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INCIDENCE OF DIABETIC KETOACIDOSIS AMONG ADULTS WITH TYPE 1 DIABETES IN SAUDI ARABIA: SYSTEMATIC REVIEW

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ABSTRACT

T1D is an autoimmune illness characterized by the death of pancreatic beta cells by the immune system, which results in a reduction in, or full stoppage of, insulin synthesis and secretion, necessitating the need for exogenous insulin for life. Diabetic ketoacidosis (DKA) is a serious complication that can arise before T1DM is diagnosed. DKA has been linked to several negative consequences. Cerebral edema is still the most prevalent cause of death in children with DKA. DKA is prevalent when a juvenile is diagnosed with diabetes, with children being the most vulnerable, presumably because diabetes symptoms are more likely to go unnoticed in younger children. In this study, we aim to: report on previous literature on the incidence of diabetic ketoacidosis in type 1 diabetes mellitus that was carried out in Saudi Arabia. PubMed database and EBSCO Information Services were used for article selection. All relevant articles to our review with the topics regarding ketoacidosis in type 1 diabetes mellitus and other articles have been used. We excluded other articles which are not related to this field. The data will be extracted according to a specific form in which it is going to be reviewed by the group members. In conclusion, studies reported variably different prevalences of DKA in Saudi Arabia. Compared to previous literature, DKA is assembling a common catastrophic complication among diabetic Saudi patients. Public awareness campaigns are needed to keep the public informed of the possible dangers of this case.

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Introduction

High blood glucose levels are a symptom of diabetes caused by faulty insulin synthesis, function, or both. T1D is an autoimmune illness characterized by the death of pancreatic beta cells by the immune system [1]. The immune system regulates this damage, which results in a reduction in, or full stoppage of, insulin synthesis and secretion, necessitating the need for exogenous insulin for life [2]. T1D usually has an acute clinical course, with polyuria, polydipsia, and weight loss being common symptoms [3]. T1D affects roughly 542 000 children aged 0 to 14, according to the International Diabetes Federation, with 86 000 new cases diagnosed each year [4]. While there are regional variations, the overall yearly increase in the incidence of T1D is estimated to be between 3% and 4%. T1D is usually diagnosed in youth; in the United States, the peak (mean) diagnosis age is 14 years [5].

Diabetic ketoacidosis (DKA) is a serious complication that can arise before T1DM is diagnosed. The data situation in determining the present stage of diagnosis is still uncertain. In all, 47 000 children and adolescents were included in a review that evaluated 34 research. DKA rates ranged from 14.7 percent in Denmark to 79.8 percent in (Saudi Arabia). Although DKA rates remain high, some articles include evidence of a downward trend. According to the meta-regression, DKA rates are moderated by latitude and the human development index (HDI). The frequency with which DKA rates arise varies greatly

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between nations. The observed variability is partially explained by both latitude and HDI, whereas other modifiers, such as physician density, showed no evident link [6].

DKA has been linked to several negative consequences. Cerebral edema is still the most prevalent cause of death in children with DKA. It affects 0.5 percent to 0.9 percent of DKA patients, with a 21 percent to 24 percent fatality rate. Late presentation in DKA increases the patient's risk of morbidity and death and raises healthcare expenses. Patients with DKA are usually hospitalized in the critical care unit and may have a lengthy hospital stay with various problems, all of which add to the expense. Furthermore, early DKA presentation is associated with a worse prognosis and has been linked to reduced residual cell activity following diagnosis as well as poorer glycemic management [7].

DKA is prevalent when a juvenile is diagnosed with diabetes, with children being the most vulnerable, presumably because it is hard to diagnose the disease from diabetes symptoms at that age. Children who are uninsured or underinsured and children from minority racial and ethnic groups are at greater risk. It is unlikely for children whose parents have diabetes also to develop diabetes and be in DKA; however, the total rate is still alarmingly high (24 percent vs. 41 percent in the Type 1 Diabetes Exchange Registry) [8-16].

Study Objective

The study aims to explore the current evidence concerning the incidence of Diabetic Ketoacidosis among Adults with Type 1 Diabetes

Materials and Methods

Study Design

Systematic Review.

Study Duration

Data was collected from 1– 29 October 2022.

