Case Report

Diabetes in the Pediatric Age Group: A Case Series and Review of Literature

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ABSTRACT

Background: Diabetes mellitus (DM) is characterized by sustained hyperglycemia (HG), which has multiple etiologies. The American Diabetes Association (ADA) classifies DM into four major groups. In the pediatric age, DM can be caused by several etiologies.

Case Presentation: We present a series of four case reports of DM among pediatric patients caused by different etiologies, to discuss several clinical presentations of DM among children and the teenage population, as well as diverse therapeutic options for the different DM subtypes.

Conclusions: We conclude that DM in the pediatric age group has multiple etiologies and presentation variants. Type 1 DM still represents the highest incidence in this age group, however, several factors have aided in the awareness and diagnosis of other types of DM previously considered as rather infrequent in this age group.

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Introduction

Diabetes mellitus (DM) is characterized by sustained hyperglycemia (HG), which has multiple etiologies. The American Diabetes Association (ADA) [1] classifies the different DM types as the following: 1) Type 1 DM (DM1) is distinguished by an absolute insulin deficiency as a result of autoimmune destruction of pancreatic beta-cells; 2) Type 2 DM (DM2) is characterized by insufficient insulin secretion by beta-cells, associated with insulin resistance; 3) Other types of DM, e.g., those caused by drugs that prevent normal insulin activity and or cause permanent beta-cell damage, or maturity-onset diabetes of the young (MODY), which are caused by monogenic defects that affect adequate insulin secretion, appearing at an early age; and 4) Gestational DM (will not be mentioned in this review).

DM2 is one of the main worldwide causes of morbidity and mortality in adults. Nonetheless, DM2 can also be present during childhood, although it is well-known that this age group is particularly associated with DM1 cases. However, there has been an increase in the incidence of DM2 and other types of diabetes among the pediatric population [2, 3]. It is estimated that DM1 corresponds to more than 90% of all diabetes cases in children, type 2 diabetes constitutes less than 10% of all cases in this group, MODY type DM 1-6%, and drug-associated DM less than 1% [4].

We present a series of four case reports of DM among pediatric patients caused by different etiologies, to discuss several clinical presentations of DM among children and the teenage population, as well as diverse therapeutic options for the different DM subtypes.

Case Presentation

Case 1

A 6-year-old male was admitted to the emergency department with respiratory distress and an altered conscious state. Previous medical history revealed asthma diagnosed at the age of 3. The chief complaint begins 3 months prior with weight loss, nocturia, and polyphagia; the patient presented with abdominal pain with a 24-hour-onset, in addition to asthenia and adynamia. Furthermore, a couple of hours later the patient presented with oral intolerance and poor general state. The patient's vital signs on admission were heart rate 126 bpm, respiratory rate 28 rpm, along with a Glasgow coma scale of 14. Laboratory results (Table 1) showed glycemic levels of 460 mg/dL, ABG with pH 7.2, and HCO_3 5.5 mmol/L (metabolic acidosis), and urinalysis with positive ketones (500 mg/dL). therefore, the diagnosis of diabetic ketoacidosis (DKA) was established. Management was started with IV fluids and short-acting insulin infusion, along with serum electrolytes correction. Resolution of symptoms was obtained 12 hours after starting therapy. Oral administration was then initiated, along with subcutaneous basal insulin (long-acting and rapid-acting insulin boluses), and the patient did not present with any complications on follow-up visits.

Case 2

A 14-year-old male attended the outpatient clinic. The patient's family history revealed DM2 and obesity in both parents. The patient also had a history of obesity since childhood and orthopedic management with foot insoles. The chief complaint was the presence of dark spots on the neck and epigastric pain. Physical exam revealed morbid obesity, as well as clinical findings associated with insulin resistance (palpable acanthosis nigricans among the neck area, dark spots on several skin folds). Laboratory results (Table 1) evidenced glycemia of 270 mg/dL, triglycerides of 329 mg/dL, total cholesterol of 291 mg/dL, and HDL-cholesterol 27 mg/dL. Therefore, DM2, metabolic syndrome, and mixed hyperlipidemia were diagnosed. Management was initiated with lifestyle modifications (a diet with a daily intake of 2800 cal was assigned by the nutriologist, as well as a daily minimum of 60 minutes of aerobic exercise was recommended). Medical therapy was started with metformin in combination with sitagliptin, fibrates, and statins. The patient's control glycemic level were below 100 mg/dL, and evidenced improvement on the lipid panel and weight loss (1000 g) after a month of treatment.

