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Abstract

Aim of the Study: Clarification for the effect of management of diabetic ketoacidosis on both hypocalcemia and electrocardiographic "Wavy triple sign or Yasser's sign" is the target for the current study.

Background: Hypocalcemia is a well-known serious electrolyte disturbance characterized by calcium deficiency. Diabetic ketoacidosis is a life-threatening problem that affects people with diabetes that usually associated with electrocardiographic and electrolytes changes such as hypocalcemia. An electrocardiographic Wavy triple sign (Yasser's sign) of hypocalcemia is a new diagnostic sign seen in 97.3% of hypocalcemia.

Method of Study and Patients: The author reported retrospective-observational 27-case report series. The study was conducted in Fraskour Central Hospital in the intensive care unit thorough nearly 15-months, starting from January 14, 2019 and ended on July 12, 2020. All included cases were latent hypocalcemia. Oral calcium and vitamin D preparation on discharge was supplied.

Results: The mean age was: 44.6 years, with female sex predominance (63%). The main complaints in the study were tachypnea (81.48%) vs. and tachypnea with chest pain (18.5%). Diabetic ketoacidosis (70.37%) and combined diabetic ketoacidosis with ischemic heart disease (11.11%) are the most common risk factors. All cases were latent tetany. Complete electrocardiographic recovery without calcium administration in 85.19% vs. nearly normalized response in 11.11% and non-response in 3.7%.

Conclusion: The wavy triple an electrocardiographic sign (Yasser's sign) and hypocalcemia are commonly seen in diabetic ketoacidosis. Dramatic spontaneous improvement of both wavy triple an electrocardiographic sign (Yasser's sign) and hypocalcemia simultaneously after the management of diabetic ketoacidosis in most cases.

Keywords: Wavy Triple an Electrocardiographic Sign; Yasser's Sign in Hypocalcemia; Hypocalcemia; Tetany; Diabetic Ketoacidosis; Reversal Effect

Abbreviations

ABG: Arterial Blood Gases; Ca⁺⁺: Calcium; CPU: Cardiopulmonary Bypass; CRF: Chronic Renal Failure; DKA: Diabetic Ketoacidosis; ECG: Electrocardiographic; ED: Emergency Department; ICU: Intensive Care Unit; IV: Intravenous; RBS: Random Blood Sugar

Introduction

Hypocalcemia in history and description

The term tetany has emerged in the research literature since 1945 [1]. Thorough the latest decades, laboratory quantified of ionized calcium (Ca⁺⁺) entirely facilitates diagnosis [2]. Hypocalcemia is a common electrolytes disorder recognize by a net loss of calcium from the extra-cellular fluid (ECF) in large amounts that can be restored by the intestine or bone [3]. Hypocalcemia is a common biochemical disorder that can differ in severity from asymptomatic mild cases to acute fatal crisis [4].

Calcium and metabolism

Calcium is an essential electrolyte in cellular physiology and heart contractility [5]. Calcium has a crucial and constructional role in the preservation of myocardial function, cardiac output and vascular tone [6]. The calcium ion enters in various biological processes such as cardiac automaticity; excitation with contraction coupling in myocardial, smooth and skeletal muscle; blood coagulation; neuronal conduction; synaptic transmission; hormone secretion, intracellular messenger, mitotic division and many enzymes fully activity [3]. Calcium can have a substantial role in tissues and organ injury after ischemia, hypoxia, reperfusion and toxic cell death [6]. Serum Ca⁺⁺ levels are commonly organized by three central calcium-regulating hormones; parathyroid hormone (PTH), vitamin D and calcitonin via their particular influences on the gut, kidneys and bone [7,8]. About half of the total serum Ca⁺⁺ is protein-bound and the remaining free ionized Ca⁺⁺ is physiologically active [8]. So, serum Ca⁺⁺ levels should be corrected for the albumin level before confirming the diagnosis of hypercalcemia or hypocalcaemia [7].

Etiology of hypocalcemia

Hypoparathyroidism, vitamin-D deficiency and albumin are the most frequently involved causes of hypocalcemia [2,4]. Kidney disease, liver disease, eating disorders, pseudohypoparathyroidism or pseudopseudohypoparathyroidism, metastatic carcinoma, heavy metal e.g. copper and iron, parathyroid gland tumor, magnesium disorders, Hungry bone syndrome post-parathyroidectomy, iatrogenic phosphate infusion, citrated massive blood transfusions, severe critical illness, Fanconi syndrome, post-radiation of parathyroid glands, acute pancreatitis, calcium antagonists, rhabdomyolysis, tumor lysis syndrome, nutritional defect [2,4,9,10], drug-induced such as cinacalcet [11], 5-fluorouracil with leucovorin [12], high-dose of intravenous zoledronic acid [4,9,10,13], acid phenobarbital [14], phenytoin [14], deno-sumab [15], foscarnet [2] and sodium phosphate forms are another considered causes of hypocalcemia [16,17]. Ionized hypocalcemia is commonly detected in sepsis, pancreatitis, hypomagnesemia, following large blood transfusions, after neck surgery, after cessation of cardiopulmonary bypass (CPU) in cardiac surgery and after starting of extracorporeal membrane oxygenation (ECMO) [6]. The symptoms are ordinarily compatible with the extent and promptness of the diminution in serum calcium [3]. Fatal complications frequently occur if the serum ionized Ca⁺⁺ concentration decreases to below 2 mg/d [3].

