THE CHARACTER OF DIABETIC KETOACIDOSIS AMONG CHILDREN IN BINT AL-HUDA TEACHINGHOSPITAL AND AL-NASRIA DIABETIC CENTER

A Research submitted to the College of Medicine University of Thi-qaras partial fulfillment ofM.B.Ch.B graduation requirements

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بِسْمِ اللهِ الرّحَمنِ الرَحّيِم

{...وَمَا أُوتِيتُم مِّنَ الْعِلْمِ إِلَّا قَلِيلا}

(صَدَق الله العليُ العَظيمْ)

سورة الإسراء (آية85)

Dedication

Every challenging work needs self-efforts as well as guidance of orders especially those who were very close to our heart.

Father and Mother,

Whose affection, love, encouragement and prays of day and night make me able to get such success and honor.

Acknowledgements

A special word of gratitude to Dr.Razzaqjameelalrubaie**for his instructions and guidance.**

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List of abbreviations

DKA	**Diabetic ketoacidosis**
DM	**Diabetes mellitus**
T1DM	**Type 1 diabetes mellitus**
T2DM	**Type 2 diabetes mellitus**
BG	**Blood gas**
HbA1C	**glycosylated hemoglobin**

Abstract

Background: Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which leads over time to serious damage to the heart, blood vessels, eyes, kidneys and nerves. The most common is type 2 diabetes, usually in adults, which occurs when the body becomes resistant to insulin or doesn't make enough insulin. In the past three decades the prevalence of type 2 diabetes has raised dramatically in countries of all income levels. Type 1 diabetes, once known as juvenile diabetes or insulin-dependent diabetes, is a chronic condition in which the pancreas produces little or no insulin by itself. For people living with diabetes, access to affordable treatment, including insulin, is critical to their survival.Diabetes can cause immediate complications and long-term complications. The most serious immediate complication is diabetic ketoacidosis. This condition is common present in approximately one-third of children with type 1 diabetes at the time of diagnosis. It affects between 1 to 10% of children with type 1 diabetes per year, typically because they haven't taken their insulin or are having issues with insulin delivery.The groups most likely to present with diabetic ketoacidosis at diagnosis were the youngest children, particularly those younger than 2 years, and children from the most deprived communities, including children from ethnic minorities or without health insurance.

Patient and method: This study is a prospective study conducted on male and female children with diabetic ketoacidosis, performed during 1st of December 2020 to 30 of April 2021. Eighty five patients enrolled in this study that collected from **Bint AL-huda hospital** and**Al-Nasria Diabetic Center**, this was done by a direct interview according to the questioner paper which was organized and submitted by our supervisor

Aim of Study: The purpose of the study is to determine the relative risk factors among diabetic children how were developed DKA at some stage of their life, and to compare the prevalence rate between both genders in Al-Nasria Provence

Results: Out of the 85 children admitted with DKA, 40 (47.1%) were male and 45(53, 2%) were female. Also, the most effected age group from the selected cases was among those children whose age more than five years which accounted for more than 90 % compare to other age groups.

Keywords:DKA in children, Al-Nasria city

Introduction

Diabetes mellitus in children

Diabetes is a group of metabolic disorders characterized by a high blood sugar level over a prolonged period of time. Symptoms often include frequent urination, increased thirst and increased appetite. If left untreated, diabetes can cause many health complications. Acute complications can include diabetic ketoacidosis, hyperosmolar hyperglycemic state, or death. Serious long-term complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, damage to the nerves, damage to the eyes and cognitive impairment.(1)In children was almost associated with type 1 diabetes mellitus, whereas type 2 diabetes was thought to be a condition of middle age and the elderly. Over the last 10-20 years, pediatric diabetes centers in North America and around the world have recorded an unprecedented rise in the incidence of type 2 diabetes.Lifestyle factors are to blame for the global epidemic of overweight and obesity, as well as the rise in the prevalence of type 2 diabetes in adults and children. Identifying children at risk for type 2 diabetes and implementing community-wide prevention measures would be critical to turning the tide.(2) The availability of calorie-dense "fast meals," candy, and sugared soft drinks in schools and other places where children congregate must be limited.Identifying children at risk for type 2 diabetes and implementing community-wide prevention measures would be critical to turning the tide. The availability of calorie-dense "fast meals," candy, and sugared soft drinks in schools and other places where children congregate must be limited.(3)

Historically, Diabeteswasa disorder characterized by a "too great emptying of the bladder" makes its way back to antiquity in Egyptian manuscripts dating back to 1500 B.C. Since it attracted ants, Indian physicians dubbed it madhumeha (‘honey urine').Sushruta, an ancient Indian physician, and Charaka, a surgeon (400–500 A.D.), were the first to describe the two forms of diabetes, later known as Type I and Type II diabetes.Diabetes has been recognized for over three centuries, and recorded history attributes the first full accounts in the first century A.D. to Aretaeus the Cappadocian, who coined the term diabetes (Greek, ‘siphon') and dramatically said, “... no important part of the drink is consumed by the body while great masses of flesh are liquefied into urine.”Avicenna (980–1037 A.D.), the great Persian physician, not only mentioned excessive appetite and diabetic gangrene in The Canon of Medicine, but also concocted a mixture of seeds (lupin, fenugreek, zedoary) as a panacea.The word mellitus (Latin for "sweet as honey") was coined in 1798 by British Surgeon-General John Rollo to differentiate this diabetes from the other diabetes (insipidus) in which the urine was tasteless.(4,5,6)

Types of Diabetes

Diabetes in children is similar to diabetes in adults. Among the varieties are:

1. Prediabetes

Prediabetes is a disorder in which blood glucose levels are higher than average but not elevated enough to be classified as diabetes (140 to 199 mg/dL) (7.8 to 11.0 mmol/L). Obese teenagers are more likely to have prediabetes than other children. Over half of adolescents experience it temporarily, but the remainders develop diabetes, especially those who continue to gain weight.The condition can occur at any time during childhood, including infancy, but it is most common between the ages of 4 and 6 years, or between the ages of 10 and 14.(7)

