

Original Article



Calcium and Hypocalcemia: from Ancient to Recent Innovative Signs and Phenomena-Narrative Review

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Abstract

Calcium (Ca^{+2}) is an essential bivalent cation that has a pivotal role in various body functions. Chemical and body metabolic processes such as skeletal mineralization, signal transduction, neurological conduction, muscle contractility, and blood coagulation can't be completed without Ca^{+2} . Hypocalcemia is a common electrolyte disorder that is seen in surgical and medical emergencies. This review aimed to correlate the ancient findings of hypocalcemia to the recent innovative signs and phenomena rather than the initial clearing of the pathophysiology of calcium and hypocalcemia. The author collected the narrative data from Google Scholar, Medline, and a few books over a 60-year duration, from 1966 to 2025. Hypocalcemia may be life-threatening if not diagnosed and immediately treated. The author concluded that there is variability among ancient electrocardiographic (ECG) findings and recent innovative signs and phenomena of hypocalcemia. The ancient ECG findings are non-specific and non-sensitive signs of hypocalcemia. Wavy triple, an electrocardiographic sign, Yasser's sign, Wavy double, an electrocardiographic sign, and Movable-weaning off, an electrocardiographic phenomenon, are recent diagnostic and prognostic hallmarks in hypocalcemia. Wavy triple, an electrocardiographic sign, Yasser's sign, Wavy double, an electrocardiographic sign, and Movable-weaning off, an electrocardiographic phenomenon, are easy, simple electrocardiographic diagnostic, monitoring, and therapeutic signs. Unfortunately, their sensitivity and specificity have not yet been further studied.

Keywords

Calcium, Hypocalcemia, ECG, Wavy triple, an electrocardiographic sign, Yasser's sign, Wavy double, an electrocardiographic sign, Movable-weaning off, an electrocardiographic phenomenon

1. Calcium essentials

Calcium (Ca^{+2}) is a substantial bivalent cation that has a crucial role in various body functions. Chemical and body metabolic processes, including skeletal mineralization, signal transduction, neurological conduction, muscle contractility, and blood coagulation, can't be completed without Ca^{+2} ions [1]. Calcium is the most plentiful electrolyte in the human body [2], and the third most abundant metal in nature [3], the fifth mineral in order of abundance in the body, after O, C, H, and N. But it is the most predominant divalent cation in the extracellular fluid (ECF) [4] [5]. However, Calcium is a fundamental nutrient for most metabolic processes, especially in the bones and teeth, where 99% of the body's Ca^{+2} dwells [6]. So, there is no doubt that calcium, phosphate (PO_4^{-3}), and magnesium (Mg^{+2}) have essential metabolic roles for both intracellular (IC) and extracellular (EC) functions in co-association

with common hormonal signals [7]. There is a strong relationship among the triple Ca^{+2} , Mg^{+2} , and PO_4^{-3} metabolism [1]. Magnesium is a primary IC ion that acts as a metallocoenzyme in more than 300 phosphate transfer reactions. It plays a crucial role in the transfer, storage, and utilization of energy within the body. EC Mg^{+2} levels are predominantly renal dependent, with the renal tubular (RT) maximum reabsorption (TmMg) controlling the plasma Mg^{+2} level [7]. When plasma PO_4^{-3} increases, RT reabsorption also increases up to a maximum (Tm PO_4), thereafter PO_4^{-3} is excreted [7]. Following these sentences, it is essential to understand calcium homeostasis, calcium balance, and regulation. Calcium homeostasis points to the hormonal regulation of ionized Ca^{+2} by parathyroid hormone (PTH) and 1,25-dihydroxyvitamin D (1,25(OH) $_2$ D) for Ca^{+2} transport at the GIT, kidney, and bone. Hypocalcemia marks a serious disturbance of Ca^{+2} ho-