Diabetic ketoacidosis and hypocalcemia

Alkalosis may be induced by hyperventilation that can cause hypocalcemia. But, acidosis decreases symptoms, especially in chronic renal failure (CRF) who often tolerate significant hypocalcemia without complaining of symptoms [18,19]. In DKA, hypocalcemia is poorly explained and symptomatic presentations with seizures are rarely described [20].

Diagnosis and clinical impression of hypocalcemia

Acute hypocalcemia may cause severe symptoms indicating hospitalization [4,5,7] whereas patients who gradually develop hypocalcemia are more likely to be asymptomatic [4,5,7]. Severe hypocalcemia or the quick occurrence of hypocalcemia may be associated with Chvostek and Trousseau's sign [5]. Clinically, hypocalcemia may present with a numerous of clinical signs and symptoms such as

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paresthesia, muscle spasms, cramps, fatigue, weakness, tetany, circumoral numbness, convulsions, laryngospasm, bronchospasm (BS), hypotension, bradycardia, digitalis insensitivity, arrhythmias, heart failure (HF), cardiac arrest, hyperactive reflexes, neuromuscular irritability, cognitive impairment and personality disturbances [3,4,7-9,21]. The tingling feeling is the hallmark symptom of hypocalcemia [5]. The diagnosis of latent tetany is based on the clinical signs that associated with hypocalcemia; the presence of Chvostek or Trousseau signs. The term "latent tetany" is exceedingly obscure [3]. Chvostek and Trousseau signs can be tested in suspected hypocalcemia [4,9]. Conventionally, diagnosis should be confirmed with corrected Ca⁺⁺ or ionized Ca⁺⁺ level [4].

ECG in hypocalcemia

The old non-specific ECG sign of hypocalcemia remains the prolongation of the QTc interval which is directly proportional to the degree of hypocalcemia and inversely proportional to the serum calcium level [22]. Hypocalcemia is a recognized cause of QT prolongation via prolongation of the plateau phase of the cardiac action potential [23,24]. Hypocalcemia is a cause of QTc prolongation and this predisposes to ventricular arrhythmias [25]. This causes calcium ion channels to remain open for a longer period, allowing a late Ca⁺⁺ inflow and the formation of early after-depolarization [26,27]. If the threshold for depolarization is reached, new action potentials are induced, initiating a tachycardia and re-entry. Ventricular arrhythmias such as torsades de pointes (TdP) and ventricular fibrillation (VF) are serious complications of hypocalcemia [28]. Prolonged of both QT and ST-intervals, T-wave inversion and bradycardia are the ECG changes seen with hypocalcemia [3,4]. The most common mechanisms of these ECG abnormalities are coronary artery spasm [29]. Changes in the contour of the T-waves may be seen in all cases [23]. The U-wave is frequently absent or unidentifiable [30]. Hypocalcemia may cause HF, elevation in cardiac enzymes and ST-segment changes in ECG which mimics acute ST-segment elevation myocardial infarction (STEMI) [31]. Note, however, that patients may have clinically significant hypocalcemia without diagnostic ECG changes [30]. It is important to note that the electrocardiogram may be normal during life-threatening hypocalcemia and a normal ECG cannot, therefore, be relied upon to exclude this condition [3].

Wavy triple an electrocardiographic sign (Yasser Sign) and hypocalcemia

Wavy triple an electrocardiographic sign (Yasser Sign) is a recently a novel diagnostic sign innovated in hypocalcemia. Related wavy double an electrocardiographic sign also was prescribed in hypocalcemia which is mostly seen with either tachycardia or bradycardia [32,33].

The analysis for this sign in the author interpretations are based on the following:

- 1. Different successive three beats in the same lead are affected.
- 2. All ECG leads can be implicated.
- 3. An associated elevated beat is seen with the first of the successive three beats, a depressing beat with the second beat and isoelectric ST-segment in the third one.
- 4. The elevated beat is either accompanied by ST-segment elevation or just an elevated beat above the isoelectric line.
- 5. Also, the depressed beat is either associated with ST-segment depression or just a depressing beat below the isoelectric line.
- 6. The configuration for depressions, elevations and isoelectricities of ST-segment for the subsequent three beats are variable from case to case. So, this arrangement non-conditional.