2. Type 1 diabetes

When the pancreas produces little to no insulin, type 1 diabetes develops. Type 1 diabetes is the most prevalent type in children, accounting for roughly two-thirds of all diabetes cases. It is one of the most common chronic diseases in children. By the age of 18, one in every 350 children has type 1 diabetes. The number of affected children has recently increased, especially among children under the age of five.(8)

The pancreas does not provide enough insulin in type 1 diabetes because the immune system attacks and damages insulin-producing cells in the pancreas (islet cells). An attack like this may be caused by environmental factors in people who have inherited those genes that make them prone to diabetes. Certain ethnic groups have a higher prevalence of these genes (such as Scandinavians and Sardinians). (9)Near relatives of people with type 1 diabetes are at a higher risk of developing the disease. Brothers and sisters are at a 4 to 8% risk, while identical twins are at a far higher 30 to 50% risk. And if a child with a parent with type 1 diabetes has a 10% chance of developing diabetes, and a 4% chance of developing diabetes if the mother is affected. Children with type 1 diabetes are more likely to suffer from other autoimmune disorders, such as thyroid disease and celiac disease.(10)

3. Type 2 diabetes

Type 2 diabetes develops when the body's cells do not respond appropriately to insulin (called insulin resistance). Unlike in type 1 diabetes, the pancreas can still produce insulin but not in sufficient quantities to resolve insulin resistance. This is known as a relative insulin deficiency, as opposed to the absolute deficiency seen in type 1 diabetes.(11)Type 2 diabetes is more prevalent in teenagers, but it is also becoming more common in overweight or obese younger children. In the 1990s, more than 95 percent of children with diabetes had type 1 diabetes, but now about one-third of children with diabetes are diagnosed with type 2 diabetes. Type 2 diabetes normally manifests itself after adolescence has started.(12)

While many children develop type 2 diabetes between the ages of 10 and 14, the highest prevalence occurs during late adolescence, between the ages of 15 and 19. Children with type 2 diabetes are much more likely to have a first-degree relative with type 2 diabetes than children with type 1 diabetes.

Children at higher risk of developing type 2 diabetes include those who:

- Are overweight (weigh more than 85% of children of similar age, sex, and height), particularly those who are obese (weigh more than 95% of children of similar age, sex, and height).(13)
- Have a parent, sibling, aunt, uncle, or grandparent who has type 2 diabetes (60 to 90%)
- Have high blood pressure, high blood levels of lipids (fats), obstructive sleep apnea, dark and thick skinfolds on the nape of the neck (acanthosisnigricans), fatty liver, polycystic ovary syndrome (PCOS), or a small-for-gestational-age birth weight
- Have a mother who had diabetes during pregnancy (gestational diabetes) or who has a history of diabetes
- Are not physically active
- Are from Native Americans, blacks, Hispanics, Asian Americans, and Pacific Islanders.

Insulin

Insulin is a hormone produced by the pancreas. Insulin regulates the amount of glucose in the blood and enables glucose to enter cells from the blood. Glucose cannot enter cells without the required amount of insulin and accumulates in the blood. Glucose starts to appear in the urine as blood glucose levels rise.Since glucose draws more water into the urine, people urinate more (polyuria), become thirsty, and drink more (polydipsia). Electrolyte imbalances and dehydration may occur in the absence of insulin. A lack of insulin also leads to the breakdown of fat and protein.Circulating insulin also influences protein synthesis in a wide range of tissues. As a result, it is an anabolic hormone that promotes the conversion of small molecules in the blood into large molecules within the cells. Low blood insulin levels have the opposite effect, promoting widespread catabolism, especially of reserve body fat.(14)

Beta cells are glucose sensitive, secreting insulin into the blood in response to high glucose levels and inhibiting insulin secretion in response to low glucose levels. Insulin increases glucose uptake and metabolism in cells, lowering blood sugar levels. By taking signals from the beta cells, their adjacent alpha cells secrete glucagon into the blood. Secrete glucagon into the blood in the opposite direction: increased secretion when blood glucose levels are low, and reduced secretion when blood glucose levels are large. By inducing glycogenolysis and gluconeogenesis in the liver, glucagon raises blood glucose levels.The primary mechanism of glucose homeostasis is the release of insulin and glucagon into the blood in response to blood glucose concentrations.(15)

History of insulin

The human insulin protein has a molecular mass of 5808 Da and is made up of 51 amino acids. It is a heterodimer composed of an A-chain and a B-chain connected together by disulfide bonds. Insulin's structure differs slightly between animal species. Because of these differences, animal insulin is less efficient (in terms of carbohydrate metabolism effects) than human insulin.Porcine insulin is particularly similar to human insulin and was commonly used to treat type 1 diabetics before human insulin could be manufactured in large amounts using recombinant DNA technologies.

The first peptide hormone detected was insulin. In 1921, **Frederick Banting** and **Charles Herbert Best**, employed in J. J. R. Macleod's laboratory at the University of Toronto, were the first to isolate insulin from dog pancreas. In 1951, Frederick Sanger sequenced the amino acid structure of insulin, making it the first protein to be entirely sequenced.**Dorothy Hodgkin** discovered the solid-state crystal structure of insulin in 1969. Insulin was also the first protein to be chemically synthesized and manufactured using DNA recombinant technology. It is included on the WHO Model List of Essential Medicines, which includes the most important drugs required in a basic health system.(16)

Leonard Thompson, a 14-year-old diabetic dying at Toronto General Hospital, received the first insulin injection on January 11, 1922. However, the extract was so contaminated that Thompson had a serious allergic reaction, and subsequent injections were canceled. Collip worked day and night for the next 12 days to boost the ox-pancreas extract.On January 23, a second dose was injected, completely removing the glycosuria that is characteristic of diabetes without creating any apparent side effects. Elizabeth Hughes, the daughter of U.S. Secretary of State Charles Evans Hughes, was the first American patient. Future woodcut artist James D. Havens was the first patient treated in the United States; Dr. John Ralston Williams imported insulin from Toronto to Rochester, New York, to treat Havens.(17)

