

Hyper Triglyceridemia Induced Pancreatitis in Children with Diabetic Ketoacidosis

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Abstract

Diabetic ketoacidosis (DKA) is one of the most serious complications of diabetes. In DKA, the deficiency of insulin activates lipolysis in adipose tissue releasing increased free fatty acid (FFA), which accelerates formation of very low density lipoprotein (VLDL) in the liver. In extreme hypertriglyceridemia, there is an expanded danger of creating intense pancreatitis. This investigation expected to assess the serum level of triglycerides and serum level of lipase as serological markers for intense pancreatitis in kids with Diabetic Ketoacidosis (DKA). For this situation controlled investigation, subjects were arranged into 2 gatherings; quiet gathering: Included 50 sort 1 diabetic youngsters, Control gathering: included 30 clearly solid kids age and sexual orientation coordinated to Diabetic patients gathering. The current examination was directed on 50 youngsters with DKA. Their mean age was 6.4 years, they were 24 guys (48%) and 26 females (52%). Notwithstanding 30 sound benchmark group of coordinated age and sexual orientation. DKA indicated altogether higher TC, LDL, fundamentally lower HDL when contrasted with control gathering. TG was fundamentally higher in DKA bunch when contrasted with control gathering. DKA with AP demonstrated fundamentally higher TC, LDL, and altogether lower HDL when contrasted with DKA without AP. TG and lipase levels were altogether higher in DKA with AP when contrasted with DKA without AP subgroups.

Keywords: Hyper triglyceridemia, Pancreatitis, Diabetic Ketoacidosis.

1. Introduction

Diabetes mellitus (DM) is a complex metabolic issue described by ceaseless hyperglycemia coming about because of deformities in insulin discharge, insulin activity, or both [1]. Wrong insulin emission and additionally diminished tissue reactions to insulin in the intricate pathways of hormone activity bring about insufficient insulin activity on track tissues, which prompts changes of sugar, fat, and protein digestion. Weakened discharge of insulin and additionally activity may exist together in a similar patient [2]. DM is over and over associated with dyslipidemia and expanded rates of glycosylated hemoglobin. Dyslipidemia remains to a great extent undiscovered and undertreated in high hazard populaces, for example, quiet with T1DM [3].

Diabetic ketoacidosis (DKA) is one of the most genuine inconveniences of diabetes. It is described by the trio of hyperglycemia (glucose >250 mg/dl), metabolic acidosis (blood vessel pH <7.3 and serum bicarbonate <18 mEq/L) and ketosis. In DKA, the lack of insulin actuates lipolysis in fat tissue discharging expanded free unsaturated fat (FFA), which quickens formalization of extremely low thickness lipoprotein (VLDL) in the liver. What's more, diminished action of lipoprotein lipase in fringe tissue diminishes expulsion of VLDL from the plasma, coming about in hypertriglyceridemia. Moderate hypertriglyceridemia is normal during scenes of DKA. Be that as it may, extreme hypertriglyceridemia, which is sifted through as a triglyceride (TG) level >2,000 mg/dL, is uncommon [4].

In extreme hypertriglyceridemia, there is an expanded hazard for the advancement of intense pancreatitis. The component is identified with high plasma chylomicrons or TGs, which are hydrolyzed by lipase in the pancreatic vessels and accordingly trigger FFA discharge that, thusly, causes enactment of

trypsinogen and initiates pancreatic narrow harm by free extreme harm [4].

Intense pancreatitis is a conceivably deadly malady with changing broadly in clinical highlights and seriousness which go from gentle and self-constrained to a quickly dynamic ailment prompting numerous organ disappointment and demise. The death rate ranges from 0% in the mellow ailment to 10% in sterile and 25% in tainted pancreatic putrefaction [5].

Assurance of pancreatic proteins in serum remains the highest quality level for the analysis of intense pancreatitis. Amylase and lipase are the two chemicals discharged from the pancreas over the span of the sickness. The plasma levels of the two catalysts top inside the initial 24 hours of side effects, yet the half-existence of amylase in plasma is shorter than that of lipase. All the distributed arrangement investigation shows that lipase estimation has a marginally unrivaled affectability and particularity and more noteworthy generally precision than amylase. This distinction turns out to be increasingly astounding when there is a postponement in the underlying blood testing. Despite the fact that the distinction in the presentation of these two tests is little, it is clear [5].

Extreme hypertriglyceridemia is most ordinarily joined by intense pancreatitis. In kids with DKA, those unsettling influences are available in 4-7% of cases, however contrasted with grown-ups are once in a while analyzed [6].

The point of this investigation was to assess the serum level of triglycerides and serum level of lipase as serological markers for intense pancreatitis in youngsters with Diabetic Ketoacidosis (DKA).