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meostasis, and not a mirror for calcium balance. Calcium balance remarks and guide for the Ca^{+2} body stores, especially in bone, which include monitoring of dietary intake, intestinal absorption, renal excretion, and bone remodeling. Based on growth, aging, and acquired or inherited disorders, bone Ca^{+2} balance can be classified into positive, neutral, and negative [2]. Calcium balance studies directed the dietary and supplemental Ca^{+2} demands to optimize bone mass in healthy persons. Calcium balance and homeostasis can be affected by chronic kidney disease (CKD) with mineral bone disorders (CKD-MBD). Calcium supplementation can promote soft tissue calcification and cardiovascular disease (CVD) in CKD-MBD [2]. Ca^{+2} homeostasis is dependent on intestinal absorption, bone turnover, and renal reabsorption. The hormonal regulators of these processes are the PTH, calcitriol $1,25(\text{OH})_2\text{D}$, and serum ionized Ca^{+2} . Cloning of the Ca^{+2} -sensing receptor (CaSR) has been extremely implicated in the understanding of Ca^{+2} metabolism. Disorders of Ca^{+2} metabolism are easily recognized because Ca^{+2} is included in routine chemistry panels [1]. The Ca^{+2} concentration outside the cell is approximately 10,000-fold more than the intracellular concentration [8]. Calcium is tightly regulated and rarely varies from physiologic levels within the body [9]. Homeostasis must be maintained as calcium is critical in many principal cellular functions [10]. However, Calcium is tightly regulated by the PTH, calcitonin, and calcitriol, which regulate serum calcium levels. Ca^{+2} must be ingested endogenously, and absorption in the GI system is influenced by PTH and $1,25(\text{OH})_2\text{D}$ hormones [11]. The PTH, calcitonin, and $1,25(\text{OH})_2\text{D}$ actively manage Ca^{+2} levels. The PTH is an essential regulator of Ca^{+2} homeostasis, which acts on the renal, skeletal, and GI systems to increase serum Ca^{+2} levels. Initially, PTH promotes Ca^{+2} absorption in the GI by activating the synthesis of renal $1,25(\text{OH})_2\text{D}$, which targets the GI to increase Ca^{+2} absorption [12] [13]. Then, PTH catalyzes Ca^{+2} resorption from bone by enhancing osteoclastic activity [14]. Finally, PTH activates Ca^{+2} absorption in the kidney by stimulating adenylyl cyclase (AC) in the distal nephron [15]. However, the concentration and amount of calcium must be considered. The average adult body contains approximately 1 kg, 99% in the skeleton in the form of $\text{Ca}^{+2} \text{PO}_4^{-3}$ salts [2]. Total Ca^{+2} concentration is also mM inside cells. In the cytosol of most cells, the concentration of ionized Ca^{+2} (iCa^{+2}) is about 10,000-fold lower. Also, within cells, Ca^{+2} is complexed by inorganic compounds and low-MW organic molecules [3]. The ECF contains approximately 22 mmol, of which about 9 mmol is in the plasma. Approximately 10 mmol of Ca^{+2} is exchanged between bone and the ECF over a period of 24 hours [16]. The plasma level of Ca^{+2} is 2.5 mM, with a normal variation of no more than 20%. Approximately half of the plasma Ca^{+2} is bound, largely to blood proteins, with albumin being the major ligand. It is the EC iCa^{+2} concentration that is

closely regulated at around 1.2 mM. Calcium carries messages to virtually all important functions of cells. The IC iCa^{+2} concentration is typically between 50 and 100 nM; that is, it is about 104 times lower than the iCa^{+2} level outside the CM [17]. Clearly, then, the cell must have mechanisms to keep Ca^{+2} out [3]. A normal 70-kg adult male has approximately 1.4 kg of Ca^{+2} ; a 60-kg woman, around 1.1 kg; and a newborn at term close to 25 g or approximately 25 mol of Ca^{+2} [4] [18]. Calcium (99%) is found in bone; 1% is distributed in the IV, interstitial, and IC fluids. The plasma Ca^{+2} level is maintained very constant at 10 mg/dL (2.5 mM or 5 mEq/L). Normal daily Ca^{+2} fluctuations in serum are less than 3%, even when Ca^{+2} intake varies significantly. Calcium level remains unchanged throughout life; only higher values are observed in fetal cord blood (11.6 mg/dL or 2.9 mM) [4]. Serum Ca^{+2} can be measured by a venous sample, with physiologic levels ranging from 8.8 mg/dL to 10.4 mg/dL for total Ca^{+2} and 4.7 mg/dL to 5.2 mg/dL for ionized Ca^{+2} [5]. The body skeleton contains about 99% of the body's Ca^{+2} , mainly as EC crystals of an unknown structure and a composition approaching hydroxyapatite (HAp) [19]. Soft tissues and EC fluid contain about 1% of the body's Ca^{+2} . In blood, virtually all Ca^{+2} is present in the plasma [20]. About 50% of the Ca^{+2} present in circulation is free (iCa^{+2}); 40% of serum Ca^{+2} is bound to proteins, especially albumin (80%) and, secondary, to globulins (20%); and about 10% exists as various small diffusible inorganic and organic anions (eg, bicarbonate, lactate, citrate). The free Ca^{+2} fraction is biologically active [6].