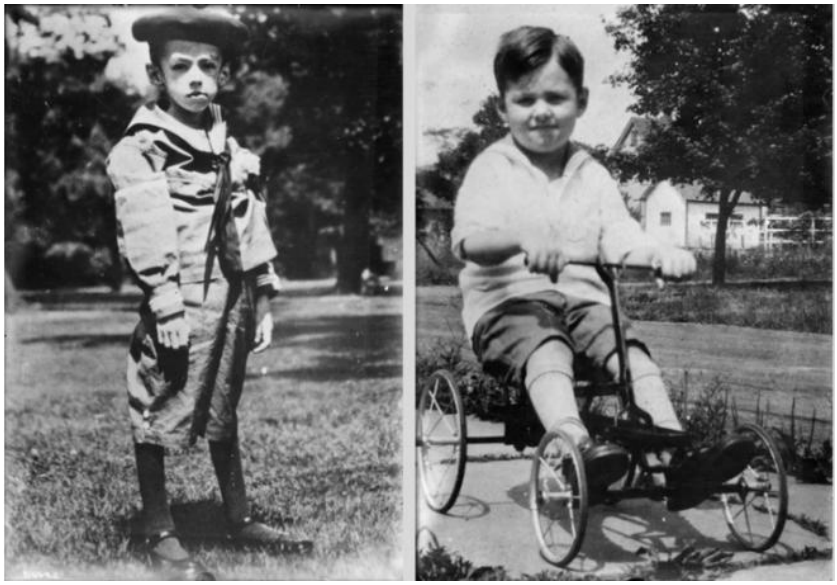
Before Banting: Treatments for Diabetes in the Pre-Insulin Era

In 1920, Frederick Banting developed the concept that led to the discovery of insulin right here at Banting House. While the concept of insulin was novel, the symptoms of diabetes were not – people had been suffering and dying from the disease for thousands of years. So, how did doctors assist them prior to the discovery of insulin?(18)

Diabetes was first mentioned around 3500 BCE in Ancient Egypt. Since then, doctors all over the world have sought to diagnose and treat the "sugar sickness," as it was dubbed; but, because insulin was still unknown, diabetics were doomed to waste away. Doctors in Egypt, India, and Greece all watched as patients they desperately sought to save passed away in comas.During the 18th century, physicians started to recognize that diet played a role in diabetes and that its

symptoms could be slowed with dietary changes. They aimed to reduce carbohydrates while increasing fat and protein levels in diabetics' diets. For the desperate at the time, fad diets included the "oat cure," "potato therapy," "rice cure," and opium – none of which worked.Dr. Frederick Allen and Dr. Elliot Joslin, the world's leading diabetologists, were promoting a new and very successful therapy only before Banting discovered insulin.For people with diabetes, the Allen Diet was an individualized starvation diet that restricted carbohydrates as well as calories. Some people's diets consisted of just 400 calories a day – hardly anything! It was difficult for patients to comply, particularly children, who often did not understand the significance of their dietary restrictions.One boy was so hungry that he ate his pet canary's birdseed, putting him into a coma and eventually killing him. Although the diet enabled some patients to live long enough to see the discovery of insulin, the majority were not so fortunate, and some even died from starvation.(19)

After Frederick Banting discovered insulin, the lives of diabetics all over the world were forever changed – they were no longer forced to survive on a starvation diet while waiting to die.Instead, they were given the opportunity to live a complete and happy life, including the ability to eat anything they desired. Banting believed that people with diabetes deserved to be able to eat normally and they deserved to live their lives to the fullest.Nevertheless, several physicians trained in the "pre-insulin school of thought," as he referred to it, tended to put diabetics on a bland diet absent of taste, flavor, and variety.(20)



The photos showed Teddy Ryder, one of Frederick Banting's first patients before and after. In the left-hand photo, Teddy is using the starvation diet treatment; in the right-hand photo, he is using the insulin treatment.

Complications of Diabetes in Children

All forms of diabetes increase the risk of long-term complications. These typically develop after many years (10–20) but may be the first symptom in those who have otherwise not received a diagnosis before that time.

The major long-term complications relate to damage to blood vessels. Diabetes doubles the risk of cardiovascular disease and about 75% of deaths in people with diabetes are due to coronary artery disease. Other macrovascular diseases include stroke, and peripheral artery disease.The primary complications of diabetes due to damage in small blood vessels include damage to the eyes, kidneys, and nerves. Damage to the eyes, known as diabetic retinopathy, is caused by damage to the blood vessels in the retina of the eye, and can result in gradual vision loss and eventual blindness. Diabetes also increases the risk of having glaucoma, cataracts, and other eye problems. It is recommended that people with diabetes visit an eye doctor once a year.Damage to the kidneys, known as diabetic nephropathy, can lead to tissue scarring, urine protein loss, and eventually chronic kidney disease, sometimes requiring dialysis or kidney transplantation. Damage to the nerves of the body, known as diabetic neuropathy, is the most common complication of diabetes. The symptoms can include numbness, tingling, pain, and altered pain sensation, which can lead to damage to the skin. Diabetes-related foot problems (such as diabetic foot ulcers) may occur, and can be difficult to treat, occasionally requiring amputation. Additionally, proximal diabetic neuropathy causes painful muscle atrophy and weakness. Diabetes can cause both immediate and long-term complications. Diabetic ketoacidosis is considered one of the most severe acute complications.(21)

Long-term complications are typically caused by social and psychological issues, as well as blood vessel disorders. While blood vessel problems can take years to develop, the better the diabetes management, the less likely complications may occur.(21)

Diabetic ketoacidosis (DKA)

Diabetic ketoacidosis (DKA) in children is characterized as a blood glucose level greater than 11 mmol/L, a venous pH less than 7.3 or a serum bicarbonate level less than 15 mmol/L, and either ketonemia (blood -hydroxybutyrate level greater than 3 mmol/L) or moderate to high ketonuria. This disease, along with the major complication of cerebral edema, is the leading cause of death and serious morbidity in pediatric diabetes cases, especially at the time of initial diagnosis. If death and disability are to be prevented, early detection and careful treatment of ketoacidosis—a metabolic derangement caused by an absolute or relative deficiency of the anabolic hormone insulin—is critical.(22)

Epidemiology

Exact figures for the incidence of diabetic ketoacidosis are not available. The estimated incidence of diabetic ketoacidosis in pediatric type 1 diabetes mellitus in resource-rich countries appears to be 1-10% per year.