Case 3

A 14-year-old female with a diagnosis of insulin-dependent DM diagnosed 2 years prior, treated with basal insulin boluses (0.25 IU/kg) was admitted to the emergency department. Family history showed the prevalence of early-onset DM (before the age of 30) in the patient's mother and maternal grandmother, along with a previous history of an appendectomy at the age of 12. The previous follow-up laboratory (Table 1) results demonstrated fasting glycemia of 208 mg/dL and triglycerides of 208 mg/dL. The patient also referred to several hypoglycemic episodes during fasting periods. The patient's physical exam revealed overweight, along with the absence of acanthosis nigricans. Due to the patient's family history of early-onset diabetes, hypo-

glycemic episodes with low-dose insulin-preserved pancreatic reserve, and negative islet cell antibodies (ICA), MODY type DM was suspected. Therapy was initiated by suspending insulin boluses and starting oral insulin secretagogues, along with lifestyle modifications (aerobic exercise and diet changes). The patient's follow-up fasting glycemic levels were below 100 mg/dL and the patient did not refer to any hypoglycemic episodes after a month of treatment.

Case 4

A 13-year-old woman attended the outpatient clinic because of altered glucose levels, steatorrhea, and hypertriglyceridemia. History of being on surveillance for acute lymphoblastic leukemia (ALL) diagnosed at 4 years old where she required management with L-asparaginase, presenting as complication necrotizing pancreatitis, evolving to improvement and remission of ALL, since 6 years of age in Pediatric Oncology surveillance. At 11 years, she presents impaired fasting glucose of 110 mg/dL without being overweight, management is used based on lifestyle changes. During follow-up, the patient complains of osteomuscular pain and steatorrhea; current physical examination with overweight without insulin resistance features, laboratory testing (Table 1) reported capillary glycemia of 200 mg/dL, triglycerides of 200 mg/dL, and vitamin D of 10.7 ng/mL, and stool analysis shows the presence of fat vacuoles.

Considering all of the above, diagnosis of pancreatic insufficiency, vitamin D deficiency, and DM are integrated. Treatment given was based on basal-bolus subcutaneous insulin regimen using long-acting and ultra-rapid-acting insulin, oral pancreatic enzymes, and oral vitamin D. After one month of treatment, during follow-up, laboratory testing reports normal fasting glycemia, clinically with remission of steatorrhea, and improvement of osteomuscular pain.

Discussion

DM is characterized by a state of sustained hyperglycemia which can vary in its pathophysiology and translates into variability in its clinical and laboratory features and presentation.

In Case 1, we present a schoolboy, who debuts with DKA, which is the most severe form of DM1 and is characterized by hyperglycemia with metabolic acidosis and dehydration due to total or near-total insulin deficiency, leading to a state of cellular hypoglycemia resulting in increased production of hyperglycemic hormones (cortisol, catecholamines, glucagon, and growth hormone) as well as increased appetite (polyphagia). This circumstance perpetuates the presence of hyperglycemia, which leads to osmotic diuresis as well as the use of proteins and fats as energy sources, which clinically presents as polyuria, polydipsia, and weight loss. The production of ketonic bodies and dehydration maintain and aggravate metabolic acidosis; clinically we observe a deep and labored breathing pattern (Kussmaul breathing), a fruity odor to the breath, and an altered state of consciousness which varies in severity [5, 6].

The cornerstone of management for this acute decompensation is rehydration with crystalloid solutions, initiating rapid-acting insulin infusion, and correction of electrolyte alterations until resolving the state of acidosis (pH>7.3 and HCO_3>15 mmol/L). Currently, the treatment protocol suggested by the International Society for Pediatric and Adolescent Diabetes (ISPAD) is the most widely used [7]. Once the acute complication has been solved, the maintenance treatment with a basal-bolus insulin regimen should be initiated, which consists in applying a long-acting insulin once daily and a prepandrial ultra-rapid-acting insulin bolus.

