Research Article

A Prospective Study on Risk Factors and Drug Utilization Review Based on Clinical Profiles in Diabetic Emergency in a Tertiary Care Hospital

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ABSTRACT

Background: Diabetic Ketoacidosis (DKA) is a triad of Diabetes, ketosis and metabolic acidosis. **Aim:** To estimate the risk factors and drug utilization review based on clinical profiles in diabetic emergency (DKA) in a tertiary care hospital prospectively. **Objectives:** To determine the demographic characters (Gender, Age and Sex), type of diabetics, clinical manifestations, precipitating factors, comorbidities, biochemical parameters and therapeutic drug monitoring parameters like Drug interactions, ADR's, untreated indications. **Methods:** A Prospective cross-sectional study was conducted on 50 patients in both male and female general medicine units at Government General Hospital, Kurnool. The patients were selected based on the inclusion criteria. Newly diagnosed diabetic patients with Diabetic Ketoacidosis and past history of hospitalization due to occurrence of Diabetic Ketoacidosis were also included in the study. **Results:** Diabetic Ketoacidosis was seen in both types I and type II diabetes. Among the study population female patients were higher in number. Presentation of Diabetic ketoacidosis was higher among the type II diabetes. Diabetic Ketoacidosis among adults was more common amongst the patients in age groups of 30-40 and 50-60 years of age. Nausea, vomiting and shortness of breath were the most common presenting complaints. Most common precipitating factors include Drug Incompliance and Infection. Random blood sugar levels were more than 300 mg/dL in majority of patients. The treatment had seven adverse drug reactions and nine untreated indications in the study. **Conclusion:** Most common precipitating factors include Drug Incompliance (32%) and Infection.

Key words: Diabetes, Diabetic Ketoacidosis, Drug utilization review, Drug incompliance, Precipitating Factors and Therapeutic drug monitoring.

INTRODUCTION

Diabetic Ketoacidosis (DKA) results from absolute or relative deficiency of circulating insulin and the combined effects of increased levels of the counter regulatory hormones: glucagon, catecholamines, growth hormone and cortisol. Absolute insulin deficiency presents in previously undiagnosed type 1 diabetes mellitus and patients on treatment who deliberately, inadequately or do not take insulin, especially the long-acting component of a basal-bolus regimen. Patients who are all on insulin pump can also develop Diabetic Ketoacidosis when insulin delivery fails for any reason.

Relative insulin deficiency can occur when the concentrations of counter regulatory hormones by increase in response to stress in such conditions like trauma, sepsis, or diarrhoea and vomiting.[1]

In condition where there is low serum insulin and high counter regulatory hormones. There occurs an increased catabolic state with increased glucose production by the liver and kidney through glycogenolysis and gluconeogenesis. Impairment in peripheral glucose utilization results in hyperglycemia, increased lipolysis, hyperosmolality and ketogenesis.[1] This causes ketonemia and metabolic acidosis. If hyperglycemia increases more than renal threshold (approximately 10 mmol/L [180 mg/dL] it results in osmotic diuresis and obligatory loss of electrolytes,

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causing dehydration which is aggravated by vomiting. These changes also stimulate further stress hormone production.[2]

This leads to worsening hyperglycemia, more severe insulin resistance and hyperketonemia. If this progression is not controlled with exogenous insulin, fluid and electrolyte therapy, it will cause fatal dehydration and metabolic acidosis. Ketoacidosis is also aggravated by lactic acidosis caused from poor tissue perfusion and sepsis.[3]

MATERIALS AND METHODS

Place of Study

Government General Hospital, Kurnool, a 1000 bed teaching hospital.

Period of Study

The study period was Six months i.e., from August 2018 to January 2019.

Study Population

50 patients fit into inclusion criteria from both female and male General Medicine departments.

Study Design

A Prospective cross-sectional study

Inclusion Criteria

The patient should be previously diagnosed diabetic or *de novo* diabetic and pediatrics are excluded.

Biochemical Inclusion criteria

The patient should have high glycemic levels.

The patient should be positive for ketone bodies in the blood.

Acidic PH values in a patient which are estimated by the physician.

IRB Approval

The research protocol was duly approved by IRB of Dr. K. V. Subba Reddy Institute of Pharmacy vide approval number KVSP/IRB 2018-2019/Pharm.D/PROJ/001.

Method of Study

The study begins with the selection of the patients based on the inclusion criteria followed by the collection of all the baseline parameters of the patient's demographic details, medical history, past allergies, personal history, family history, laboratory data and present treatment and all the data of the data of the subjects are collected by using the patient proforma.