At the time of type 1 diabetes diagnosis, an estimated one-third of children have diabetic ketoacidosis. **According to a multicenter in the USA**, population-based analysis, approximately 25% of new cases of type I diabetes mellitus presented with ketoacidosis, resulting in an annual

incidence of 4 cases per 100,000 children.The youngest children were the most vulnerable, with more than 37% developing diabetic ketoacidosis. The prevalence of diabetes in children rises with age.

As in the United States, little information was available on the prevalence of diabetic ketoacidosis. On the other hand, a**massive multicenter European study** found that rates of diabetic ketoacidosis at diagnosis ranged from 26 to 67 percent, with rates inversely linked to the overall incidence of childhood diabetes.Diabetic ketoacidosis rates in children with proven diabetes differ greatly; in **a national prospective study** conducted in the United Kingdom, 60 percent of all cases occurred in patients with documented diabetes. Diabetic ketoacidosis at the time of diagnosis is more common in the poorest neighborhoods.

A 2011 analysis of 46 published papers confirmed the preceding assertions. The youngest children, especially those younger than two years old, and children from the most vulnerable populations, including ethnic minorities or those without health insurance, were the groups most likely to present with diabetic ketoacidosis at diagnosis.Having a first-degree relative with type 1 diabetes, having better-educated parents, and living in a neighborhood with a high history incidence of childhood diabetes were all protective factors against diabetic ketoacidosis at diagnosis.

Etiology

Twenty-five percent of children with a new diabetes diagnosis have diabetic ketoacidosis; the most common cause, especially in young children, is a missed diabetes diagnosis. The causes of diabetic ketoacidosis in children with proven diabetes differ with age. In the prepubescent boy, infection is the most probable precipitant; in the older adolescent, missed injections or emotional upset are more common. The most common cause of diabetic ketoacidosis in adolescents is failure to administer prescribed insulin.(23)

Children with high glycosylated hemoglobin (HbA1c) levels (a measure of control over an 8- to 12-week period) may only receive one-third or less of the recommended insulin dose. Total insulin deficiency clearly causes diabetic ketoacidosis, inadequate doses; on the other hand, make the child more likely to overcompensate with other pressures such as infection, mental turmoil, or food bingeing. Children on regular insulin infusion are particularly vulnerable to diabetic ketoacidosis if the system fails or if insulin delivery is interrupted, since they lack an efficient insulin depot and rapidly become insulin-deficient. Diabetic ketoacidosis is most likely to develop within the first year of starting continuous subcutaneous insulin infusion. Diabetic ketoacidosis sometimes may present with vomiting and stomach pain, which are misdiagnosed as gastroenteritis or food poisoning. Some children experience diabetic ketoacidosis on a regular basis (so-called brittle diabetics).(24) These children typically have profound psychological disturbances related to home, education, or peer relationships. They will repeatedly present in a

critical condition, but they will still deny any failure to comply. It is incredibly difficult to assist them.(25)

Managements of DKA

- **DIAGNOSTIC WORK-UP:**

DKA diagnosis should be performed precisely due to the risk of a misleading clinical image, such as dehydration, meningitis, acute abdomen, pneumonia, and so on. The general principles in Pediatric Advanced Life Support may be used to conduct an emergency assessment. Immediate interventions include a brief history and a prompt diagnosis, all of which are critical.The degree of dehydration, level of consciousness as measured by the Glasgow Coma Scale, body weight, and height, if the person is mobile, are all part of the initial immediate assessment or investigation. Baseline tests include measuring BG levels, beta-hydroxybutyric acid, serum electrolytes, and renal function.During a physical exam, a doctor can look for signs of dehydration, acidosis, and electrolyte imbalance, such as shock, hypotension, acidotic breathing, and a malfunctioning central nervous system.(26)

The biochemical criteria required for a diagnosis of DKA to be made are:

a) Acidosis - indicated by blood pH of <7.3 or bicarbonate <18 mmol/L:
b) pH ≥7.1 indicates mild or moderate DKA.
c) pH<7.1 indicates severe DKA.
d) Ketonaemia (indicated by blood beta-hydroxybutyrate above 3 mmol/L) or ketonuria (indicated by ++ or more on urine dipstick).

There is usually raised blood glucose >11 mmol/L. However, children and young people with normal blood sugar levels can develop DKA.

- **THERAPEUTIC OPTIONS*:***

The following is based on National Institute for Health and Care Excellence and British Society for Pediatric Endocrinology and Diabetes DKA guidelines.(27)

1-Always begin with resuscitation of the patient

Airway - check the airway is patent, attempt to open it if not. Seek urgent anesthetic review and discuss with pediatric critical care specialist if airway is not protected due to a reduced level of consciousness as intubation may be indicated. Consider need for nasogastric tube to decompress and empty the stomach and lower the risk of aspiration, particularly if there is reduced consciousness.

Breathing - consider need for oxygen -eg, if altered level of consciousness (if necessary 6-10L/min via Hudson mask)(28)

Circulation - insert two intravenous (IV) cannula if possible, one for fluid and medications and one for blood sampling line. Attach cardiac monitor. Assess cardiovascular status and only give a fluid bolus (10 ml/kg 0.9% sodium chloride) if there is hypotensive shock. Discuss any further bolus and the use of inotropes with a pediatric critical care specialist.