7. Mostly, there is no participation among the involved leads. The author intended that is not conditionally included in an especial coronary artery for the affected leads [32].

Laboratory and radiology in hypocalcemia

Determination of serum albumin, magnesium, phosphate levels and arterial blood gas (ABG) analysis are essential emergency workups in hypocalcemia. These measures should be early assessed before correction of hypocalcemia. Calcium replacement may be started without waiting for the laboratory results if the patient has serious neuromuscular complications of hypocalcemia, e.g. seizures, bronchospasm, laryngospasm, arrhythmias [18]. The ECG is indicated in hypocalcemia. Imaging studies such as plain radiography or CT scans may be helpful in hypocalcemic disorders e.g. rickets or osteomalacia [2]. Ionized calcium is the decisive method for diagnosing hypocalcemia. A serum Ca⁺⁺ level less than 8.5 mg/dL or an ionized calcium level less than 1.0 mmol/L is considered hypocalcemia [2].

Prognostic value

Depending on the cause; idiopathic or poorly treated acute hypocalcemia can cause considerable morbidity or mortality [34]. Ionized hypocalcemia commonly can be detected in critically ill cases [10]. A poorer prognosis was reported in those cases of ionized hypocalcemia [6].

Acute management of hypocalcemia

Suspicion of the patient's symptoms and signs is essential in the management of hypocalcemia [18]. The cause, severity, the existence of symptoms and rapidly the hypocalcemia developed hypocalcemia are the main determinants in the management [2]. Most mild cases only require supportive treatment and future laboratory follow-up [2]. Intravenous calcium is given if serum calcium levels fall below 1.9 mmol/L, or ionized calcium levels are less than 1 mmol/L, or if patients are symptomatic [4]. Oral calcium and vitamin D preparations are considered in management [18]. Calcium supplementation may correct a biochemical abnormality with an improvement of cardiovascular status, hemodynamic stability and significant amelioration in cardiac output [6]. Serum level of hypocalcemia is often corrected within several days post-calcium supplementation [5]. Patients with acute symptomatic hypocalcemia (serum calcium usually below 7.0 mg/dl and ionized calcium usually below 3.2 mg/dl) should be treated promptly with IV calcium [35]. Calcium gluconate is preferred over calcium chloride because it causes less tissue necrosis if extravasated. The first 100 to 200 mg of elemental calcium (1 - 2 ampoules of 10% calcium gluconate [93 mg/10 ml ampoule]) should be given over 10 to 20 minutes. Calcium for infusion should be diluted in 50 to 100 ml of saline or dextrose solution to avoid vein irritation [18]. Calcium supplement dosages are 1 to 2 g of elemental calcium 3 times daily (level III evidence) [21]. Elemental calcium supplements can be started at 500 to 1000 mg 3 times daily and titrated upward (level III evidence) [21]. Asymptomatic ECG changes usually normalize with calcium and calcitriol supplementation (level II evidence) [36]. Intravenous calcium is given if serum calcium levels fall below 1.9 mmol/L, or ionized calcium levels are less than 1 mmol/L, or if patients are symptomatic (level III evidence) [7,8]. Cardiac monitoring during IV calcium supplementation is necessary [7,21]. Intravenous calcium administration restores normal polarity transiently in patients with negative T-waves [37]. Long-term therapy results in permanent normalization of the ECG [37]. The marked improvements of the ECG abnormalities following replacement of calcium and vitamin D [38].

Method of Study and Patients

My case study was a retrospective-observational 27-case report series. The study was conducted in Fraskour Central Hospital in both the emergency department and intensive care unit. The author reported the 27-cases thorough nearly 16-months, started from January 14, 2019 and ended on July 12, 2020 (Table 1). The cases were investigated hypocalcemia that was undergoing serial ECG before and after DKA administration. This group also investigated ionized calcium before and after the management of DKA. Other electrolytes, random

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blood sugar and urine acetone were done for all cases. Arterial blood gases, troponin test, serum albumin and echocardiography were done in selected cases. All cases of DKA were admitted to the ICU. All initial ECG tracings were examined for the new sign-in hypocalcemia; "Wavy Triple An Electrocardiographic Sign (Yasser Sign)" (Figure 1). All cases that were tested for latent hypocalcemia are included. Oral calcium preparation on discharge was supplied. Responses were reported (Table 2). Initial oral calcium preparation was only supplied for mild cases or cases of latent tetany. The oral calcium and vitamin-D preparation were supplied after discharge for all the cases. For more details on general, clinical and laboratory data for the cases (Table 2 and 3).