2. Patients and methods

This case controlled examination was directed on the patients taking care of pediatric divisions in Elnil medical clinic of health care coverage, and pediatric

emergency unit bahtim clinic of medical coverage after educated assent from the guardians. This work has been led in Clinical Pathology Departments of wellbeing insuranc emergency clinics.

All subjects were arranged into 2 gatherings as following:

Quiet gathering: Included 50 sort 1 diabetic youngsters 24 guys (48%) and 26 females (52%) analyzed by the accompanying rules [2].

Control gathering: Included 30 clearly solid youngsters 14 guys (46.7%) and 16 females (53.3%) age and sexual orientation coordinated to Diabetic patients gathering.

2.1 Inclusion criteria

- 1- All of the diabetic patients receive insulin therapy during the investigation.
- 2- Males and females with the age range 3-15 years old.

2.2 Exclusion criteria

1- Patient group

- The patients with malnutrition, liver disease and end stage renal disease.
- The patients with chronic illnesses such as gastrointestinal disorders, malabsorption and celiac disease.

2- Control group

Healthy children who were on vitamin D, calcium supplementation, or multivitamins were excluded from control group.

Ethical consideration

Approval of the study protocol by Ethical Scientific Committee of Benha University Hospital has been obtained and informed consent has been obtained from the parents before enrollment in the study.

All participants were subjected to the following:

- 1- Full history taking:
- 2- Thorough clinical examination
- 3- Laboratory Investigation including-:
 - Random blood glucose.
 - Serum triglycerides, HDL, LDL cholesterol.
 - Aceton in urine.
 - Glycosylated Hb (HbA1c).
 - Serum lipase
 - Serum urea and creatinine
 - Liver function test
 - Serum electrolytes Na&K + ABG
 - Complete blood count

2.3 Statistical analysis

The collected data was revised, coded and tabulated using Statistical package for Social Science (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). Data were presented and suitable analysis was done according to the type of data obtained for each parameter. Descriptive statistics: Mean, Standard deviation (\pm SD) for parametric numerical data, while Median and range for non-parametric numerical data. Frequency and percentage of non-numerical data. Kolmogorov Smirnov test was done to test the normality of data distribution. Significant data was considered to be nonparametric.

3. Results

The present study was conducted on 50 children with DKA. Their mean age was 6.4 years, they were 24 males (48%) and 26 females (52%). In addition to 30 healthy control group of matched age and gender. Table (1).

Table (1) Comparison of age and gender between cases and control groups.

		Control N=30		DKA N=50		P
Age (years)	mean \pm SD	6.6	2.2	6.4	2.1	0.625 ^T
Males	N; %	14	46.7	24	48	0.908 ^C
Females	N; %	16	53.3	26	52	

DKA showed significantly higher TC, LDL, significantly lower HDL when compared to control group Table (2).

Table (2) Comparison of lipid profile between cases and control groups.

	Control N=30		DKA N=50		P
	Mean	SD	Mean	SD	
TC (mg/dL)	139.7	17.1	321.4	106	<0.001 ^T
LDL (mg/dL)	71.2	15.5	115.94	22.68	<0.001 ^T
HDL (mg/dL)	64.4	6.4	49.8	7.6	<0.001 ^T

SD, standard deviation; T, t test, p, predictive value.

RBG and HA1C concentration were significantly higher in DKA when compared to control groups. Table 3

Table (3) Comparison of RBG and HA1C concentrations between cases and control groups.

	Control N=30		DKA N=50		P
	mean	SD	mean	SD	
RBG (mg/dL)	102.2	9.3	449.86	59.19	<0.001 ^T
HbA1C (%)	6.2	0.7	11.88	1.12	<0.001 ^T

TG was significantly higher in DKA group when compared to control group. Lipase level did not differ significantly between both groups Table (4).

Table (4) Comparison of serum TG and lipase concentrations between cases and control groups.

	Control N=30		DKA N=50		P
	median	range	Median	range	
TG (mg/dL)	100	12-180	681.50	100-10500	<0.001 ^M
Lipase	54	45-100	71	34.0-500.0	0.239 ^M

Mann-Whitney tes, p, predictive value.

TG and lipase levels were significantly higher in DKA with AP when compared to DKA without AP subgroups Table (5).

Table (5) Comparison of TG and lipase levels between DKA with and without AP subgroups.

	DKA without AP N=45		DKA with AP N=5		P
	Median	Range	Median	Range	
TG (mg/dL)	600	100-7010	8000	7000-10500	<0.001 ^M
Lipase	70	34-150	400	300-500	<0.001 ^M

M, Man Whitney test, p, predictive value.

TG showed significant positive correlation with lipase, TC, LDL, HA1C and creatinine. Otherwise, no

significant correlations were found between TG with other studied parameters in all studied cases Table (6).