RESULTS

Age Distribution

A total of 50 patients were analyzed for a period of 6 months.

Table 1 furnishes the details of patient's age distribution. Among 50 patients Diabetic Ketoacidosis (DKA) was more common among the age group of 30-40 and 50-60 years of age as shown in Figure 1. The average age was found to be 36.98 (SD±16.48) years.

Gender Distribution

Table 2 furnishes the details of patient's gender distribution. Among 50 Patients the distribution of gender is as follows i.e., Females are 27(54%) and Males are 23(46%) as shown in Figure 2.

Distribution of Diabetic Population

Table 3 furnishes the details of distribution of diabetic population. Among 50 Patients, 21 (42%) were type – I and 29 (58%) were types – II patients as shown in Figure 3.

De novo Diabetic Population

Table 4 furnishes the details of *de novo* diabetic population. Among the *de novo* presentations in 13 patients, 3 (24%) patients were type – I and 10(76%) patients were types – II *de novo* diabetics as shown in Figure 4. Average *de novo* diabetics among 13 patients were 6.5 SD±4.94.

Precipitating Factors in DKA Patients

Table 5 furnishes the details of precipitating factors in DKA patients. Among 50 patients, the most common precipitating factor was Drug incompliance 16 (32%) and followed by Urinary tract infections 12 (24%), pancreatitis 3 (6%), Gastroenteritis 3(6%), Acute febrile illness 2(4%), sepsis 2(4%), Diabetic foot ulcer 1(2%), starvation 1(2%). Among 50 patients first presentations of DKA were 13 (26%) and unknown causes for Diabetic Ketoacidosis (DKA) were 8(16%) as shown in Figure 5.

Clinical Manifestations

Table 6 furnishes the details of clinical manifestations in DKA. Among the 50 patients, 34(68%) had nausea and vomiting as chief presenting symptoms. 33(66%) had

Shortness of breath, 24(48%) had the fever, 23(46%) had abdominal pain, Kussmaul respiration 12(24%) and Altered sensorium 5(10%) as shown in Figure 6.

Glycemic Levels

Table 7 furnishes the details of glycemic levels. Among the 50 patients 15 (30%) patients had Random blood sugar values of about 200-300mg/dL and 11(22%) of patients had 300-400mg/dL, 9(18%) of patients had 400-500mg/dL, 11(22%) had 500-600mg/dL and 2(4%) had 600-700 mg/dL of Random blood sugar as shown in Figure 7. Average RBS value among 50 patients was found to be 383 mg/dL SD ± 130.6989.

Distribution of Co-morbidities

Table 8 furnishes the details of distribution of co-morbidities. Among previous co-morbidities 15 (30%) of patients had hypertension, 3(6%) had pancreatitis, 1 (2%) had AKI, 1(2%) had CKD, 1(2%) had 1(2%) had Diabetic foot ulcer, 1(2%) had Hypothyroidism as shown in Figure 8. The average number of patients having co-morbidities was found to be 3.66 SD± 5.609.

Ketone Index in DKA Patients

Table 9 furnishes the details of ketone index in diabetic ketoacidosis patients. Among 50 patients, 11 (22%) of patients were found with Small, 17(34%) of patients with Moderate and 22 (44%) of patients with Large levels of ketone bodies in urine as shown in Figure 9.

Therapeutic Drug Monitoring

Table 10 furnishes the details of therapeutic drug monitoring (occurrence of adverse drug reactions and drug interactions) in diabetic ketoacidosis patients. Therapeutic Drug Monitoring in 50 patients reveals that the treatment has 9(18%) Untreated indications, 7(14%) Adverse Drug Reactions, 1(2%) Drug interactions as shown in Figure 10. The average number of patients having therapeutic drug errors was found to be 5.6 (SD ±4.16).

Untreated Indications

Table 11 depicts the number of untreated indicatons in patients. Among 50 patients treatment, 9(18%) untreated indications were found as shown in Figure 11.

Adverse Drug Reactions

Table 12 depicts the number of adverse drug reactions in patients. It depicts the total of 7(14%) ADR's occurred among 50 patients as shown in Figure 11.

Table 1: Age Distribution of DKA Patients (*n*= 50).