Disability - assess conscious level early on. All patients should have GCS assessment or a modification of the verbal response score for younger children, and one-hourly neurological observations. If the patient is comatose or semi-conscious, consider cerebral edema and institute treatment and arrange transfer to PICU/HDU (but do not delay therapy).(29)

2-The next step in the management is correction of fluid loss

The essential principles of DKA treatment include careful replacement of fluid deficits, correction of dehydration, correction of acidosis and hyperglycemia with insulin administration, maintenance of glucose levels at the normal range, correction of electrolyte imbalance and treatment of any precipitating cause. Successful management of DKA requires constant clinical and biochemical monitoring and timely adjustment of insulin dose, fluid and electrolyte status. Antibiotics, oxygen, and cardiac monitoring can be used if required. Fluid therapy is initially used for the treatment of DKA, followed by insulin therapy if required. The main importance of fluid therapy is: Restoration of circulating volume, replacement of electrolytes, improvement of renal function and clearance of glucose and ketones from the blood. (29)

Before starting fluid therapy, the physician should check if the child was treated earlier before the current admission. During fluid therapy, water and salt deficit are replaced using 0.9% normal saline and a 10-20 mL/kg normal bolus may also be used for approximately 1-2 h. If the patient is in shock, several boluses may be given. Subsequent therapy is used for deficit replacement. Normal saline or Ringer lactate is used over a period of 4-6 h. Consequently, maintenance fluids are used. Usually, half normal saline (0.45%) with potassium chloride is given depending on the state of hydration and electrolyte levels. Fluid therapy is usually planned for a period of 48 h. However, a child may improve earlier than 48 h. Normal circulation is often achieved in 12 ± 6 h. In cases of mild DKA, no bolus is needed. The main principle of fluid therapy is to never infuse fluids more than 1.5-2 times the normal daily requirement. Moreover, constant monitoring and assessment of hydration is absolutely essential.(30)

3- Replace insulin

Insulin therapy is essential to return the blood sugar level to normal limits, and to prevent further lipolysis and ketogenesis. Insulin should be given as an IV infusion at a dosage between 0.05 and 0.1 units/kg/hour. Use pre-filled syringes containing 50 Units of soluble insulin in 50 ml 0.9% sodium chloride. An initial bolus is not recommended.it is worth mentioning that Continuous subcutaneous insulin pumps should be stopped while the IV infusion is given, but long-acting insulin treatment may be continued. Subcutaneous insulin may only be used along with oral

fluids where the child or young person is alert, not nauseated or vomiting, and not clinically dehydrated.(30)

4- Potassium replacement

Potassium replacement therapy is used when the total body potassium deficit is nearly ~3-6 mmol/kg. If the patient is hypokalemic, start potassium replacement at the time of initial volume expansion and before starting insulin therapy. Otherwise, start replacing potassium after initial volume expansion and concurrent with starting insulin therapy. If the patient is hyperkalemic, defer potassium replacement therapy until urine output is documented. If children are hypokalemic on presentation, potassium should be replaced, and as long as the patient has adequate renal function, rehydration fluid should contain potassium. Depletion of intracellular phosphate is also seen in DKA due to losses from osmotic diuresis, and severe hypophosphatemia should be treated. Bicarbonate administration is not recommended because this has not shown benefit in the resolution of DKA, and bolus administration has been historically associated with worse outcomes. Administration of bicarbonate potentially may cause harm due to paradoxical central nervous system acidosis. Therefore, bicarbonate administration should be reserved for the treatment of severe hyperkalemia or severe acidosis (pH $\leq$6.9) causing impaired cardiac contractility.(31)

Patient and method

This study is a prospective study conducted on male and female children with diabetic ketoacidosis, performed during 1st of December 2020 to 30 of April 2021. Eighty five patients were enrolled in this study that collected from Bint AL-huda hospital and Al-Nasria Diabetic Center, this was done by a direct interview with the patients' parents mostly their mother according to the questioner paper which was organized and submitted by our supervisor.

Inclusive criteria:

1) Children with a known case of diabetes mellitus.
2) Newly diagnosed cases of diabetes mellitus and its complication.

Exclusive criteria:

1) Children with other chronic diseases.
2) Children with different complication rather than DKA.

Aim of Study

The purpose of the study is to determine the relative risk factors among diabetic children how were developed DKA at some stage of their life, and to compare the prevalence rate between both genders in Al-Nasria Provence.

Statistical analysis

Data was entered and analyzed using Microsoft excel program, also the mean and standard deviation was calculated by free online site for mean and standard deviation.

Results

Table 1: basic information regarding sex and age distribution

Age variation	sex		P value <0.05
	male	Female	
Less than 1 years	1	1	
1-2 years	0	3	
3-5 years	3	2	
More than 5 years	36	39	
Total	40	45	

The relationship between sex and age is significant

Table 2: the address and the type of treatments among the selected patients

Type of treatment	address		Total	P value <0.05
	Rural	Urban		
Mixed two doses regimen	16	42	58	
Basal and bolos	4	7	11	
Other	4	5	9	
Unknown	1	6	7	
Total	27	58	85	

The relationship between treatment and address is significant

Table 3: shows the number of DKA attacks in each age group and the diagnosis state of DM

Attacks	Old diagnosis	New diagnosis	Total	P value <0.05
First attack	3	21	24	
2-5 attacks	26	-	26	
6-10 attacks	8	-	8	
More than 10 attacks	12	-	12	
Unknown	1	14	15	
Total	50	35	85	

