Sudan University of Science and Technology

College of Graduated Studies

Effect of Acidosis on Uropathogenic Bacterial Growth among Diabetic ketoacidosis Patients in East Nile Locality, Khartoum state

تأثير الحمضيه على نمو بكتريا البول الممرضه وسط مرضى الحُماض الكيتوني السكري في محليه شرق النيل - ولايه الخرطوم

A Dissertation Submitted in partial Fulfillment for The Requirements of M.Sc Degree in Medical Laboratory Science (Microbiology)

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Dedication

TO MY COUNTYRY YEMEN

TO MY DEAR PARENTS

TO ALL MEMBER OF MY FIMALIY

TO MY FRIENDS

Acknowledgement

First I would like to thank Allah for blessing me …..

I would like to express my immense gratitude and appreciation to my supervisor

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I would like to thank my teachers in Sudan University of Science and Technology

I am deeply indebted to my second family the staff of Microbiology Lab in Laboratory Administration for their good advice and aid

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Abstract

Diabetes is a group of metabolic disease characterized by hyperglycemia resulting from defect in insulin secretion, insulin action or both. Diabetic ketoacidosis (DKA) is a type of diabetes complication lead to coma and death, the main characteristic of Diabetic ketoacidosis (DKA) are: hyperglycemia and ketoacidosis. Urinary tract infection is the most type of infection in diabetic patients especially in females more than males.

This study aimed to detect bacterial growth in diabetes ketoacidosis urine and to compare the percentage of growth between Diabetic ketoacidosis patients and Diabetes patients without Ketoacidosis. Out of 50 cases of diabetic ketoacidosis 20 males (40 %) and 30 females (60 %), the age group between 23-33 years have high occurrence of diabetic ketoacidosis 24% .The duration period of onset diabetic between1 -5 years was 41.9 % and reflect high incidence rate of diabetic in the last five years. 14 (28%) and 36(72%) were symptomatic and asymptomatic of UTI respectively . 74% of diabetes ketoacidosis having urine pH 5 while those with pH 6 were 26%. The present results show inhibition action of acidosis against urine pathogens among diabetic ketoacidosis patients in East Nile province only 2% of bacterial growth while 98% was inhibited. The only bacteria in acidic urine in this study was *Klebseilla pneumoniae* may be due to presence of large capsule. Among 25 diabetes patients non- ketoacidosis 13 (52 %) were females and 12 (48 %) were males with age group between 36- 70 years old and blood glucose level between 170 – 295 mg \dl , four microorganisms isolates were detected in the urine samples of non- ketoacidosis 4 (16%) two *Esherichia coli* (50%) , one *Klebseilla pneumoniae* (25%) and one *Candidia spp (25 %)*

مستخلص الاطروحه

يعد مرض السكرى من أمراض الايض والإستقلاب ومن أشهر أمراض الغدد الصماء متمثلا بارتفاع سكر الدم الناتج من وجود خلل في إفراز الانسولين أو عمله . الحُماض الكيتوني السكرى هو نوع من أخطر مضاعفات مرض السكري الذى يؤدى للغيبوبه والوفاه وتتمثل علاماته بارتفاع معدلات السكر مع وجود الحمضيه الكيتونيه يمثل التهاب البول وتكراره المشكله التى تؤرق أغلب مرضى السكر.

الغرض من هذه الدراسه هو تحديد مدى نمو البكتريا في عينات البول لدى مرضى الحماض الكيتوني السكري بالمقارنه مع مرضى السكري من دون الحماض الكيتوني حوالى ٥٠ حاله من حالات الحماض الكيتوني السكري كانت تحت الدراسه ٢٠ (٤٠%) من الذكور و ٣٠(٦٠%) من الاناث .الفئه العمريه الاكثر اصابه بهذه الحاله كانت فئه الشباب بين (٢٣-٣٣ عام) بنسبه ٢٤% .الفتره الزمنيه لظهور السكري خلال الخمسه اعوام الاخيره كانت الاعلى مما يدلل على زياده حالات السكري المسجله سنويا . ١٤ (٢٨%) و ٣٦(٧٢ %) مابين المرضى الذين لديهم اعراض التهاب في البول من الذين لا يعانون من هذه الاعراض تباعا . ٧٤% من مرضي الحُماض الكيتوني السكري كانت حمضيه البول لديهم تساوى ٥ بينما من يحملون حمضيه تساوي ٦ كانوا ٢٦%. النتائج المقدمه اظهرت تأثير مثبط للحمضيه على البكتريا المسببه لالتهاب البول وسط مرضى الحماض الكيتوني السكري في محليه شرق النيل ٢% فقط كان النمو البكتيري لعينات البول بمقابل ٩٨% من دون نمو، البكتريا الوحيده التى تم عزلها هي بكتريا كلبسيليه الرئويه ربما بسبب وجود كبسول ضخم يحميها من العوامل الخارجيه بالمقارنه مع نسبه نمو تقدر ب ٤ (١٦%) في مجتمع ٢٥ حاله من حالات السكر الخالى من الحماض الكيتوني الذي كان الذكور يمثلوا فيه حوالى ١٢ (٤٨%) والاناث بنسبه تقدر ب ١٣ (٥٢%) كان مدى الفئات العمريه محصورا بين (٣٦ – ٧٠ عام) وكانت نسب السكر مابين (١٧٠-٢٩٥) كانت البكتريا القولونيه (اي كولاي) هي الاعلى بنسبه ٥٠ % وتم عزل بكتريا الكلبيسله الرئويه بنسبه ٢٥ % مناصفه مع المبيضات بنسبه ٢٥%

Table of contents

No	Subjects	Page No
	Dedication	**I**
	Acknowledgement	**II**
	Abstract	**III**
	المستخلص	**IV**
	Tables of contents	**V**
	List of tables	**IX**
	List of figures	**IX**
1	**Chapter one : Introduction**	
1.1	Background	**1**
1.2	Rationale	**3**
1.3	Objectives	**3**
1.3.1	General objective	**3**
1.3.2	Specific objectives	**3**
1.4	Hypothesis	**4**
2	**Chapter two : Literature Review**	
2.1	Diabetes Mellitus	**5**
2.1.1	The History of Diabetes Mellitus	**5**
2.1.2	Definition and classification of Diabetes	**5**
2.1.3	Pathophysiology	**6**
2.1.4	Signs and Symptoms	**7**
2.1.5	Diagnosis of Diabetes Mellitus	**7**
2.2	Diabetic Ketoacidosis	**8**

2.2.1	Definition of Diabetic Ketoacidosis (DKA)	**8**
2.2.2	Pathophysiology	**8**
2.2.3	Signs and Symptoms	**9**
2.2.4	Causes of Diabetic Ketoacidosis	**10**
2.2.5	Diagnosis	**10**
2.2.6	Frequency of Diabetic Ketoacidosis	**11**
2.2.7	Management	**11**
2.3	Urinary Tract Infection (UTI)	**12**
2.3.1	Definition and classification of Urinary Tract Infection	**12**
2.3.2	Pathophysiology	**14**
2.3.3	Signs and Symptoms	**14**
2.3.4	Causative agents of urinary tract infection	**15**
2.3.5	Diagnosis of urinary tract infection	**15**
2.3.5.1	Laboratory Methods	**16**
2.3.6	Treatment	**17**
2.4	Urinary Tract infection between Diabetic patients and non-Diabetic patients	**17**
2.5	Prevalence of Urinary Tract infection among Diabetic patients	**18**
2.6	The effect of pH and glucose on the growth of bacteria in urine	**19**
2.7	Antibacterial action of acidosis in urine	**20**
3	**Chapter three : Materials and Methods**	
3.1	Study design	**21**
3.2	Study area	**21**
3.3	Study population	**21**

3.4	Study duration	**21**
3.5	Sample size	**21**
3.6	Data collection	**21**
3.7	Ethical considerations	**21**
3.8	Samples collection	**22**
3.9	Laboratory methods	**22**
3.9.1	Urine culture	**22**
3.9.2	Urine investigation (Macroscopic, Microscopic investigation)	**22**
3.9.3	Gram stain	**22**
3.9.4	Biochemical test	**23**
3.9.4.1	Citrate Utilization test	**23**
3.9.4.2	Urease test	**23**
3.9.4.3	Indole test	**23**
3.9.4.4	Killigler iron agar (KIA)	**24**
4	**Chapter four: Results**	
4.1	Distributions of Diabetic ketoacidosis (DKA) patients according to gender	**25**
4.2	Distributions of Diabetic ketoacidosis (DKA) patients according to age	**25**
4.3	Duration period of onset diabetic among Diabetic ketoacidosis (DKA) patients	**26**
4.4	Risk factors of Diabetic Ketoacidosis (DKA) among patients	**27**
4.5	Symptoms of urinary tract infection among Diabetic ketoacidosis (DKA) patients	**28**
4.6	laboratory investigations results	**28**