Issue	Definition
Title	Wavy triple sign of hypocalcemia or Yasser's sign-in diabetic ketoacidosis; reversal effect and
	diverse management; retrospective-observational study
Estimated enrollment	27 participants
Study type	Observational
Observational model	Case-only
Time	Retrospective
Study date	Jan 14, 2019 and, ended on Jul 12, 2020





Figure 1: Author caricaturing diagrammatic clarification for the effect of management of DKA on both hypocalcemia and ECG " wavy triple sign". Red arrow = elevated beat, green arrow = isoelectric beat, blue arrow = depressed beat.

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Case	Age	Sex	The main	BP mg	Pulse	RR	Associated	Severity	Number	Given	Final	Outcome
No.	Per		complaints	Hg	bpm		RF	Ū.	of	Calcium	diagnosis	(Response to
	year		-		-				affected	and	C	Ca++)
	,								ECG leads	Vitamin D		2
1.	29	М	Tachypnea	90/60	74	32	DKA	Mild	4	Oral	Latent tetany	Clinical+ ECG
2.	40	М	Tachypnea	110/70	71	24	DKA	Mild	1	Oral	Latent tetany	Clinical+ ECG
3.	22	F	Tachypnea	100/70	120	28	DKA	Mild	3	Oral	Latent tetany	Clinical+ ECG
4.	70	F	Tachypnea	90/70	125	36	DKA-IHD	Severe	5	Oral	Latent tetany	Clinical+ ECG
5.	47	М	+CP	130/80	73	23	DKA	Severe	5	Oral	Latent tetany	Clinical+ ECG
6.	30	М	Tachypnea	90/70	115	34	DKA	Severe	6	Oral	Latent tetany	Clinical+ ECG
7.	58	М	Tachypnea	140/70	108	34	DKA	Severe	7	Oral	Latent tetany	Clinical+ ECG
8.	50	М	Tachypnea	90/60	76	25	DKA	Severe	11	Oral	Latent tetany	Clinical+ ECG
9.	65	F	Tachypnea	100/80	80	30	DKA	Severe	5	Oral	Latent tetany	Clinical+ ECG
10.	19	F	Tachypnea	90/60	81	27	DKA	Severe	5	Oral	Latent tetany	Clinical+ ECG
11.	60	М	Tachypnea	140/90	102	22	DKA-IHD	Mild	3	Oral	Latent tetany	Clinical+ ECG
12.	35	F	Tachypnea	100/80	108	34	DKA-AF	Severe	8	Oral	Latent tetany	Clinical+ ECG
13.	18	F	+CP	90/60	100	22	DKA	Mild	2	Oral	Latent tetany	NN ECG
14.	52	F	Tachypnea	110/70	122	24	DKA-RBBB	Mild	2	Oral	Latent tetany	Clinical+ ECG
15.	53	F	Tachypnea	130/70	81	29	DKA	Severe	5	Oral	Latent tetany	Clinical+ ECG
16.	58	F	Tachypnea	100/80	80	33	DKA	Severe	12	Oral	Latent tetany	Clinical+ ECG
17.	24	F	Tachypnea	90/60	100	21	DKA	Mild	1	Oral	Latent tetany	Clinical+ ECG
18.	20	F	Tachypnea	90/70	126	32	DKA	Severe	12	Oral	Latent tetany	Clinical+ ECG
19.	65	F	Tachypnea	120/80	118	38	DKA	Severe	12	Oral	Latent tetany	Clinical+ ECG
20.	23	F	Tachypnea	110/80	99	30	DKA	Severe	10	Oral	Latent tetany	Clinical+ ECG
21.	31	F	Tachypnea	90/70	107	34	DKA	Severe	12	Oral	Latent tetany	NN ECG
22.	53	М	Tachypnea	110/70	116	30	DKA-STD	Mild	1	Oral	Latent tetany	Clinical+ ECG
23.	63	М	Tachypnea	140/80	84	27	DKA-IHD	Severe	10	Oral	Latent tetany	NN ECG
24.	26	F	Tachypnea	90/70	88	24	DKA	Mild	2	Oral	Latent tetany	Clinical+ ECG
25.	73	М	Tachypnea	130/80	102	22	DKA-UB C.	Mild	4	Oral	Latent tetany	Clinical+ ECG
26.	70	F	+CP	100/60	110	35	DKA-LBBB	Severe	9	Oral	Latent tetany	Clinical+ ECG
27.	50	F	Tachypnea	100/70	92	28	DKA	Severe	12	Oral	Latent tetany	Clinical+ ECG
			Tachypnea									Clinical+ ECG
			+CP									Clinical+ ECG
			Tachypnea									Non-response
			+CP									Clinical+ ECG
			Tachypnea									

Table 2: Summary of the history, clinical and management Data for all the study cases.