Despite these essentials, the role of calcium can't be ignored. Calcium has a vital physiological role in the body [12]. Calcium is a prominent molecule involved in several biochemical body processes and pathways. This mineral is fundamental for cardiac function, blood clotting, nerve excitability, the structural integrity of bone, muscular contraction, and the regulation of enzymatic signal in biochemical [4] [19]. Extracellular Ca^{+2} provides Ca^{+2} ions for maintaining IC Ca^{+2} , bone mineralization, blood coagulation, and plasma membrane potential [12]. Calcium stabilizes the plasma membranes and influences permeability and excitability. A lowering in the plasma iCa^{+2} level causes an increase in neuromuscular excitability and tetany, but its rise level reduces this excitability [21].

So, the physician should be taken in consideration the forms of plasma calcium. There are 3 different forms of Ca^{+2} in plasma: 1. Ionized Ca^{+2} (iCa^{+2}), which represents approximately 50% of the total Ca^{+2} . 2. Bounded Ca^{+2} to proteins, primarily albumin (~ 40% of the total), which is in dynamic equilibrium with the plasma Ca^{+2} . 3. Nonionic (or diffusible), associated with anions, such as citrate or lactate. Ionized Ca^{+2} is the physiologically active form of Ca^{+2} . Its level varies between 4.6 and 5.2 mg/dL (1.25 and 1.3 mM) [20]. Calcium is physiologically either IC or EC. IC Ca^{+2} is key for numerous vital physiological body functions, such as muscle contraction,

hormone secretion, glycogen metabolism, and cell division. The IC level of Ca^{+2} in the cytosol of unstimulated cells is around 0.1 $\mu\text{mol/L}$, which is less than 1/20,000 of that in EC fluid [22].

Indeed, calcium is independent of PH. The balance between iCa^{+2} and protein-bound Ca^{+2} is relevant to changes in blood pH. Alkalosis causes a decrease in Ca^{+2} , and the opposite occurs with acidosis. For every 0.1 unit of pH increase, the Ca^{+2} ion level is reduced by 0.4% [20]. But in vitro, for each 0.1-unit change in pH, approximately 0.2 mg/dL (0.05 mmol/L) of inverse change occurs in the iCa^{+2} level [23]. Because Ca^{+2} binds to negatively charged sites on proteins, its binding is pH-dependent. Alkalosis causes an increase in the negative charge of proteins, increasing binding and decreasing iCa^{+2} ; conversely, acidosis leads to a decrease in negative charge, decreasing binding and increasing iCa^{+2} [24]. Calcium can be redistributed among the 3 plasma pools, acutely or chronically, by alterations in the levels of protein and small anions, changes in pH, or changes in the amounts of iCa^{+2} and total Ca^{+2} in the plasma [9].

But the albumin level plays a pivotal role in calcium concentration. Total Ca^{+2} values should be corrected for current albumin levels, which act as a carrier protein and can affect the reported results. Urine analyses can also assess Ca^{+2} level, urine Ca^{+2} to creatinine ratio (UCA: UCr), or fractional excretion of Ca^{+2} (FeCa) [18]. Albumin is a carrier protein for Ca^{+2} and can result in an inaccurately reported serum Ca^{+2} level. Evaluating albumin levels to correct for total Ca^{+2} and differentiate actual versus factitious Ca^{+2} dysregulation is important [25]. The equation for albumin correction is as follows: True Ca^{+2} (mg/dL) = reported total Ca^{+2} (mg/dL) + 0.8 (4.0 – serum albumin (g/dL))

If the corrected serum total Ca^{+2} levels are between the normal levels of 8.8 mg/dL to 10.4 mg/dL, then the laboratory-reported Ca^{+2} is fictitious due to impaired serum albumin levels [26].