4.6.1	Blood glucose level	**28**
4.6.2	Blood urea level	**29**
4.6.3	Glucosuria and ketonuria in Diabetic ketoacidosis (DKA)	**29**
4.6.4	Proteinuria in Diabetic ketoacidosis (DKA)	**29**
4.6.5	Urine pH in Diabetic ketoacidosis (DKA)	**29**
4.6.6	Pyuria in urine of Diabetic ketoacidosis (DKA)	**30**
4.6.7	Uropathogenic growth in Diabetic ketoacidosis (DKA)	**30**
4.6.8	Uropathogenic growth in Diabetes patients without ketoacidosis	**31**
5	**Chapter five : Discussion**	
5.1	Discussion	**32**
5.2	Conclusion	**34**
5.3	Recommendations	**34**
	Reference	**35**
	Appendix	

List of Tables

Legend	Page No
Table .1 Distributions of diabetic ketoacidosis (DKA) patients according to gender	25
Table .2 Distributions of diabetic ketoacidosis (DKA) patients according to age group	25
Table. 3 Regularity of taking doses among patients	27
Table. 4 Frequency of symptomatic and asymptomatic patients	28
Table .5 Blood glucose levels among males and females ketoacidosis patients	28
Table .6 ketonuria and glucosuria among DKA patients	29
Table .7 Appearance of protein in urine patients	29
Table 8. Pus in urine of Diabetes ketoacidosis patients	30

List of Figures

Legend	Page No
Figure .1 Distribution of age between males and females	26
Figure. 2 duration period of diabetes for more than one year	27
Figure. 3 Urine PH in ketoacidosis patients	30
Figure. 4 uropathogenic growth between DKA and non -DKA	31

Chapter one

Introduction

1. Introduction

1.1Background

Diabetic is a group of metabolic disease characterized by hyperglycemia resulting from defect in insulin secretion, insulin action or both. The chronic hyperglycemia of diabetic is association with long term damage, dysfunction and failure of different organs especially the eyes, kidneys nerves, heart and blood vessels. Several pathogenic processes are involved in the development of diabetes these range from autoimmune destruction of the pancreatic beta cells with consequent insulin deficiency to abnormalities that result in resistance to insulin action. Symptoms of marked hyperglycemia include polyuria, poly dipsia , weight loss sometimes with polyphagia and blurred vision (American Diabetes Association , 2014). Diagnosis of diabetes according to WHO criteria 2006 , 2011 are random blood sugar more than 11 mmole\L about (200 mg \ dl) fasting blood sugar more than 7 mmole \L about (127 mg \dl) and HbA1c more than 6.5 (Rees *et al* , 2017) .

Diabetic ketoacidosis (DKA) is an important complication of diabetes mellitus , accounting for a majority of deaths mainly in younger adult and also in known diabetic patient who misses insulin doses. The main characteristic of DKA are: hyperglycemia (due to lack of insulin) – ketoacidosis and acidosis (due to elevated counter regulatory hormone promoter lipolysis in adipose tissue and inhibit lipogenesis leading to release of fatty acid and glycerol and formation ketone body) – dehydration and electrolyte imbalance) . Clinical presentation included: polydipsia – polyuria – nocturia – polyphagia – weight loss – nausea, vomiting and abdominal pain Laboratory diagnosis included : serum glucose more than 11 mmole \ L arterial blood gas PH below 7.2 –

ketonuria and glycosuria- elevated in blood urea and creatinine through protein catabolism – decrease in serum potassium .The first management of DKA is by fluid replacement by normal saline second electrolyte replacement by potassium then insulin therapy take place (Oakes and Cole , 2007) The incidence of Diabetic ketoacidosis (DKA) among Diabetic patients is about 50-100 events per 1000 (Farsani *et al* , 2017)

Urinary tract infection (UTI) is the most type of infection in diabetic patients especially in females more than males. Bacteria are the most common cause of this infection. Urinary tract comprising of the upper and lower urinary tract. The infection is named after the part that gets infected and is referred to as cystitis (bladder infection) and phylonephritis (kidney infection). The symptoms associated with the cystitis includes: sudden need to urinate and difficult painful urination and dysuria. The symptoms associated with pylonephritis incudes: fever and lower back pain. (Vasudevan , 2014). The most type of bacteria that called uropathogenic bacteria are *: Esherichia coli , Klebseilla pneumoniae , Staphylococcus saprophyticus , Proteus mirablis , Enterococcus faecalis , Pseudomonas aeruginosa, Candidia spp and Staphylococcus aureus* . Diabetic patients have the high prevalence of UTI by the following mechanism: diabetic neuropathy lead to dysfunction of the bladder thus creating the chance for UTI development .Autonomic neuropathy involved the genitourinary tract causes dysfunction voiding and urinary retention which lead to decrease bacterial clearance by micturition, this facilitating bacterial growth .Also impaired immune response play a role in reduced capacity to defend against bacterial (Alrwithy *et al* , 2017)

1.2 Rationale

The number one of non – communicable diseases in Sudan is diabetes with high incidence rate, in 2017 there was over 2,247,000 patients and about 425 million patients in the world, more than 39 million in Middle East and North Africa region (MENA), by 2045 this will rise to 67 million (International Diabetes Federation. 2017). The high incidence of diabetic mellitus was the reason to choice diabetic patients as study population. In this population recurrent urinary tract infection is a big problem in diabetic mellitus especially in females more than males. These days most of antibiotic failure to treat UTI because of formation high level of resistance mechanism by the bacteria because of misuse of antibiotic with and without symptoms the patient takes a lot of antibiotic. Most of doctors in developing countries give the patient antibiotics without making culture and sensitivity due to lake of microbiology lab, materials and to save the patient time and his money. In this research I aimed to study if the acidosis has effect on the growth of bacteria that causes UTI and how to treat UTI without using antibiotic by control the pH level.

1.3 Objectives

1.3.1 General objectives

To study the effect of acidosis on uropathogenic bacterial growth among Diabetic ketoacidosis patients in East Nile province, Khartoum state

1.3.2 Specific objectives

1. To detect bacterial growth in urine of diabetic ketoacidosis (DKA) and diabetics non -ketoacidosis.

2. To compare the percentage of growth between diabetic ketoacidosis (DKA) patients and non-ketoacidosis patients.

3. To investigate blood glucose , urea , urine general in diabetic ketoacidosis (DKA)

4. To determine urine pH in diabetic ketoacidosis (DKA)

1.4 Hypothesis

Decrease urine pH (acidic urine) affect in urinary tract infection and may help to reduce of urinary tract infection (UTI) without use antibiotic except some type of bacteria that have virulence factors that can cause infection .

Chapter two
Literature Review

2. Literature Review

2.1 Diabetes Mellitus:

2.1.1 The History of Diabetes Mellitus

Diabetes mellitus is a chronic endocrine disease, diabetes comes from Greek means to pass through and mellitus also from Greek means sweetened with honey. Ancient egyptians described features similar to diabetes mellitus around 3000 years ago but the actual term 'diabetes' was only first used by the physician aretaeus of Cappadocia in the 2nd century AD. Later, in 1675, 'mellitus' was added by Thomas Willis, a physician who re-discovered the urine's sweet taste. A major turning point in the history of diabetes was the discovery and use of insulin by Banting and Best in 1921. The first oral hypoglycaemic agents were marketed in 1955. (Rees *et al* , 2017).

2.1.2 Definition and classification of Diabetes

Diabetes mellitus is a general term for heterogeneous disturbances of metabolism for which the main finding is chronic hyperglycaemia. The cause is either impaired insulin secretion or impaired insulin action or both.(Kerner and Brückel , 2014). Diabetes can be classified into the following general categories:

1. Type 1 diabetes (due to autoimmune b-cell destruction, usually leading to absolute insulin deficiency)
2. Type 2 diabetes (due to a progressive loss of b-cell insulin secretion frequently on the background of insulin resistance)
3. Gestational diabetes mellitus (GDM) (diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation)

4. 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 drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation). (American Diabetes Association, 2017)

But in the new study which published in March 2018 in the journal "The Lancet Diabetes and Endocrinology" researcher classify diabetes into five clusters: Cluster 1: (severe autoimmune diabetes) similar to type 1. Cluster 2: (severe insulin deficient diabetes) similar to cluster 1but in this case the immune system was not the cause of their disease and they didn't have auto antibiotic people in this group may have a deficiency in the cell that produce insulin. Cluster 3 : (severe insulin resistance diabetes) overweight people and had high insulin resistance ,meaning their bodies are making insulin but their cells aren't responding to it and had high risk of kidney disease . Cluster 4: (mild obesity –related diabetes) this form in people who had a milder form of the disease without as metabolic problem as those in cluster 3 . Cluster 5: (mild age related diabetes) this forms was similar to cluster 4 but the people were older at the age of diagnosis (BBC News , 2018)

2.1.3 Pathophysiology

The autoimmune process, involving both humoral and cellular immunity, results in CD8 T-cell lymphocyte-mediated destruction of the insulin-secreting β-cells. The chronic inflammatory changes which ensue include infiltration with CD4+ and CD8+ lymphocytes and macrophages, causing an insulinitis. β-Cell destruction subsequently occurs, with a loss in β-cell mass and consequent insulinopenia. In the absence of insulin action in muscle and adipose tissue, glucose is not transported into the cells by the GLUT4 transporter. A number of islet-related antibodies are present in

patients with Type 1 diabetes. In the case of type 2 the defect in both insulin sensitivity and insulin secretion. Insulin resistance occurs at the level of the peripheral tissues (skeletal muscle, adipose tissue) and liver,

Resulting in reduced glucose uptake in skeletal muscle and impaired inhibition of hepatic glucose output. In adipose tissue, insulin resistance leads to increased non-esterified fatty acid production, which stimulates gluconeogenesis and triglyceride synthesis. As a result of β-cell dysfunction, insulin secretion is already reduced by half by the time of diagnosis of disease (Rees *et al*, 2017)..

