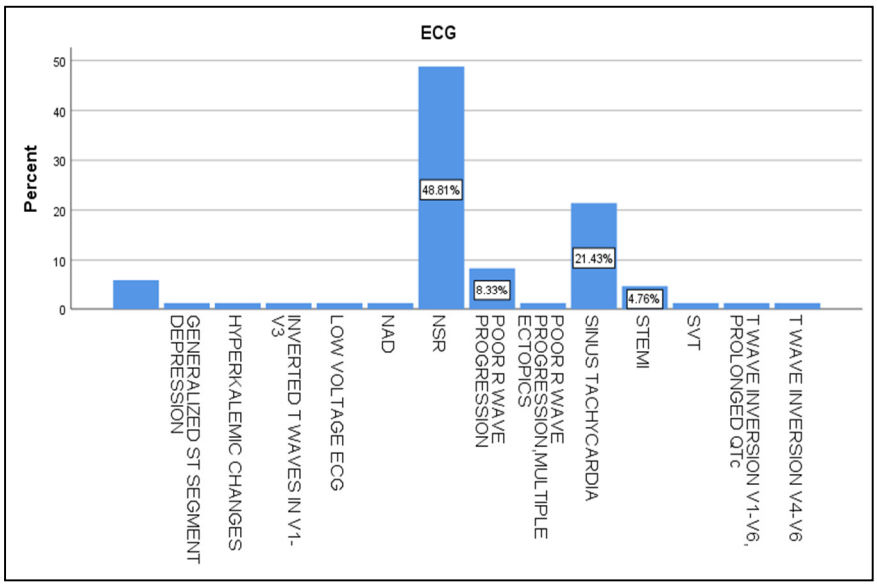

Fig. 27: Bar chart representation of ECG findings at presentation(N=84)

Table 21 24 hour urine protein findings in patients admitted with DKA(N=65)

	N	Minimum	Maximum	Mean
24 Urinary protein (mg/24 hour)	65	20	6540	794±973(+/-973.18)

A 24 hour urinary protein was done for 65 patients after 6 weeks after the patients were discharged from the hospital and the average urinary protein 794±973 mg/24 hours.

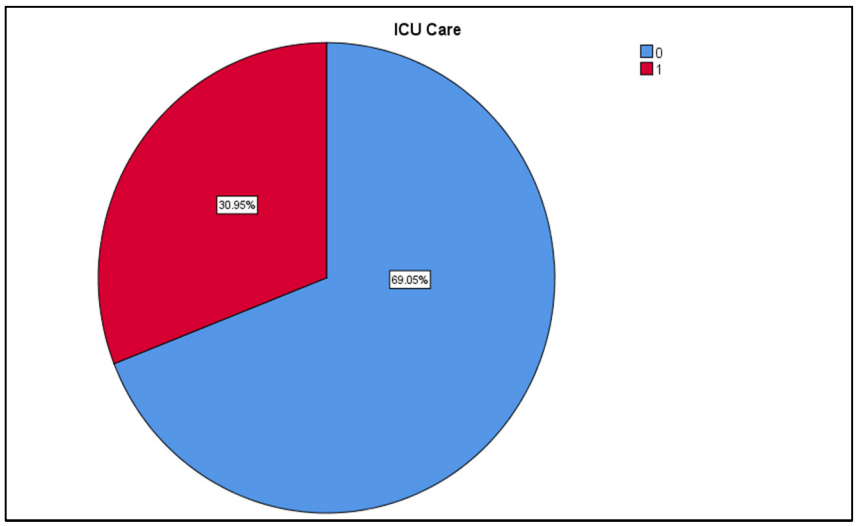

Fig. 28: Pie chart representation of ICU care requirement (N=84)

Table 22: ICU requirement in patients with DKA (N=84)

	Frequency
YES	26(31%)
Total	84

A total of 26 patients required ICU admission out of the 84 patients with a total of 13 patients admitted in view of COVID19

Table 23: Mean ICU stay in patients presenting with DKA (N=26)

	N	Minimum	Maximum	Mean
Duration of ICU stay	26	1	15	4.15± 3.48)

The mean hospital stay was 8.5 days± 5.715 and the average ICU stay was 4.15 days with SD of 3.48 days

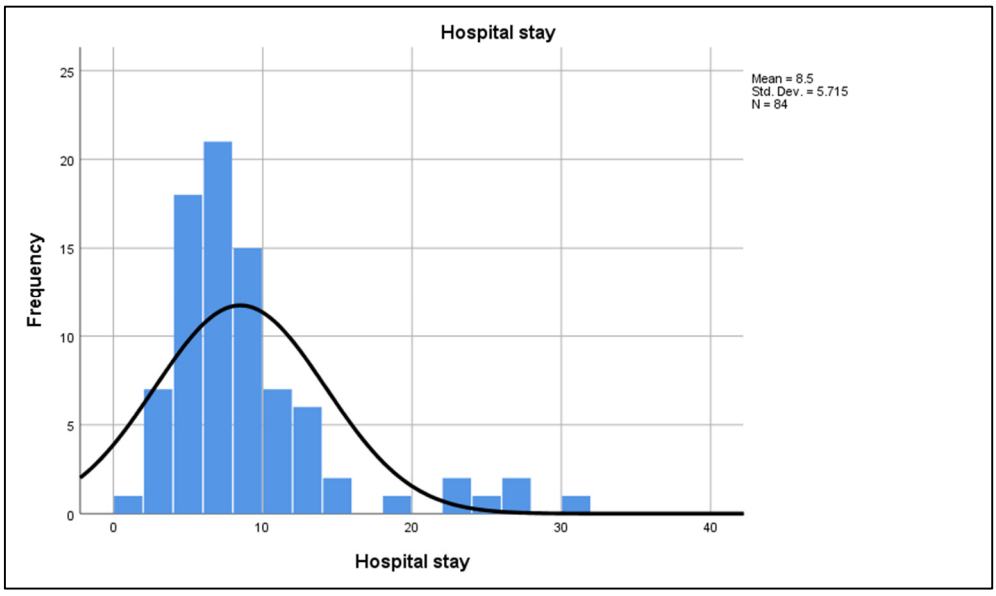

Figure 29: frequency histogram of hospital stay (N=84)

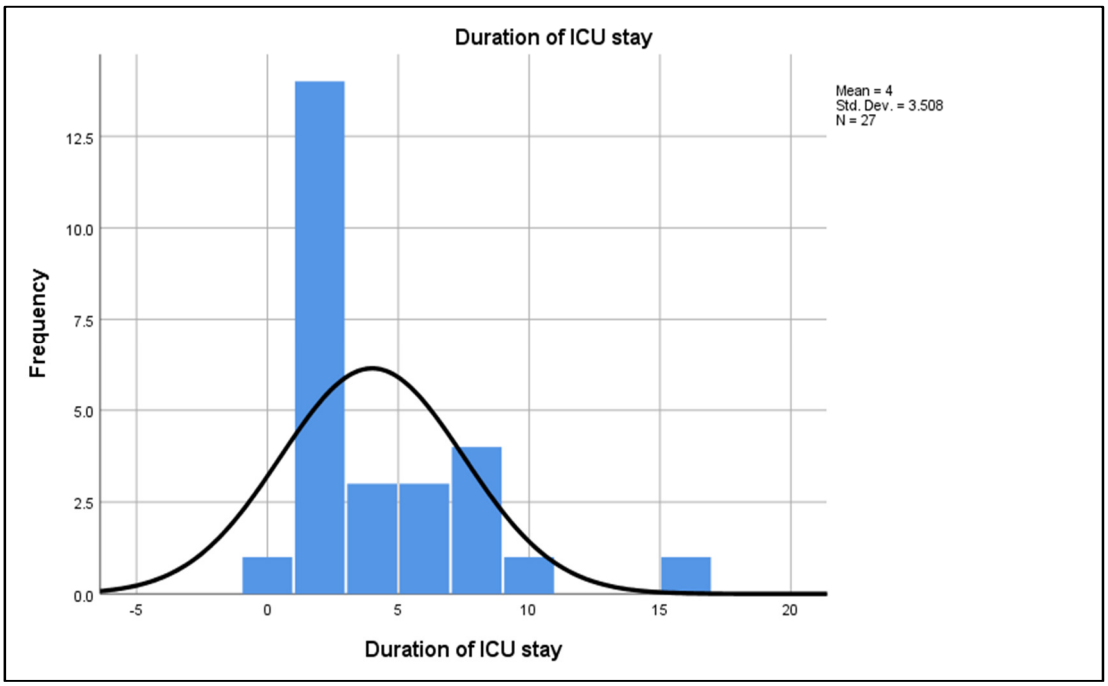

Figure 30: frequency histogram of ICU stay (N=26)

Table 24: Hypoglycemia episodes during hospital stay(N=84)

Hypoglycemia attack	Frequency
Yes	8(9.5%)
No	76(90.5%)

In 8 patients Hypoglycemia was attack developed during the hospital stay.