DM1 is characterized by hyperglycemia due to a lack of insulin production secondary to the autoimmune destruction of β cells in the pancreas. This type of diabetes corresponds to only 5-10% of DM in the general population but accounts for up to 90% of DM cases in children and adolescents. A positive autoantibodies test, which are antibodies that mistakenly destroy components of the pancreas or β cell, is required to confirm the diagnosis of DM1; the most commonly found is anti-glutamate decarboxylase (GAD), but there are also others such as ICA, anti-insulin (IAA), anti-tyrosine phosphatase 2 (IA2), and anti-Zn8 transporter (ZnT8) [8].

Treatment in patients with DM1 is based on a balance between insulin administration, adequate nutritional management, and exercise, all of this adjusted for the age and sex of the patient. Self-monitoring with capillary glycemia is imperative in managing treatment adjustment [7].

Although the basal-bolus regimen was used in our patient for the administration of insulin, currently, continuous subcutaneous insulin infusion methods are more effective to reach and maintain adequate glycemic control in patients with DM1 [9].

Table 1. Comparison of laboratory values in the case series

Case	Glycemia (mg/dL)	HbA 1c (%)	Insulin (µUI/mL)	C peptide (ng/mL)	Islet-cell Antibodies(UI/mL)*	BMI (Zs)	IR**	Glucosuria	Presentation at Diagnosis	Medical History	Others	Diagnosis
1	480	10.4	1.8	0.6	3.8	17.7(+1.2)	No	Yes	Ketoacidosis	Irrelevant	No family history of DM	DM1
2	270	8.3	28.3	NA	0.6	34.4 (+2.7)	Yes	Yes	Fasting hyperglycinemia	Family history of DM2	Mixed dyslipidementia (TG) 329 mg/dL (ChoT) 291 mg/dL (HDL) 27 mg/dL	Type 2 DM
3	145	6.7	4.2	1.5	0.9	26.6(+1.7)	No	No	Fasting hyperglycemia	Family history of DM <30 years	Hyperglycemia (208 mg/dL)	MODY
4	226	11	4.9	1	NA	23.4(+1.1)	No	Yes	Fasting hyperglycemia	ALL treated with L-asparagase	Hyperglycemia (216 mg/dL)	Medication induced DM

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Abbreviations: TG: Triglycerides; ChoT: Total cholesterol; HDL: High-density lipoprotein; ALL: Acute lymphoblastic leukemia; NA: Data not available.

Glycemia: 60-100, HbA1c<5.7%, Insulin: 1-15, C peptide: 0.5-3.5.

*Detection of anti-GAD antibodies,**Presence of clinical signs of insulin resistance (acanthosis nigricans, abdominal obesity).

In Case 2, we present a teenage male with severe obesity and clinical features of insulin resistance who also had metabolic syndrome, in which we confirm the diagnosis of DM by laboratory criteria. Since there were elevated insulin levels and negative pancreatic autoantibodies in testing, the diagnosis of DM2 was confirmed.

Although these cases are not common in pediatrics, their number is increasing, predominantly in teenagers. These disorders have a poli-genetic origin, but their main etiology is not established yet. They demand the presentation of precipitant factors such as obesity, bad nutrition, a sedentary lifestyle, and others. Obesity and insulin resistance triggers a pro-inflammatory status in the organism and demands high insulin levels, which causes an altered production of this hormone and its receptor that manifest in hyperglycemia, dyslipidemia, systolic hypertension, and other metabolic alterations [10].

This patient presented metabolic syndrome, characterized by hypertriglyceridemia, hypoalphalipoproteinemia, obesity, and insulin resistance, which are considered cardiometabolic risk factors in adults. It should be noted that it is not the main objective of this review to discuss the criteria of metabolic syndrome in pediatric patients. The treatment for DM2 in pediatrics continues to be discussed. Changes in lifestyle including diet and exercise are part of the therapeutic cornerstone. Although first option drugs are those that increase insulin sensitivity as biguanides, the pharmacologic treatment is still in the study [10].