Table (6) Correlations of lipase with other studied parameters in all studied cases.

	Lipase	
	R	P
TG	0.512	<0.001
Age	-0.061	0.544
Weight	-0.067	0.510
Height	0.026	0.800
BMI	-0.124	0.221
TC	0.311	0.002
LDL	0.370	<0.001
HDL	0.170	0.076
RBG	-0.118	0.130
HbA1C	0.127	0.209
Creatinine	0.355	<0.001
Urea	0.200	0.046
TLC	-0.042	0.677
Hemoglobin	0.110	0.277
Platelets	0.351	<0.001
pH	0.056	0.580
PCO2	0.144	0.152
HCO3	0.017	0.867

Table (6) Continue

Na	0.119	0.238
K	0.265	0.008

r, Pearson correlation coefficient.

TG showed significant positive correlation with BMI, TC, LDL in DKA with no AP subgroup; lipase, LDL in DKA with AP. Otherwise, no significant correlations

were found between TG with other studied parameters in DKA with and without AP subgroups Table (7).

Table (7) Correlations of TG with other parameters in DKA with and without AP subgroups.

	TG			
	No AP		AP	
	r	P	r	P
Lipase	-0.179	0.093	0.794	0.003
Age	0.107	0.318	-0.378	0.252
Weight	0.227	0.032	-0.253	0.452
Height	0.039	0.715	-0.417	0.202
BMI	0.224	0.035	0.330	0.322
TC	0.799	<0.001	0.124	0.717
LDL	0.705	<0.001	0.698	0.017
HDL	0.200	0.058	0.290	0.388
RBG	0.195	0.067	0.575-	0.064
HbA1C	0.062	0.566	0.172	0.613
Creatinine	0.207	0.052	0.506	0.112
Urea	-0.176	0.099	0.237	0.482
TLC	-0.067	0.531	0.331	0.320
Hemoglobin	-0.001	0.994	0.454	0.161
Platelets	-0.164	0.124	0.041	0.904
pH	0.003	0.977	-0.004	0.990
PCO2	-0.159	0.136	-0.196	0.565
HCO3	-0.204	0.054	-0.048	0.888
Na	0.029	0.784	-0.557	0.075
K	-0.122	0.257	0.124	0.716

r, Pearson correlation coefficient.

AP, acute pancreatitis, TG, triglycerides.

4. Discussion

In the current examination, the occurrence of DKA was very higher in the recently analyzed cases contrasted with the ones with a built up T1DM (56% and 44%, separately). The announced pervasiveness of DKA as a first introduction in the writing is generally factor; going from 12.8% to 80% [7]. A few specialists ascribed the higher frequency of DKA at the beginning of the illness to the absence of guardians' familiarity with hyperglycemia manifestations. Actually, having a first degree relative with diabetes was seen as related with a lower danger of DKA at conclusion [8].

We additionally found that DKA cases had higher complete cholesterol, LDL, and lower HDL contrasted with the sound controls. Then again, the decrease in plasma HDL level is a result of hypertriglyceridemia saw in this condition.

We found that triglyceride level was essentially higher in the DKA bunch when contrasted with the benchmark group. In DKA, insulin lack advances

lipolysis and discharges free unsaturated fats from fat tissue and muscle. These free unsaturated fats are additionally changed over into exceptionally low-thickness lipoprotein (VLDL) by the liver. Likewise, their freedom from blood is additionally diminished because of low degrees of lipoprotein lipase, which inevitably results in hypertriglyceridemia [9]. Variations from the norm in the quality for this catalyst have additionally been embroiled for another situation of serious hyperlipidemia and DKA in a kid [10].

Likewise, we found that lipase at a cut-off worth 160.5 mg/dL had 100% affectability, 87.6% explicitness in distinguishing intense pancreatitis in DKA patients. Doctors normally face numerous difficulties in diagnosing intense pancreatitis in DKA patients. To start with, epigastric torment is very normal in DKA, and one-fourth of these patients have raised degrees of serum lipase and amylase with no clinical or radiological proof of pancreatitis. What's more, albeit a

three-overlap ascend in serum lipase and amylase levels is viewed as explicit for the conclusion of intense pancreatitis; yet, in hypertriglyceridemia-instigated pancreatitis, the catalyst levels can at present seem typical. Actually, intense pancreatitis in DKA patients giving ordinary serum lipase level has been recently depicted [9].