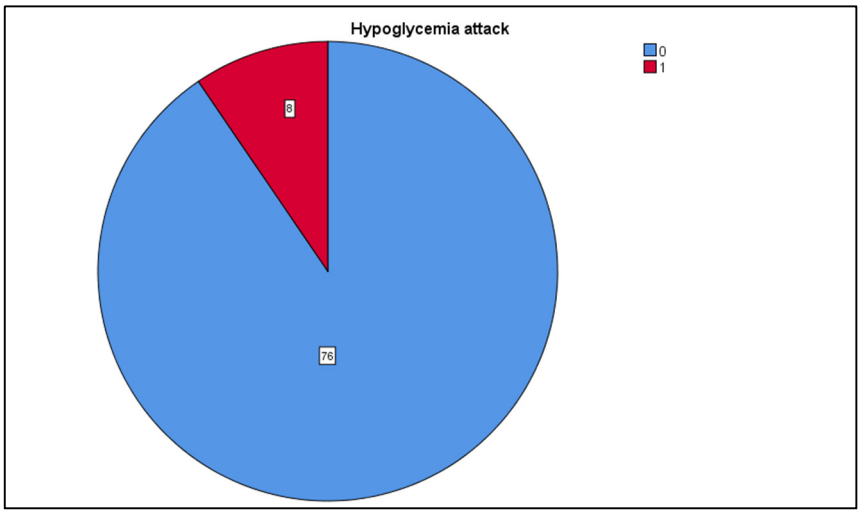

Figure 31: Pie chart representation of number and frequency of Hypoglycemia attacks(N=84)

A total of 26 patients received bicarbonate supplementation during the treatment for DKA

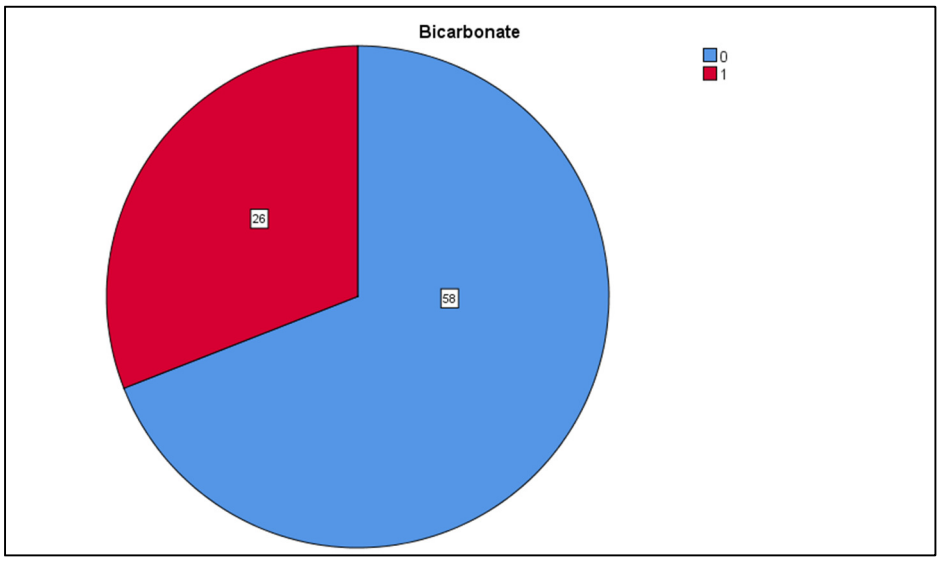

Figure 32: Pie chart representation Bicarbonate supplementation requirement(N=84)

A total 40 patients received potassium supplementation during DKA management in the hospital.

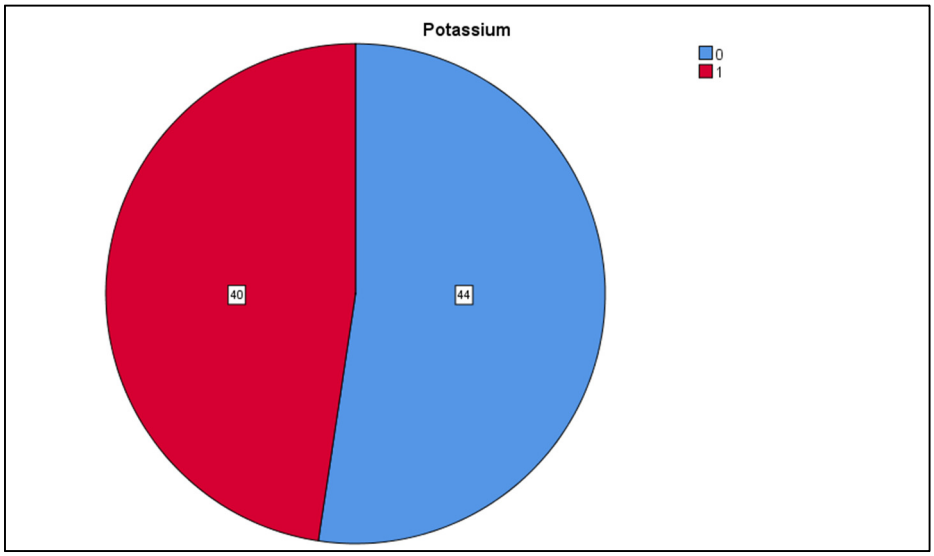

Figure 33: Pie chart representation Potassium supplementation requirement(N=84)

Table 25: Complications during Hospital stay (N=84)

	Frequency
None	69(82.1%)
Intubation	8(9.5%)
Hemodialysis	2(2.4%)
Anterior wall ST elevation Myocardial infarction	1(1.2%)
Cerebral edema	1(1.2%)
Chronic kidney disease- Fluid Overload	1(1.2%)
High flow nasal canulae	1(1.2%)
Resistant fluid overload	1(1.2%)

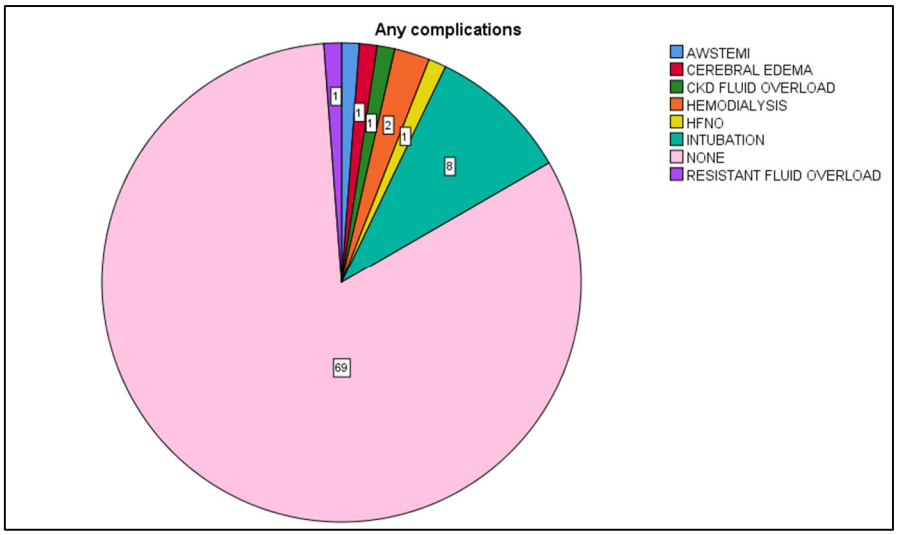

Fig. 34: Pie chart representation of complications during management of DKA patients (N=84)

The patient illustrates the complications encountered in patients admitted with DKA with maximum being secondary to the Primary etiology. Only 1 patient can be said to have encountered a complication directly being attributed to DKA with Cerebral edema being observed.

OUTCOME

Table 26: Outcome of patients presenting with DKA (N=84)

Outcome	Frequency
Discharge	74(88.1%)
Mortality	10(11.9%)
Total	84

From 84 admitted patients, 74 patients were discharged, 9 died during hospital stay and 1 patient went LAMA.