2. Calcium and body systems

Several body systems play a crucial role and have variable functions in calcium metabolism. Initially, the urinary system has significant part in calcium metabolism and regulation. The PTH acts on the urinary system by activating AC and 1-1- α -hydroxylase (1A-hydroxylase) to increase Ca^{+2} reabsorption and $\text{PO}_4\text{-3}$ excretion. AC increases Ca^{+2} reabsorption at the distal convoluted tubules (DCT). The enzyme 1A-hydroxylase increases the conversion of vitamin D to its active form, 1,25(OH) $_2$ D, resulting in increased Ca^{+2} absorption in the intestine [27]. In CKD, the effect of PTH can become muted, leading to hypocalcemia, hyperphosphatemia, and secondary hyperparathyroidism [20].

The gastrointestinal tract may have another function in cal-

cium metabolism. Calcium is an exogenous mineral in humans. So it must be ingested and absorbed in the GI tract. Calcium levels and 1,25(OH) $_2$ D influence Ca^{+2} absorption in the gut. Age, gender, race, and comorbidities can change Ca^{+2} absorption. 1,25(OH) $_2$ D is increased in response to low serum Ca^{+2} and triggers an active process in the duodenum to absorb more Ca^{+2} [13]. Elevated serum Ca^{+2} levels shut off the active process, and Ca^{+2} absorption occurs passively at the jejunum and ileum, resulting in lower Ca^{+2} absorption rates [20]. Since Ca^{+2} is absorbed in ionic form, dietary intake of compounds that interact with Ca^{+2} will reduce the amount of Ca^{+2} available for absorption. These are primarily oxalate, phosphate, sulfate, citrate, fiber, and fats [13].

The musculoskeletal system may have a different role in calcium regulation. Bone tissue stores Ca^{+2} as HAp, deposited when serum Ca^{+2} levels are elevated and released when levels are low. This process is linked with the endocrine system via the thyroid and parathyroid glands. When serum Ca^{+2} levels are elevated, the thyroid gland releases calcitonin, which inhibits bone resorption by halting osteoclast activity. The PTH effect on bone tissue is dependent on continuous versus intermittent exposure [14]. In continuous exposure, PTH activates osteoclasts more readily by enhancing RANKL, which increases Ca^{+2} resorption and bone loss, promoting an osteoporotic state [27]. Intermittent PTH exposure favors osteoblast activation, which promotes bone formation. The chronic reduction in PTH levels may precipitate decreased bone remodeling, producing weak and brittle bones [28]. Calcium is necessary for muscle contraction. Actin and myosin subunits interact to initiate contraction, and two regulatory subunits, troponin and tropomyosin, actively inhibit this process. Tropomyosin obstructs the actin-myosin binding site, which prevents contraction by blocking actin and myosin interaction [29]. Muscle contraction occurs when Ca^{+2} , released from the sarcoplasmic reticulum, binds to troponin to force tropomyosin out of the binding site, thus allowing for actin and myosin interaction [30].

But calcium is essential for the contraction of cardiac muscle. The calcium in the myocytes stabilizes the membrane potential [9]. Calcium influx during the plateau phase of myocardial contractility sets the speed of pacemaker potential. Dysregulation of either Ca^{+2} or K^{+} can affect this delicate balance. In severe hyperkalemia, an ECG will be indicated to evaluate for serious associated changes. So, giving of Ca^{+2} gluconate is the initial step to stabilize the myocardium and prevent arrhythmias [31]. In the past, prospective cohort studies had shown no relationship between dietary Ca^{+2} intake and the risk of heart disease, sudden cardiac death (SCD), or acute myocardial infarction (AMI) [32]. Study results conclude an unclear interpretation of whether absorption of dietary Ca^{+2} versus Ca^{+2} supplements has any indications regarding cardio-