BP: Blood Pressure; Ca: Calcium; CP: Chest Pain; DKA: Diabetic Ketoacidosis; ECG: Electrocardiography; F: Female; HVS: K⁺: Potassium; Mg⁺⁺: Magnesium; M: Male; Na⁺: Sodium; NN: Nearly Normalized; RA: Risk Factor; RR: Respiratory Rate; STD: Sexual Transmitted Disease; UB C: Urinary Bladder Carcinoma.

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Case	Ionized Ca++	Total Ca++	Na⁺	K⁺	Mg ⁺⁺	S creatinine	RBS	S albumin	ABG	Troponin
no.	mg/dl	mg/dl	mg/dl	mg/dl	mg/dl	mg/dl	mg/dl	mg/dl		test
1	4.1	7.8	131	5	1.8	0.7	Hi	3.5	RA*	-
2	4.3	8	133	5.3	2.2	1.7	566	.4	RA	-
3	4.2	7.8	132	4.9	1.7	1.1	Hi	3.9	RA	-
4	4	7.3	134	4	2	0.8	Hi	4.2	RA	-VE
5	3.8	7.4	132	5.4	1.9	1.4	587	3.5	RA	-
6	3.3	7.2	132	3.9	1.85	1.3	508	1.4	RA**	-
7	3.9	7.1	129	5.2	2	1.1	499	4.1	RA	-
8	3.7	7	134	4.9	1.8	1.1	Hi	3.4	RA	-
9	4	7.7	131	5.2	1.9	0.7	Hi	3.6	RA	-
10	4	7.6	135	5	2	1	Hi	3.5	RA	-
11	4.3	7.7	143	5.4	1.8	0.7	484	3.7	RA	-VE
12	3.3	7	132	4.1	1.8	1.4	Hi	4	RA	-
13	4.2	8.1	130	5.2	2	0.7	513	3.6	RA	-
14	4.3	7.9	134	4.9	1.9	0.7	Hi	3.5	RA	-
15	3.4	7.2	131	4.8	1.86	1.2	489	3.7	RA	-
16	3.3	7	133	5	1.92	1.4	Hi	4	RA	-
17	4.2	7.9	129	5.3	2	0.7	456	3.8	RA	-
18	3.6	7.6	134	4.6	2.2	0.9	Hi	3.6	RA	-
19	3.5	7.2	129	5.1	1.9	0.8	501	4.2	RA	-
20	3.7	7.1	122	5.4	2.1	1.2	511	3.5	RA	-
21	3.5	7.3	128	5	1.8	1.5	Hi	3.9	RA	-
22	4.2	8	134	4.8	2.1	0.8	500	3.5	RA	-
23	3.9	7.8	128	4.6	1.85	1	436	3.7	RA	
24	4.3	8.1	133	5.1	1.9	1.5	Hi	4.2	RA	-
25	4.1	8.2	134	4.9	2	0.7	Hi	3.5	RA	-VE
26	3.6	7.2	136	5.4	2.2	1	Hi	3.6	RA	-VE
27	3.4	7	127	5.1	1.9	0.9	576	3.5	RA	-

Table 3: Laboratory data for all study cases

ABG: Arterial Blood Gases; BP: Blood Pressure; Ca*+: Calcium; DKA: Diabetic Ketoacidosis: HR: Heart Rate; K*: Potassium; Mg++: Magnesium; Na*: Sodium; RA: Respiratory Alkalosis; RBS: Random Blood Sugar; RR: Respiratory Rate.

Suggesting hypothesis and research objectives

- **Suggesting hypothesis**: Electrocardiographic Wavy triple or Yasser's sign can be improved spontaneously in parallel to the management of DKA.
- The research objectives to evaluate this hypothesis might include: What is Electrocardiographic Wavy triple or Yasser's sign? What is diabetic ketoacidosis? How can management of DKA do improvement of Electrocardiographic Wavy triple or Yasser's sign? Is the study supported by past publicized literature studies? Is there a relationship between the DKA and the improvement of electrocardiographic Wavy triple or Yasser's sign? What is the magnitude of both electrocardiographic Wavy triple or Yasser's sign and DKA in the study?

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The cases were divided into three groups:

- 1. Group I: It included 23 patients (85.17%) of DKA.
- 2. Group II: It included 3 patients (11.11%) of DKA.
- 3. Group III: It included 1 patient (3.7%) of DKA.

Response was reported after the first nearly recovery of DKA. For more details see the summary of the study data (Table 2).

Assessment of treatment response was done with the presence of either:

- Entirely (dramatic improvement) or partially reliving of electrocardiographic Wavy triple or Yasser's sign (weak improvement) or (non-response).
- All the above criteria were assessed in parallel to the clinical status.
- Simple randomization was used in the assignment of patients for both groups with the electrocardiographic Wavy triple or Yasser's sign-in DKA.
- Electrocardiographic Wavy triple or Yasser's sign is defined according to the author's literature in his study as the presence of. The target time in the author's opinion referred to the defined international guidelines of acute management of DKA as in the above literature.
- The treatment was administered according to international guidelines of DKA management.