It is frequently used in the health disciplines to identify novelties and discover new approaches to health services, enabling evidence-based health care, ensuring high-quality services, and enhancing patient welfare and safety. A systematic review is a technique for gathering previously published studies to synthesize suggestions on a subject. Six steps must be completed in order: Explaining the purpose of the study, defining the sample, evaluating the included papers, interpreting the results, and presenting the Systematic review synthesis.

After searching and defining the sample, a thorough examination of the papers with the same objective as our study was conducted.

Due to their reputation as reliable databases, PubMed and EBSCO Information Services were preferred as the exploration databases for the papers utilized in the study. One of the biggest online digital libraries, PubMed, was created by the National Center for Biotechnology Information (NCBI), a division of the National Library of Medicine of the United States. The article was created using subjects relating to the incidence of Diabetic Ketoacidosis among Adults with Type 1 Diabetes. The topics and summaries of the established papers will be scrutinized.

Inclusion Criteria

The subjects were selected for addition founded on their applicability to the research, which must have at least one of the following subjects; the incidence of diabetic ketoacidosis among adults with Type 1 diabetes.

Exclusion Criteria

All additional papers, recurring research, and reviews of research that do not possess one of these themes as their major end were disregarded.

Analysis of Data

The data was not analyzed by any program. The information was taken from a specified form, including the research topic, author's designation, aim, executive summary, results, conclusions, and outcomes. To guarantee rationality and reduce errors, each affiliate's results will be double-revised.

To ensure that the research we contained within the study applies to the goal line of our study and to avert or diminish slips in the results, studies will be double-reviewed during the article selection process.

Results and Discussion

Figure 1 shows the selection and identification of studies. The search of the mentioned databases returned a total of 105 studies that were included for title screening. 63 of them were included for abstract screening, which lead to the exclusion of 32 articles. The remaining 31 publications' full texts were reviewed. The full-text revision led to the exclusion of 19 studies, and 12 were enrolled for final data extraction **(Table 1)**.

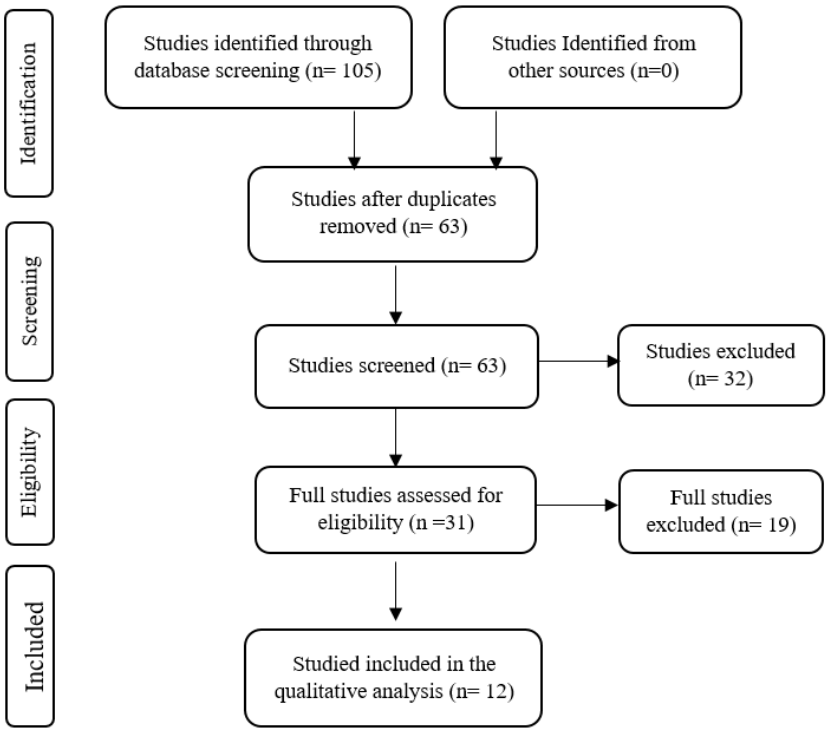

Figure 1. Flow chart the included studies had different study designs

Al-Shaikh, A., *et al*. (2019) found that moderate and severe DKA cases were significantly higher among female children. Patients diagnosed with DKA had lower BMI. The median length of hospital stay was higher among severe DKA compared to moderate and mild cases (5.0, 4.5, and 4.0 days, respectively) [17].