vascular risks. Therefore, further investigations are recommended to discover the role of these supplements in cardiovascular prevention [33]. Calcium is a key cofactor in the coagulation cascade and is necessary for appropriate coagulability. During primary hemostasis, von Willebrand Factor (vWF) is released from injured tissue to act as a bridge for the endothelium and platelet GpIb receptors for proper platelet adhesion. After a platelet adheres to the endothelium, Ca^{+2} is released to assist with other coagulation factors of the clotting cascade [34]. The tissue factor released from subendothelial tissue binds to Ca^{+2} and factor VII to promote thrombin formation. Calcium is also involved in forming the prothrombinase complex, which converts prothrombin to thrombin and further creates insoluble fibrin [35]. Results from a study of intracerebral hemorrhage (ICH) among 2103 patients showed that hypocalcemia was associated with subtle coagulopathy and correlated with increased bleeding in patients with ICH [36].

3. Basics of Hypocalcemia

Hypocalcemia is a common biochemical abnormality that can range in severity from asymptomatic to mild and to acute life-threatening episodes [37]. Hypocalcemia is usually an electrolyte disorder in surgical and medical presentations. Hypocalcemia can be caused by a wide spectrum of diseases. It may be fleeting and rapidly reversed with treatment of the underlying cause. But it may be chronic and lifelong, such as in a genetic disorder, post-operative irreversible damage of the parathyroid glands, and autoimmune destruction [38]. Hypocalcemia is defined as a total serum Ca^{+2} level below 8.8 mg/dL (< 2.20 mmol/L) in the presence of normal plasma protein concentrations, or as a serum iCa^{+2} concentration below 4.7 mg/dL (< 1.17 mmol/L). Reference ranges for serum Ca^{+2} vary by age and sex [39]. Hypocalcemia may be life-threatening if not diagnosed and immediately treated [2].

So, the levels of evidence can be used for the assessment of hypocalcemia [28]. Level I: At least one of randomized controlled trials, systematic reviews, and meta-analyses, Level II: Preferably more than one study of comparative trials, non-randomized, cohort, case-control, or epidemiologic studies, and Level III: Expert opinion or consensus statements. Unfortunately, there are numerous causes for hypocalcemia. Hypocalcemia (corrected serum total Ca^{+2} level < 2.12 mmol/L) is most commonly a consequence of vitamin D inadequacy or hypoparathyroidism, or a resistance to these hormones [37] [40]. Chronic hypocalcemia is commonly due to inadequate levels of PTH or vitamin D, or due to resistance to these hormones [28]. The following are implicated causes in hypocalcemia: 1. PTH deficiency (inadequate PTH production/hypoparathyroidism), including postsurgical, autoimmune, abnormal parathyroid gland development, parathyroid gland destruction, and functional hypoparathyroidism. 2.

High PTH, including: absolute or relative vitamin D deficiency (inadequate vitamin D), CKD, and Pseudohypoparathyroidism (PHP). 3. Drug-inducing, such as antiepileptics (denosumab, cisplatin, foscarnet, and cinacalcet), antiepileptics, aminoglycosides, IV bisphosphonate, diuretics, and proton pump inhibitors. 4. Miscellaneous causes, including: massive blood transfusion of citrated blood, pseudohypocalcemia, acidosis/alkalosis, acute pancreatitis, severe sepsis, critical illness, trauma, shock, hypomagnesemia/hypermagnesemia, acute hyperphosphatemia, pregnancy, osteoblastic metastasis, and severe COVID-19 infection [41-61]. (For more details, see Table 1). Hypocalcemia can develop in individuals with inadequate 25(OH)D levels following the start of bisphosphonate and should be excluded before starting IV bisphosphonate, especially in cases of osteoblastic metastases (level III [62-66] and level I evidence) [67]. Serum 25(OH)D and 1,25(OH)₂D levels should be monitored in cases of hypocalcemia (level III evidence) [68].