The relationship between attack and diagnosis state is significant

Figure 1: shows the percentage of the male and female in the selected cases

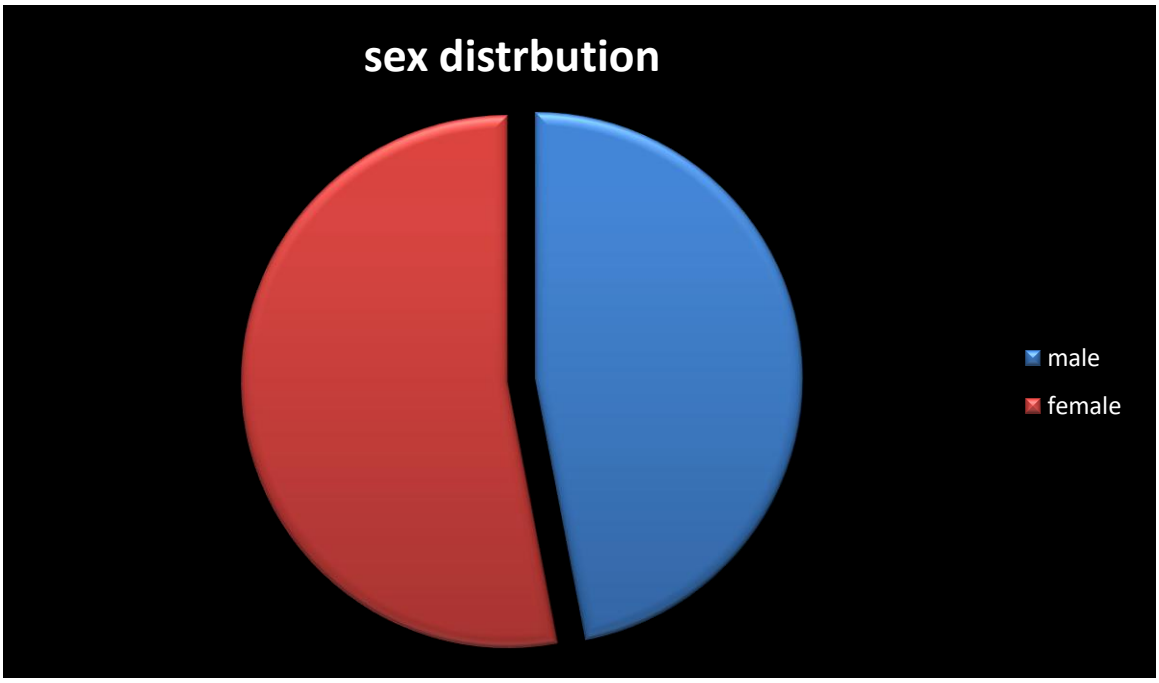


Figure 2 : represents the difference in the age group between both genders

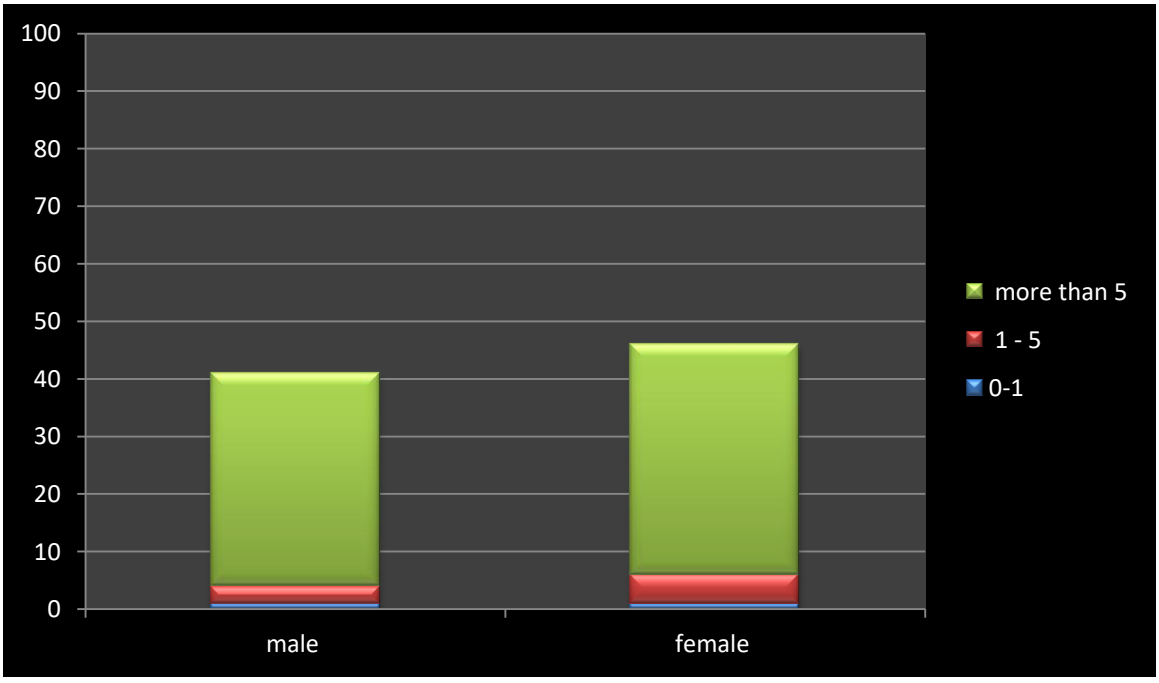


Figure 3: the proportion of children who were diagnosed newly and those with old dm