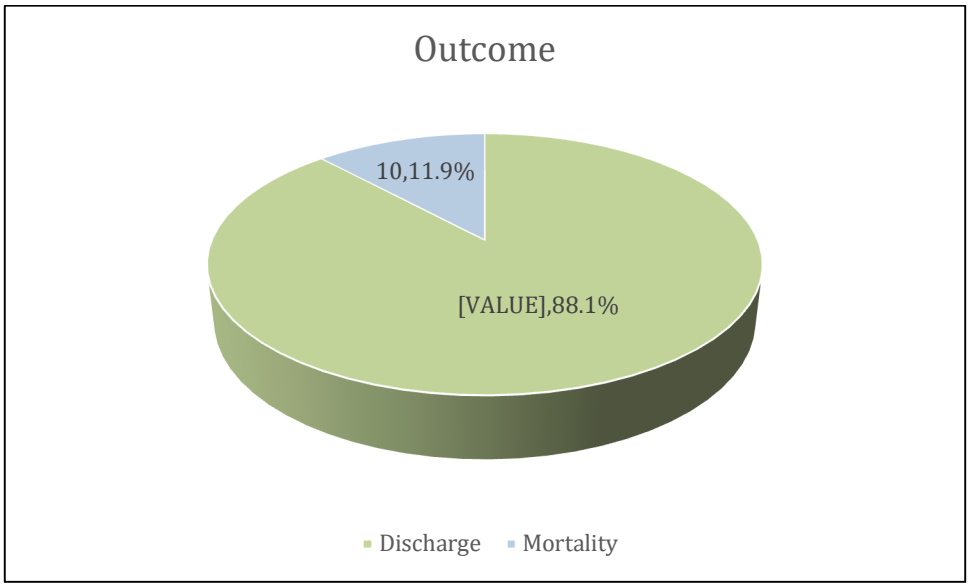

Figure 35: Bar chart representing the outcome of patients presenting with DKA (N=84)

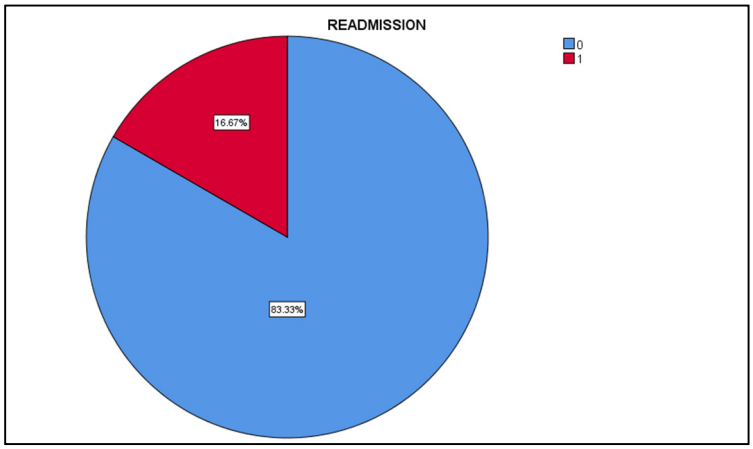

Figure 36: Pie chart indicating readmission rates for DKA (N=84)

Table 27: Readmission rates with DKA (N=84)

Readmissions	Yes	No
Frequency	14	70

Table 28: Outcome of patients with Subtypes of Diabetes (N=84)

	Discharge	Mortality	Total
TYPE 1	39	1	40
TYPE 2	25	9	34
Latent autoimmune diabetes in adults	8	0	8
Maturity onset diabetes of young	1	0	1
Secondary	1	0	1
	74	9	84

The maximum mortality was observed in patients with Type 2 DM while only one patient with type 1 DM expired . Rest all patients were discharged without any treatment incurred complications

MORTALITY

Using univariate logistic regression p value, odds ratio and the confidence interval was calculated for the association of mortality with the variables and a significant association was found for fever with the p value of 0.01, Shortness of breath and COVID19 infection were also significantly associated with the p values of 0.004 and 0.002 respectively and the odds ratio of 0.093 and .104 repectively.T2DM and increasing age were also significantly associated with the p value of 0.008 and 0.002 respectively with the odds ratio of 17.64 and 1.082.

Table 29: Univariate regression analysis for predictors of Mortality in patients presenting with DKA(n=84)

S.no	Variable	Frequency	Odds Ratio, CI	P-value
1	**Age**		**1.08(1.02-1.13)**	**0.002**
2	Gender	43/84	.947(.25 – 3.54)	0.936
3	BMI		1.19(.99 – 1.43)	0.051
4	Comorbidities	37/84	3.42(.81 – 14.29)	0.92
5	Diabetic Complications	31/84	0.73(.16 – 2.94)	0.631
6	**T2DM**	**34/84**	**17.64(2.11 – 147.16)**	**0.008**
7	Past DKA Admission	43/84	.59(.15 – 2.29)	0.454
8	**Fever**	**30/84**	**.19(.04 - .81)**	**0.02**
9	Starvation	25/84	.98(.23 -4.17)	0.98
10	**Shortness of breath**	**28/84**	**0.09 (0.18 - .47)**	**0.004**
11	**COVID**	**12/84**	**.10 (.02 -.45)**	**0.002**
12	Infection	35/84	3.83 (.91 -16.04)	0.066
13	Severe DKA	20/84	0.77 (.15 -4.00)	0.764
14	>7 Admission days	36/84	0.27 (.05-1.40)	0.122
15	HbA1c		1.25 (.90 – 1.74)	0.170
16	Hemoglobin		.85 (.67 – 1.09)	0.219
17	Sinus Tachycardia		0	0.998

SEVERITY

Using univariate logistic regression the risk factor associated with severe disease were analysed and presence of comorbidities, increasing age and higher HbA1c were associated with significant p values of 0.018,0.007, and HbA1c of 0.002 respectively and the odds ratio of .516, .950 and 1.539 respectively.

Table 30: Univariable regression analysis for predictors of Severe DKA in patients presenting with DKA(n=84)

S.no	Variable	Frequency	Odds Ratio	P value
1	**Age**		**.95 (.91 - .98)**	**.007**
2.	Female Sex	43/84	2.10 (.74 – 5.96)	.161
3	BMI		.93 (.82 – 1.05)	.287
4.	T2DM	34/84	.40 (.13 – 1.24)	0.113
5	Readmission	20/84	.85 (.21 – 3.40)	.819
6.	**Comorbidities**	**37/84**	**.51 (.07 - .78)**	**0.018**
7.	Complications	31/84	.34 (.10 -1.14)	0.081
8.	>7 Admission days	36/84	.50 (.17 – 1.50)	0.221
9	**HbA1C**		**1.53 (1.17 -2.01)**	**.002**
10	Infection	35/84	.51 (.17 -1.51)	.230

Readmission in our Hospital

The variables associated with the readmission were assessed by the univariable logistic regression and the presence of significant association was checked for Insulin diabetes mellitus, severe disease, comorbidities, complications, HBA1c, >7 day admission, Age and BMI. On calculation Patients on Insulin presence of comorbidities and increasing age were significantly associated with chances of readmission with the p values of 0.021,0.025 and 0.010 respectively and the odds ratios of 11.59,0.167 and .937 respectively.

Table 31: Univariate regression analysis for predictors of Readmission in patients presenting with DKA(n=84)

S.no	Variable	Frequency	Odds Ratio,CI	P value
1	**Age**		**.93 (.89 - .98)**	**0.010**
2	BMI		.84 (.70- 1.00)	0.053
3	Female Sex	43/84	2.80 (.80 - 9.79)	0.106
4	**Patients on Insulin**	**50/84**	**11.59 (1.43 – 93.49)**	**0.021**
5	Severe Disease	20/84	.85 (.21 – 3.40)	0.819
6	**Comorbidities**	**37/84**	**.16 (.03-.80)**	**0.025**
7	Complications	31/84	.94 (.28 – 3.10)	0.919
8	HBa1C		1.02 (.82 – 1.26)	0.851
9	>7 Day Admission	36/84	.45 (.12 – 1.57)	0.212
10	Diabetes Education	40/84	869871005.7	.997

ICU ADMISSION

Univariate logistic regression suggested a association between T2DM, Age, Fever and Starvation with the p values of 0.010,0.014,0.022 and 0.012 and the odds ratio of 3.556,1.036,3.907 and 0.0165 respectively. Any respiratory/skin/lung infection was also significantly associated with ICU admission with Odds ratio of 4.198 and the p value of 0.004 with CI of 1.574- 11.195. No significant associations were found for past DKA, Severity of the DKA and the HbA1c of the patient.