2.1.4 Signs and Symptoms

Only about half of patients of type 2 present with the classic symptoms of thirst, polydipsia, polyuria and tiredness. Secondary to hyperglycaemia, although these symptoms are often less marked than in type 1. Weight loss is an unusual feature at presentation. The most common symptoms in type 1 are thirst, polydipsia, polyuria and weight loss. Hyperglycaemia results in a marked osmotic effect, often more severe than type 2 . The increased osmotic effect can lead to profound. Dehydration, hypovolaemia and drowsiness hyperglycaemia causes osmotic changes in the lens of the eye, with subsequent blurred vision. In addition, a hyperglycaemic environment predisposes patients to cutaneous *Candida* infections, particularly genital thrush. Absolute insulin deficiency also results in protein breakdown and muscle wasting, fatigue and weight loss. (Rees *et al* , 2017)..

2.1.5 Diagnosis of Diabetes Mellitus

Diabetes may be diagnosed based on plasma glucose criteria, either the fasting plasma glucose (FPG) or the 2-h plasma glucose (2-h PG) value after a75-g oral glucose tolerance test (OGTT) or A1C criteria.

FPG >126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h .Or 2-h PG>200 mg/dL (11.1 mmol/L) during an OGTT.

The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water. Or A1C>6.5% (48 mmol/mol). Or In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma Glucose>200mg/dL(11.1mmol/L). (American Diabetes Association, 2017)

2.2 Diabetic Ketoacidosis

2.2.1 Definition of Diabetic Ketoacidosis (DKA)

Diabetic ketoacidosis (DKA) is an extreme metabolic state caused by insulin deficiency. The breakdown of fatty acids (lipolysis) produces ketone bodies (ketogenesis), which are acidic. Acidosis occurs when ketone levels exceed the body's buffering capacity. (Misra and Oliver , 2015) . Diabetic ketoacidosis (DKA), a life-threatening complication of diabetes mellitus (DM), occurs more commonly in children with type 1 DM than type 2 DM. (Sivanandan *et al* , 2010) .

2.2.2 Pathophysiology

DKA results from insulin deficiency from new-onset diabetes, insulin noncompliance, prescription or illicit drug use, and increased insulin need because of infection. This insulin deficiency stimulates the elevation of the counter regulatory hormones (glucagon, catecholamines, cortisol, and growth hormone). Without the ability to use glucose, the body needs alternative energy sources. Lipase activity increases, causing a breakdown of adipose tissue that yields free fatty acids. These components are converted to acetyl coenzyme A, some of which enter the Krebs cycle for energy production; the remainder is broken down into ketones (acetone, acetoacetate, and β-hydroxybutyrate). Ketones can be used for energy, but accumulate rapidly. Glycogen and proteins are catabolized to form glucose. Together, these factors promote hyperglycemia, which leads to an osmotic diuresis resulting in

dehydration, metabolic acidosis, and a hyperosmolar state (Westerberg, 2013) The most common acid – base disorder is associated with many life threatening condition .Metabolic acidosis(a state produce by excessive acid production , reduce acid excretion , or loss of body alkaline) . Arterial blood gas analysis typically show the PH to be less than 7.35 and serum bicarbonate ($HCO_3^{-)}$ to be less than 18 Eq\L .The signs and symptoms of metabolic acidosis are non-specific and it's diagnosis is associated with increase morbidity and mortality Pathophysiology: cellular metabolism produce CO_2 by a reverse intracellular process CO_2 combined with water to form $H_2CO_3^{-}$then $H_2CO_3^{--}$ dissociate into H^+ and HCO_3^-. Acidemia is the state of elevated H^+ concentration and is measured in units of PH . The primary responses to a metabolic acidosis is an increase in ventilation resulting in increased CO_2 excretion by diffusion in the lungs (Chaeles and Heilman , 2005)

2.2.3 Signs and Symptoms

The clinical signs and symptoms of Diabetic ketoacidosis (DKA) include: Feeling unwell for a short period, often less than 24 hours . Polydipsia and increased thirst. Polyuria/ nocturia . Polyphagia . Weight loss. Nausea and vomiting, vomitus can have coffee-ground colour due to haemorrhagic gastritis. Abdominal pain, due to dehydration and acidosis. Weakness . Neurologic signs: restlessness, agitation, lethargy and drowsiness, coma. Increased osmolality is the main factor that contributes to altered mental status . Visual disturbances due to hyperglycaemia . Deep and rapid breathing, known as Kussmaul breathing, may have acetone odour on breath.. Signs of dehydration due to fluid loss through polyuria, vomiting and breathing . Reduced skin turgor, dry mucous membranes. Signs of hypovolaemia: tachycardia, hypotension, postural hypotension due to fluid loss over 3 litres . Mild hypothermia due to acidosis-induced peripheral vasodilation, warm dry skin fevers are rare

despite infection. Severe hypothermia is a poor prognostic sign (Oakes and Cole , 2007)

2.2.4 Causes of Diabetic Ketoacidosis

The main Causes of Diabetic Ketoacidosis included the follows:

Drugs : Antipsychotic agents clozapine (Clozaril) , olanzapine(Zyprexa), risperidone (Risperdal) , Illicit drugs (cocaine) and alcohol. Infection: Pneumonia, sepsis, urinary tract infection. Lake of insulin: Insulin pump failure . Nonadherence to insulin treatment plans. Unrecognized symptoms of new- onset diabetes mellitus Other physiologic stressors : Acromegaly, arterial thrombosis, cerebrovascular accident , Cushing disease, hemochromatosis, myocardialinfarction,, pancreatitis, pregnancy, psychological stress, Shock/hypovolemia, trauma. (Westerberg, 2013)

2.2.5 Diagnosis

The biochemical criteria for the diagnosis of diabetic ketoacidosis (DKA) are: Hyperglycemia (serum glucose concentration >200 mg/ dL) in the presence of metabolic acidosis (blood pH<7.3 with serum bicarbonate level <15 mEq/L) and ketonemia (presence of ketones in blood) .As measurement of ketones in blood is not readily available, ketonuria is used as a marker of ketonemia. When measured, serum ketones (ß hydroxybutyrate plus acetoacetate) exceed 31 mg/dL with or without ketonuria >80 mg/dL. The severity of DKA is defined by the degree of acidosis. Mild DKA is defined by venous pH between 7.2 and 7.3 or bicarbonate between 10 and15 mEq/L; moderate by pH between 7.1 and 7.2 or bicarbonate between 5 and10 mEq/L; and severe by venous pH below 7.1 or bicarbonate below 5 mEq/L. (Sivanandan *et al* , 2010) .

2.2.6 Frequency of Diabetic Ketoacidosis

There is wide geographic variation in the frequency of Diabetic ketoacidosis (DKA) at onset of diabetes; rates inversely correlate with The regional incidence of type 1 diabetes. Frequencies range from approximately 15–70% in Europe and North America. (Wolfsdorf *et al* . 2014) Diabetic ketoacidosis (DKA) continues to have high rates of morbidity and mortality despite advances in the treatment of diabetes mellitus. 14 percent occurred in persons older than 70 years, 23 percent in persons 51 to 70 years of age, 27 percent in persons 30 to 50 years of age, and 36 percent in persons younger than 30 years. 94 percent had no episodes of DKA, 5 percent had one episode, and 1 percent had at least two episodes. Additionally, DKA occurred more often in females, DKA has a case fatality rate of 1 to 5 percent. Although the highest rate of mortality is in older adults and persons with comorbid conditions, DKA is the leading cause of death in persons younger than 24 years with diabetes, most often because of cerebral edema. Most persons with DKA have type 1 Diabetes. There is also a subgroup of persons with type 2 diabetes who have ketosis-prone diabetes; this subgroup represents 20 to 50 percent of persons with DKA. Persons with ketosis-prone diabetes have impaired insulin secretion; however, with proper glucose management, beta cell function improves and the clinical course resembles that of type 2 diabetes. These persons are often black or Latino, male, middle-aged, overweight or obese, have a family history of diabetes, and have newly diagnosed diabetes (Westerberg, 2013)