S. No.	Age	No. of Patients	Percentage (%)
1	10 – 20	11	22
2	21 – 30	7	14
3	31 – 40	12	24
4	41 – 50	6	12
5	51 – 60	12	24
6	61 – 70	2	4

Mean ± SD 36.98 ± 16.48

Table 2: Gender Distribution (*n*= 50).

S. No.	Gender	No. of Patients	Percentage (%)
1	Male	23	46
2	Female	27	54

Table 3: Distribution of Diabetic population (*n*= 50).

S. No.	Type of Diabetes	No. of Patients	Percentage (%)
1	Type - I	21	42
2	Type - II	29	58

Table 4: *De novo* diabetes (*n*= 13).

S. No.	Type of *de novo* Diabetes	No. of Patients	Percentage (%)
1	Type – I	3	24
2	Type – II	10	76

Mean ± SD6.5 ± 4.94

Table 5: Precipitating Factors (*n* = 50).

S. No.	Precipitating Factors	No. of Cases	Percentage (%)
1	Drug Incompliance	16	32
2	Urinary Tract Infections	12	24
3	Sepsis	2	4
4	Diabetic Foot Ulcer	1	2
5	Gastroenteritis	3	6
6	Acute Febrile illness	2	4
7	Pancreatitis	3	6
8	Starvation	1	2
9	First Presentation	13	26
10	Unknown	8	16

Type of ADR

Table 13 depicts the type of adverse drug reactions as shown in Figure 12. During the treatment of 50 DKA patients, 7(14%) were found. Out of which 4(8%) were

Table 6: Clinical Manifestations (*n*= 50).

S. No.	Clinical Manifestations	No. of. Cases	Percentage (%)
1	Nausea/Vomiting	34	68
2	Abdominal Pain	23	46
3	Shortness of Breath	33	66
4	Fever	24	42
5	Kussmaul Respiration	12	24
6	Altered Sensorium	5	10
7	Lethargy	36	72
8	Constitutional Symptoms	29	58

Table 7: Glycemic Levels (*n*= 50).

S. No.	Glycemic Range (mg/dL)	No. of Patients	Percentage (%)
1	100 – 200	2	4
2	200 – 300	15	30
3	300 – 400	11	22
4	400 – 500	9	18
5	500 – 600	11	22
6	600 – 700	2	4

Mean ± SD 383 ± 130.6989

Table 8: Co morbidities in DKA Patients (*n*= 50).

S. No.	Type of Co morbidity	No. of Patients	Percentage (%)
1	Hypertension	15	30
2	Acute Kidney Injury	1	2
3	Chronic Kidney Disease	1	2
4	Pancreatitis	3	6
5	Diabetic Foot Ulcer	1	2
6	Hypothyroidism	1	2

Mean ± SD 3.66 ± 5.609

Table 9: Ketone Index (*n*= 50).

S. No.	Ketone Range	No. of Patients	Percentage (%)
1	Small	11	22
2	Moderate	17	34
3	Large	22	44

Diarrhea, 2(4%) were Dyspepsia and 1(2%) were Allergic reaction. Average number of ADR in 50 patients was found to be 2.3 (SD ± 1.5).

Table 10: Therapeutic Drug Monitoring (*n*= 50).

S. No.	Factor	No. of patients	Percentage %
1.	Untreated indications	9	18
2.	Adverse Drug Reactions	7	14
3.	Drug Interactions	1	2
4.	Patient factors	0	0

Mean ± SD 5.6 ± 4.16

Table 11: Untreated indications (*n*= 50).

S. No.	FACTOR	No. of patients	Percentage%
1.	Untreated indication	9	18

Table 12: Adverse Drug Reactions (*n*= 50).

S. No.	FACTOR	No. of patients	Percentage %
1.	Adverse Drug Reactions	7	14

Table 13: TYPE OF ADR's (*n*= 50).

S. No	TYPE OF ADR	No. of patients	Percentage %
1.	Diarrhea	4	8
2.	Dyspepsia	2	4
3.	Allergic Reaction	1	2

Mean ± SD 2.3 ± 1.5

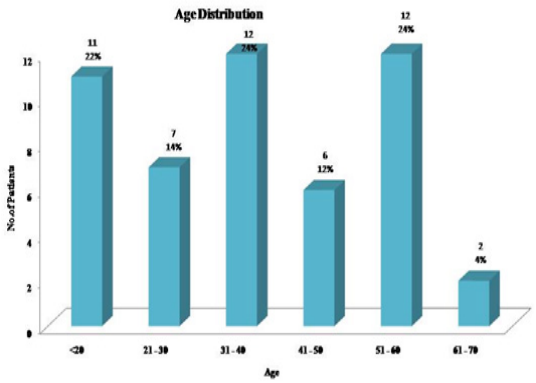

Figure 1: Age Distribution of DKA Patients (*n* = 50).