Table 32: Univariable regression analysis for predictors of ICU admission in patients presenting with DKA(n=84)

S.no	Variable	Frequency	Odds Ratio	P value
1	**Age**		**1.03(1.00 -1.06)**	**0.014**
2	BMI		1.10 (.99 -1.23)	.054
3	Past DKA	43/84	.47 (.18- 1.12)	.121
4	**T2DM**	**50/84**	**3.55 (1.35 – 9.34)**	**0.010**
5	Any complications	31/84	.81 (.29 – 2.62)	.816
6	Blood Sugar		1.00 (.99 -1.00)	.675
7	**Fever**	**31/84**	**3.90 (1.21 -12.55)**	**0.022**
8	**Starvation**	**25/84**	**.16(0.04 -.67)**	**0.012**
9	Shortness of breath	28/84	.35 (.64 – 11.19)	.351
10	**Infection**	**35/84**	**4.19 (1.57 – 11.19)**	**.004**
11	Severe DKA	20/84	.68 (.21 – 2.13)	.511
12	HbA1c		.98 (.81 -1.19)	.903

7 HOSPITAL STAY

The variables associated with the >7-day hospital stay were analysed with the univariate logistic regression and no significant association was found with female, HBA1c, Blood sugar, Age, Past DKA, T2DM, Complications, Comorbidities, Bicarbonates, Potassium supplementation

Table 33: Univariable regression analysis for predictors of prolonged hospital stay(>7 days) in patients presenting with DKA(n=84)

S.no	Variable	Frequency	Odds Ratio,CI	P value
1	Age		1.01(.98-1.04)	.426
2	Female Sex	43/84	1.01(.42 – 2.39)	.979
3	T2DM	34/84	.75 (.23 – 2.44)	.638
4	Comorbidities	37/84	.82 (.87 – 7.28)	.085
5	Complications	31/84	1.01 (.29 – 2.28)	.709
6	HBA1c		.96 (.79 – 1.16)	.695
7	Blood Sugar		1.00 (.99 – 1.00)	.369
8	Past DKA	43/84	.37 (.23 – 7.28)	.077
9	Bicarbonate	26/84	.71 (.29 – 1.72)	.453
10	Potassium	40/84	1.49 (.56 -3.93)	.414
11	Infection	35/84	2.04 (.84 – 4.94)	.112
12	Hemoglobin		.961 (.82 – 1.11)	.603
13	Sinus Tachycardia	19/84	1.18(.42 – 3.31)	.740

MORATLITY

Using multivariate logistic regression significant association was tested for the parameters found significant in the univariate logistic regression as well the parameters deemed important for the outcome analyses. Only Shortness of breath was significantly associated with mortality with the odds ratio of 4.340 and the p value of 0.044 with CI

Table 34: Multivariate regression analysis for predictors of Mortality in patients presenting with DKA(n=84)

S.no	Variable	Frequency	Odds Ratio,CI	P value
1	Age		1.04 (0.96-1.13)	.288
2	Infection	35/84	.41 (0.07-2.14)	.292
3	**Shortness of breath**	**28/34**	**6.34 (1.05 - 38.26)**	**.044**
4	Male gender	41/84	.85 (.17-4.31)	.850
5	T2DM	34/84	2.14(.07 – 61.66)	.656

COVID-19 and DKA

In our study there were 13 patients with COVID 19 infection. The average age was 51.2±18.36. T2DM patients were 69.2%(9/13) and the average Blood sugar was 471± 97.The HbA1c levels were 12.92 ± 2.52 and the average pH was 7.05 ± 0.15.Hospital stay was 10.6 ± 8.7 days and mortality was 38.4%(5/13). There was a significant association with the Age and the COVID 19 positive patients as the patients with COVID 19 had significant higher age as compared to COVID 19 patients and there was also significant association of Mortality with COVID 19 positive status

Table 35: Comparison of clinical, biochemical and outcome between COVID and non-COVID patients

	COVID 19 positive	COVID 19 negative	P values,CI
Age	**51.3 ± 18.36**	**38.7 ± 16.74**	**0.024(-22.88 - -1.67)**
T2DM	9/13(69.2%)	25/71(35.2%)	0.060
Blood sugar	471±97	435 ± 114.75	0.102
HbA1c	12.92±2.52	12.02 ± 2.69	0.255
pH	7.05±0.15	7.14 ± 0.15	0.076
Hospital stay	10.6±8.7	8 ± 4.9	.117
Mortality	**5/13(38.4%)**	**5/71(7.04%)**	**0.001(2.11 – 147.16)**

DISCUSSION

Our study enrolled 84 patients out of which 43(51.2%) were females while 41(48.8%) patients were males suggesting a nearly equal gender distribution. A study by Basha K et all published in 2013 reported a distribution of 72% in males and 28% in female (54) while a study by Singh H et all reports a male to female ration of 2:1[55].

The mean age of patients enrolled was 40.7±7.5 years which was greater than the mean age of the patients reported in the studies published by Singh H et all in 2019 and a study on DKA published by Almalki H et all in 2016 reported mean age to be29.4 ±14.4 years and 21.4 ± 10.1 years[45]. The slightly higher mean age of our patients can be attributed the number of COVID 19 and the slightly greater proportion of Type 2 DM cases in our study. Also, we did not enrol paediatric population in the present study.

T1DM patients accounted for 40 patients (47.62%) while 34 (40.48%) patients belonged to the T2DM category. LADA accounted for 8 cases (9.5%) while MODY and secondary accounted for 1 patient each (1.2%). In the study by f by Almalki H et all Type 1 cases accounted for 71% cases while the study by Singh H et all reported type 1 cases to account for 74% of DKA presentations while a study by Ooi et all from UK in 2021 reported 76% proportion for Type 1 diabetes[55]. Only the study by Singh H reported LADA patients with DKA presentations while none of the above studies reported patients with MODY and secondary diabetes presenting as DKA. Higher age in present study can be explained by inclusion criteria of >18 years and exclusion of patients in pediatric age group, while other studies have included pediatric patients. The results obtained call for raise in awareness of the possibility of the Type 2 DM and the other forms of diabetes presenting as DKA.

The mean duration of diabetes was 7.81 ±8.2 years which was almost equal to the mean age reported in the study by Almalki H et all which was 7.6 ±5.3 years[37].

Forty-three (51.2%) patients belonged to the moderate severity of DKA while 20(23.8%) belonged to severe while 21(25%) belonged to mild severity. Harpreet Singh et all observed mild DKA in 11 (22%), moderate in 25 (50%) and severe DKA in 14 (28%) patients in their study[56]. These findings were similar to our results.

Pain abdomen (17 patients,20.2%) followed by fever and shortness of breath (7 patients,8.3%) were the most common presentations in patients presenting with DKA which

was similar to the studies by Singh H and Almalki et all who also reported nausea, vomiting, fever and SOB as the most common presenting symptoms[56][45].

A total of 41 out of 84 (48.8%) patients presented with DKA for the first time while 43 patients had prior history of DKA. Out of these patients, 16 patients (19%) were diagnosed as diabetic for the first time. Prior history of DKA was present in 65% patients in a study from Riyadh[45] and 37% in a study from India (Singh H et all) In a study from India reported 20% newly diagnosed diabetes with the DKA episode[57]. Our study had a lesser number of patients with past history as compared to the cited studies the likely possibility holds that the number of T2DM cases in our study were more and the likelihood of them having a recurrent episode of DKA is less in comparison to the patients with T1DM.Also likely causes include the precipitating factors the above-mentioned studies conclude the noncompliance to be the most common precipitating factor while as discussed later in our study

Infection ,44 patients (52.3%) followed by noncompliance (13 patients 15.5%) were the most common precipitating factor with 12 patients had COVID (14.3%) and 7 patients had Lower respiratory tract infection(8.3%) as the precipitating fact which was in concordance to the various Indian studies which suggested infections followed by non-compliance as the major contributing factor for DKA. Although the 2019 published study by Singh H et all suggested non-compliance (52%) f/b infections (36%) as the most common precipitating factor[57], 2021 study from UK concluded infections (39.8%) followed by noncompliance (26.8%) as the commonest precipitating factors. Among infection urinary tract infection was the commonest, however, infection at any site contributed to development of DKA. Our study also highlighted the heterogenicity of the causal factors for the DKA precipitation with a variety of medical, surgical, gynaecological and psychiatric complications leading to DKA including opioid withdrawal, Acute coronary syndrome, Cerebrovascular accident, electrocution, Upper GI bleed.