According to the response of electrocardiographic Wavy triple or Yasser's sign to DKA treatment; there are two types of response in the study:

- **The "dramatic improvement**": It is meaning that the presence of entirely and acutely reliving of complete recovery of electrocardiographic Wavy triple or Yasser's sign after DKA treatment.
- The "weak improvement": It is meaning that is still the presence of Wavy triple or Yasser's sign-in some ECG leads despite DKA treatment.

The patients was secondly classified according to "author opinion based on the completeness recovery of electrocardiographic Wavy triple or Yasser's sign into:

- A complete recovery: Is defined as a completeness recovery of electrocardiographic Wavy triple or Yasser's sign after DKA treatment.
- A partial recovery: It is defined as a partial recovery of electrocardiographic Wavy triple or Yasser's sign after DKA treatment.

Eligibility criteria

Inclusion criteria: All cases with diabetic ketoacidosis. Patients' ages started from 18 and up to 73 years old.

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Exclusion criteria:

- 1. Controlled diabetes mellitus.
- 2. Hypoglycemia.

Electrocardiographic recovery had happened after the management of diabetic ketoacidosis.

Case Presentations

Case No. 1: A 29-year-old married male carpenter Egyptian patient was admitted to the ICU due to DKA and respiratory distress. He was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis (Figure 2).



Figure 2: Serial ECG tracings; A-tracing of the presentation showing "Wavy triple sign" in V2,4, 5 and V6 leads. B-tracing was done within 78 minutes of B-tracing showing no "Wavy triple sign". Red arrows =elevated beats, green arrows = isoelectric beats and blue arrows =depressed beats.

Case No. 2: A 40-year-old married male Paramedic Egyptian patient was admitted to the ICU due to DKA and tachypnea. He was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis (Figure 3).

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Figure 3: Serial ECG tracings; A-tracing of the presentation showing "Wavy triple sign" in V4 lead. B-tracing was done within 30 minutes of B-tracing showing no "Wavy triple sign". Red arrows =elevated beats, green arrows = isoelectric beats and blue arrows =depressed beats.

Case No. 3: A 22-year-old single female student Egyptian patient was admitted to the ICU due to DKA and tachypnea. She was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis (Figure 4).



Figure 4: Serial ECG tracings; A-tracing of the presentation showing "Wavy triple sign" in V4,5 and 6 leads. B-tracing was done within 20 hours of B-tracing showing no "Wavy triple sign". Red arrows =elevated beats, green arrows = isoelectric beats and blue arrows =depressed beats. There are missed V5 lead (purple arrows).

Case No. 4: A 70-year-old married housewife female Egyptian patient was admitted to the ICU due to DKA, chest pain and tachypnea. She was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis (Figure 5).



Figure 5: Serial ECG tracings; A-tracing of the presentation showing "Wavy triple sign" in aVL, aVF and V1-3 leads. B-tracing was done within 10 hours of A-tracing showing no "Wavy triple sign". Red arrows =elevated beats, green arrows = isoelectric beats and blue arrows =depressed beats. There are pathological Q-waves in inferior (III and aVF) and anterior leads (V1-6) lead (lime arrows). There are missed V1 lead (purple arrows).

Case No. 5: A 47-year-old married male farmer Egyptian patient was admitted to the ICU due to DKA and tachypnea. He was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis (Figure 6).



Figure 6: Serial ECG tracings; A-tracing of the presentation showing "Wavy triple sign" in I, II, III, aVL and aVF leads. B-tracing was done within 19 hours of A-tracing showing no "Wavy triple sign". Red arrows =elevated beats, green arrows = isoelectric beats and blue arrows =depressed beats. There are ST-segment depressions in anterior leads (V5-6) leads (lime arrows). There are tremor artifacts in I, III and aVF leads (black arrows).

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Case No. 6: A 30-year-old married painter Egyptian male patient was admitted to the ICU due to DKA and tachypnea. He was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis (Figure 7).



Figure 7: Serial ECG tracings; A-tracing of the presentation showing "Wavy triple sign" in I, III and V1- 4 leads. B-tracing was done within 14 hours of A-tracing showing no "Wavy triple sign". Red arrows =elevated beats, green arrows = isoelectric beats and blue arrows =depressed beats.

Case No. 7: A 58-year-old married housewife female Egyptian patient was admitted to the ICU due DKA and tachypnea. She was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis (Figure 8).