2.2.7 Management

Subsequent Fluid Management It is recommended that 0.9% saline or Ringer's acetate be used in the initial 4–6 h of Management, fluid containing 5% dextrose and with tonicity between 0.45% saline should be

used. Insulin Therapy: is essential to reverse the metabolic derangements like lipolysis and ketogenesis, and to normalize the blood glucose Dose Low dose intravenous insulin therapy at 0.1 Unit per kg per hour is the standard of care. Potassium Replacement: Addition of potassium to intravenous fluids is essential in DKA because of an actual deficit in the total body Potassium (Sivanandan *et al* , 2010)

2.3 Urinary Tract Infection (UTI)

2.3.1 Definition and classification of Urinary Tract Infection

Urine like other body fluid can be either acidic or alkaline. Acidic substance have pH less than 7 and alkaline substance have pH higher than 7. Normal urine is slightly acidic with a pH around 6. The pH of urine is dependent on the time of day, diet, health status and medication (Manickam *et al* , 2017) Urinary tract infections are a group of common diseases that occur predominantly by ascension of normal enteric flora through the urethra into the bladder. These infections more frequently affect women due to anatomic differences including a shorter urethra. Diagnosis is made by identifying related clinical symptoms in combination with an abnormal urinalysis and growth on urine culture. (Levinson , 2014) It is understood that the infection targets the different parts of the urinary tract and as a consequence results in the contagion of the lower and the upper urinary tracts. The infection is named based on the site of infection. The infection of urethra and ureter are referred to as urethritis and ureteritis respectively where as cystitis and phylonephritis corresponds to bladder and kidney infections. Cystitis is a common type of infection where as the infection associated with the renal damage is an issue of serious concern. Therefore the infection of bladder and urethra are referred as the infection of the lower urinary tract whereas the kidney and ureter infection is an indication of upper tract infection. Generally UTIs are classified based on the factors that trigger the infection and the

nature of occurrence. Taking these aspects in to consideration, UTIs can be classified as follows: i. Uncomplicated or complicated (based on the factor that Triggers the infection) this is a consequence of bacterial infection and the prevalence is higher in women than men. This includes the common form Of the infection like the cystitis and phylonephritis which affects. In contrast, complicated urinary tract infection occurs in men and women at any point of their life and has the tendency to produce severe outcomes resulting in death under serious circumstances. These infections are highly intricate and are difficult to treat and they are persistent. These complicated urinary tract infections can lead to outcomes like structural anomalies that blights that capability of the urinary tract to flush out the urine and this in turn provides better scope for the growth of bacteria as urine is considered to be a suitable growth medium and leads to dire consequences and ii. Primary or recurrent (depending on the nature of occurrence) This is a common phenomenon that is observed among women who have Experienced uncomplicated UTIs and they are classified as reinfection and relapse. Major cases of UTIs are referred to as reinfections and the condition is encountered by the patient after several weeks of antibiotic treatment. The less frequent type of recurrent UTI is known as relapse which is an outcome of treatment failure and the patient encounters the condition within two weeks of the previous infection. Relapse UTIs are usually associated with phylonephritis which results in renal failures, usually associated with kidney impediments through kidney stones and anatomical abnormalities in men and women. In addition, the classification of UTIs is also based on the extent of symptoms exhibited by the patients which groups the UTIs in to symptomatic and asymptomatic UTIs.(Vasudevan , 2014)

2.3.2 Pathophysiology

Bacteria (rarely fungi) reach the bladder via ascension through the urethra. This is much more common in women due to the short urethra and close approximation of the urethra to the vagina and anus. Preceding infection, the vagina, which is normally colonized by *Lactobacillus* species, will become colonized by enteric organisms such as *Escherichia coli* instead. *E. coli* are able to adhere to the urethral mucosa via pili. Once bacteria enter the bladder, they are able to reproduce and cause an inflammatory response, resulting in the symptoms of infection. Medical conditions that cause abnormal emptying of bladder increase risk for urinary tract infections. These include anatomic abnormalities such as cystoceles, neurologic disorders such as spinal cord injuries and multiple sclerosis, and the presence of foreign bodies such as indwelling Foley catheters. In infants less than 3 months of age, uncircumcised boys are at higher risk for urinary tract infections than girls. However, after infancy, girls are at higher risk for infection than all boys. Pyelonephritis may occur either by ascension of bacteria from the urethra to the bladder and then to the kidney(s) or, less commonly, through hematogenous spread from other sites of infection such as endocarditis. Kidney stones predispose to pyelonephritis Urinary tract infections in children can be associated with anatomic abnormalities, and additional workup for diseases such as vesicoureteral reflex should be considered (Levinson , 2014)

2.3.3 Signs and Symptoms

The characteristic symptoms of UTI in the adult are primarily dysuria with irritating voiding symptoms like urinary urgency, frequency, nocturia, painful voiding, bladder discomfort or stranguria which greatly distress the patient. A sensation of bladder fullness or lower abdominal

discomfort is usually present. Pain occurring at the beginning of or during urination suggests a urethral site of disease, whereas pain after voiding Implies pathology within the bladder or prostate area. Sometimes a patient will relate a history of pain in the suprapubic area. Because of the referred pain pathways, even simple lower UTI may be accompanied by flank pain and costovertebral angle tenderness. In the emergency department, however, it is assumed that the presence of these symptoms represents upper UTI. Fevers, chills and malaise may be noted in patients with cystitis, though these findings are associated more frequently wit pyelonephritis.(Hotchandani and Aggarwal , 2012)

2.3.4 Causative agents of urinary tract infection

E. coli is the most common cause of urinary tract infections. Other enteric Gram-negative rods such as *Klebsiella* species and *Proteus* species are regular culprits. *Pseudomonas aeruginosa* can cause urinary tract infection, but this is most common in health care–associated infections, patients with anatomic/neurologic abnormalities afflicting their urinary tract, or heavily antibiotic- experienced patients. Gram-positive pathogens include *Enterococcus* species and *Staphylococcus saprophyticus*.is common in younger women. *Candida* species can cause infection in patients who have extensive prior antibiotic use and indwelling Foley catheters. Rarely, viruses such as adenovirus, BK virus, and cytomegalovirus can cause a hemorrhagic cystitis. These viruses almost exclusively cause cystitis in immunocompromised hosts such as those who have undergone stem cell transplants. Hematogenous spread also occurs with *Mycobacterium tuberculosis* and can been seen in disseminated fungal infection as well. (Levinson , 2014)

2.3.5 Diagnosis of urinary tract infection

The gold standard for the diagnosis of a urinary tract infection is the detection of the pathogen in the presence of clinical symptoms. The

pathogen is detected and identified by urine culture (using midstream urine). This also allows an estimate of the level of the bacteriuria. However, the minimum level of bacteriuria demonstrating an infection of the urinary tract has not been defined in scientific literature or standardized by microbiological laboratories. Many laboratories define 10^5 colony forming units (cfu)/mL urine as the threshold. (Schmiemann , *et al* , 2010)

2.3.5.1 Laboratory Methods

Suprapubic aspiration is the best method of collection to avoid contamination of specimens with bacteria in the distal urethra. Most urine specimens are obtained from adult patients via the clean-catch midstream technique. The urine specimens are plated within 2 h after collection unless specimens have been refrigerated or kept in a preservative. The types of media used for routine cultures should be limited to blood Agar and MacConkey's agar. (Wilson and Gaido , 2004) . the urine was cultured on CLED agar (cysteine lactose electrolyte deficient agar) which is a differential medium of urine because it support the growth of all urinary pathogens it consists lactose , tryptone ,beef extract , cysteine and pH indicator is the bromothymol blue . This medium identified of Gram negative bacteria on the basis of lactose fermentation and colony appearance. Also it inhibits the swarming of *proteus* spp . (Cheesbrough , 2006) Bacteriuria can be detected microscopically using Gram staining of urine specimens, reliably positive only if the concentration of bacteria in the urine is $>10^5$ cfu/mL; infections with bacterial concentrations of 10^2–10^3 cfu/mL may not be detected by this test. Pyuria can be detected and quantified microscopically by measuring the urinary leukocyte UTIs and bacterial concentrations of $>10^5$ cfu/ mL have urine leukocyte counts of more than 10 leukocytes per field. (Wilson and Gaido , 2004)

2.3.6 Treatment

Recommended treatment for patients with uncomplicated cystitis Included Nitrofurantoin or Trimethoprim-sulfamethoxazole or Fosfomycin trometamol or Fluoroquinolones or Beta-lactams (amoxicillin-clavulanate, cefdinir, cefa-clor, or cefpodoxime-proxetil)

Recommended treatment for patients with Acute Pyelonephritis Included Ciprofloxacin or Levofloxacin or Trimethoprim-sulfamethoxazole or Beta-lactam (amoxicillin-clavulanate, cefdinir, cefaclor, or cefpodoxime-proxetil) . (Gibson, and Toscano , 2012)