DISCUSSION

In Past few decades, DKA was considered to be more prone in Type – I diabetics. But now DKA prevalence of occurring is much into Type –II diabetics also.[4] Primary development of DKA is due to absolute or relative lack of circulating insulin and enhanced by counter regulatory hormones like Glucagon, catecholamine's, cortisol and growth hormone.[5] We conducted a prospective cross – sectional study in G.G.H, Kurnool. During a period of six months and collected 50 DKA cases during August 2018 to January 2019. Out of a total of 50 patients, 21

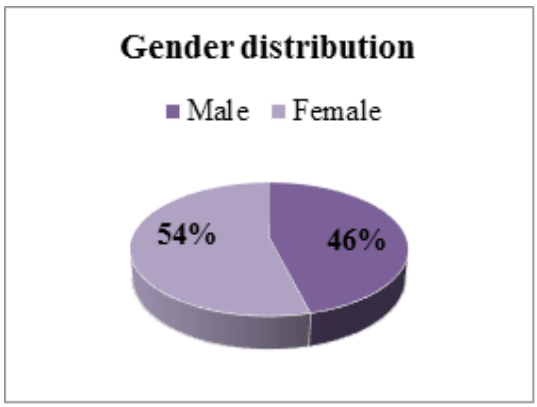

Figure 2: Gender Distribution (*n*= 50).

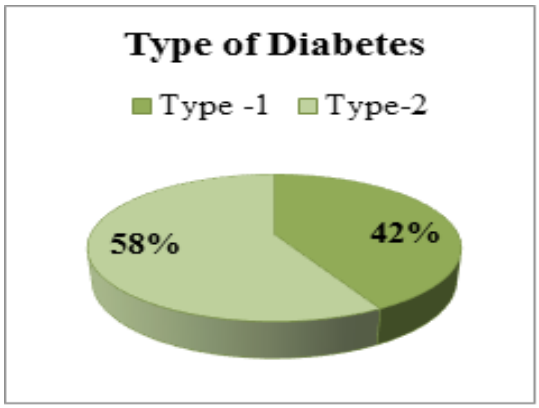

Figure 3: Diabetic Population: (*n*= 50).

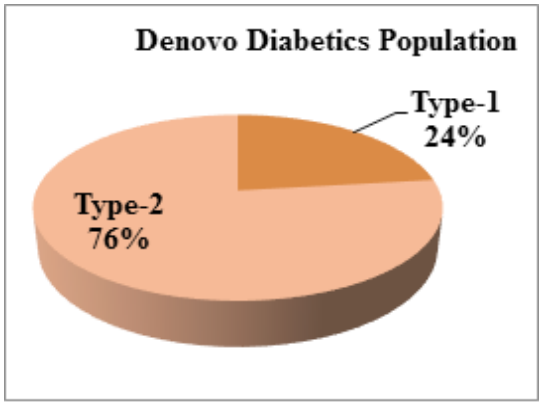

Figure 4: *De novo* Diabetic Population: (*n*= 50).

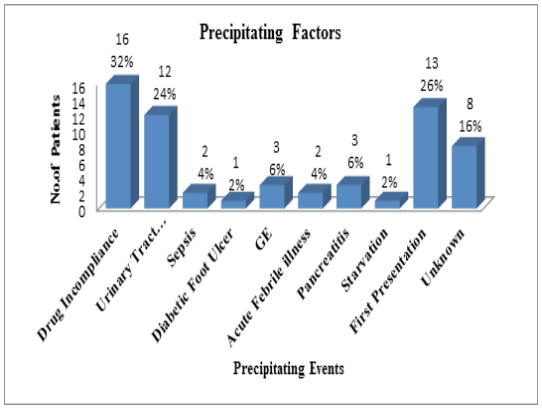

Figure 5: Precipitating Factors: (*n*= 50).

