

**Epidemiology of Diabetes Mellitus in School-Aged Children in Qena Governorate****Khaled Abdullah<sup>a</sup>, Ali Helmy<sup>a</sup>, Maha Hossny Abu Elhassan<sup>a\*</sup>**<sup>a</sup>Department of Pediatrics, Faculty of Medicine, South Valley University, Qena, Egypt.**Abstract**

**Background:** Previously called juvenile diabetes, this autoimmune illness causes the pancreas' islets of Langerhans to generate little or no insulin. Frequent urination, thirst, hunger, and weight loss are symptoms. DM has many causes.

**Objectives:** To assesses demographic characteristics of type 1 diabetes mellitus in children aged 6-12 years in Qena governorate.

**Patients and methods:** This is an analytical observation cross-sectional study conducted at the Outpatient Pediatric Clinic, Pediatric Department of Qena University Hospital, and General Hospital in Qena on 100 children. Assessment of these children was done using a written questionnaire based on WHO criteria for the diagnosis of DM.

**Results:** The mean age of studied patients was  $8.72 \pm 1.67$  years, there were 63 males (63%) and 37 females (37%), there were 19 patients (19%) of white race and 81 patients (81%) of black race. there were 54 patients (54%) from rural areas and 46 patients (46%) from urban areas. As regard SES, there were 77 patients (77%) of low SES and 23 patients (23%) of moderate SES in the studied patients. There were 17 patients (17%) of positive consanguinity and 6 patients (60%) of positive family history in the studied patients. The mean BMI of studied patients was  $17.1 \pm 2.2$  (median = 16.5).. As regard comorbidities, there were 3 patients (3%) had bronchial asthma, 2 patients (2%) had Celiac disease and 1 patient (1%) had epilepsy in the studied patients. There were 3 patients (3%) on steroid inhaler in the studied patients. There was history of acute complications in 59 patients (59%), history of repeated infection in 65 patients (65%) and hospital admission in 59 patients (59%). 17 patients (28.8%) were admitted once, 22 patients (37.3%) were admitted twice and 20 patients (33.9%) were admitted 3 times. There were 26 patients (44.1%) admitted due to DKA, 23 patients (39 %) admitted due to hyperglycemia and 10 patients (16.9%) admitted due to hypoglycemia.

**Conclusion:** The mean age of studied patients was  $8.72 \pm 1.67$  years, with predominance of males (63%). 54% from rural areas. Acute complications were occurred in 59% of patients.

**Keywords:** Type 1 diabetes; School-Aged Children; Epidemiology.

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## Introduction

Previously known as juvenile diabetes, is an autoimmune disease that is a form of diabetes in which very little or no insulin is produced by the islets of Langerhans (containing beta cells) in the pancreas. Insulin is a hormone required for the cells to use blood sugar for energy and it helps regulate normal glucose levels in the bloodstream. Before treatment this results in high blood sugar levels in the body (Deshmukh et al., 2015).

The role of the gut microbiota in the pathophysiology of T1DM has been shown by a number of earlier investigations done on non-obese diabetic mice. (Zheng et al., 2018). In fact, gut dysbiosis may be involved in the altered balance of pro-inflammatory vasculature. Signals that are tolerated, encourage the growth of pancreatic autoimmunity (Paun et al., 2016).

The American Diabetes Association (ADA) recommends including patient age as one factor in the development of glycemic objectives because patients ages 0-6, 6-12, and 13-19 have different targets for preprandial, bedtime/overnight, and haemoglobin A1c (HbA1c) values. Tight glycemic control has numerous advantages, including significant differences in cardiovascular events and total mortality as well as ongoing decreases in the rates of microvascular complications (Fibmsdch et al., 2017).

Real-time continuous glucose monitoring with continuous glucose monitors (CGMs) can improve patients' glycemic management. Every one to five minutes, subcutaneous sensors in CGMs measure the interstitial glucose levels and sound an alert if they are abnormally high or low, rising or falling quickly (Cameron et al., 2018).

Insulin therapy is required for life for those with type 1 diabetes. Most people need two or more insulin injections every day, with doses adjusted based on personal

blood glucose monitoring. Giving basal insulin plus the preprandial (premeal) insulin helps to replenish lost insulin. It is used to administer either the intermediate-acting or long-acting basal insulin (glargine or detemir) (NPH). The preprandial insulin is either rapid-acting (insulin inhaled) or short-acting (glulisine, lispro, aspart) (regular) (Das., 2017)

This study's objectives were to assess demographic characteristics of type 1 diabetes mellitus in children aged 6-12 years in Qena Governorate.