Figure 8: Serial ECG tracings; A-tracing of the presentation showing "Wavy triple sign" in I, II, III, aVR, aVL, aVF and V1 leads. B-tracing was done within 19 hours of A-tracing showing no "Wavy triple sign". Red arrows =elevated beats, green arrows = isoelectric beats and blue arrows =depressed beats.

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Case No. 8: A 50-year-old married worker Egyptian male patient was admitted to the ICU due to DKA and tachypnea. He was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis (Figure 9).



Figure 9: Serial ECG tracings; A-tracing of the presentation showing "Wavy triple sign" in all leads except aVL. B-tracing was done within 15 hours of A-tracing showing no "Wavy triple sign". Red arrows =elevated beats, green arrows = isoelectric beats and blue arrows =depressed beats.

Case No. 9: A 65-year-old married housewife female Egyptian patient was admitted to the ICU due to DKA and tachypnea. She was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis (Figure 10).



Figure 10: Serial ECG tracings; A-tracing of the presentation showing "Wavy triple sign" in aVF, V2, 3, 4 and V6 leads. B-tracing was done within 15 hours of A-tracing showing no "Wavy triple sign". Red arrows =elevated beats, green arrows = isoelectric beats and blue arrows =depressed beats.

Case No. 10: A 19-year-old single female student Egyptian patient was admitted to the ICU due to DKA and tachypnea. She was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis (Figure 11).



Figure 11: Serial ECG tracings; A-tracing of the presentation showing "Wavy triple sign" in II, III, aVF, V2 and V3 leads. B-tracing was done within 35 hours of A-tracing showing no "Wavy triple sign". Red arrows =elevated beats, green arrows = isoelectric beats and blue arrows =depressed beats.

Case No. 11: A 60-year-old married male farmer Egyptian patient was admitted to the ICU due to DKA, tachypnea and chest pain. He was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis (Figure 12).



Figure 12: Serial ECG tracings; A-tracing of the presentation showing "Wavy triple sign" in aVR, aVL and aVF leads. B-tracing was done within 24 hours of A-tracing showing no "Wavy triple sign". Red arrows =elevated beats, green arrows = isoelectric beats and blue arrows =depressed beats. There are ST-segment depressions in anterior leads (V4-6; lime arrows).

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Case No. 12: A 35-year-old married female officer Egyptian patient was admitted to the ICU due to DKA and tachypnea. She was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and movable phenomenon. Complete clinical and but nearly normalized electrocardiographic recovery had happened after the management of diabetic ketoacidosis (Figure 13).



Figure 13: Serial ECG tracings; A-tracing of the presentation showing AF and "Wavy triple sign" in II, III, aVF, V2, 3, 4, 5 and V6 leads. B-tracing was done within 7 hours of A-tracing showing "Wavy triple sign" in V4 and V5. Red arrows =elevated beats, green arrows = isoelec-tric beats and blue arrows =depressed beats.

Case No. 13: A 18-year-old single female student Egyptian patient was admitted to the ICU due to DKA and tachypnea. She was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis.

Case No. 14: A 52-year-old married housewife female Egyptian patient was admitted to the ICU due to DKA and tachypnea. She was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis.

Case No. 15: A 19-year-old single female student Egyptian patient was admitted to the ICU due to DKA and tachypnea. She was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis.

Case No. 16: A 58-year-old married Egyptian housewife female patient was admitted to the ICU due to DKA and tachypnea. She was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis.

Case No. 17: A 24-year-old married Egyptian housewife female patient was admitted to the ICU due to DKA and tachypnea. She was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis.

Case No. 18: A 20-year-old single female student Egyptian patient was admitted to the ICU due to DKA and tachypnea. She was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and movable phenomenon. Complete clinical and but nearly normalized electrocardiographic recovery had happened after the management of diabetic ketoacidosis.

Case No. 19: A 65-year-old married Egyptian housewife female patient was admitted to the ICU due to DKA and tachypnea. She was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and movable phenomenon. Complete clinical and but nearly normalized electrocardiographic recovery had happened after the management of diabetic ketoacidosis.

Case No. 20: A 23-year-old married Egyptian housewife female patient was admitted to the ICU due to DKA and tachypnea. She was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis.

Case No. 21: A 31-year-old married Egyptian housewife female patient was admitted to the ICU due to DKA and tachypnea. She was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis.

Case No. 22: A 53-year-old married male worker Egyptian patient was admitted to the ICU due to DKA and tachypnea. He was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis.

Case No. 23: A 63-year-old married male carpenter Egyptian patient was admitted to the ICU due to DKA, tachypnea and chest pain. He was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis.

Case No. 24: A 26-year-old married female teacher Egyptian patient was admitted to the ICU due to DKA and tachypnea. She was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis.