2.4 Urinary Tract infection between Diabetic patients and non-Diabetic patients

Urinary tract infections frequently occur in diabetic patients due to an impaired immune status and increased glucose content of the urine, among other reasons. This makes UTI very important to investigate. Complicated cases of UTI may be infrequent but are more common in diabetics with far more severe consequences, and so warrant further investigation. The proper management of UTI in diabetics is crucial, as prompt diagnosis and correct use of antibiotics is vital for treatment. Future research in this regard will hopefully decrease the burden of UTI in diabetic patients.**(** Alrwithey , 2017) . In Ajman, UAE The frequency of UTI amongst the diabetic compared to non-diabetic participants higher, and the relationship was highly significant(35.5% Vs 12%,) (Mubarak *et al* , 2012) Prevalence of UTI in diabetics was 32.0% and in non-diabetics 22.0% The most commonly isolated pathogens for both groups were *E. coli* (48.1%), *Enterobacter* (24.1%), *Klebsiella* spp (13%), *Candida albicans* (9.3%), and *S. aureus* (3.7%) The present study in Iran identified older age, female gender, hyperglycemia, elevated HbA1c, glycosuria, albuminuria as risk factors of UTI in diabetics.(Borj

et al , 2017) . In Nepal Among culture positivity rate was noted between diabetic and non diabetic patients (34.5% Vs 26.7%). *Escherichia coli* was the most frequent organism (64.5%) in diabetic and (66.7%) non diabetic followed by *Klebsiella* sps (22.6% in diabetic and 12.5% in non diabetic). (Acharya *et al* , 2015)

2.5. Prevalence of Urinary Tract infection among Diabetic patients

A total of 200 diabetic patients were enrolled in Sudan, (60.5%) men and (39.5%) women; (96.5%) had type II DM. The overall prevalence of UTI was (19.5%). Among the total population, 17.1% and 20.9% had symptomatic and asymptomatic bacteriuria, respectively. According to multivariate logistic regression, none of the investigated factors (age, sex, type of DM and duration) were associated with UTI. The predominant isolates were *Escherichia coli* (56.4%), and *Klebsiella pneumoniae*, (23%) *E. faecalis*(12.8%), and *P. mirabilis* (7.6%) **.** About one-fifth of diabetic patients in Sudan had UTI (Hamdan *et al* , 2015) .The prevalence of UTI was 13.8% in Ethiopia (Nigussie and Amsalu , 2017) . There is high prevalence of UTI among diabetic patients in Uganda. Age, sex and high blood glucose were associated with UTI in this group of diabetic patients The overall prevalence of UTI is about 22.0% (Nabaigwa and Mwambi , 2018) Urinary tract infections (UTI) are common in diabetic patients in Iraq. This investigation was based to evaluate the incidence of UTI in patients with DM. The prevalence of UTI among the diabetic patients was found to be (35 %). Commonly recovered UTI isolates were *E.coli, K.pneumoniae, Pseudomonas* . and *S. aureus*.. (Almazini , 2016) Urinary tract infection is a significant problem in diabetics in India the prevalence about 43 % a. Early diagnosis and treatment is essential to prevent any complication. (Sharma, 2012) Among three groups of patients type 1, diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM) and diabetes ketoacidosis (DKA) patients. Urine samples of

T1DM patients and ketoacidosis patients were collected from children department and intensive care unit respectively, in Egypt. The prevalence of UTI among T1DM patients (64.28%) T2DM (77.77%) ketoacidosis patients, (73.68 %). (Adly *et al* , 2015)

2.6 The effect of pH and glucose on the growth of bacteria in urine

It has long been known that urine is a nutritive medium for organisms; in Fact, Pasteur used urine, as well as wine and beer, in his researches on The phenomenon of fermentation. Exactly how good a medium it is Will be brought out in the present work, and the effect of acidification of The urine will be shown in detail for numerous strains of bacteria obtained from clinical cases of urinary tract infection. The work is thought to be of interest as it shows the lethal and bacteriostatic pH levels for each Organism in urine, in vitro, and gives an indication of the practicability of treatment of urinary infections by acidification of the urine. The general conclusions reached, from experimental work, were that urine of pH 5.00 or below, had a lethal or growth inhibitory influence on E. coli. (Bentley , 1940). Glucosuria is one of the most important reasons for the high prevalence of urinary tract infections in diabetics. No differences were observed between the bacterial growth rates of uropathogenic and non-uropathogenic strains. Moderate and severe glucosuria enhance bacterial growth and diabetics to urinary tract infections. The growth inhibition found at extremely high glucose concentrations is probably caused by the decreasing pH (to 5.0) (Geerlings *et al* , 1999) The increase in Urine pH is also a risk factor for the development of UTI in Type 2 Diabetes mellitus patients. (Manickam *et al* , 2017)

2.7 Antibacterial action of acidosis in urine

Urinary acidification induces strong antibacterial effect against different bacterial types involved in urinary tract infections *E.coli* bacteria have been isolated from the urine of patients with urinary tract infection

Ascorbic acid (40 mM) alone and sodium nitrite (200 mM) alone are considered to be a weak antibacterial agents on uropathgenic *E. coli*, while mixing 10 mM ascorbic acid with 625 μM sodium nitrite at pH 5 became a strong antibacterial agent. Strong antibacterial agent can be formed in acidified urine containing nitrite. This antibacterial agent is strongly pH and nitrite dependent and is increased by addition of ascorbic acid. (Waheda *et al*, 2010)

Chapter Three
Materials and Methods

3. Materials and Methods

3.1 Study design

Descriptive cross sectional study

3.2 Study area

Emergency Internal Medicine Department in Albangadeed Educational Governmental Hospital in East Nile Province.

3.3 Study population

Diabetic ketoacidosis patients (DKA) admissioned in emergency wards. And Diabetic patients without ketoacidosis

3.4 Study duration

The study was carried out during five months between March and July 2018

3.5 Sample size

The sample size was 50 cases of Diabetic ketoacidosis patients and 25 cases of Diabetic patients without ketoacidosis .

3.6 Data collection

The data collected by questionnaire direct from patients also from admission file

3.7 Ethical considerations

Permission to carry out this study was obtained from College of Graduate Studies, Sudan University of Science and Technology. All patients were informed about the purpose of the study and verbal consent was taken.

3.8 Sample collection

Midstream urine for culture was taken from the patients in clean sterile containers, and aliquots of three ml of whole venous blood were collected using sterile disposable syringes. Blood samples were centrifuged for 3000 r.p.m for five minutes and serum was separated to estimate random blood glucose and urea by biosystem reagents. .

3.9 Laboratory methods

3.9.1 Urine culture

After collection of urine from patients the urine was cultured on CLED agar (cysteine lactose electrolyte deficient agar) .The urine was mixed using sterile calibrated wire loop 0.002 ml a loopful of urine was streaked on the CLED agar , incubated aerobically at 35- 37C° overnight. (Cheesbrough , 2006)

3.9.2 Urine investigation (Macroscopic, Microscopic investigation)

After the step of culture the samples were tested for macroscopic and microscopic investigation of urine , this step was made by physical ,chemical and microscopic examination Urine strip (Mission Expert 4K) was used to determine ketone , glucose , protein and pH by immersing strip and read within 1 minute . The purpose of microscopic examination to determine the presence of pus and bacteria in the urine samples.

3.9.3 Gram's stain

The procedure was carried out according to Cheesbrough , (2006) as follows : smear was prepared from overnight culture on a clean and dry slide . The smear was left to air dry , fixation was done by heat . Crystal violet stain was added to smear for one minute and was washed by tap

water . lugol's iodine was added for one minute then washed by tap water and decolorized rapidly (few seconds) with acetone alcohol and washed immediately by tap water . Finally the smear was covered with safranin for 2 minutes and washed by tap water . On the dry smear , a drop of oil was added to the dried smear and examined under the light microscope by oil lens.

3.9.4 Biochemical test

Were carried out according to Cheesbrough (2006)

3.9.4.1 Citrate Utilization test

By using of sterile loop under aseptic condition the organism under test incubated in Simmons citrate agar and incubated at 37C° for 24 hr. The change in colour from green to blue is positive result, no change in the colour of medium is negative result

3.9.4.2 Urease test

By using of sterile loop under aseptic condition the organism under test incubated in urea media and incubated at 37C° for 24 hr. The change in colour from yellow to pink is positive result, no change in the colour of medium is negative result

3.9.4.3 Indole test

By using of sterile loop under aseptic condition the organism under test incubated in trypton water and incubated at 37C° for 24 hr after incubation drop of kovac's regent is added appearance of red surface layer is positive result and appearance of yellow surface layers is negative result

3.9.4.4 Killigler iron agar (KIA)

By using of sterile loop under aseptic condition the organism under test incubated in KIA media and incubated at 37C° for 24 hr. KIA reaction based on the fermentation of lactose and glucose and the production of hydrogen sulphide . A yellow butt (acid production) and red - pink slope indicate the fermentation of glucose only , yellow slope and yellow butt indicate the fermentation of lactose and possible glucose ,red –pink slope and butt indicate no fermentation of glucose or lactose . Cracks and bubbles in the medium indicate gas production from glucose fermentation blackening along the stab line or throughout the medium indicates hydrogen sulphide (H_2S) production .