Dipeptidyl peptidase 4 (DPP-4) inhibitors as sitagliptin have been used by individuals that do not respond to this treatment; glucagon like peptide-1 (GLP-1) agonists have improved the management of infant obesity and DM2. Liraglutide is currently approved for its use in obesity for 10 years of age, which has the disadvantage of being for daily subcutaneous use. As semaglutide, recently GLP-1 agonists' weekly dosage has been approved for its use in young people 12 years old [11-13]. It is important to note that GLP-1 agonist therapy is not indicated in pediatrics with DM, but a great improvement in glycemic control has been observed as they improve corporal weight [13, 14]. Although insulin secretagogues are employed, they are not well accepted because of their risk of hypoglycemia and poisoning. The use of SGLT-2 inhibitors is currently not approved in children. If glucose control is not achieved with the aforementioned therapies, the use of subcutaneous insulin would be the treatment of choice. In patients where the meta-

bolic syndrome is associated with DM2, pharmacologic therapy is indicated when there is no good control with conventional management. Statins are used when hypercholesterolemia is present. Fibrates can be used in hypertriglyceridemia with their side effects as myalgias and arthralgias or some occasional complications such as myositis or rhabdomyolysis [10].

Omega-3 fatty acids with an appropriate diet and exercise do not show the side effects as fibrates and they have demonstrated good response in the management of hypertriglyceridemia in children. The use of angiotensin-converting enzyme inhibitors (ACE) or angiotensin receptor blockers (ARBs) has shown good results when patients have systemic hypertension [10]. Our patient responded correctly to the combined management of modified lifestyle, metformin, and DPP-4 inhibitors. We added fibrates and statins to treat hyperlipidemia, but because the patient showed osteomuscular ache, it was suspended.

The third reported case is about a young woman with DM who presented multiple hypoglycemias using low doses of insulin. We suspected a monogenic origin of diabetes because the patient has familiar records of DM early start before 30 years old in her mother and grandmother; also she did not present clinical signs of insulin resistance and had a C-peptide normal range (>0.6 ng/mL).

Monogenic DM occurs when abnormalities in the production or secretion of insulin are caused by a mutation in a specific gene. The most common cause is MODY which has an autosomal dominant inheritance pattern [15, 16]. This type of DM represents 2-3% of all diabetes causes in the general population and 1% in children. More than 10 different subtypes of MODY genes had been discovered. Although subtype 3 is the most frequent and the possible origin of our patient disorder, subtypes 1, 2, 3, and 5 together stand for 90% of all cases [4, 15, 16].

Both HNF4A-MODY (MODY-1) and HNF1A-MODY (MODY-3) present with a mutation in 1A and 4A hepatic nuclear factor genes respectively, both of which facilitate the release of insulin from the pancreatic β-cell. The specific mutations involving these genes result in a non-insulin-dependent DM, which eventually progresses until insulin therapy is required later in life. Upon diagnosis, management usually begins with dietary measures, oral secretagogues such as glyburide, and if deemed necessary, biguanides or dipeptidyl peptidase 4 inhibitors [15].

GCK-MODY (MODY-2) is caused by a mutation of the GCK gene which codifies the enzyme glucokinase. When a mutation to this gene occurs, there exists a decreased glucose phosphorylation and glucose sensitivity in the pancreatic β-cell, thus a shift in the glucose-stimulated insulin secretion occurs. Individuals with GCK-MODY are generally present with fasting hyperglycemia <200 mg /dL. Pharmacological treatment is not often required, due to adequate production of insulin in these individuals, and microvascular complications are rarely reported. HNF1β-MODY (MODY-5) is caused by the mutation of HNF1β, which regulates HNF4A expression, therefore, presenting similarities with MODY-1 in regards to disease progression and treatment. Renal and urogenital tract malformations are a characteristic finding of this subtype due to the role of HNF1β expression in various tissues including the kidney [15, 16].

The definitive diagnosis of MODY is achieved through molecular diagnostic methods; however, the costs of these procedures hinder their accessibility in middle and low- income countries. Multiple clinical algorithms have been published to correctly select patients that are more suitable for molecular diagnostic methods with more precision [17, 18, 19]. Genetic testing is considered a necessary clinical tool due to its important prognostic implications [19]. In patients where genetic testing is not a possibility, therapeutic tests can be carried out to assess treatment response and improve patient care.

In case 4, we present the case of an adolescent with a previous diagnosis of ALL that received chemotherapy with L-asparaginase. Subsequently, the patient presented in follow-up examinations with persistent hyperglycemia, vitamin D deficiency, hypertriglyceridemia, and pancreatic insufficiency.