## Patients and methods

This study is an analytical observation cross-sectional Study. This study was carried out in the outpatient Clinic of Pediatrics Department of Qena University Hospital, and from Qena General Hospital; from October 2021 to April 2022.

**Inclusion criteria:** Diabetic children presented to the outpatient clinic and diabetic children admitted in Pediatric department, Qena University Hospital and Qena General Hospital; aged from 6-18 years old.

**Exclusion criteria:** All patients less than 6 years and patients who refuse to participate in the study.

## Methods

**All patients were subjected to the following:**

**Full history taking including:** Age, sex, presence of parental consanguinity, age at onset of diabetes, family history, comorbidities, associated complications drug history, and level of plasma glucose at the time of diagnosis, duration of the disease and history of acute complications or vascular complications, treatment of types 1 diabetes, and insulin dose (unit/kg/day). Socioeconomic state was assessed according to Abdel-Tawab socio-economic status scale, This scale consisted of four dimensions, namely, level of education, employment, total family monthly income, and lifestyle of the family. (Abdel-Tawab, 2012).

Complete clinical examination: Physical appearance, including assessment of weight, height, the arterial blood pressure and vital data Such as temperature, heart rate, respiratory rate and blood pressure were recorded (CDC, 2014).

The following has been done to these kids: initial phase The child or his parents completed a written questionnaire based on WHO (2010) criteria for the diagnosis of DM, paying particular attention to the following: the T1DM family history. Consanguinity's past symptoms and red flags for DM. Then, these kids were tested using the Medi Test for quick detection of glucose in urine (Machery Nagel, Düren, Germany).

A second stage Hoffman Auto Analyzer (Hoffmanla Roche, Basel, Switzerland) and other diagnostic techniques were utilised to estimate random blood glucose levels in order to determine if children with positive glucotest findings had diabetes mellitus. The third stage: The following tests were run on diabetic children: Complete blood counts for haemoglobin level, red blood cells, white blood cells, and platelets should be performed using the DIRUI BCC 3000B Hematology Analyzer (Diamond Diagnostics, Holliston, Massachusetts, USA). The amount of glycosylated haemoglobin was calculated using BioSystems S.A. (Barcelona, Spain).

**Operational design:** All of the participants' parents were introduced to the researcher, who then asked them to take part in the study by outlining its objectives. All chosen parents of participants received thorough information about the study's purpose and anticipated advantages. The entire project was conducted with the utmost ethical attention. The parents of the subjects verbally consented after being fully informed, and information confidentiality was guaranteed. Additionally, approval from the faculty of medicine's ethics committee was received.

### Statistical analysis

Microsoft Excel 2016 and the SPSS application (Statistical Package for Social Sciences) version 26.0 were used to tabulate and statistically analyse the gathered data. For inferential studies, children of two independent groups with parametric data underwent independent t-tests, whereas those of two independent groups with non-parametric data underwent Mann Whitney U analysis. For inferential analysis of qualitative data, the chi square test for independent groups was employed.

### Results

This cross-sectional study was carried out on 100 children presented to the outpatient clinic or admitted in Pediatric department at Qena University Hospital and General Hospital in Qena.

The mean age of studied patients being  $8.72 \pm 1.67$  years, there were 63 males (63%) and 37 females (37%), the mean maternal age was  $38.25 \pm 3.84$ , the mean paternal age was  $44.31 \pm 5.5$  (median = 45), there were 19 patients (19%) of white race and 81 patients (81%) of black race. As regard residence, there were 54 patients (54%) from rural and 46 patients (46%) from urban. As regard SES, there were 77 patients (77%) of low SES and 23 patients (23%) of moderate SES in the studied patients. There were 17 patients (17%) of positive consanguinity and 6 patients (60%) of positive family history in the studied patients. Artificial feeding was the commonest type of feeding (62%) in studied children followed by normal breastfeeding in 38% of children. The mean BMI of studied patients was  $17.1 \pm 2.2$  (median = 16.5) (**Table.1**).

The mean age at diagnosis was  $7.7 \pm 1.65$  (median = 8) with mean duration of symptoms being  $8.97 \pm 6.58$  years, as showed in (**Table 2**).