The mean blood glucose was 442.15±113.243. The mean HBA1c was 12.1% ±2.677 and the range of 6.0 to 19.0. The average pH was 7.12±.155 at presentation. Singh et all study observed a mean blood sugar of 406.8 ± 130.4 mg/dl and pH of 7.128 ± 0.157[57]. A 2004 study published by Newton CA et all from USA reported average haemoglobin A_{1c} level of 13.0% ± 2.5%. (58).Almalki H et all study reported pH levels of 7.2 ±±0.2 and HbA1c levels of 11.9(+/-) 2.6.We could infer that the mean HBA1c levels and the blood glucose levels varied from study to study and belonging to our study population did not infer poorer blood

glucose control levels inferred by HBA1c. Also, we could not infer that the well-controlled diabetes that is HBA1c levels <7 did not offer insurance from DKA as 6 patients presented with DKA even with HBA1c <8 and one patient presented with DKA with HBA1c of 5.6.A total of three patients presented with euglycemic DKA defined as blood sugar <250 with positive urinary ketones and acidosis on blood gas analysis. The three patients shared among them the post referral status and had received insulin therapy from outside hospital before presenting to the AIIMS. We could not encounter the patients with classic associations with euglycemic DKA. The average anion gap in our study was 21±6 and the mean bicarbonate was 8.9 ±4.59 and the average Total leucocyte counts were 14.08 with SD of 8.38. Singh H et all in their study reported the anion gap to be 23.4 ±6.7, bicarbonate to be 8.20±5.) and counts to be 13.2±7.2 which were similar to the values observed in our study[57].

A total of 26 patients (31%) required ICU care during the course of hospital stay and the mean duration of hospital stay for our patients was 8.5 ±5. 71 days. The average duration of stay in the USA study was 4.5 ± 3.3 days (58) while the study from north India observed average hospital duration stay of 8.2. ± 5.0 days. Our average hospital stay was longer than that described by the national average of 4.5 by CDC in the US. The slightly greater hospital stay could be explained by the multiple comorbidities in our patients and severe underlying precipitating factors in our patients including the COVID-19 infection

A total of 40 out of 84 patients (47.6%) patients required Pottasium supplementation while 26 patients out of 84(30.9%) patients required Bicarbonate supplementation,comparing to the other studies Almalki H et all reported Bicarbonate supplementation in 18% cases(45). 8 patients had hypoglycemia attack during the DKA management. Christopher et all in their study reported 4 episodes of DKA out of 138 admissions (2.9%) and there was one patient developing Cerebral edema after the initiation of DKA treatment[58]. Christopher et al report no such or other complications in their study. It is notable that other studies do not mention the complications associated with the DKA presentation, treatment or as a direct con sequence of underlying precipitating factors.

The mortality rate in our patients was 9 out of 84 (10.7 %) which was comparable to the mortality rate (16.3%-23.7%) reported in studies by Adhikari et al (16.3%) (59and Matoo et al (23.7%) (60)[60] and Sonwani et al (7%)[61]. The studies by Almalki H et all and Singh H et all reported no mortality in patients presenting with DKA. The mortality rate in our study got

exacerbated by the COVID-19 related deaths in our study population as 5 out of 13 patients admitted with DKA died in our study

The readmission rate in our patients was 14 out of 84 (16.6%) while Almalki et all reported readmission rates of 65%[45] while a study from USA reported recurrence rates of 55.5% in their population[48]. All the patient discharged from our hospital received comprehensive diabetic education during the hospital stay and at the time of discharge which was further consolidated during OPD visits. We believe our diabetic education to be responsible for comparatively lower recurrent DKA episodes however further studies need to be done on our education model.

COVID-19 and DKA

Our study included 13 patients with DKA and COVID 19 out of which 9 patients (69.2%) were of T2DM while 4 patients had T1DM (30.8%). The average age was 51.3 ± 18.6 years. Out of the 13 patients enrolled 6 patients (46.1%) were diagnosed to have diabetes with the DKA episode of which 4 patients (66.6%) were T2DM and 2 patients were T1DM (33.3%).4 patients had past history of DKA and the average blood glucose levels were 471(+/-) 97 at presentation. Mean HBA1c levels were 12.98±2.52, pH levels were 7.07±.15 and the average hospital stay was 10.6±8.7 days. The patients with COVID 19 had more severity of DKA as compared to the non-COVID patients according to the pH values at presentation, prolonged hospital stay and poorer outcome as calculated with the mortality rate of 5 of 13 patients (38.4%).Singh B et all published study of 43 patients in 2021 which concluded mean age to be 52, newly diagnosed diabetics to be 10(23.3%).Median blood glucose at presentation to be 553mg/dl(300.0-1927.0) and the median HBA1c to be 13.9%.The mortality rate observed by them in their study was 25(58.1%) and Age and D-dimer that were significantly associated with mortality. The mortality rate and the HBA1c levels in their study were significantly higher than our study and it could be because of the greater percentage of newly diagnosed diabetics in our study. Analyzing our data Blood glucose at presentation were significantly associated with mortality (p=0.05)(OR-1.01,1.00-1.03) and there was significant association with Age, Type of diabetes and HBA1c.

Predictors of Outcome

Mortality

Age, T2DM, BMI, presence of fever, and Shortness of breath at admission and COVID 19 infection were associated with significant risk factors of mortality as outcome. Matoo et al reported association with duration of DKA prior to admission, severity of acidosis, and severity of peripheral vascular insufficiency (60) while Sonwani et al reported >10 years of Diabetes, poor compliance, Cardiovascular disease and Acute coronary syndrome as predictors of mortality[61].

But on using multivariate logistic regression only shortness of breath was associated with significant association with mortality. The high contribution of COVID 19 towards our mortality numbers can explain these results as these patients predominantly presented with shortness of breath at presentation.

Severity

Our analysis did not support the associations with severe DKA.

Readmission

Age, Female sex, Insulin dependent diabetes mellitus and presence of comorbidities was significantly associated with risk of readmission. Bradford et al concluded younger age, comorbid behavioural health problems (especially depression), poor baseline glucose control, drug and alcohol abuse, ethnic minority status as risk factors for readmission[47]. Cooper et al did not find any significant association with recurrent DKA admissions in their study[62]. Prior diabetic education did not have any significant association with DKA recurrence. This highlights the point that although diabetic education in our institution reduced the rate of recurrence. The prevention at an individual level was not inferred and thus patient assessment of the disease posts the education should be assessed. However further study needs to be performed.

ICU Admission and prolonged hospital stay (>7 days)

We could infer fever, age, T2DM, starvation and infection to be associated to risk of ICU admission in our patients presenting with DKA. No significant associations could be found for prolonged hospital stay. Singh et all in their study found tachycardia and low hemoglobin

to be associated with prolonged hospital stay. Basha et al concluded low bicarbonate values (<10) to be associated with prolonged hospital stay[54]. However we did not find such associations in our study.

CONCLUSION

DKA is a acute complication of diabetes which is contributor to significant morbidity and preventable mortality in both Type 1 and Type 2 Diabetes and can be precipitated equally in females and males and irrespective of age. Various medical, surgical, gynaecological, and psychiatric factors can precipitate DKA with infections followed by noncompliance being the most common precipitants in our study. Age, T2DM, BMI, history of fever, Shortness of breath and COVID19 infection were significantly associated with mortality. However, we advocate further studies with greater sample size on this topic to validate our findings.

BIBLIOGRAPHY

1. Association AD. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 2014 Jan 1;37(Supplement 1) S81–90.

2. Association AD. 2. Classification and Diagnosis of Diabetes. Diabetes Care. 2015 Jan 1;38(Supplement 1) S8–16.

3. Ramachandran A. Know the signs and symptoms of diabetes. Indian J Med Res. 2014 Nov;140(5) 579–81.

4. Pippitt K, Li M, Gurgle HE. Diabetes Mellitus Screening and Diagnosis. Am Fam Physician. 2016 Jan 15;93(2) 103–9.

5. Sapra A, Bhandari P. Diabetes Mellitus. In StatPearls [Internet]. Treasure Island (FL) StatPearls Publishing; 2021 [cited 2021 Nov 17]. Available from http //www.ncbi.nlm.nih.gov/books/NBK551501/

6. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic Crises in Adult Patients With Diabetes. Diabetes Care. 2009 Jul 1;32(7) 1335–43.

7. Ahmed AM. History of diabetes mellitus. Saudi Med J. 2002 Apr;23(4) 373–8.

8. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045 Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract [Internet]. 2019 Nov 1 [cited 2020 May 29];157. Available from https //www.diabetesresearchclinicalpractice.com/article/S0168-8227(19)31230-6/abstract

9. Mobasseri M, Shirmohammadi M, Amiri T, Vahed N, Hosseini Fard H, Ghojazadeh M. Prevalence and incidence of type 1 diabetes in the world a systematic review and meta-analysis. Health Promot Perspect. 2020 Mar 30;10(2) 98–115.