Ahmadi, S., *et al*. (2018) reported that the mean age of patients was (22.82 ± 5.567) years, and females constituted (66.7%) of this group. Poor medication compliance was the commonest risk factor associated with DKA. Patients with multiple DKA episodes reported fewer visits to the diabetes educator compared to the single DKA group [18].

Babiker, A., *et al*. (2022) reported that the frequency of DKA admissions 2 were 146/562, 26%, of which (n=42/146, 28.7%) were newly diagnosed vs. (n=104/146, 71.2%) known patient of T1DM. The majority were 10-14 years ($p \leq 0.001$) and 55.5% were females. Missing insulin was the main precipitating cause of DKA (p=0.001) among known patients with T1DM. Recurrent episodes (n=30/164, 20.5%) occurred in 15/116 patients and were more common in children ≥10 years of age (P=0.024). The mean length-of-stay was 2.67±2.04 days and increased with DKA severity (P=0.008) [19].

Alotaibi, R., *et al*. (2022) found that factors that precipitated DKA were most commonly noncompliance to treatment (55.1%), followed by infections (31.8%) and nonadherence to diet (25.6%). The most common symptoms were nausea and vomiting (87.5%), followed by abdominal pain (72.7%). 32.4% of the sample was read-mitted with DKA [20].

Al Sahib, Y. H., *et al.* (2021) study included 228 males (59.2%), and 44.2% were diabetic for more than 5 years. The last recorded HbA1c levels of 53.5% were >9%. The main predisposing factors for DKA were first presentation (59%) or treatment discontinuation (53.1%). DKA occurred significantly more in patients with a family history of diabetes (p ($p<0.001$), in patients with poor glycemic control ($p<0.001$), and in patients whose parents were less educated or unemployed [21].

In their study, Alhaji, R., *et al.* (2021) revealed that 44.1% were diabetic for more than 5 years. The main causes of DKA were "first presentation of the disease" (40.9%) and "discontinued treatment" (37%). The HbA1c among 53.6% was above 9%. Almost all cases who experienced DKA were hospitalized (98.8%). Out of them, 9 (5.4%) suffered complications. Female patients were more likely to suffer from episodes of DKA than males (76% and 68.3%, respectively). Ketoacidosis was significantly more frequent among patients with parents' consanguinity ($p<0.001$) [22].

Batwa M, Alharthi L, Ghazal R, *et al*. (2022) reported that polyuria (98.1%), polydipsia (86.8%), weight loss (62.3%), and abdominal pain and vomiting (45.3%) were the most frequent symptoms. The mean random blood glucose was 424.09 ± 108.67 mg/dL, and the mean venous pH was 7.15 ± 0.36 mmol/L. Of patients, 66% had no associated complications, 24.4% had hypokalemia, 20.8% developed hypoglycemia, and 18.9% developed hyperchloremic metabolic acidosis. One patient had cerebral edema and coma. Based on metabolic acidosis, 24.5% had mild DKA, an equal percentage had severe DKA, and 9.4% had moderate DKA [23].

Albi, L. A., *et al.* (2017) found that female patients and those aged 0 - 3 years exhibited the highest likelihood of developing DKA. Moreover, underweight children had a greater DKA incidence than healthy, overweight, or obese children ($p = 0.02$) [24].

Al-Hayek, A. A., *et al*. (2015) reported that adolescents who stopped insulin and those with lipodystrophy at the injection site had a higher frequency of RDKA. Discontinuing insulin (67%) was the major reason for RDKA, followed by infection (31%) [25].

Al Hayek, A. A., *et al*. (2020) revealed a significant relationship in terms of gender, age, body mass index (BMI), hemoglobin A1c (HbA1c), duration of diabetes, and clinic appointments. Bivariate analysis between patients with DKA and those without DKA revealed significant relationships in terms of gender ($p = 0.014$), age ($p = 0.0001$), body mass index (BMI) ($p = 0.017$), hemoglobin A1c (HbA1c) ($p = 0.0001$), duration of diabetes ($p = 0.001$) and clinic appointments ($p = 0.001$). Those in the age category of 20–29 years and teenagers faced a higher risk of having DKA episodes. Compared with patients with HbA1c levels <8%, those with HbA1c levels 8–9.9% and ≥10% revealed a higher risk for DKA [26].