Also, we found that triglycerides at cut-off worth 4130 mg/dL had 100% affectability, 97.8% particularity in recognizing intense pancreatitis in DKA patients. This has not been recently concentrated in the pediatric populace; in any case, an investigation included 144 grown-up patients who created hypertriglyceridemia instigated pancreatitis, not really because of diabetes, and revealed that a triglyceride level of 2648 mg/dL was the ideal cut-off an incentive for anticipating progressively serious type of hypertriglyceridemia-initiated pancreatitis, with an affectability and particularity of 75% and 64.5%, individually [11]

Concerning lipase levels, we found that the lipase level didn't vary fundamentally between the two gatherings. Nonetheless, it's been accounted for that pancreatic catalysts; particularly lipase, are usually raised in kids with DKA and that the greatness of lipase rise is connected with the level of acidosis.

Then again, pancreatic proteins height is accounted for to be substantially less basic in recently analyzed T1DM without DKA. The pathogenesis of pancreatic compound rises in DKA stays muddled. It is hypothesized to result from direct injury to the pancreas with protein spillage from the acini, discharge of amylase and lipase from non-pancreatic sources, and diminished renal leeway [12].

In the current examination, we found that serum triglyceride and lipase levels are essentially higher in DKA patients with intense pancreatitis. It has been concurred that triglyceride levels over 1000 mg/dl can regularly trigger a scene of intense pancreatitis. The discharged free unsaturated fat from triglycerides in pancreatic vessels by lipase further initiates pancreatic catalyst trypsinogen and makes free extreme harm the pancreatic tissue [9]. The past case reports of DKA youngsters and teenagers who have created intense pancreatitis detailed high serum levels of triglyceride and lipase [13].

We concur with sharma et al, [13] that detailed a 4-year-old youngster with extreme hypertriglyceridemia, pancreatitis, and diabetic ketoacidosis.

Intense pancreatitis as an entanglement of DKA in youngsters is viewed as an uncommon condition and has been limitedly portrayed in the writing. Just a couple of reports portrayed instances of youngsters who created intense pancreatitis as a result of DKA-actuated hypertriglyceridemia.

We concur with, Wolfgram and Macdonald [14] that announced an instance of a 10-year-old young lady who gave extreme DKA and created horrifying stomach torment. She was determined to have intense pancreatitis optional to hypertriglyceridemia.

In any case, as far as anyone is concerned, none of the distributed work incorporated a few patients. In the current investigation, we included 5 DKA patients who have created intense pancreatitis. We found that DKA patients who have created intense pancreatitis had essentially higher all out cholesterol and LDL levels, and altogether lower HDL levels when contrasted with DKA without intense pancreatitis. Ongoing examinations have recommended that raised serum triglyceride and low HDL levels are related with Acute pancreatitis [15], [16].

We concur with haddad et al, [12] that announced A previous investigation distributed in 2004 included 50 kids with DKA and found that 19% created hyperlipidemia, though just a single patient grew clinically critical intense pancreatitis.

We can't help contradicting [17] in her report about an instance of a 10-years of age young lady gave ketoacidosis and serious hyperlipidemia; serum glucose, triglyceride, all out cholesterol, LDL-cholesterol and HDL-cholesterol levels were discovered raised. Along these lines, this perspective needs further examinations in the setting of hypertriglyceridemia-actuate intense pancreatitis related with DKA.

All the more critically, serum lipase has been seen as better than serum amylase in diagnosing intense pancreatitis. This is because of the way that serum amylase levels may show up erroneously low if serum triglycerides surpass 500 mg/dL because of amylase examine obstruction [18]. Curiously, for the situation by Wolfgram and Macdonald [14], in spite of the fact that the patient's underlying serum amylase level was ordinary, her underlying serum lipase esteem was more twice more prominent than typical. A prior investigation detailed that in grown-up DKA patients who created intense pancreatitis, serum lipase at a 3-crease rise had an affectability of 81%, explicitness of 91%, and a positive prescient estimation of 52% [19].

When all is said in done, triglyceride was emphatically related with lipase, cholesterol, LDL and HDL and creatinine., Musa et al, [20] announced a positive relationship between's triglyceride, complete cholesterol, and lipoproteins focuses. Another investigation revealed a critical positive relationship between's serum triglyceride and pancreatic lipase resistant reactivity [21]. In the interim, we found that in DKA patients who created intense pancreatitis, triglyceride level was just related with lipase and LDL, yet such relationships are limitedly announced in the writing. Concerning lipase, when all is said in done, it was decidedly related with triglyceride, cholesterol LDL, Hba1c, creatinine, urea, platelets, and potassium. In any case, in patients with intense pancreatitis, lipase was just associated with triglycerides.

5. Conclusion

Hypertriglyceridemia was detected in most patients of T1DM during episodes of DKA that significantly declined with insulin therapy. The level of serum triglycerides correlated with the DKA severity BG

levels and duration of ICU stay. The level of serum TG inversely correlated with the modified Glasgow coma scale (GCS) level. Serum TG during DKA did not affect glycemic control or insulin dose later.

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