10. Khan MAB, Hashim MJ, King JK, Govender RD, Mustafa H, Al Kaabi J. Epidemiology of Type 2 Diabetes – Global Burden of Disease and Forecasted Trends. J Epidemiol Glob Health. 2020 Mar;10(1) 107–11.

11. Diabetic Ketoacidosis - an overview | ScienceDirect Topics [Internet]. [cited 2021 Nov 18]. Available from https //www.sciencedirect.com/topics/medicine-and-dentistry/diabetic-ketoacidosis

12. Farsani SF, Brodovicz K, Soleymanlou N, Marquard J, Wissinger E, Maiese BA. Incidence and prevalence of diabetic ketoacidosis (DKA) among adults with type 1 diabetes mellitus (T1D) a systematic literature review. BMJ Open. 2017 Aug 1;7(7) e016587.

13. Ohiagu FO, Chikezie PC, Chikezie CM. Pathophysiology of diabetes mellitus complications Metabolic events and control. Biomed Res Ther. 2021 Mar 31;8(3) 4243–57.

14. Skyler JS, Bakris GL, Bonifacio E, Darsow T, Eckel RH, Groop L, et al. Differentiation of Diabetes by Pathophysiology, Natural History, and Prognosis. Diabetes. 2017 Feb 1;66(2) 241–55.

15. Schwartz SS, Epstein S, Corkey BE, Grant SFA, Gavin JR, Aguilar RB. The Time Is Right for a New Classification System for Diabetes Rationale and Implications of the β-Cell–Centric Classification Schema. Diabetes Care. 2016 Feb 1;39(2) 179–86.

16. Todd JA. Etiology of type 1 diabetes. Immunity. 2010 Apr 23;32(4) 457–67.

17. Leslie RD. Predicting adult-onset autoimmune diabetes clarity from complexity. Diabetes. 2010 Feb;59(2) 330–1.

18. Gregg BE, Moore PC, Demozay D, Hall BA, Li M, Husain A, et al. Formation of a human β-cell population within pancreatic islets is set early in life. J Clin Endocrinol Metab. 2012 Sep;97(9) 3197–206.

19. Ziegler A-G, Nepom GT. Prediction and pathogenesis in type 1 diabetes. Immunity. 2010 Apr 23;32(4) 468–78.

20. Noble JA, Valdes AM, Varney MD, Carlson JA, Moonsamy P, Fear AL, et al. HLA class I and genetic susceptibility to type 1 diabetes results from the Type 1 Diabetes Genetics Consortium. Diabetes. 2010 Nov;59(11) 2972–9.

21. The 0.1% of the Population With Glucokinase Monogenic Diabetes Can Be Recognized by Clinical Characteristics in Pregnancy The Atlantic Diabetes in Pregnancy Cohort | Diabetes Care [Internet]. [cited 2021 Dec 9]. Available from https //care.diabetesjournals.org/content/37/5/1230?ijkey=5112652c67542ce53cae04e36726a703ab67d24d&keytype2=tf_ipsecsha

22. JCI - Prediction algorithms pitfalls in interpreting genetic variants of autosomal dominant monogenic diabetes [Internet]. [cited 2021 Dec 9]. Available from https //www.jci.org/articles/view/133516

23. Screening for Prediabetes and Type 2 Diabetes US Preventive Services Task Force Recommendation Statement | Guidelines | JAMA | JAMA Network [Internet]. [cited 2021 Dec 10]. Available from https //jamanetwork.com/journals/jama/fullarticle/2783414#jus210018r14

24. Handelsman Y, Bloomgarden ZT, Grunberger G, Umpierrez G, Zimmerman RS, Bailey TS, et al. American association of clinical endocrinologists and american college of endocrinology - clinical practice guidelines for developing a diabetes mellitus comprehensive care plan - 2015. Endocr Pract Off J Am Coll Endocrinol Am Assoc Clin Endocrinol. 2015 Apr;21 Suppl 1 1–87.

25. Fong DS, Aiello LP, Ferris FL, Klein R. Diabetic Retinopathy. Diabetes Care. 2004 Oct 1;27(10) 2540–53.

26. Diabetic Nephropathy Diagnosis, Prevention, and Treatment | Diabetes Care [Internet]. [cited 2021 Dec 12]. Available from https //care.diabetesjournals.org/content/28/1/164?ijkey=02c1a5952afc4faaa5c5c152909b3d5080b4df28&keytype2=tf_ipsecsha

27. Adler AI, Stevens RJ, Manley SE, Bilous RW, Cull CA, Holman RR, et al. Development and progression of nephropathy in type 2 diabetes The United Kingdom Prospective Diabetes Study (UKPDS 64). Kidney Int. 2003 Jan 1;63(1) 225–32.

28. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators. Lancet Lond Engl. 2000 Jan 22;355(9200) 253–9.

29. Rossing K, Jacobsen P, Pietraszek L, Parving H-H. Renoprotective Effects of Adding Angiotensin II Receptor Blocker to Maximal Recommended Doses of ACE Inhibitor in Diabetic Nephropathy A randomized double-blind crossover trial. Diabetes Care. 2003 Aug 1;26(8) 2268–74.

30. Boulton AJM, Vinik AI, Arezzo JC, Bril V, Feldman EL, Freeman R, et al. Diabetic Neuropathies A statement by the American Diabetes Association. Diabetes Care. 2005 Apr 1;28(4) 956–62.

31. Simovic D, Isner JM, Ropper AH, Pieczek A, Weinberg DH. Improvement in chronic ischemic neuropathy after intramuscular phVEGF165 gene transfer in patients with critical limb ischemia. Arch Neurol. 2001 May;58(5) 761–8.

32. Kosiborod M, Gomes MB, Nicolucci A, Pocock S, Rathmann W, Shestakova MV, et al. Vascular complications in patients with type 2 diabetes prevalence and associated factors in 38 countries (the DISCOVER study program). Cardiovasc Diabetol. 2018 Nov 28;17(1) 150.

33. Kitabchi AE, Umpierrez GE, Murphy MB, Barrett EJ, Kreisberg RA, Malone JI, et al. Management of hyperglycemic crises in patients with diabetes. Diabetes Care. 2001 Jan;24(1) 131–53.

34. Metabolic Effects of Low-Dose Insulin Therapy on Glucose Metabolism in Diabetic Ketoacidosis | Diabetes [Internet]. [cited 2021 Dec 13]. Available from https //diabetes.diabetesjournals.org/content/37/11/1470?ijkey=29d903175f705fd972627760ba498f8bd3b0e940&keytype2=tf_ipsecsha

35. Chupin M, Charbonnel B, Chupin F. C-peptide blood levels in keto-acidosis and in hyperosmolar non-ketotic diabetic coma. Acta Diabetol Lat. 1981 Jun;18(2) 123–8.

36. Pasquel FJ, Umpierrez GE. Hyperosmolar Hyperglycemic State A Historic Review of the Clinical Presentation, Diagnosis, and Treatment. Diabetes Care. 2014 Nov 1;37(11) 3124–31.

37. Almalki MH, Buhary BM, Khan SA, Almaghamsi A, Alshahrani F. Clinical and Biochemical Characteristics of Diabetes Ketoacidosis in a Tertiary Hospital in Riyadh. Clin Med Insights Endocrinol Diabetes. 2016;9 7–11.

38. Nyenwe EA, Kitabchi AE. The evolution of diabetic ketoacidosis An update of its etiology, pathogenesis and management. Metabolism. 2016 Apr;65(4) 507–21.

39. Rabbone I, Maltoni G, Tinti D, Zucchini S, Cherubini V, Bonfanti R, et al. Diabetic ketoacidosis at the onset of disease during a national awareness campaign a 2-year observational study in children aged 0-18 years. Arch Dis Child. 2019 Oct 9;

40. Second-generation (atypical) antipsychotics and metabolic effects a comprehensive literature review. - PubMed - NCBI [Internet]. [cited 2019 Nov 14]. Available from https //www.ncbi.nlm.nih.gov/pubmed/15998156

41. Taylor SI, Blau JE, Rother KI. SGLT2 Inhibitors May Predispose to Ketoacidosis. J Clin Endocrinol Metab. 2015 Aug;100(8) 2849–52.

42. Abu-Abed Abdin A, Hamza M, Khan MS, Ahmed A. Euglycemic Diabetic Ketoacidosis in a Patient with Cocaine Intoxication. Case Rep Crit Care. 2016;2016 4275651.