Several medications are known to induce a hyperglycemic state, glucocorticoids being among the most studied and characterized up to date [20]. However, L-asparaginase, a bacterial enzyme that is used as an antineoplastic agent in leukemia, can induce both hyperglycemia and pancreatic insufficiency [21]. These reported side effects of L- asparaginase are predominantly transitory and tend to resolve after the suspension of the medication, nonetheless, there is a minority of cases that can progress to DM and pancreatic insufficiency [22]. The exact mechanism by which L-asparaginase induces pancreatic injury has yet to be fully determined, although there is evidence that suggests it is linked to an imbalance in plasma amino acids [21]. Follow-up examinations are necessary for patients that received or will receive chemotherapy with this agent to ensure optimal treatment.

Management of L-asparaginase-induced diabetes is based on controlling adequate glycemia levels based on the degree of pancreatic injury; therefore, it is important to determine both insulin and C peptide levels to establish the remaining pancreatic reserve and justify the indication of oral hypoglycemic medication or insulin if deemed necessary [22]. Furthermore, the management of pancreatic insufficiency is based on oral pancreatic enzymes, and dietary measures, for instance, the supplementation of liposoluble vitamins.

Conclusion

We conclude that DM during the pediatric age group has multiple etiologies and presentation variants. DM1 still represents the highest incidence in this age group [3]; however, lifestyle changes, more accessibility to genetic testing, and changes in medical treatments have aided in the awareness and diagnosis of other types of DM previously considered as rather infrequent in this age group.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles are considered in this article. The participants were informed of the purpose of the research and its implementation stages. They were also assured about the confidentiality of their information and were free to leave the study whenever they wished, and if desired, the research results would be available to them. A written consent has been obtained from the subjects. principles of the Helsinki Convention were also observed.

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Authors contributions

Study design and conceptualisation: Valenzuela-Ruiz, Bobadilla-Olaje, and Ruiz-Quiroz. Acquisition of data: Valenzuela-Ruiz, Bobadilla-Olaje, and Ruiz-Quiroz; Analysis and interpretation of data, drafting of the manuscript: All authors; Critical revision of the manuscript: Calleja-López, Ruibal-Tavares, Rivera-Rosas, Aguilera-Duarte, and Bobadilla-Olaje; Study supervision: Bobadilla-Olaje and Calleja-López.

Conflicts of interest

The authors declared no conflict of interest.

References

1. Elsayed NA, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, et al. 2. Classification and diagnosis of diabetes: Standards of care in diabetes-2023. Diabetes Care. 2023; 46(Suppl 1):S19-40. [DOI:10.2337/dc23-S002] [PMID] [PMCID]

2. Greeley SAW, Polak M, Njølstad PR, Barbetti F, Williams R, Castano L, et al. ISPAD clinical practice consensus guidelines 2022: The diagnosis and management of monogenic diabetes in children and adolescents. Pediatr Diabetes. 2022; 23(8):1188-211. [DOI:10.1111/pedi.13426] [PMID] [PMCID]

3. Nevo-Shenker M, Phillip M, Nimri R, Shalitin S. Type 1 diabetes mellitus management in young children: Implementation of current technologies. Pediatr Res. 2020; 87(4):624-9. [DOI:10.1038/s41390-019-0665-4] [PMID]

4. Pihoker C, Gilliam LK, Ellard S, Dabelea D, Davis C, Dolan LM, et al. Prevalence, characteristics and clinical diagnosis of maturity-onset diabetes of the young due to mutations in HNF1A, HNF4A, and glucokinase: Results from the SEARCH for Diabetes in Youth. J Clin Endocrinol Metab. 2013; 98(10):4055-62. [DOI:10.1210/jc.2013-1279] [PMID] [PMCID]

5. Bauer W, Gyenesei A, Krętowski A. The multifactorial progression from the islet autoimmunity to type 1 diabetes in children. Int J Mol Sci. 2021; 22(14):7493. [DOI:10.3390/ijms22147493] [PMID] [PMCID]

6. von Oettingen JE, Wolfsdorf JI, Feldman HA, Rhodes ET. Utility of diabetes- associated autoantibodies for classification of new onset diabetes in children and adolescents. Pediatr Diabetes. 2016; 17(6):417-25. [DOI:10.1111/pedi.12304] [PMID] [PMCID]

7. Glaser N, Fritsch M, Priyambada L, Rewers A, Cherubini V, Estrada S, et al. ISPAD clinical practice consensus guidelines 2022: Diabetic ketoacidosis and hyperglycemic hyperosmolar state. Pediatr Diabetes. 2022; 23(7):835-56. [DOI:10.1111/pedi.13406] [PMID]