Al-Ghamdi, A. H., & Farah, A. A. (2018) found that hyperglycemic symptoms were the most frequent symptoms at presentation (59.2% vs. 40.8% with diabetic ketoacidosis (DKA)), and 37% of them presented with loss of weight. Most of the ketoacidosis was mild to moderate (80.2%), while only 19.8% of children had the severe type, and DKA was more common (55.2%) among females. The mean age at diagnosis of T1DM was 8.2±3.5 years for all patients, and 8.3±3.9 and 8.9±3.6 years for boys and girls, respectively (p=0.06). Hyperglycemic symptoms were more common in spring (15.9%) [27].

Table 1. Author, country, year of publication, methodology, and results

Author, year	Study type	Method	Outcomes
Al Shaikh, A., *et al*. (2019) [17]	Jeddah, Saudi Arabia	This retrospective chart review was conducted on newly diagnosed T1DM children during the study period were investigated (n = 390). Data were collected on the demographic characteristics, body mass index (BMI), DKA severity, length of hospital stay, and follow-up data on the type of diabetes therapy.	The incidence of DKA among newly diagnosed T1DM pediatric patients was 37.7%.
Alahmadi, S., *et al*. (2018) [18].	Jeddah, Saudi Arabia	Retrospective review of DM1 patients at King Abdul-Aziz Medical City who was presented with DKA during the past six and half years.	The average annual DKA onset was (6.2%).
Babiker, A., *et al*. (2022) [19]	Riyadh, Saudi Arabia	A retrospective review of all DKA admissions at King Abdullah Specialized Children's Hospital, Riyadh. Data were gathered from newly diagnosed T1DM and known patients ≤14-year-old with DKA criteria.	A total of 20.6% of patients with T1DM DKA, of which 26/116 (34%) were newly diagnosed.
Alotaibi, R., *et al*. (2022) [20]	Jeddah, Saudi Arabia	We identified all patients aged 15 years and older admitted with DKA from 2018 to 2020.	During the study period, 32.4% of the sample was read-mitted with DKA. The median duration between the first and second admission was 12 (4-25) weeks.
Al Zahib, Y. H., *et al*. (2021) [21]	Abha City, Saudi Arabia	A cross-sectional study was conducted among 385 type-1 diabetics in Abha City, Saudi Arabia	70.9% of participants reported a history of DKA.
Alhajaji, R., *et al*. (2021) [22].	Makkah Al-Mukarramah City, Saudi Arabia	A cross-sectional study was conducted among 236 type-1 diabetics in Makkah AlMukarramah City, Saudi Arab	70.8% of participants reported a history of DKA.
Batwa M, Alharthi L, Ghazal R, *et al*. (2022) [23]	Jeddah, Saudi Arabia	This retrospective cohort study analyzed the medical records of patients ≤ 16 years old seen in the emergency department at King Abdulaziz University Hospital, Jeddah, Saudi Arabia, between April 2015 and June 2019.	Of 207 patients with T1DM, 53 presented with DKA as a new onset.
Albishi, L. A., *et al*. (2017) [24]	Tabuk, Saudi Arabia	This retrospective observational study was based on the clinical records of pediatric diabetes outpatients at KSMH. All children aged <12 years who were diagnosed with T1DM and were followed up at the diabetes clinic from 2000 to 2010 were enrolled.	Diabetic ketoacidosis (DKA) was the presenting feature in 38.0% of patients
Al-Hayek, A. A., *et al*. (2015) [25]	Riyadh, Kingdom of Saudi Arabia	A cross-sectional study was conducted among 103 T1DM adolescents (aged 13-18 years, 57 males) who were hospitalized for diabetic ketoacidosis (DKA) between January 2013 and May 2014 at Prince Sultan Military Medical City (PSMMC), Riyadh, Kingdom of Saudi Arabia.	54.3% of participants had experienced one episode of DKA, 41 had 2 episodes, and 6 had ≥3 episodes.