As regard clinical presentation at onset, there were 12 patients (12%) presented by polyuria, 63 patients (63%) presented by weight loss and 25 patients (25%) presented by both polyuria and

weight loss in the studied patients. As regard comorbidities, there were 3 patients (3%) had bronchial asthma, 2 patients (2%) had Celiac disease and 1 patient (1%) had epilepsy in the studied patients. As regard other drug therapy, there were 3 patients (3%) on steroid inhaler in the studied patients. As regard maternal drug intake during pregnancy, there were 6 mothers (6%) taking drugs, 2 mothers (33.3%) taking insulin therapy, 3 mothers (50%) taking methyldopa and 1 mother (16.7%) taking steroid inhalation (**Table.3**).

Table 4 shows the description of History of complications and hospital admission in all studied patients. There was history of acute complications in 59 patients (59%), history of repeated infection in 65 patients (65%) and hospital admission in 59 patients (59%). 17 patients (28.8%) were admitted once, 22 patients (37.3%) were admitted twice and 20 patients (33.9%) were admitted 3 times. There were 26 patients (44.1%) admitted due to DKA, 23 patients (39 %) admitted due to hyperglycemia and 10 patients

(16.9%) admitted due to hypoglycemia (**Table.4**).

The mean hemoglobin level was  $10.73 \pm 1.29$  g/dl. The mean HBA1C at presentation was  $11.33 \pm 1.57$  while the mean HBA1C at follow up was  $9.73 \pm 1.29$ . The mean C-peptide level was  $0.93 \pm 0.62$ . The mean ALT and AST levels were  $36.88 \pm 4.15$  U/L and  $39.03 \pm 7.26$  U/L respectively. The mean levels of Ca, K, Na and Vitamin D were  $8.22 \pm 0.57$  mg/dl,  $8.22 \pm 0.43$  mEq./L,  $139.28 \pm 3.98$  mEq./L and  $21.7 \pm 7.6$  U/L respectively. The mean creatinine level was  $0.74 \pm 0.36$  mg/dl while the mean pus in urine analysis was  $1.68 \pm 0.94$ . The mean free T4 and TSH levels were  $2.75 \pm 1.43$  U/L and  $2.70 \pm 1.12$  U/L respectively (**Table.5**).

**Table 1. Demographic data in all studied patients**

Parameters		Studied children (N=100)	
		N	%
Gender	Male	63	63.0%
	Female	37	37.0%
Age (years)	Mean± SD	8.72± 1.67	
	Median	9.0	
	Range	6.0 – 12.0	
Maternal age (years)	Mean± SD	38.25± 3.84	
	Median	39.0	
	Range	29.0 – 46.0	
Paternal age (years)	Mean± SD	44.31± 5.5	
	Median	45.0	
	Range	30.0 – 56.0	
Black or white	White	19	19.0%
	Black	81	81.0%
Residence	Rural	54	54%
	Urban	46	46%
SES	Low	77	77%
	Moderate	23	23%
Consanguinity	No	83	83%

	<b>Yes</b>	17	17%
<b>Family history</b>	<b>No</b>	94	94%
	<b>Yes</b>	6	6%
<b>Feeding type</b>	<b>Breastfeeding</b>	38	38%
	<b>Artificial feeding</b>	62	62%

**Table 2. Anthropometric measures in all studied patients**

Parameters		Studied children (N=100)	
		N	%
<b>Weight (kg)</b>	<b>Mean± SD</b>	25.7± 5.4	
	<b>Median</b>	25	
	<b>Range</b>	19 – 38.6	
<b>Height (cm)</b>	<b>Mean± SD</b>	122.4± 10.7	
	<b>Median</b>	119	
	<b>Range</b>	108 – 151	
<b>BMI (kg/m<sup>2</sup>)</b>	<b>Mean± SD</b>	17.1± 2.2	
	<b>Median</b>	16.5	
	<b>Range</b>	10.9 – 24.1	

**Table 3. Clinical data in all studied patients**

Parameters		Studied children (N=100)	
		N	%
<b>Age at diagnosis (years)</b>	<b>Mean± SD</b>	7.7 ± 1.65	
	<b>Median</b>	8	
	<b>Range</b>	5 – 11	
<b>Duration of symptoms at onset (Days)</b>	<b>Mean± SD</b>	8.97 ± 6.58	
	<b>Median</b>	7.0	
	<b>Range</b>	1.0 – 30.0	
<b>Disease duration</b>	<b>Mean± SD</b>	3.7 ± 1.65	
	<b>Median</b>	4	
	<b>Range</b>	1 - 7	
<b>Clinical presentation at onset</b>	<b>Polyuria</b>	12	12.0%
	<b>Wt. Loss</b>	63	63.0%
	<b>Wt. Loss + Polyuria</b>	25	25.0%
<b>Comorbidities</b>	<b>No</b>	94	94%
	<b>Bronchial asthma</b>	3	3%
	<b>Celiac disease</b>	2	2%
	<b>Epilepsy</b>	1	1%
<b>Other drug therapy</b>	<b>No</b>	97	97%
	<b>Steroid inhaler</b>	3	3%
<b>Maternal drug intake during pregnancy</b>	<b>No</b>	94	94%
	<b>Yes</b>	6	6%
<b>Maternal drugs</b>	<b>Insulin therapy</b>	2	33.3%
	<b>Methyldopa</b>	3	50%
	<b>Steroid inhalation</b>	1	16.7%