Chapter four

Results

4. Results

4.1 Distributions of Diabetic ketoacidosis (DKA) patients according to gender

Fifty patients of Diabetics Ketoacidosis were involved in the study, 20 were males (40 %) and 30 were females (60 %) as shown in table 1

Table1: Distributions of diabetic ketoacidosis (DKA) patients according to gender

Gender	Frequency	Percent
Males	20	40%
females	30	60%
Total	50	100%

4.2 Distributions of Diabetic ketoacidosis (DKA) patients according to age

The patients ages ranged from 13 – 83 years old. And the highest age group that has Diabetic ketoacidosis was between 23 -33 years old as in table 2

Age group	Frequency	Percent
13-23	8	16 %
23-33	12	24 %
33-43	8	16%
43- 53	11	22%
53- 63	8	16%
63-73	2	4%
73-83	1	2%
Total	50	100%

Table2: Distributions of diabetic ketoacidosis (DKA) patients according to age group

The age of females group was higher than that in males in as in figure 1

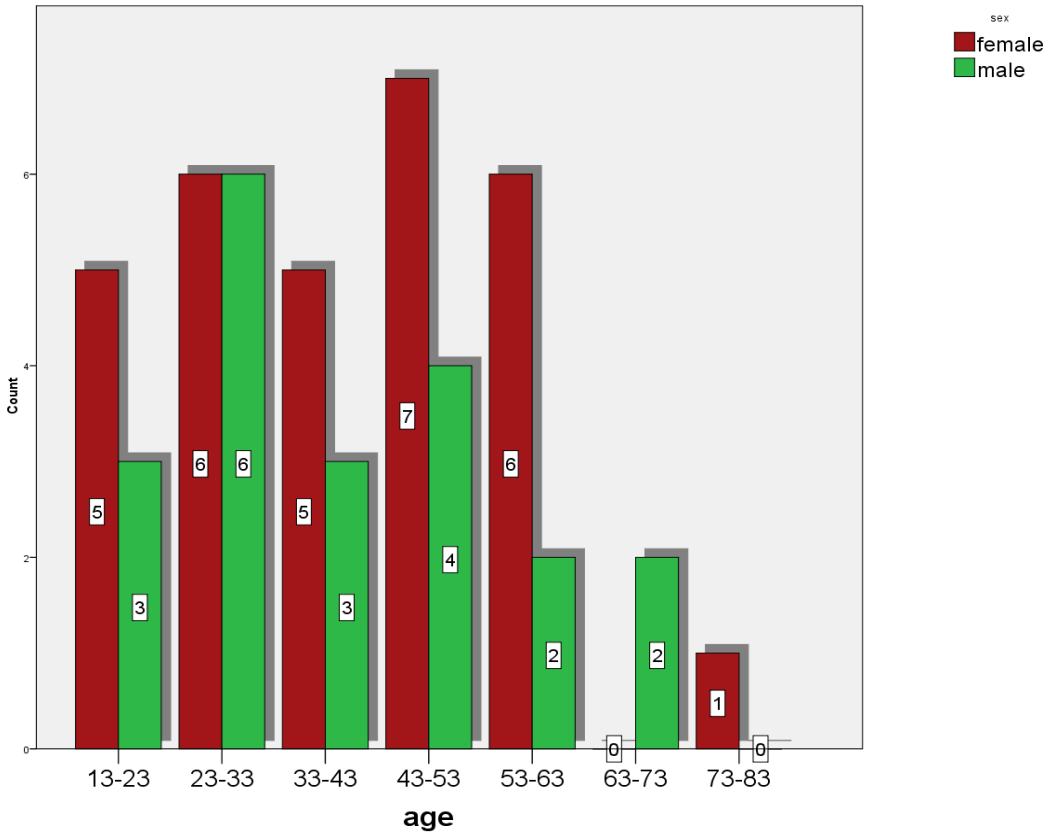


Fig1 : Distribution of age between males and females

4.3 Duration period of onset diabetic among Diabetic ketoacidosis (DKA) patients

Forty three (86 %) of cases have diabetes for more than one year , 2 (4%) have diabetes for less than one year and about 5 (10 %) patients with unknown diabetes . patients of un known diabetes five patients admitted to the hospital with symptoms other than those of hyperglycemia but when check for diabetes , they be diabetes patients

Patients with duration period between 1-5 years was 41.9 % in 6-10 years 27.9% , in 11 -15 years 18.6 % and in group between 16- 20 years 11.6% as shown in figure 2

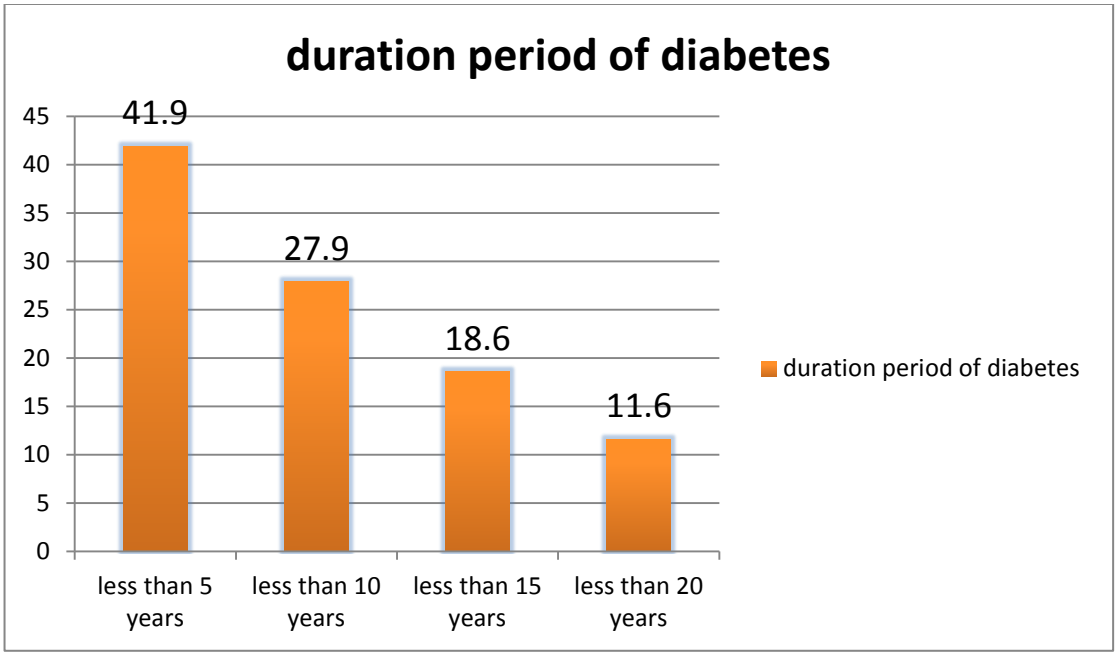


Fig 2: The Distribution of patients who suffered from diabetes for more than one year

4.4 Risk factors of Diabetic Ketoacidosis (DKA) among patients

4.4.1 Irregular treatment

There were 45 cases of DKA have treatment . The other five who have not known their disease didn't take medicine. 69% regularly take their doses and 31 % missing their doses The regularity of taking dose among 45 patients shown in table 3

Table 3: Regularity of taking treatment among DKA patients

Regularity of taking doses	Frequency	Percent
Regular	31	69%
Irregular	14	31%
Total	45	100%

4.4.2 Smoking among diabetic ketoacidosis (DKA) patients

The majority 98% of the diabetic ketoacidosis patients were nonsmoker

4.5 Symptomatic of urinary tract infection among Diabetic ketoacidosis (DKA) patients

72 % of ketoacidosis patients showed no symptoms of urinary tract infection in table 4

Table 4: Frequency of symptomatic and asymptomatic patients

UTI symptoms	Frequency	Percent
Symptomatic	14	28%
Asymptomatic	36	72%
Total	50	100%

4.6 Laboratory investigations results

4.6.1 Blood glucose level

Among DKA patients 9\ 20 male and 13\30 female have random glucose level between 300- 400 mg\dl this represent the high frequency composed to other in table 5

Table 5: Blood glucose levels among males and females ketoacidosis patients

Gender	Males		Females		Total
Blood glucose	Frequency	Percent	Frequency	Percent	
230- 300 mg\dl	2	10%	11	36.7%	13 (26%)
300-400 mg\dl	9	45%	13	43.3%	22 (44%)
400-500 mg\dl	8	40%	6	20%	14 (28 %)
500-600 mg\dl	1	5%	0	0%	1(2%)
Total	20	100%	30	100%	50(100%)