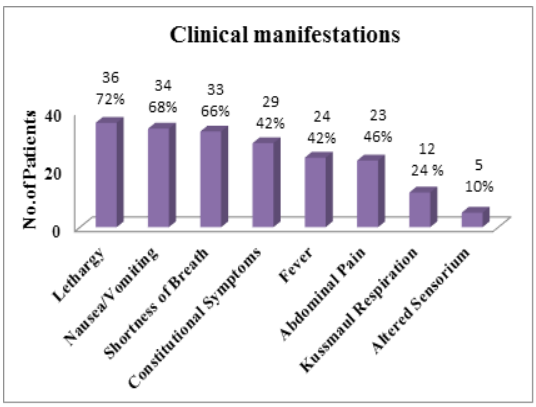

Figure 6: Clinical Manifestations: (*n*= 50).

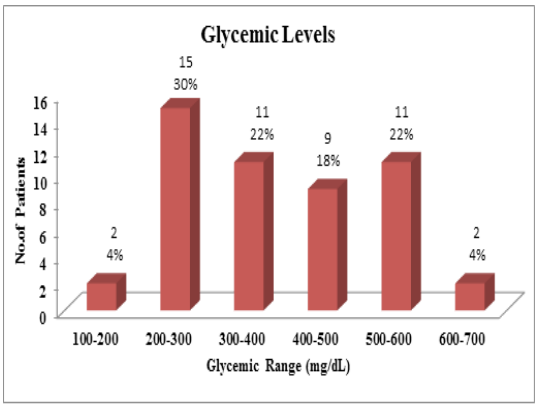

Figure 7: Glycemic Levels (*n*=50).

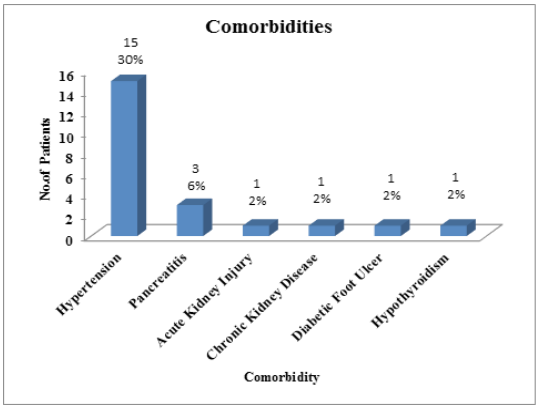

Figure 8: Co morbidities in DKA Patients: (*n*= 50).

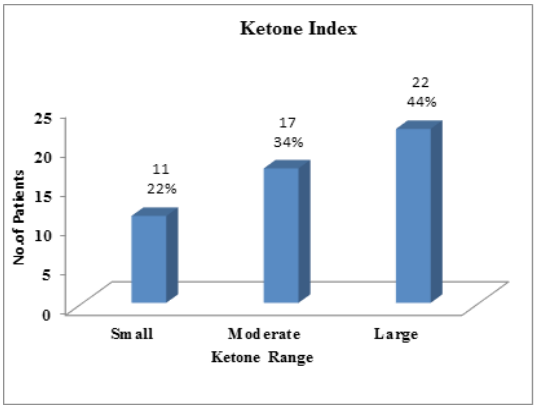

Figure 9: Ketone Index: (*n*= 50).

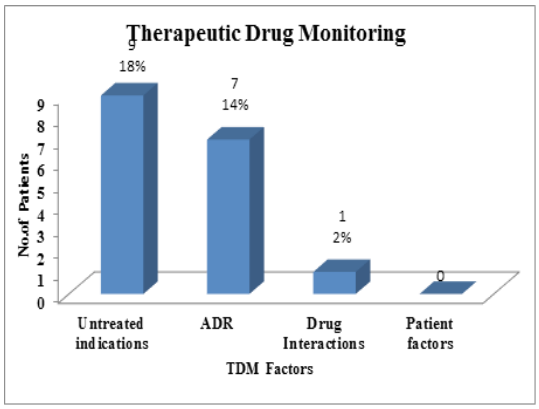

Figure 10: Therapeutic Drug Monitoring (*n*= 50).

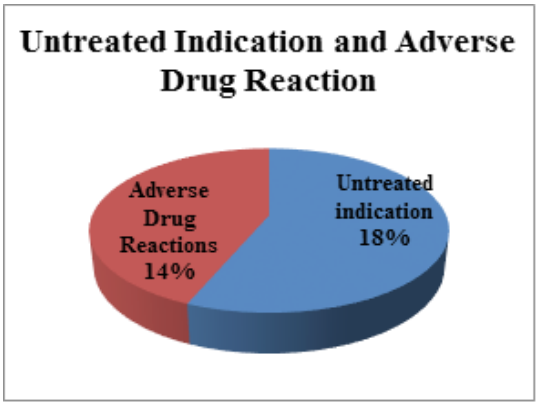

Figure 11: Untreated Indication and Adverse Drug Reaction (*n*= 50).