**Table 4. Frequency of history of complications and hospital admission in all studied patients.**

Parameters		Studied children (N=100)	
		N	%
History of acute complications	No	41	41%
	Yes	59	59%
History of repeated infections	No	35	35%
	Yes	65	65%
Hospital admissions	No	41	41%
	Yes	59	59%
Frequency of hospital admissions	Once	17	28.8%
	Twice	22	37.3%
	3 times	20	33.9%
Causes of hospital admissions	DKA	26	44.1%
	Hyperglycemia	23	39%
	Hypoglycemia	10	16.9%

**Table 5. Distribution of studied children as per laboratory data**

Variables	Mean	±SD	Median	Min.	Max.
HBA1C at presentation	11.33	1.57	11.10	7.10	14.00
HBA1C at follow up	9.73	1.29	10.00	7.20	13.00
Hgb (g/dl)	10.73	0.80	10.90	9.00	13.00
ALT	36.88	4.15	34.00	17.00	46.00
AST	39.03	7.26	35.00	13.00	51.00
Creatinine	0.74	0.36	0.70	0.30	1.30
Ca	8.22	0.57	8.00	7.00	9.00
K	3.62	0.43	3.60	2.00	4.60
Na	139.28	3.98	139.00	128.00	145.00
Vit D	21.7	7.6	17.00	11.00	28.00
Urinalysis (Pus)	1.68	0.94	2.00	0.00	4.00
C-peptide	0.93	0.62	1.00	0.02	2.20
Free T4	2.75	1.43	2.75	0.91	7.50
TSH	2.70	1.12	2.70	1.20	5.10

## Discussion

Type 1 diabetes mellitus (T1DM) is one of the most common endocrine and metabolic conditions in childhood. Data from the International Diabetes Federation (IDF) reported that the estimated number of children and adolescents with T1DM aged 0–20 years was 1.1 million, with about 128,900 new cases diagnosed every year (Saad et al., 2020).

The disease usually first appears in infancy, while it can occasionally strike persons in their late 30s and early 40s. A combination of hereditary and environmental variables contributes to

T1DM, which ultimately results in pancreatic cell death (Aathira and Jain., 2014). In the Egyptian governorates of Fayoum, North Sinai, and Suez, a study examining the prevalence and incidence of T1DM in children and adolescents discovered prevalence rates of 0.7/1000 and incidence rates of 4.01/100 000. (Salem et al., 2007).

The main objective of this study was to evaluate the epidemiological profile and risk factors of Diabetes Mellitus type 1 in School-aged children of Qena governorate.

Regards demographic data; the age of children ranged from 6 to 12 years with mean  $\pm$ SD was  $8.72 \pm 1.67$  years and a median was 9 years. The total number of males was 63 (63%) and females was 37 (37%) with male: female ratio was 1.7:1. The maternal age ranged from 29 to 46 years with mean  $\pm$ SD of  $38.25 \pm 3.84$  years while the paternal age ranged from 30 to 56 years with mean  $\pm$ SD was  $44.31 \pm 5.5$  years. The majority of children (81%) were black.

Our results were supported by the study of **Hassan et al., 2019** as they stated that among the 8000 pupils they surveyed, girls outnumbered boys by a margin of 52.8% to 47.2%. In total, 50% of people lived in cities and 50% in rural areas. Students who were male were more affected than those who were female (66.7 vs. 33.3%). The mean age of diabetic kids was  $11.3 \pm 2.8$  years. According to **Chong et al** study 's from 2007, there are age-specific differences in the incidence of paediatric T1DM. The typical pattern of T1DM incidence by age in most registries revealed that the incidence rises with age and typically peaks in the peripubertal phase with the corresponding gender effect, which starts in girls 1-2 years sooner than in boys. The DIAMOND Project Group found that among children under the age of 15, those aged 10 to 14 had a higher chance of acquiring T1DM, while those aged 5 to 9 had a medium risk and those aged 0 to 4 had a reduced risk. When compared to children under the age of 5, those aged 10 to 14 had roughly double the risk of acquiring T1DM, and this pattern was consistent regardless of gender (**DIAMOND Project Group, 2006**).