4.6.2 Blood urea level

All 50 cases of diabetic ketoacidosis have normal urea level less than 45mg\dl

4.6.3 Glucosuria and ketonuria in Diabetic ketoacidosis (DKA)

Table 6 shows the frequency of glycosuria and ketonuria respectively and it's between two to three crosses

Degree	+	++	+++	++++	Total
Glucosuria	4%	26%	56%	14%	100%
ketonuria	22%	52%	16%	10%	100%

4.6.4 proteinuria in Diabetic ketoacidosis (DKA)

Most of the patients have no protein 44 (88%) in the urine table 7

Table 7: Appearance of protein in urine patients

proteinuria	Frequency	Percent
+	5	10.0%
++	1	2.0%
without protein	44	88.0%
Total	50	100.0%

4.6.5 Urine pH in Diabetic ketoacidosis (DKA)

Urine samples with pH 5 were 37 (74%) and those with pH were 13 (26%) in figure 3

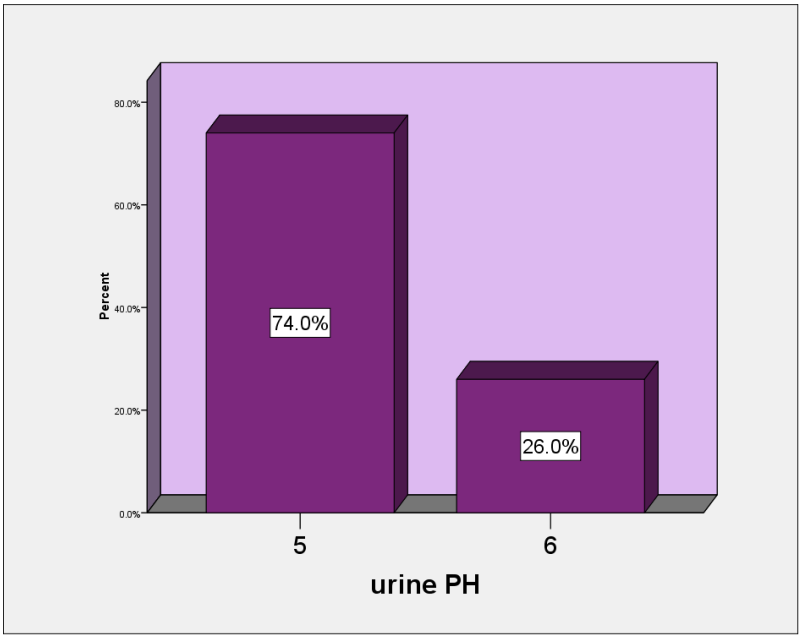


Fig 3 : Urine PH in ketoacidosis patients

4.6.6 Pyuria in urine of Diabetic ketoacidosis (DKA)

Five patients (10%) had pyuria while 45 (90 %) showed no pus cell in their urine table 8

Table 8: Pus in urine of Diabetes ketoacidosis patients

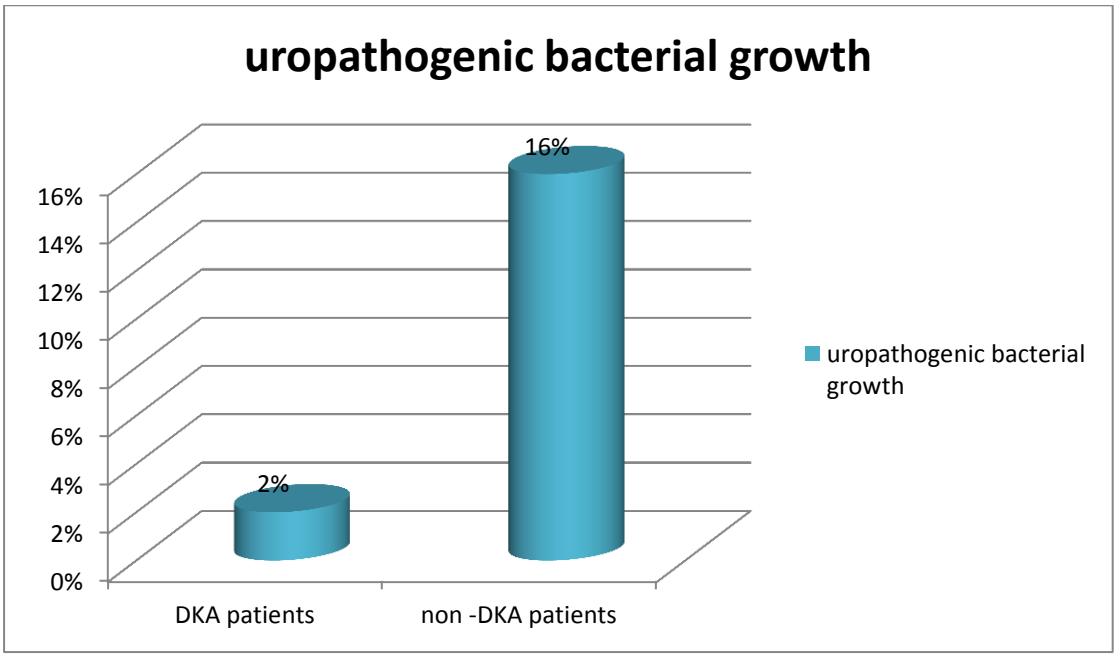
Pus in urine	Frequency	Percent
Sterile urine	45	90.0%
Pyuria	5	10.0%
Total	50	100.0%

4.6.7 Uropathogenic growth in Diabetic ketoacidosis (DKA)

The growth of pathogenic microorganism isolated from urine among diabetic ketoacidosis (DKA) patients has occurred only one female (2%) had bacteria *Klebseilla pneumonia*e in their urine while 49 (98 %) showed no bacterial growth

4.6.8 Uropathogenic growth in Diabetes patients without ketoacidosis

Among 25 diabetes patients without ketoacidosis 13 (52 %) females and 12 (48 %) males with age group between 36- 70 years old and random blood glucose level between 170 – 295 mg \dl bacterial growth was only in 4 (16%) one male 1(25%) and 3 (75%) females , 11 (44%) with pyuria and 14(56 %) without pyuria .The urine pH level between 5 – 8. The four isolated microorganisms from urine of non-diabetic ketoacidosis were : *Esherichia coli* 2 (50%) , *Klebseilla pneumoniae* 1 (25%) and *Candida spp 1 (25 %)*



Chapter five

Discussion

5. Discussion

5.1 Discussion

The present results show lethal action of acidosis against urine pathogens among diabetic ketoacidosis patients in East Nile province by percent about 98% . The only bacteria grow in acidic urine in this study was *Klebseilla pneumoniae* may be due to presence of large capsule by percent about 2% , in compered to 16 % of growth among diabetes without ketoacidosis. No notable reports or researches about urinary tract infection (UTI) in Diabetic ketoacidosis patients in Sudan or other country upon to my knowledge.

In this study Diabetic ketoacidosis (DKA) more common in females 30(60%) than males 20 (40%) , also common in young patients less than 40 years than old patients the age group between 23-33 years have high occurrence of diabetic ketoacidosis 24% with similar percent between males 12 % and females 12 % as reported Westerberg (2013), may be because absolute insulin deficiency type 1 diabetes found in young people The duration period of onset diabetic between (1 -5 years) was the highest (41.9 %) may be due to high incidence rate of diabetes in the last five years. In our study patients who used their treatment regularly were 31 (69%) and those with irregular treatment were 14 (31%) there are different causes for diabetic patients to enter in ketoacidosis in addition to missing their doses, we need more research and knowledge to determine the other causes. According to this study Smoking has no role in ketoacidosis development nonsmokers were 49 (98 %) the acidity only by ketone body , Blood urea was normal in all 50 diabetic ketoacidosis patients that discordance between our result and the criteria of elevated urea among diabetic ketoacidosis in Oakes and Cole (2007) may be due to the Sudanese people have low level of urea than

other people . Blood glucose level between 300- 400 mg\dl was the highest concentration of glucose among diabetic ketoacidosis patients 22(44%) followed by 400 – 500 mg\dl 14 (28 %) , more common in male than female may be due to this level is the upper limit of random blood glucose in Sudanese diabetes patients . majority of DKA patients have no symptoms of urinary tract infection 36(72%) due to acidosis ,pyuria found only in 10% of DKA patients in compare 44% of non – DKA , the urinary tract infection depend on this result found in non-diabetic ketoacidosis more than diabetic ketoacidosis .

The present results disagreed with Adly *et al* (2015) in Egypt who found Out of the 57 ketoacidosis patients, 42 patients (73.68 %) showed positive urine culture and pyuria. The main reasons for these results that the samples were collected from children department and intensive care unit, intensive care unit have high rate of infections. The present results agreed with results Geerlings *et al* (1999) who reported that glucosuria is one of the most important reasons for the high prevalence of urinary tract and the growth inhibition was at extremely high glucose concentrations is probably caused by the decreasing pH (to 5.0).