Al-Agha, A. E., Alafif, M. M., & Abd-Elhameed, I. A. (2015) [28]	Jeddah, Saudi Arabia	a cross-sectional study of 228 T1DM children and adolescents visiting the pediatric diabetes clinic at the King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia, from January 2013 to January 2014. The clinical and laboratory characteristics of the patients were recorded. Metabolic control, complications, and associated autoimmune diseases were evaluated.	Acute complications included ketoacidosis in 65.4% of patients
Al Hayek, A. A., *et al*. (2020) [26]	Riyadh, Saudi Arabia	This descriptive, retrospective study was conducted among 1118 patients with T1D at the Prince Sultan Military Medical City, Riyadh, Saudi Arabia.	336 patients were selected for analysis. Among these, 105 patients with T1D were hospitalized for DKA
Al-Ghamdi, A. H., & Fureeh, A. A. (2018) [27]	AL-Baha region, Saudi Arabia	The clinical and laboratory data of 471 children and adolescents who presented with T1DM and received medical care at an AL-Baha diabetic center	Hyperglycemic symptoms were the most frequent symptoms at presentation [59.2% vs. 40.8% with diabetic ketoacidosis (DKA)]

Diabetic ketoacidosis (DKA) is a major life-threatening recurrent complication of T1DM and is the most common reason for death in children and adolescents with T1DM. In some cases, DKA may be the first sign of previously undiagnosed diabetes, but it may frequently happen in those who previously have diabetes [25].

Worldwide, children and adolescents aged under 15 years, to the tune of more than 96,000, develop T1DM annually, and 13% to 80% of these children present with DKA at the time of diagnosis [29]. The highest frequencies for DKA at the presentation of T1DM are seen in Saudi Arabia (44.9%) [30] and the United Arab Emirates (80%) [31]. The lowest frequencies for DKA at the presentation of T1DM are found in Hungary (23%), Finland (22%), Canada (18.6%), and Sweden (14%). A systematic review (65 studies) comprising over 29,000 children from 31 countries reported that the incidence of DKA varied sixfold, from 80% in the United Arab Emirates to 12.8% in Sweden. The study also demonstrated that the highest incidences were seen as 59% in Saudi Arabia, 80% in the United Arab Emirates, 67% in Romania, and 65% in Taiwan, and the lowest incidences were seen in Sweden (14%), Canada (18.6%), Finland (22%), and Hungary (23%). An increased risk of DKA may be due to younger age, diagnostic error, lower body mass index, ethnic minority status, earlier infection, lack of health insurance, and delayed treatment [32].

One study from the USA in 2018 showed that DKA mortality had been reduced from 2000-2014 from 1.1% to 0.4%. Similarly, in the United Kingdom, Adult DKA mortality has been reported to be less than 0.16%. And an isolated incident of DKA was associated with a 5.2% risk of death, while recurrent DKA admissions were associated with a 23.4% risk of death. Also, those patients with more than 5 DKA admissions died over 2.4 years [33]. DKA mortality in adults in Italy is 7.4%25. The DKA mortality in adults in Australia and New Zealand is 1.4%. In China, one study of adult DKA showed that mortality is 0.67% 28. Recently in 2016, one study from India reported very high inpatient mortality of 30%, and most of these patients who died were above the age of 20 years (81.5%) [34, 35].

The proportion of children with incident type 1 diabetes who arrive with DKA at or near the time of diabetes diagnosis is likewise rising, and changes in incident type 1 diabetes demographics aren't to blame. Between 2010 and 2016, DKA at or near the diabetes diagnosis of youth-onset type 1 diabetes grew at a 2% annual rate. Overall, 38.5 percent of type 1 diabetes case subjects had DKA at or near the time of diagnosis, up from a previously estimated frequency of 30 percent between 2002 and 2010. Younger children have the largest frequency of DKA found at or near type 1 diabetes diagnoses, which is consistent with previous SEARCH studies. On the other hand, adolescents may be at a higher risk of DKA at the time of diagnosis [36, 37]. In one research, teenagers aged 10–14 had a greater prevalence of DKA at the time of type 1 diabetes diagnosis than older adolescents aged 15. Compared to their non-Hispanic White and privately insured counterparts, youth with Hispanic ethnicity identity and from households without private insurance showed a greater frequency of DKA. For children aged 10–14 years, those diagnosed in the spring season, and those registered in South Carolina, there are growing trends in the prevalence of DKA at or near type 1 diabetes diagnosis [8, 37].