8. Wadwa RP, Reed ZW, Buckingham BA, DeBoer MD, Ekhlaspour L, Forlenza GP, et al. Trial of hybrid closed-loop control in young children with type 1 diabetes. N Engl J Med. 2023; 388(11):991-1001. [DOI:10.1056/NEJMoa2210834] [PMID]

9. Yu L, Zhao Z, Steck AK. T1D Autoantibodies: Room for improvement. Curr Opin Endocrinol Diabetes Obes. 2017; 24(4):285-91. [DOI:10.1097/MED.0000000000000348] [PMID] [PMCID]

10. Serbis A, Giapros V, Kotanidou EP, Galli-Tsinopoulou A, Siomou E. Diagnosis, treatment and prevention of type 2 diabetes mellitus in children and adolescents. World J Diabetes. 2021; 12(4):344-65. [DOI:10.4239/wjd.v12.i4.344] [PMID] [PMCID]

11. Jepsen MM, Christensen MB. Emerging glucagon-like peptide 1 receptor agonists for the treatment of obesity. Expert Opin Emerg Drugs. 2021; 26(3):231-43. [DOI:10.1080/14728214.2021.1947240] [PMID]

12. Ryan PM, Seltzer S, Hayward NE, Rodriguez DA, Sless RT, Hawkes CP. Safety and efficacy of glucagon-like peptide-1 receptor agonists in children and adolescents with obesity: A meta-analysis. J Pediatr. 2021; 236:137-47.e13. [DOI:10.1016/j.jpeds.2021.05.009] [PMID]

13. Danne T, Biester T, Kapitzke K, Jacobsen SH, Jacobsen LV, Petri KCC, et al. Liraglutide in an adolescent population with obesity: A randomized, double-blind, placebo-controlled 5-week trial to assess safety, tolerability, and pharmacokinetics of liraglutide in adolescents aged 12-17 years. J Pediatr. 2017; 181:146-53.e3. [DOI:10.1016/j.jpeds.2016.10.076] [PMID]

14. Jastreboff AM, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, et al. Tirzepatide once weekly for the treatment of obesity. N Engl J Med. 2022; 387(3):205-16. [DOI:10.1056/NEJMoa2206038] [PMID]

15. Anık A, Çatlı G, Abacı A, Böber E. Maturity-onset diabetes of the young (MODY): An update. J Pediatr Endocrinol Metab. 2015; 28(3-4):251-63. [DOI:10.1515/jpem-2014-0384]

16. Peixoto-Barbosa R, Reis AF, Giuffrida FMA. Update on clinical screening of maturity-onset diabetes of the young (MODY). Diabetol Metab Syndr. 2020; 12:50. [PMID] [PMCID]

17. Sanyoura M, Philipson LH, Naylor R. Monogenic diabetes in children and adolescents: Recognition and treatment options. Curr Diab Rep. 2018; 18(8):58. [PMID] [PMCID]

18. Broome DT, Pantalone KM, Kashyap SR, Philipson LH. Approach to the patient with MODY-monogenic diabetes. J Clin Endocrinol Metab. 2021; 106(1):237-50. [DOI:10.1210/clinem/dgaa710] [PMID] [PMCID]

19. Bobadilla-Olaje GF, Calleja-López JRT, Ruibal-Tavares E, Rivera-Rosas CN, Aguilera-Duarte LJ. Maturity-onset diabetes of the young (MODY). Rev Mex Pediatr. 2022; 89(1):27-31. [DOI:10.35366/106857]

20. Tosur M, Viau-Colindres J, Astudillo M, Redondo MJ, Lyons SK. Medication- induced hyperglycemia: Pediatric perspective. BMJ Open Diabetes Res Care. 2020; 8(1):e000801. [DOI:10.1136/bmjdrc-2019-000801] [PMID] [PMCID]

21. Minowa K, Suzuki M, Fujimura J, Saito M, Koh K, Kikuchi A, et al. L-asparaginase- induced pancreatic injury is associated with an imbalance in plasma amino acid levels. Drugs R D. 2012; 12(2):49-55. [PMID] [PMCID]

22. Hwangbo Y, Lee EK. Acute hyperglycemia associated with anticancer medication. Endocrinol Metab (Seoul). 2017; 32(1):23-9. [DOI:10.3803/EnM.2017.32.1.23] [PMID] [PMCID]

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