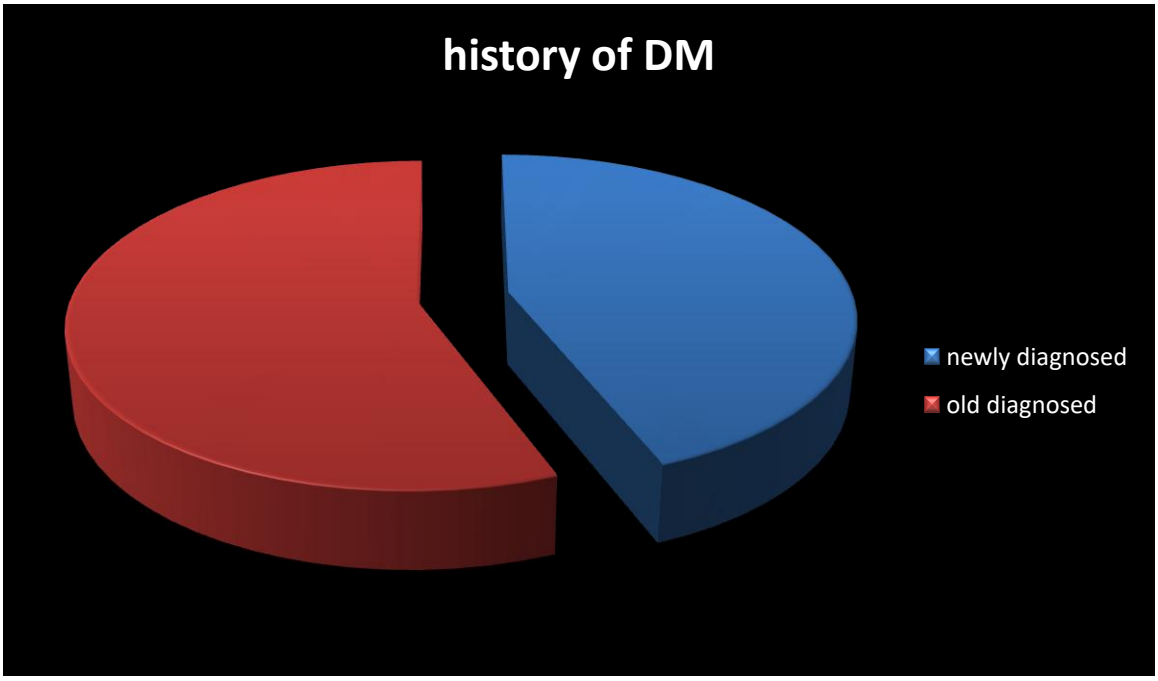


Figure 4: the proportion of DKA attacks among selected cases

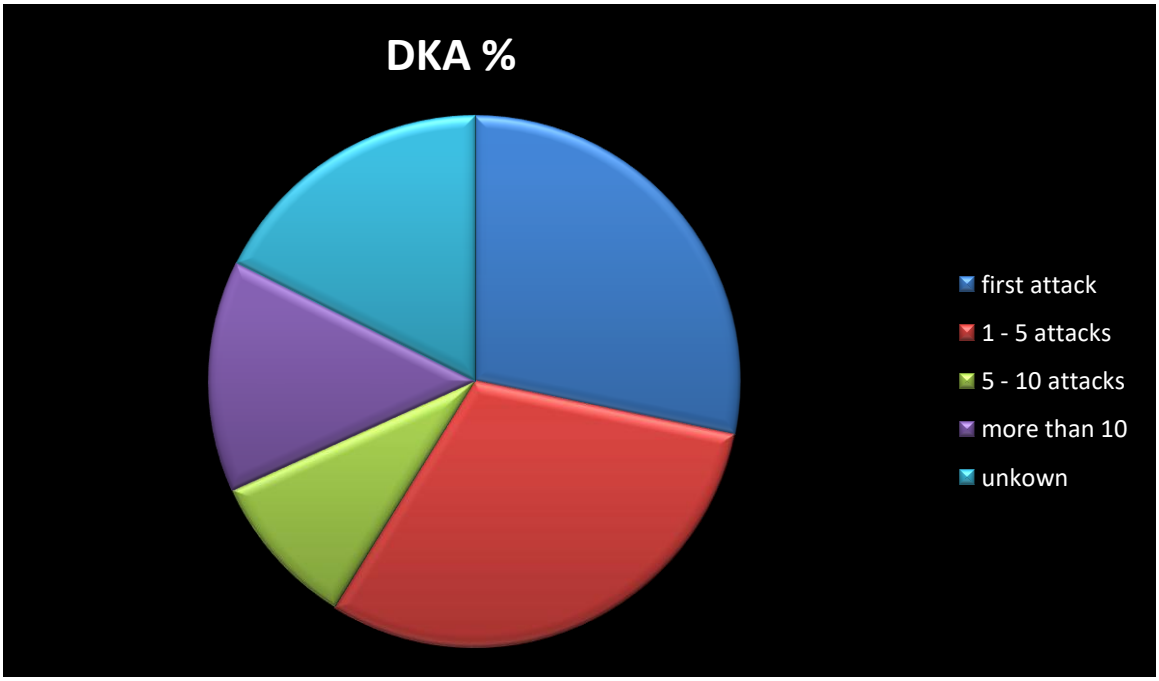
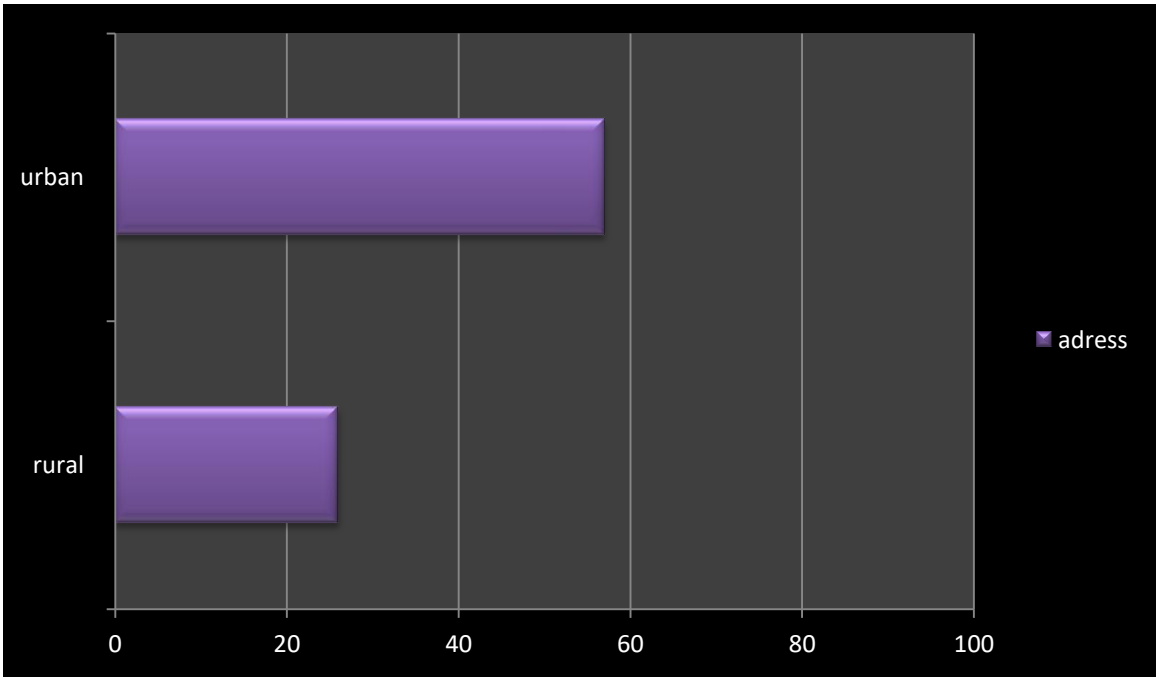