DKA at the time of type 1 diabetes diagnosis is linked to poorer overall glycemic control (higher overall HbA1c levels) and a deteriorating glycemic trajectory beyond the first year of illness. These links were found to be independent of demographic (sex, race/ethnicity, and age at diagnosis), socioeconomic (household income and insurance status), treatment-related factors (frequency of glucose monitoring and insulin regimen), and residual insulin secretion around the time of diagnosis; all of which are linked to both the presence of DKA and long-term glycemic control [36]. Some findings show that DKA at the outset of type 1 diabetes is not only an acute consequence but also a risk factor for long-term glycemic control deterioration [38-40].

Conclusion

In conclusion, studies reported variably different prevalence of DKA in Saudi Arabia. Compared to previous literature, DKA is assembling a common catastrophic complication among diabetic Saudi patients. There is no doubt that diabetic ketoacidosis is a serious case that requires some attention not only in newborns but also for adolescents, as some papers suggest that

teenagers can also present with severe conditions because most diagnoses focus on infants. However, it is also noteworthy to mention that juveniles are the ones who can present the most severe symptoms of DKA. Public awareness campaigns are needed to keep the public informed of the possible dangers of this case.

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References

1. Fazeli Farsani S, Brodovicz K, Soleymanlou N, Marquard J, Wissinger E, Maiese BA. Incidence and prevalence of diabetic ketoacidosis (DKA) among adults with type 1 diabetes mellitus (T1D): a systematic literature review. BMJ Open. 2017;7(7):e016587. doi:10.1136/bmjopen-2017-016587. Erratum in: BMJ Open. 2017 Sep 1;7(8):e016587corr1.
2. Centers for Disease Control and Prevention. National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States. 2014. Available from: www.cdc.gov/diabetes/pubs/statsreport14/national-diabetes-report-web.pdf.
3. Maahs DM, West NA, Lawrence JM, Mayer-Davis EJ. Epidemiology of type 1 diabetes. Endocrinol Metab Clin North Am. 2010;39(3):481-97. doi:10.1016/j.ecl.2010.05.011
4. International Diabetes Federation. IDF Diabetes Atlas. 7th Edition, 2015. Available from: www.diabetesatlas.org.
5. Patterson CC, Dahlquist GG, Gyürüs E, Green A, Soltész G, EURODIAB Study Group. Incidence trends for childhood type 1 diabetes in Europe during 1989-2003 and predicted new cases 2005-20: a multicentre prospective registration study. Lancet. 2009;373(9680):2027-33. doi:10.1016/S0140-6736(09)60568-7
6. Große J, Hornstein H, Manuwald U, Kugler J, Glauche I, Rothe U. Incidence of Diabetic Ketoacidosis of New-Onset Type 1 Diabetes in Children and Adolescents in Different Countries Correlates with Human Development Index (HDI): An Updated Systematic Review, Meta-Analysis, and Meta-Regression. Horm Metab Res. 2018;50(3):209-22. doi:10.1055/s-0044-102090. Erratum in: Horm Metab Res. 2018;50(3):e2.