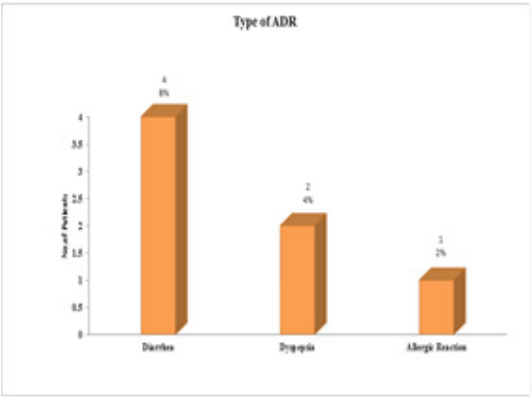

Figure 12: Type of Adverse Drug Reaction (n= 50).

(42%) of patients are type I Diabetics and 29 (58%) of patients had type II diabetics. Females are more prone to DKA than male population in our study. Majority of the patients 12 (24%) were in the age group of about 30-40 years and 50-60 years of age. The average age was found to be 36.98 years. Most of the DKA patients 34 (68%) had nausea and vomiting as chief presenting symptoms. The most common precipitating factor was Drug incompliance 16 (32%) and followed by Urinary tract infections 12 (24%). First presentations of DKA was seen in 13 patients. Among previous comorbidities, in DKA patient's hypertension is about 30% and is considered as most frequently occurring fatal comorbidity. High Random glycemic levels were noticed in most of the DKA patients. The average Random blood sugar levels are more than 300 mg/dL in 48 (96%) of patients in majority of patients at time of presentation. 22 (44%) of DKA.[6]

Patients had developed a large range of ketone bodies in urine among 50 patients. Newly diagnosed diabetes were about 13 (26%) patients. Out of thirteen newly detected type I diabetics was 3 (23%) and 10 (76.9%) were type II diabetics. Out of the 50 patients 9 (18%) untreated indications, 7 (14%) Adverse drug reactions and 1 (2%) of Drug interactions were found in the treatment. Among 7(14%) ADR's Diarrhea 4(8%), Dyspepsia 2(4%), Allergic Reactions 1(2%) was found in the treatment.[7]

Role of Clinical Pharmacist in Dka Management

The ultimate goal of counseling is to provide information directed at encouraging safe and appropriate use of medications, thereby enhancing therapeutic outcomes.

Because of the rapid expansion of available therapeutic agents to treat diabetes, the pharmacist's role in caring for diabetic patients has expanded. The pharmacist can educate the patients about the proper use of medication, screening for drug interactions, explain monitoring devices and make recommendations for ancillary products and services.[8,9]

Essential components of diabetic counseling

Counseling regarding lifestyle modifications

Carbohydrates: 45–60 g per meal and 10–25 g per snack, totaling about 135–230 g per day.

Fat: It is wise to restrict saturated fats and to substitute them with unsaturated fats

Fiber: 25 to 50g daily.

CONCLUSION

From the above study, it was concluded that DKA was seen in both types I and type II diabetes. Among the study population female patients (54%) were high in number. Presentation of Diabetic ketoacidosis (DKA) was high among the type II diabetes (58%). DKA among adults was more common among patients in the age group of 30-40 (24%) and 50-60 (24%) years of age. Nausea/vomiting (68%) and shortness of breath (66%) were the most common presenting complaints. Most common precipitating factors include Drug Incompliance (32%) and Infection. Random blood sugar levels are 200- 300

mg/dL (30%) in the majority of patients at the time of presentation. Hypertension (30%) is the major co-morbidity among the patients. Many of these cases can be prevented with proper education and effective communication. All patients' treatment was evaluated with regards to Therapeutic Drug Monitoring and concluded that the treatment has Seven Adverse drug reactions (14%) and nine untreated indications (18%) in the study population.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

ADR: Adverse Drug Reaction, **AKI:** Acute Kidney Injury; **CKD:** Chronic Kidney Disease; **DKA:** Diabetic Ketoacidosis; **RBS:** Random Blood Sugar.

SUMMARY

- Among diabetic population type – II diabetics were more prone to Diabetic ketoacidosis.
- The most common Precipitating factor was Drug incompliance and infection.
- Hypertension was the major Comorbidity among the patients.
- Seven ADRs and nine untreated indications were identified in this study.

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