Figure 5: the number of patients in rural and urban areas



Discussion

Out of the 85 children admitted with DKA, 40 (47.1%) were male and 45(53, 2%) were female (Table 1). Also, the most effected age group from the selected cases was among those children whose age more than five years which accounted for more than 90 % compare to other age groups.

In terms of living environment which may be a leading risk factor for DKA among children in different age group, those children who lives in urban areas are more prone to have DKA attacks compare with those who lives in rural areas as it shown in table (2) 27 child were from different rural areas and 58 were living in urban site.A study was made by AgnieszkaSzypowska which consisted of new-onset type 1 diabetic patients admitted to the hospital between January 2006 and March 2008. One hundred and eighty-seven children were identified (95 females and 92 males) and their mean age was 8.9 ± 4.6 yr (0.8–17.8). Hemoglobin A1C, blood gases, and fasting c-peptide level were evaluated in all children. DKA was defined as a capillary pH < 7.3 and blood glucose >11 mmol/L. the results reveled that at the time of T1DM diagnosis, 26% of children had DKA. Misdiagnosis was significantly associated with the incidence of DKA. In this study the incidence of DKA among newly diagnosed patients with T1DM remains unacceptably high and indicates greater necessity of medical alertness for this diagnosis, especially in the youngest children. Children under 2 yr of age remain the most prone to DKA, which may be related to delay in diagnosis and more aggressive β-cell destruction.in comparison with our study which show compatible results with the study which made by AgnieszkaSzypowska as the Marjory of children were new-onset DM .

While the majority of children (50 children) were admitted to the hospital with (1-5) attacks of DKA as it is shown in table (3), the remaining (35 children) were between five to fifteen attack during their diseased life od DM . Weather being diagnosed newly with DM or before a certain period of time, this may counter as a risk factor for having DKA later in life. In our study the number of children who were admitted to the hospital with first time diagnosis of DM was around 60% while those children who already had established diagnosis were about 30%.

Another cohort study which made byElzbietaNiechcialcomprised 735 children aged 0–18 years with newly diagnosed T1DM. Clinical and biological features were collected at diagnosis and during follow-up. DKA was defined as blood pH <7.30. To confirm autoimmune diabetes origin typical autoantibodies were tested. DKA was diagnosed in 36.0% of patients: 12.9% had mild form, while 14.5% and 8.7% moderate and severe, respectively. In children aged 0–4, 5–9, 10–14 and 15–18 years DKA was present in 48.5, 34.7, 31.4 and 28.2%, respectively. In individuals aged <4 years DKA occurred significantly often (P=0.001). The highest severe DKA frequency

was associated with symptoms' duration (>28 days) (P=0.014) and diabetes misdiagnosis (P=0.001). The prevalence of DKA is high in children from Wielkopolska. Children aged <4 years have the greatest risk of developing ketoacidosis. The highest frequency of severe DKA is related to symptoms' duration and diabetes misdiagnosis. This study results is opposite to our results in the study which revealed that most of effected children with DKA were more than five years of age.

FikadenBerheHadgustudy was done to assess prevalence and associated factors of diabetic ketoacidosis in children with newly diagnosed type 1 diabetes in hospitals of the Tigray region, Ethiopia. The results revealed that more than three-quarters, 258/328 (78.7%) of the newly diagnosed type 1 diabetes patients, presented with diabetic ketoacidosis at initial diagnosis. Median age of diabetic ketoacidosis patients was 11 years. The patients with diabetic ketoacidosis were younger than nondiabetic ketoacidosis patients (11 vs 13 years, P=0.002). The mortality rate of diabetic ketoacidosis was 4.3%. Young age, presence of precipitating factors and symptoms of DKA/diabetes were found to be highly associated with diabetic ketoacidosis at initial diagnosis.The prevalence of diabetic ketoacidosis was alarmingly high. Young age group patients, precipitating factors and the presence of symptoms of diabetes/DKA like excessive drinking, vomiting and fatigue were highly associated with diabetic ketoacidosis.

Conclusion

Diabetic ketoacidosis is a common presentation of both T1DM and T2DM in children DKA arises due to lack of adequate insulin in the body. For successful DKA management, meticulous monitoring of the patient's clinical and biochemical response using a flow chart is essential. Neurological observations, for warning signs and symptoms of cerebral edema, and capillary BG concentration should be measured on an hourly basis. Every 2-4 h electrolytes, blood gases, and beta-hydroxybutyrate should be measured.

Recommendations

1) We need community education about diabetes mellitus and its serious acute and chronic complications.
2) The avoidances of herbal medicine in the treatment of diabetes mellitus, is one of the essential recommendation which we have to clarify it for our community.
3) The use of social media for social education will promote the rate of distribution of our clarification about DKA.
4) Print more educational posters about the life style of patient with diabetes and how he or she can live a normal life without any complication.

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