7. Mencher SR, Frank G, Fishbein J. Diabetic Ketoacidosis at Onset of Type 1 Diabetes: Rates and Risk Factors Today to 15 Years Ago. Glob Pediatr Health. 2019;6:2333794X19870394. doi:10.1177/2333794X19870394
8. Jensen ET, Stafford JM, Saydah S, D'Agostino RB, Dolan LM, Lawrence JM, et al. Increase in Prevalence of Diabetic Ketoacidosis at Diagnosis Among Youth With Type 1 Diabetes: The SEARCH for Diabetes in Youth Study. Diabetes Care. 2021;44(7):1573-8. doi:10.2337/dc20-0389
9. Wolfsdorf JI, Allgrove J, Craig ME, Edge J, Glaser N, Jain V, et al. International Society for Pediatric and Adolescent Diabetes. ISPAD Clinical Practice Consensus Guidelines 2014. Diabetic ketoacidosis and hyperglycemic hyperosmolar state. Pediatr Diabetes. 2014;15(Suppl. 20):154-79.
10. Rewers A, Klingensmith G, Davis C, Petitti DB, Pihoker C, Rodriguez B, et al. Presence of diabetic ketoacidosis at diagnosis of diabetes mellitus in youth: the Search for Diabetes in Youth Study. Pediatrics. 2008;121(5):e1258-66.
11. Bui H, To T, Stein R, Fung K, Daneman D. Is diabetic ketoacidosis at disease onset a result of missed diagnosis? J Pediatr. 2010;156(3):472-7.
12. De Vries L, Oren L, Lazar L, Lebenthal Y, Shalitin S, Phillip M. Factors associated with diabetic ketoacidosis at onset of type 1 diabetes in children and adolescents. Diabet Med. 2013;30(11):1360-6.
13. Maahs DM, Hermann JM, Holman N, Foster NC, Kapellen TM, Allgrove J, et al. National Paediatric Diabetes Audit and the Royal College of Paediatrics and Child Health, the DPV Initiative, and the T1D Exchange Clinic Network. Rates of diabetic ketoacidosis: international comparison with 49,859 pediatric patients with type 1 diabetes from England, Wales, the U.S., Austria, and Germany. Diabetes Care. 2015;38(10):1876-82.
14. Dhatariya KK, Glaser NS, Codner E, Umpierrez GE. Diabetic ketoacidosis. Nat Rev Dis Primers. 2020;6(1):40.
15. Rewers A, Chase HP, Mackenzie T, Walravens P, Roback M, Rewers M, et al. Predictors of acute complications in children with type 1 diabetes. JAMA. 2002;287(19):2511-8.
16. Fox LA, Mubasher M, Wolfsdorf JI, Buckingham BA, Peters AL, Tamborlane WV, et al. T1D Exchange Clinic Network. Characteristics of youth with type 1 diabetes (T1D) with and without a parent with T1D in the T1D exchange clinic registry. J Diabetes. 2016;8(6):834-8.
17. Al Shaikh A, Farahat F, Saeedi M, Bakar A, Al Gahtani A, Al-Zahrani N, et al. Incidence of diabetic ketoacidosis in newly diagnosed type 1 diabetes children in western Saudi Arabia: 11-year experience. J Pediatr Endocrinol Metab. 2019;32(8):857-62. doi:10.1515/jpem-2018-0548
18. Alahmadi S, Ragaban A, Alblowi S, Aljumail E, Zarif H. Diabetic ketoacidosis; annual incidence and precipitating factors at King Abdulaziz Medical City, Jeddah. Egypt J Hosp Med. 2018;72(7):4831-5.