Case No. 25: A 73-year-old married male farmer Egyptian patient was admitted to the ICU due to DKA, tachypnea and chest pain. He was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon. Complete clinical and electrocardiographic recovery had happened after the management of diabetic ketoacidosis.

Case No. 26: A 70-year-old married Egyptian housewife female patient was admitted to the ICU due to DKA, tachypnea and chest pain. She was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and the movable phenomenon. A complete clinical but non-responded electrocardiographic changes had happened after the management of diabetic ketoacidosis.

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Case No. 27: A 50-year-old married female nurse Egyptian patient was admitted to the ICU due to DKA and tachypnea. She was tested for latent tetany which was positive. Oral calcium-vitamin D tab was prescribed for two weeks after discharge. Serial ECG tracings (A-B) showing an electrocardiographic wavy triple sign of hypocalcemia and Weaning-off pattern of the movable phenomenon.

Results and Findings

Age averages in the study: Mean: 44.6, Median: 50, Mode: 70.

Sex in the study: Female (F) 63% (17 cases) vs. Male (M) 37% (10 cases).

The main complaints in the study were tachypnea (81.48%) vs. and tachypnea with chest pain (18.5%) (Figure 14).



The associated risk factors (RF) and etiology in the study:

- DKA: 70.37% (19 cases)
- Combined RF:
 - DKA + IHD: 11.11% (3 cases)
 - DKA + AF: 3.7% (1 case)
 - DKA + RBBB: 3.7% (1 case)
 - DKA + LBBB: 3.7% (1 case)
 - DKA + UB carcinoma: 3.7% (1 case)
 - DKA + STD: 3.7% (1 case) (Figure 15).

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Figure 15: Bar chart showing the associated risk factors (RF) and etiology in the study.

The averages in the number of affected ECG leads: Mean: 6.25, Median: 5, Mode: 7.

The response after the treatment of DKA:

- Complete recovery: 85.19% (23 cases)
- Nearly normalized response: 11.11% (3 cases)
- No response: 3.7% (1 case) (Figure 16).



Figure 16: Bar chart showing the response after the treatment of DKA.

Discussion

Despite diabetic ketoacidosis is a life-threatening problem that affects people with diabetes that usually associated with electrocardiographic and electrolytes changes [39] but hypocalcemia is not a famously associated electrolyte disorder.

Clarification for the effect of management of diabetic ketoacidosis on both hypocalcemia and electrocardiographic "Wavy triple sign or Yasser's sign" is the target for the current study.

Although, the electrocardiographic Wavy triple sign (Yasser's sign) of hypocalcemia is a new diagnostic sign and seen in 97.3% of hypocalcemia [32,33], unfortunately, there were no relevant studies in the current and past diabetes literature.

The wavy curve for the subsequent three beats from depressions, elevations and isoelectricities are noticed and prescribed (Figure 17).



Figure 17: Author caricaturing diagrammatic clarification with a case example for "wavy triple sign". Red arrow =elevated beat, blue arrow = isoelectric beat, black arrow = depressed beat.

Zhu H., *et al.* (2015) reported one case of hypocalcemia, hypophosphatemia and transient hypoparathyroidism in diabetic ketoacidosis possibly associated with the use of proton-pump inhibitor (PPI) [39].

There are no well-known mechanisms for the causes of hypocalcemia in the cases of diabetic ketoacidosis.

Alkalosis may be induced by hyperventilation that can cause hypocalcemia. But, acidosis decreases symptoms, especially in chronic renal failure (CRF) who often tolerate significant hypocalcemia without complaining of symptoms [18,19]. In DKA, hypocalcemia is poorly explained and symptomatic presentations with seizures are rarely described [20].

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Significant Ca²⁺ and Mg²⁺ losses have been demonstrated during ketoacidosis and the first hours of recovery. Negative Ca²⁺ and Mg²⁺ balance occurs immediately following insulin withdrawal, progresses with acidosis and continues through the first few days of recovery [39].

Movable-weaning off an electrocardiographic phenomenon is another interpretation for spontaneous disappearance of Wavy triple or double electrocardiographic signs (Yasser signs) of hypocalcemia with DKA. Movable-weaning off an electrocardiographic phenomenon is a guide for both Wavy triple or double electrocardiographic signs (Yasser signs) of hypocalcemia. Don't angry if the staring electrocardiography or the last one was normal [40].

Conclusion

- "The wavy triple an electrocardiographic sign (Yasser's sign) and hypocalcemia are commonly seen in diabetic ketoacidosis.
- Dramatic spontaneous improvement of both wavy triple an electrocardiographic sign (Yasser's sign) and hypocalcemia simultaneously after the management of diabetic ketoacidosis in most cases.
- Further investigations for the "Wavy triple an electrocardiographic sign (Yasser sign)" for more evaluation and assessment are recommended.

Conflicts of Interest

There are no conflicts of interest.

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