**Patterson et al. (2009)** noted that a multicenter research for youth T1DM in Europe found an increased incidence of the disease among children under the age of five compared to children in older age groups. The present study showed that breastfeeding was the commonest type of feeding (62%) in studied of children

followed by artificial feeding in 38% OF children. The mean ( $\pm$ SD) time of weaning was  $1.70 \pm 0.19$  years and ranged from 1.7 to 2 years.

Also, **Lund-Blix et al., 2017**, during follow-up, type 1 diabetes was discovered in 504 kids, with incidence rates of 30.5 in the Norwegian cohort and 23.5 in the Danish cohort per 100,000 person-years. Type 1 diabetes risk was two times higher in children who were never breastfed than in those who were (HR 2.29 [95% CI 1.14-4.61]). According to **Holmberg et al. (2007)**, children under the age of five are more likely to develop beta-cell autoimmunity if they receive full-time breastfeeding for less than four months.

According to a different study by **Cardwell et al. (2012)** nursing exclusively during the first few weeks of life can lower a child's chance of developing type 1 diabetes by 15%. But it was unable to explain how type 1 diabetes and exclusive breastfeeding were related without additionally taking into account other DM risk variables, such as gestational diabetes, birth weight, gestational age, mother's age, birth order, and delivery method.

The current study showed that the majority had low socioeconomic status and 23% had moderate socioeconomic status. Regarding residence, more than half studied children were living in rural areas (54%) and only 46% were living in urban areas.

Our findings were corroborated by a study conducted by El-Ziny et al. in 2014, which revealed that out of 1600 patients, 935 were from the Nile Delta region's rural parts and 665 were from its urban ones. In the entire patient population and for each gender separately, this increased rate of T1DM in rural compared to urban settings was statistically significant ( $p=0.000$ ). The much greater incidence of T1DM in rural areas may be caused by children living there being accidentally exposed to certain environmental chemicals, like organophosphorus compounds (OPCs), which include insecticides, rodenticides

(Vacor), and pediculicides (malathion). The reported epidemiological evidence suggesting exposure to specific environmental chemicals is implicated in the aetiology of type 1 diabetes through the direct apoptosis of beta cells or the onset of T1DM autoimmunity in people lends weight to this concept. While in **Içekli and Durusoy's (2022) study**, there was no discernible difference in the child's living situation with parents and parents' educational attainment.

Our results showed that as regard different laboratory data, the mean hemoglobin level was  $10.73 \pm 1.29$  g/dl. The mean HBA1C at presentation was  $11.33 \pm 1.57$  while the mean HBA1C at follow up was  $9.73 \pm 1.29$ , whereas in the study of **Wafaa. (2017)** Regarding every laboratory profile, there was no discernible difference between diabetic male and female students. Children with diabetes had a mean random blood sugar of 288.760.2 mg/dl. Environmental triggers (viruses, poisons, emotional stress, etc.) cause autoimmunity in those with genetic susceptibility (HLA groups at risk), which leads to the onset of progressive beta-cell destruction. When beta-cell reserves are diminished by 80–90%, clinical symptoms of diabetes start to appear. (**Turkey Endocrinology and Metabolism Society, 2019**).

### Conclusion

The mean age of studied patients was  $8.72 \pm 1.67$  years, with predominance of males (63%). 54% from rural areas. Acute complications were occurred in 59% of patients.

### Limitations

Our study has some limitations, this study was conducted on small sample size, further studies with large sample size was needed in this field at a single center. secondly, a long term follow up was not done in this study.

### Abbreviations

ALT: Alanine Transaminase, AST: Aspartate Transaminase, BMI: body mass index, SES: socio-economic status, ADA; American Diabetes Association, HbA1c;

Haemoglobin A1c, Type 1 diabetes mellitus; T1DM.