Anyway, an understanding of the pathophysiological processes of hypocalcemia is vital. Physiologically, blood Ca^{+2} is strictly regulated within a narrow range in cellular metabolism. The blood Ca^{+2} occurs in three essential forms: proteins bound (mainly albumin), anions bound to such as phosphate and citrate, and as free (iCa^{+2}). Only the iCa^{+2} is physiologically active. Normal blood Ca^{+2} level is between 8.5 and 10.5 mg/dL (2.12 to 2.62 mmol/L), and that of unbound Ca^{+2} is 4.65 to 5.25 mg/dL (1.16 to 1.31 mmol/L) [69]. Hypocalcemia causes irritability and tetany. Alkalosis induces tetany due to a decrease in iCa^{+2} , whereas acidosis is protective. This pathophysiology is important in patients with renal failure who have hypocalcemia, because rapid correction of acidosis or development of alkalosis may trigger tetany [70-72]. Patients with a decrease in total serum Ca^{+2} may not have "true" hypocalcemia, which is defined as a decrease in iCa^{+2} . A total hypocalcemia can result from a hypoalbuminemia secondary to liver disease, nephrotic syndrome, or malnutrition [69].

The clinical diagnosis still represents the cornerstone of the management of hypocalcemia.

Acute hypocalcemia varies from gradually asymptomatic hypocalcemia to severe symptoms indicating of hospitalization [37]. The most common symptoms of hypocalcemia are paresthesia, muscle spasms, cramps, tetany, circumoral numbness, and seizures [37][68][73]. It may be present with laryngospasm, irritability, cognitive impairment, personality disturbances, QT prolongation in ECG, mimic MI changes, and congestive heart failure (CHF) [68][73]. However, the manifestations of hypocalcemia can be divided into 1. Neuromuscular irritability: Chvostek's sign, Trousseau's sign, paresthesia, tetany, seizures, muscle cramps, weakness, laryngospasm, bronchospasm. 2. Neurological signs and symptoms: extrapyramidal signs due to calcification of the basal ganglia, calcification of the cerebral cortex or cerebellum, personality dis-

turbances, irritability, impaired intellectual ability, non-specific EEG changes, increased intracranial tension (ICT), Parkinsonism, choreoathetosis, and dystonic spasms. 3. Mental symptoms: confusion, disorientation, psychosis, fatigue, anxiety, poor memory, and reduced concentration. 4. Ectodermal changes: hair, brittle nails, alopecia, enamel hypoplasia, shortened premolar roots, thickened lamina dura, delayed tooth eruption, increased dental caries, atopic eczema, exfoliative dermatitis, psoriasis, and impetigo herpetiformis. 5. Smooth muscle manifestations: dysphagia, abdominal pain, biliary colic, dyspnea, and wheezing. 6. Ophthalmologic manifestations: subcapsular cataracts and papilledema. 7. Cardiac: prolonged QT interval, CHF, and cardiomyopathy (CMP) [41]. Critical initial laboratory testing involves measuring serum PO_4^{3-} , Mg^{+2} , intact PTH, 25(OH)D, and 1,25-dihydroxyvitamin D levels [38]. Diagnosis should generally be confirmed by determining the corrected Ca^{+2} or iCa^{+2} level [28]. Abnormal changes may also be seen in an ECG [74]. The hallmark of acute hypocalcemia is neuromuscular irritability. Patients often complain of numbness and tingling in their fingertips, toes, and the perioral region. Paresthesia of the extremities may occur, along with fatigue and anxiety. Muscle cramps can be very painful and progress to carpal spasm or tetany. In extreme cases of hypocalcemia, bronchospasm and laryngospasm with stridor may occur. Muscle symptoms can be so severe as to present with a polymyositis-like picture with elevated muscle isoenzymes. These symptoms are corrected by Ca^{+2} replacement. Chvostek and Trousseau signs can be elicited in patients with hypocalcemia [28][75]. Clinically, neuromuscular irritability can be demonstrated by eliciting Chvostek's or Trousseau's signs. Chvostek's sign is elicited by tapping the skin over the facial nerve anterior to the external auditory meatus. Ipsilateral contraction of the facial muscles occurs in hypocalcemia. Chvostek's sign is also present in 10% of normal people [28][38][75]. Trousseau's sign is elicited by inflation of a BP cuff to 20 mm Hg above the patient's SBP for 3-5 minutes. Carpal spasm presents as flexion of the wrist and of the metacarpal phalangeal joints, extension of the interphalangeal joints, and abduction of the thumb. It can be very [28][38][76]. Trousseau sign is a more reliable sign present in 94% of hypocalcemia and only 1% to 4% of healthy people [38][75][76]. Acute hypocalcemia may have fairly common prolongation of the QT-interval due to lengthening of the ST-segment. Abnormal T-waves occurs in about 50% of patients [77]. Acute anteroseptal injury in ECG without MI has been associated with hypocalcemia and other electrolyte abnormalities [78]. Hypomagnesemia with hypocalcemia may magnify the ECG abnormalities. Rarely, CHF may occur [77][79][80]. Reversible CMP due to hypocalcemia has been reported [81]. In cases of mild, asymptomatic hypocalcemia, Ca^{+2} replacement can result in improved cardiac output and exercise tolerance [82]. Measurement of iCa^{+2} is the preferred way to as-