19. Babiker A, Aljahdali GL, Alsaeed MK, Almunif AF, Mohamud MS, Al Mutair A, et al. Frequency and Risk Factors of Diabetic Ketoacidosis in a Specialized Children's Hospital, Riyadh: A Cross-sectional Study. Oman Med J. 2022;37(1):e341.
20. Alotaibi R, Alsulami M, Hijji S, Alghamdi S, Alnahdi Y, Alnahdi H, et al. Diabetic ketoacidosis in Saudi Arabia: factors precipitating initial admission and readmission. Ann Saudi Med. 2022;42(2):119-26. doi:10.5144/0256-4947.2022.119
21. Al Zahib YH, Alshaikhi SA, Alshaikh AA, Al Zahib MH, Alshehri HM, Alamri SA, et al. Risk Factors of Diabetic Ketoacidosis among Type 1 Diabetic Patients in Abha City, Saudi Arabia. Middle East J Family Med. 2021;19(7).
22. Alhajaji R, Almasodi K, Alhajaji A, Alturkstani A, Samkari M. Prevalence and Associated Factors of Diabetic ketoacidosis among Patients Living with Type 1 Diabetes in Makkah Al-Mukarramah City. Middle East J Family Med. 2021;7(10):16.
23. Batwa M, Alharthi L, Ghazal R, Alsulami M, Slaghour R, Aljuhani R, et al. Diabetic Ketoacidosis at the Onset of Type 1 Diabetes Mellitus Among Children and Adolescents in Jeddah, Saudi Arabia: A Study from the Emergency Department. Cureus. 2022;14(4):e24456. doi:10.7759/cureus.24456
24. Albishi LA, Altoonisi MM, Alblewi SM, Osman RH, Ahmed NA, Fararjeh M. Clinical demographic patterns of type 1 diabetes in saudi children in Tabuk City, 2000-2010. J Diabetes Mellitus. 2017;7(2):41-54.
25. Al-Hayek AA, Robert AA, Braham RB, Turki AS, Al-Sabaan FS. Frequency and associated risk factors of recurrent diabetic ketoacidosis among Saudi adolescents with type 1 diabetes mellitus. Saudi Med J. 2015;36(2):216-20. doi:10.15537/smj.2015.2.10560
26. Al Hayek AA, Robert AA, Ruqayah AS, Alhojele M, Aloufi S, Sabri D, et al. Factors associated with the presence of diabetic ketoacidosis: a retrospective analysis of patients with type 1 diabetes in Saudi Arabia. Diabetes Metab Syndr. 2020;14(6):2117-22.
27. Al-Ghamdi AH, Fureeh AA. Prevalence and clinical presentation at the onset of type 1 diabetes mellitus among children and adolescents in AL-Baha region, Saudi Arabia. J Pediatr Endocrinol Metab. 2018;31(3):269-73.
28. Al-Agha AE, Alafif M, Abd-Elhameed IA. Glycemic control, complications, and associated autoimmune diseases in children and adolescents with type 1 diabetes in Jeddah, Saudi Arabia. Saudi Med J. 2015;36(1):26-31. doi:10.15537/smj.2015.1.9829
29. Usher-Smith JA, Thompson M, Ercole A, Walter FM. Variation between countries in the frequency of diabetic ketoacidosis at first presentation of type 1 diabetes in children: a systematic review. Diabetologia. 2012;55(11):2878-94.
30. Ahmed AM, Al-Maghamsi M, Al-Harbi AM, Eid IM, Baghdadi HH, Habeb AM. Reduced frequency and severity of ketoacidosis at diagnosis of childhood type 1 diabetes in Northwest Saudi Arabia. J Pediatr Endocrinol Metab. 2016;29(3):259-64.
31. Shaltout AA, Channanath AM, Thanaraj TA, Omar D, Abdulrasoul M, Zanaty N, et al. Ketoacidosis at first presentation of type 1 diabetes mellitus among children: a study from Kuwait. Sci Rep. 2016;6(1):1-9.
32. Robert AA, Al-Dawish A, Mujammami M, Dawish MA. Type 1 diabetes mellitus in Saudi Arabia: a soaring epidemic. Int J Pediatr. 2018;2018. doi:10.1155/2018/9408370
33. Lombardo F, Maggini M, Gruden G, Bruno G. Temporal trend in hospitalizations for acute diabetic complications: a nationwide study, Italy, 2001–2010. PLOS one. 2013;8(5):e63675.
34. Agarwal A, Yadav A, Gutch M, Consul S, Kumar S, Prakash V, et al. Prognostic factors in patients hospitalized with diabetic ketoacidosis. Endocrinol Metab. 2016;31(3):424-32.
35. Lizzo JM, Goyal A, Gupta V. Adult diabetic ketoacidosis. InStatPearls [Internet] 2022 Jul 12. StatPearls Publishing.
36. Duca LM, Reboussin BA, Pihoker C, Imperatore G, Saydah S, Mayer-Davis E, et al. Diabetic ketoacidosis at diagnosis of type 1 diabetes and glycemic control over time: The SEARCH for diabetes in youth study. Pediatr Diabetes. 2019;20(2):172-9. doi:10.1111/pedi.12809
37. Peng W, Yuan J, Chiavaroli V, Dong G, Huang K, Wu W, et al. 10-Year Incidence of Diabetic Ketoacidosis at Type 1 Diabetes Diagnosis in Children Aged Less Than 16 Years From a Large Regional Center (Hangzhou, China). Front Endocrinol (Lausanne). 2021;12:653519. doi:10.3389/fendo.2021.653519
38. Segerer H, Wurm M, Grimsmann JM, Karges B, Neu A, Sindichakis M, et al. Diabetic Ketoacidosis at Manifestation of Type 1 Diabetes in Childhood and Adolescence—Incidence and Risk Factors. Dtsch Arztebl Int. 2021;118(22):367-72. doi:10.3238/arztebl.m2021.0133
39. Mengistu K. A Prevalence and associated factors of diabetic ketoacidosis among pediatrics: Hospital Based Cross Sectional Study in Hawassa University, Comprehensive specialized Hospital. Ethiop Med J. 2020;58(03). Available from: https://emjema.org/index.php/EMJ/article/view/1382.
40. Phillips MÓ, Quesada VM, Esquivel RN. Hyperglycemic emergencies. Rev Méd Sinergia. 2020;5(02):353.