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5.2 Conclusion

Antibacterial action of acidosis against urine pathogens among diabetic ketoacidosis patients in East Nile province by percent 98%. The chance for bacteria to grow in urinary tract of diabetic ketoacidosis is low, acidosis helps to protection against urinary tract infection in non-ketoacidosis patients

5.3 Recommendations

(1) Further studies with large sample size and different study areas are recommended to make confirmation for this study results.

(2) Creation the same acidic urine condition that found in Diabetic ketoacidosis by nutritional diet or pharmaceutical clinical trials instead antibiotic to treat urinary tract infection.

(3) Further studies to determine the real causes of diabetic ketoacidosis among diabetic patient.

References

1) **Acharya D** , Bogati B , Shrestha GT, Gyawali P (2015) . Diabetes mellitus and Urinary Tract Infection: Spectrum of Uropathogens and their Antibiotic Sensitivity Pattern. *JMMIHS* .**1**(4) 24 -28

2) **Adly** N.N, Ragab Y.M, Hashem A.M, Ahmady A.K(2015) . Effect of Diabetes on occurrence of urinary tract infection and asymptomatic Bacteriuria among diabetic and ketacidosis patients in Egypt. *International Research Journal of Microbiology* . **6** (3) 027-036

3) **Almazini** M. (2016) . Incidence and sensitivity of bacterial Uropathogens among diabetic patients. *Euro. J. Exp. Bio*., **6**(3):8-12

4) **Alrwithy** FA , , Alahmadi AE , Alshehri AM, Abalhassan IB , Alhamad FM , Khedher YZ , *et al* (2017) . Urinary Tract Infection in patients with Diabetes Mellitus. *The Egyptian Journal of Hospital Medicine* **69** (3) 2133-2136

5) **American Diabetes Association** (2014).Diagnosis and classification of Diabetes Mellitus . *Diabetes care* **37** (1) 81- 90

6) **American Diabetes Association** (2017).Diagnosis and classification of Diabetes Mellitus . *Diabetes care* **40** (1) 11-24

7) **BBC News** (2018) . Diabetes is actually five separate diseases research suggests. Available from http// www. bbc.com/ news / health43246261

8) **Bentley** J (1940) . The effect of PH on the growth of bacteria in urine. American Urological Association. p 699

9) **Borj** MR , Taghizadehborojen S , Shokati A , Sanikhani N , Pourghadamyari H , Mohammadi A *et al* (2017) . Urinary Tract Infection Among Diabetic Patients with Regard to the risk factors, causative organisms and their antimicrobial susceptibility profiles . *International journal of live science and pharma research* . 7(3) 38 – 47

10) **Chaeles** J C and Heilman R L (2005) . Metabolic Acidosis .*Hospital Physician* 37-42

11) **Cheesbrough**,M (2006). District laboratory practice in Tropical countries, ,Cambridge University press, UK, 2 nd Ed . part 2 ,p :38-70

12) **Cheesbrough**,M (2006). District laboratory practice in Tropical countries, ,Cambridge University press, UK, 2 nd Ed . part 2 ,p :111-114

13) **Cheesbrough**,M (2006). District laboratory practice in Tropical countries, ,Cambridge University press, UK, 2 nd Ed . part 2 ,p :395-396

14) **Farsani** SF, Brodovicz K, Soleymanlou N , Marquard J ,Wissinger E , Maises B (2017) . Incidence and prevalence of diabetic ketoacidosis (DKA) among adult with type 1 diabetes mellitus. *BMJ Open* **7** 1- 15

15) **Hamdan** H Z , Kubbara E , Adam A M , Hassan O S , Suliman S O , Adam I (2015) Urinary tract infections and antimicrobial sensitivity among diabetic patients at Khartoum, Sudan . *Annals of Clinical Microbiology and Antimicrobials* **14**:26 DOI 10.1186/s12941-015-0082-4

16) **Hotchandani** R and Aggarwal kk,(2012) Urinary Tract Infections in Women. *Indian Journal of Clinical Practice*. **23** (4) 187 -192

17) **International diabetes federation \ Sudan** (2017) . Prevalence of Diabetes Mellitus in Sudan. available from http// www. Idf .org/ Sudan

18) **Geerlings** S E , Brouwerp E C, Gaastras W , Verhoeft J , Hoepelman A I.M (1999) Effect of glucose and pH on uropathogenic and non-uropathogenic *Escherichia coli:* studies with urine from diabetic and non-diabetic individuals . *J. Med. Microbiol*. **49** : 535 -539

19) **Gibson** K and Toscano J (2012). Urinary Tract Infection Update. *American Journal of Clinical Medicine* **9** (2) 82 -86

20) **Kerner**.W and Brückel J , (2014). Definition, Classification and Diagnosis of Diabetes Mellitus. German Diabetes Associaton: Clinical Practice Guidelines .p 384–386

21) **Levinson** W (2014) . Review of Medical Microbiology and Immunology. 13 nd Ed .p 1391-1394

22) **Manickam** K, Raveendran SR, Romi S , Rita J (2017) . Urine pH As An Indicator For Urinary Tract Infections In Patients With Type 2 Diabetes Mellitus. *Journal of Dental and Medical Sciences*. **16** (7): 09-12

23) **Misra** S and Oliver N S ,(2015) . Diabetic ketoacidosis in Adults. *BMJ Open* clinical review 28 : 1-8: doi: 10.1136

24) **Mubarak** AA , Ashraf1 AM , El-hag M , Raza MA , Majed A , Al-Sharbatti S , *et al* (2012) . Prevalence of urinary tract infections among

diabetes mellitus and non- diabetic patients attending a teaching hospital in Ajman, UAE . *Gulf Medical journal* **1**(1): 228-232

25) **Nabaigwa** BI, Mwambi B, Okiria J, Oyet C (2018) . Common uropathogens among diabetic patients with urinary tract infection at Jinja Regional Referral Hospital, Uganda. *Afr J Lab Med*.;**7**(1), 621

26) **Nigussie** D and Amsalu A (2017). Prevalence of uropathogen and their antibiotic resistance pattern among diabetic patients. *Turk J Urol* **43**(1): 85-92 • DOI: 10.5152/tud.2016.86155

27) **Oakes** EE and. Cole L (2007). Diabetic ketoacidosis (DKA) . Resource Folder. P 12- 25

28) **Rees** A , Levy M , Lansdown A (2017) . Clinical Endocrinology and diabetes at a clance , Wiley Blackwell , 1nd Ed . p : 120- 170

29) **Schmiemann** G , Kniel E , Gebhardt K , Matgczyk MM , Pradier EH (2010) The Diagnosis of Urinary Tract Infection . *Dtsch Arztebl Int* **107**(21): 361–7

30) **Sharma** V , Gupta V , Mittal M (2012) Prevalence Of Uropathogens In Diabetes patients and their Antimicrobial susceptibility . *National Journal of Laboratory Medicine*., **1**(1): 26-28

31) **Sivanandan** S , Sinha A , Jain V , Lodha R (2010) . Management of Diabetic Ketoacidosis . *The Indian Journal of Pediatrics* · DOI: 10.1007/s12098-010-0294-8

32) **Vasudevan** R (2014) .Urinary tract infection : an overview of the infection and associated risk factors . *Journal of Microbiology and Experimentation* **1**(2) 1-15

33) **Waheda** N , Bazzaz P. H.A ,.Mansoor E Y, Toma S (2010) . The antibacterial effect of acidified nitrite on uropathogenic *Escherichia coli*: In vitro study. *Zanco J. Med. Sci*.,**14**(1) 31 -36

34) **Westerberg** D. P (2013) . Diabetic Ketoacidosis: Evaluation and Treatment *American Family Physician* **87** (5) 337 – 346

35) **Wilson** M. L and Gaido L (2004) . Laboratory Diagnosis of Urinary Tract Infections in Adult Patients. . Medical Microbiology . CID 38 p 1150- 1158

36) **Wolfsdorf** JI, Allgrove J, Craig ME , Glaser N, Jain V, Lee WWR, *et al* (2014) , Diabetes: Diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Pediatric Diabetes*. **15** (20): 154–179. doi: 10.1111/pedi.12165

Appendix

Questionnaire

Diabetic ketoacidosis Patient Research number : ……

Admission file information

- **Name of patient:…….**
- **Gender : …….**
- **Age :……..**

Patient information

- **Duration period of diabetes:…….**
- **Treatment regularity:……..**
- **Antibiotic use :…….**
- **Smoking :…….**
- **Symptoms of urinary tract infection :……**

Laboratory information

- **Random blood glucose level :…….**
- **Blood urea :……**
- **Glucosuria :……**
- **Ketonuria :……..**
- **Protein uria :……..**
- **Urine pH :…….**
- **Pyuria :……**
- **Bacteria growth :……..**

Questionnaire

Non -ketoacidosis Patient Research number: ……

Admission file information

- **Name of patient:…….**
- **Gender: …….**
- **Age:…….**

Laboratory information

- **Random blood glucose level :…….**
- **Urine pH :…….**
- **Pyuria :……**
- **Bacteria growth:……..**