43. Jayashree M, Sasidharan R, Singhi S, Nallasamy K, Baalaaji M. Root Cause Analysis of Diabetic Ketoacidosis Admissions at a Tertiary Referral Pediatric Emergency Department in North India. Indian J Endocrinol Metab. 2017 Oct;21(5) 710–4.

44. George J, Mishra A, Iyadurai R. Correlation between the outcomes and severity of diabetic ketoacidosis A retrospective pilot study. J Fam Med Prim Care. 2018 Jul 1;7 787.

45. Clinical and Biochemical Characteristics of Diabetes Ketoacidosis in a Tertiary Hospital in Riyadh - PubMed [Internet]. [cited 2021 Dec 10]. Available from https //pubmed.ncbi.nlm.nih.gov/27226739/

46. Brandstaetter E, Bartal C, Sagy I, Jotkowitz A, Barski L. Recurrent diabetic ketoacidosis. Arch Endocrinol Metab. 2019 Jul 29;63 531–5.

47. Bradford AL, Crider CC, Xu X, Naqvi SH. Predictors of Recurrent Hospital Admission for Patients Presenting With Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar State. J Clin Med Res. 2017 Jan;9(1) 35–9.

48. Randall L, Begovic J, Hudson M, Smiley D, Peng L, Pitre N, et al. Recurrent diabetic ketoacidosis in inner-city minority patients behavioral, socioeconomic, and psychosocial factors. Diabetes Care. 2011 Sep;34(9) 1891–6.

49. Agarwal A, Yadav A, Gutch M, Consul S, Kumar S, Prakash V, et al. Prognostic Factors in Patients Hospitalized with Diabetic Ketoacidosis. Endocrinol Metab Seoul Korea. 2016 Sep;31(3) 424–32.

50. Vyas C, Dalal L, Talaviya P, Saboo B. Multiple educational programs improves glycemic control, quality of life with diminishing the impact of diabetes in poorly controlled type 1 diabetics. Diabetes Metab Syndr. 2017 Dec;11 Suppl 2 S601–6.

51. Is a priming dose of insulin necessary in a low-dose insulin protocol for the treatment of diabetic ketoacidosis? - PubMed [Internet]. [cited 2021 Dec 13]. Available from https //pubmed.ncbi.nlm.nih.gov/18694978/

52. Mazer-Amirshahi M, Chen E. Is Subcutaneous Administration of Rapid-Acting Insulin as Effective as Intravenous Insulin for Treating Diabetic Ketoacidosis? Ann Emerg Med. 2009 Mar 1;53 259–63.

53. Treatment of diabetic ketoacidosis with subcutaneous insulin aspart - PubMed [Internet]. [cited 2021 Dec 13]. Available from https //pubmed.ncbi.nlm.nih.gov/15277410/

54. Sathik Basha K. A Study on Clinical and Biochemical Profile in Diabetic Ketoacidosis [Internet] [masters]. Madurai Medical College, Madurai; 2013 [cited 2021 Dec 18]. Available from http //repository-tnmgrmu.ac.in/6393/

55. Ooi E, Nash K, Rengarajan L, Melson E, Thomas L, Johnson A, et al. Clinical and biochemical profile of 786 sequential episodes of diabetic ketoacidosis in adults with type 1 and type 2 diabetes mellitus. BMJ Open Diabetes Res Care. 2021 Dec 1;9(2) e002451.

56. Singh H, Saroch A, Pannu AK, Sachin HJ, Sharma N, Dutta P. Clinical and biochemical profile, precipitants and prognostic factors of diabetic ketoacidosis A retrospective study from a tertiary care center of north India. Diabetes Metab Syndr. 2019 Aug;13(4) 2357–60.

57. Singh H, Saroch A, Pannu A. Clinical and biochemical profile, precipitants and prognostic factors of diabetic ketoacidosis A retrospective study from a tertiary care center of north India. Diabetes Metab Syndr Clin Res Rev. 2019 Jun 10;13.

58. Newton CA, Raskin P. Diabetic Ketoacidosis in Type 1 and Type 2 Diabetes Mellitus Clinical and Biochemical Differences. Arch Intern Med. 2004 Sep 27;164(17) 1925–31.

59. Adhikari PM, Mohammed N, Pereira P. Changing profile of diabetic ketosis. J Indian Med Assoc. 1997 Oct;95(10) 540–2.

60. Matoo VK, Nalini K, Dash RJ. Clinical profile and treatment outcome of diabetic ketoacidosis. J Assoc Physicians India. 1991 May;39(5) 379–81.

61. Sonwani S, Arya A, Saxena RS. A Prospective Study of Risk Factors, Clinical Profile and Outcome in Patients of Diabetic Ketoacidosis (DKA) in Type II Diabetes Patients. Int J Contemp Med Res IJCMR [Internet]. 2018 Apr [cited 2021 Dec 22];5(4). Available from https //www.ijcmr.com/uploads/7/7/4/6/77464738/ijcmr_1969_v3.pdf

62. Cooper H, Tekiteki A, Khanolkar M, Braatvedt G. Risk factors for recurrent admissions with diabetic ketoacidosis A case-control observational study. Diabet Med J Br Diabet Assoc. 2015 Oct 22;33.

63. Singh B, Kaur P, Patel P, et al. (January 30, 2021) COVID-19 and Diabetic Ketoacidosis: A Single Center Experience. Cureus 13(1): e13000. doi:10.7759/cureus.13000

IEC CERTIFICATE

अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur
संस्थागत नैतिकता समिति
Institutional Ethics Committee

No. AIIMS/IEC/2020/2060

Date: 01/01/2020

ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: AIIMS/IEC/2019-20/960

Project title: **"Clinical profile and outcomes of patients with diabetic ketoacidosis in a tertiary care hospital in western Rajasthan"**

Nature of Project:	**Research Project**
Submitted as:	**M.D. Dissertation**
Student Name:	**Dr.Kartikey Saini**
Guide:	**Dr.M.K.Garg**
Co-Guide:	**Dr.Maya Gopalakrishnan**

This is to inform that members of Institutional Ethics Committee (Annexure attached) met on **23-12-2019** and after through consideration accorded its approval on above project. Further, should any other methodology be used, would require separate authorization.

The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:

- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

On behalf of Ethics Committee, I wish you success in your research.

Dr. Praveen Sharma

Enclose:

1. Annexure 1

Page 1 of 2

Basni Phase-2, Jodhpur, Rajasthan-342005, **Website:** www.aiimsjodhpur.edu.in, **Phone:** 0291-2740741 Extn. 3109
Email: ethicscommittee@aiimsjodhpur.edu.in

APPENDIX-1

All India Institute of Medical Sciences

Jodhpur, Rajasthan

Informed Consent Form

Title of Thesis/Dissertation

CLINICAL PROFILE AND OUTCOMES OF PATIENTS WITH DIABETIC KETOACIDOSISIN A TERTIARY CARE HOSPITAL IN WESTERN RAJASTHAN

Name of PG Student **Dr. Kartikey Saini 9799789859**

Patient/Volunteer Identification No. _____

I,_____S/o or D/o_____

R/o_____give my full, free, voluntary consent to be a part of the study**CLINICAL PROFILE AND OUTCOMES OF PATIENTS WITH DIABETIC KETOACIDOSISIN A TERTIARY CARE HOSPITAL IN WESTERN RAJASTHAN** the procedure and nature of whichhas been explained to me in my own language to my full satisfaction. I confirm that I havehad the opportunity to ask questions.

I understand that my participation is voluntary and I am aware of my right to opt out of the study at any time without giving any reason.

I understand that the information collected about me and any of my medical records may be looked at by responsible individual from _____(Company Name) or from regulatory authorities. I give permission for these individuals to have access to my records.

Date _____ _____

Place _____ Signature/Left thumb impression

This to certify that the above consent has been obtained in my presence.