### References

- **Aathira R, Jain V. (2014)**. Advances in management of type 1 diabetes mellitus. *World J Diabetes*, 5:689–696.
- **Abd El-Tawab AA (2012)**. Family socio-economic status scale. *Journal of Faculty of Education, Assiut University*, 28(1).
- **Cameron, Dawn, Fiona Harris, and Josie MM Evans. (2018)** "Self-monitoring of blood glucose in insulin-treated diabetes: a multicase study." *BMJ Open Diabetes Research and Care*, 6.1: 538.
- **Cardwell CR, Stene LC, Ludvigsson J, Rosenbauer J, Cinek O, Svensson J, et al. (2012)**. Breast-feeding and childhood-onset type 1 diabetes: A pooled analysis of individual participant data from 43 observational studies. *Diabetes Care*, 35:2215–25.
- **Chong JW, Craig ME, Cameron FJ, Clarke CF, Rodda CP, Donath SM, et al. (2007)**. Marked increase in type 1 diabetes mellitus incidence in children aged 0–14 yr in Victoria, Australia, from 1999 to 2002. *Pediatr Diabetes*, 8:67–73.
- **Çiçekli İ, Durusoy R. (2022)**. Breastfeeding, nutrition and type 1 diabetes: a case-control study in Izmir, Turkey. *International Breastfeeding Journal*, 17(1):1-1.
- **Das, A. K. (2017)**. Insulin Therapy. *CDiC Textbook of Pediatric Diabetes*, 1, 1.
- **Deshmukh CD, Jain A, Nahata B. (2015)**. Diabetes mellitus: a review. *Int. J. Pure Appl. Biosci*, 3(3):224-30.
- **DIAMOND Project Group. (2006)**. Incidence and trends of childhood Type 1 diabetes worldwide 1990-1999. *Diabet Med*, 23:857–866.
- **El-Ziny MA, Salem NA, El-Hawary AK, Chalaby NM, Elsharkawy AA. (2014)**. Epidemiology of childhood type 1 diabetes mellitus in Nile Delta, northern Egypt - a retrospective study.



- J Clin Res Pediatr Endocrinol, 6(1):9-15.
- **FibmsdCH, Raid K. Dehiol, Mohammed A, Challab A. (2017).** "Factors associated with uncontrolled type 1 Diabetes Mellitus in children and adolescents in Thi-Qar 2016-2017."
  - **Hassan FM, Khatab AA, Abo El-Fotoh WM, Ganh IN (2019).** Prevalence of diabetes mellitus among school-age children. *Menoufia Med J*,32:305-10
  - **Holmberg H, Whalberg J, Vaarala O, Ludvigsson J. (2007).** Short duration of breast-feeding as a risk-factor for  $\beta$ -cell autoantibodies in 5-year-old children from the general population. *Br J Nutr*, 97:111–6.
  - **Lund-Blix NA, Dydensborg SS, Størdal K, Nybo A AM, Rønningen KS, Joner G et al. (2017).** Infant Feeding and Risk of Type 1 Diabetes in Two Large Scandinavian Birth Cohorts. *Diabetes Care*, 40(7):920-927.
  - **McNeilly, Alison D., and Rory J. (2018).** McCrimmon. "Impaired hypoglycaemia awareness in type 1 diabetes: lessons from the lab." *Diabetologia*, 61.4: 743-750.
  - **Patterson CC, Dahlquist GG, Gyürüs E, Green A, Soltész G EURODIAB Study Group. (2009).** Incidence trends for childhood type 1 diabetes in Europe during 1989-2003 and predicted new cases 2005-20: a multicentre prospective registration study. *Lancet*, 373:2027–2033 .
  - **Paun A, Yau C, Danska JS. (2016).** Immune recognition and response to the intestinal microbiome in type 1 diabetes. *J Autoimmun*, 71:10–8.
  - **Saad FM, Mahmoud LA, Mohammedali AM, Abdullah MA, Omer IM (2020).** Incidence and prevalence of type 1 diabetes mellitus in children and adolescents aged 6 months–19 years in Khartoum State, Sudan. *Sudan J Paediatr*, 20(2):163–169.
  - **Salem M, El Sawi MA, Ibrahim WE, Abdel Aziz MM, Abdo KM, Ragab IAM. (2007).** Vitamin D receptor gene polymorphism and susceptibility to T1DM and its complications in Egyptian children. *Egypt J Pediatr*, 84:1–25.
  - **Turkey Endocrinology and Metabolism Society. (2019).** Endocrinology and Metabolism Association Guideline 2019. 14th edition. Ankara,129-137.
  - **Wafaa Moustafa M. Abo El Fotoh. (2017).** Prevalence of Diabetes Mellitus among School Age Children in Menoufia Governorate. .
  - **Zheng P, Li Z, Zhou Z. (2018).** Gut microbiome in type 1 diabetes: a comprehensive review. *Diabetes Metab Res Rev*, 34:e3043.