Date _____ _____

Place _____ Signature of PG Student

Witness 1 Witness 2

Signature Signature

Name _____ Name _____

Address _____ Address _____

APPENDIX-2

अखिल भारतीय आयुर्विज्ञान संस्थान

जोधपुर, राजस्थान

सूचित सहमति प्रपत्र

थीसिस का शीर्षक डायग्नोस्टिक क□□ॉसीडोसिन क□साथ रोगियों की नैदानिक शख्सियत और नतीज□

पीजी छात्र का नाम - कार्तिक□मसैनी दूरभाष संख्या 9799789859

रोगी / स्वयं स□ी पहचान संख्या. _____

मैं,_____पुत्र/पुत्री_____

नि□ासी_____मर□ी पूर्ण, निशुल्क, स्वैच्छिक सहमति दे□ा हु निम्नलिखित □ ध्ययन का हिस्सा बनन□क□लिए " डायग्नोस्टिक क□□ॉसीडोसिन क□साथ रोगियों की नैदानिक शख्सियत और नतीज□ जिसकी प्रक्रिया और प्रकृति मर□ी पूरी संतुष्टि क□लिए मर□ी □ पनी भाषा में मुझ□समझाया गया है। मैं पुष्टि करता हूं कि मर□□पास प्रश्न पूछन□का □ □सर था।

मैं समझता हूं कि मर□ी भागीदारी स्वैच्छिक है और किसी भी कारण क□बिना, किसी भी समय □ ध्ययन स□बाहर निकलन□क□मर□□ धिकार स□□ □गत हूं।

.मैं समझता हूं कि मर□□और मर□□किसी भी म□डिकल रिकॉर्ड क□बार□में एकत्र की गई जानकारी एम्स जोधपुर स□या नियामक प्राधिकरणों स□जिम्मे□ार व्यक्ति द्वारा दे□ी जा सकती है। मैं इन व्यक्तियों क□लिए □ पन□रिकॉर्ड तक पहुंचन□की □ नुमति दे□ा हूं।

दिनांक _____ _____

स्थान _____ हस्ताक्षर/बाएं□ंगूठ□की छाप

यहप्रमाणितकरन□क□लिएकिउपर्युक्तसहमतिमर□ीउपस्थितिमेंप्राप्तकीगईहै।

तारीख _____ _____

स्थान _____ हस्ताक्षरपीजीछात्र

साक्षी1 साक्षी2

हस्ताक्षर हस्ताक्षर

नाम _____ नाम _____

स्थान _____ स्थान _____

APPENDIX-3

PATIENT INFORMATION SHEET

Name of the patient **Patient ID.**

CLINICAL PROFILE AND OUTCOMES OF PATIENTS WITH DIABETIC KETOACIDOSIS IN A TERTIARY CARE HOSPITAL IN WESTERN RAJASTHAN

1. You are participating in a study to understand the various parameters associated with the disease condition called as Diabetic Ketoacidosis
2. We will be collecting information regarding your age, gender, duration of your disease and the treatment you have received.
3. Study procedure We will be collecting your blood sample to do your routine tests, which are done as part of our study. You will be assessed for your education level about your disease process and will be offered education about your disease following which you will be assessed for your education level again
4. Likely benefit If you will have an better idea about diabetes and its management and the likely cause of complication that you faced , this is likely to help you in managing your blood sugars in a better way and identifying beforehand any future complications.You will also be contributing to the scientific knowledge about the disease
5. **Confidentiality** All the data collected from you will be kept highly confidential.
6. **Risk** Enrolment in above study poses no substantial risk to you as all procedures performed are part of routine clinical care. You can withdraw from the study at any point of time without any consequences to yourself.

For further information / questions, the following personnel can be contacted

DrKartikey Saini, Junior Resident, Department of Internal Medicine, All India Institute of Medical Sciences, Jodhpur, Rajasthan. Ph 9799789859

APPENDIX-4

रोगी सूचना पत्र

रोगी का नाम रोगी आईडी।

पश्चिमी राजस्थान में एक तृतीयक दे□भाल □ स्पताल में मधुमे□ का□ोएसिडोसिस □ाल□रोगियों की नैदानिक प्रोफ़ाइल और परिणाम

1. आप मधुमे□ की□ोएसिडोसिस नामक बीमारी की स्थिति स□जुड़□□भिन्न मापदंडों को समझना□□लिए एक □ ध्ययन में भाग ल□रहे□हैं

2. हम आपकी उम्र, लिंग, आपकी बीमारी की □ □धि और आपक□द्वारा प्राप्त उपचार क□बार□ में जानकारी एकत्र करेंग□□

3. □ ध्ययन प्रक्रिया हम आपक□नियमित परीक्षण करना□□लिए आपक□रक्त का नमूना एकत्र करेंग□,जो हमार□□ ध्ययन क□हिस्सा□□रूप में किए जाते□हैं। आपकी बीमारी की प्रक्रिया क□बार□ में आपक□शिक्षा स्तर क□लिए आपका मूल्यांकन किया जाएगा और आपकी बीमारी क□बार□में शिक्षा की पे□ाकश की जाएगी जिसक□बाद आपक□शिक्षा स्तर क□लिए आपका □ र स□ मूल्यांकन किया जाएगा।

4. संभा□ित लाभ यदि आपको मधुमे□ और इसक□प्रबंधन क□बार□में और आपक□सामन□आन□ □ाली ज□□लता का□संभा□ित कारण क□बार□में बे□तर जानकारी होगी, तो यह आपक□रक्त शर्करा को बे□तर तरीक□स□प्रबंधित करना□और भ□□ष्य की किसी भी ज□□लता की पहचान करना□में आपकी मदद कर सकता है। रोग क□बार□में □ैज्ञानिक ज्ञान में भी योगदान द□रहे□हैं

5. गोपनीयता आपस□एकत्र किए गए सभी ड□□ा को □ त्यधिक गोपनीय रखा जाएगा।

6. उपरोक्त □ ध्ययन में जोखिम नामांकन स□आपक□लिए कोई महत्वपूर्ण जोखिम नहीं है क्योंकि निष्पादित सभी प्रक्रियाएं नियमित नैदानिक दे□भाल का हिस्सा हैं। आप बिना किसी परिणाम क□किसी भी समय □ ध्ययन स□पी□े□ह□ सकते□हैं।

□ धिक जानकारी/प्रश्नों क□लिए निम्नलिखित कर्मियों स□संपर्क किया जा सकता है

डॉ कार्तिक□सैनी, जूनियर रे□िडेंट, आंतरिक चिकित्सा □भाग, □ खिल भारतीय आयुर्□ज्ञान संस्थान, जोधपुर, राजस्थान। दूरभाष 9799789859

APPENDIX-5

SOCIO-DEMOGRAPHIC AND CLINICAL DETAIL

Patient ID **Name of patient** **Participant No**

Age/gender

Diagnosis-Type ½ Diabetes		
Severity of DKA		
Index visit/ referral		
In case of referral, type of hospital previously visited (PHC/CHC/District Hospital)		
Duration of disease		
Age at Diabetes Diagnosis		
Symptoms at admission		
First symptom experienced for the current DKA episode		
No of past episodes similar to current episodes		
If yes to the above question then the total number and duration of hospital admission		
When was the Last administered Insulin dose		
What was the dose of insulin administered		
What was the Blood sugar levels at that time		
Duration of Insulin use		
Type of Insulin taken		
OHA use –duration and class of OHA taken		
Co morbidities	**Hypertension**	
	CVA	
	CAD	
	COPD/Chronic airway diseases	
Family history of diabetes		
Other family history		
History of smoking/Alcohol /cocaine /other	**Smoking**	

substance use disorder	**Alcohol**	
	Cocaine	
	Cannabis	
	Opium	
Other drugs(Thiazide /Amphetamines/Terbutaline) if any kindly mention		
Any diagnosed psychiatric condition		
Any History of	**Starvation**	
	Alcohol Excess	
	Emotional stress	
	Pregnancy	
Any History of	**Fever**	
	Burning Micturition	
	Cough	
	SOB	
	Rashes	
	Any Pus Collection	
Prior History of Insulin/Diabetic education(Yes/No)		
If answer to above question –yes then number of times received		
D SMQ Score		

Weight/SD	
Height /SD	

Waist Hip Ratio/SD	
BMI/SD	
General Examination	
GCS	

Systemic examination	
Ophthalmological examination – Fundoscopy	
Peripheral Neuropathy (using Clinical examination and monofilament)	
Dermatological examination	

INVESTIGATIONS

Blood Sugar	
HbA1c	
Urinary Ketones	
Blood Ketones	
Ph	
Bicarbonates	
Anion Gap	
Electrolytes	
Phosphorous	
Po2/co2	
Lactates	
TLC	
Chest X-ray	
Urine C/s	
Urine r/m	
ECG	
24-hour urinary protein	

ICU care Yes/ No Duration of ICU stay-

Duration of Stay at the hospital-

1. Any episodes of Hypoglycaemia during the stay-
2. Any Requirement of Potassium /Bicarbonate /Phosphate Supplementation during stay at the Hospital –
3. If Yes above to the above question what was supplemented and how, much -
4. Any complication during the stay-
5. Eventual outcome of stay at the hospital