certain the diagnosis of hypocalcemia and hypercalcemia [1]. Because a significant portion of Ca^{+2} is bound to albumin, any alteration in the level of albumin will affect the measured level of Ca^{+2} . A corrected Ca^{+2} level based on the albumin level is: Corrected Ca^{+2} (mg/dL) = measured total Ca^{+2} (mg/dL) + 0.8 * (4.0 - serum albumin [g/dL]) [83]. Since Ca^{+2} is also bound to small anions, it may be more useful to correct total Ca^{+2} for both albumin and the anion gap (AG) [84][5].

Finally, the treatment of hypocalcemia is life-saving. However, the current treatments mostly depend on expert clinical opinion and published case reports. Acute and life-threatening Ca^{+2} deficit requires treatment with IV Ca^{+2} [28]. IV Ca^{+2} is given if serum Ca^{+2} levels fall below 1.9 mmol/L, or iCa^{+2} levels are less than 1 mmol/L, or if patients are symptomatic (level III evidence) [37] [68] [86]. There are striking inequities in Ca^{+2} intake between rich and poor populations. Appropriate Ca^{+2} intake has shown many health benefits, such as reduction of hypertension of pregnancy, lower blood pressure, particularly among young people, prevention of osteoporosis and colorectal adenomas, lower cholesterol values, and lower BP in the progeny of mothers taking sufficient Ca^{+2} during pregnancy [87]. Treatment of chronic hypocalcemia focuses on oral Ca^{+2} and vitamin D supplements, as well as magnesium if deficiency is present. Treatment can be further intensified with thiazide diuretics, PO_4^{3-} binders, and a low-salt and low- PO_4^{3-} diet when treating hypocalcemia secondary to hypoparathyroidism [28]. Current therapy is limited by serum Ca^{+2} fluctuations. Currently, management is suboptimal and marked by fluctuations in serum Ca^{+2} and a lack of approved PTH replacement therapy for hypoparathyroidism. Rapid correction of hypocalcemia can cause to cardiac arrhythmia [37] [68]. Cardiac monitoring during IV Ca^{+2} supplementation is necessary, particularly in patients taking digoxin therapy (level III evidence) [37] [73] [88]. IV Ca^{+2} gluconate administered with a CVP catheter is preferable to avoid extravasation and irritation of the surrounding tissue, which is most often seen with IV Ca^{+2} chloride administration [37] [68] [73] [87] [88] [89]. IV Ca^{+2} is given as 1 or 2 10-mL ampoules of 10% Ca^{+2} gluconate diluted in 50 to 100 mL 5% dextrose, infused over 5 to 10 minutes (level III evidence) [37] [68]. To avoid precipitation of Ca^{+2} salts, PO_4^{3-} and HCO_3^{-1} should not be infused with the Ca^{+2} [87]. Patients should also receive oral Ca^{+2} supplements and calcitriol (0.25 to 1 $\mu\text{g}/\text{day}$) as needed (level III evidence) [37]. Mg^{+2} deficiency or alkalosis should be corrected if present [68] [73] [90]. In an emergency, Mg^{+2} therapy will not elevate serum PTH or Ca^{+2} , as peripheral PTH resistance can last for many days [87].

4. Ancient and traditional ECG Findings of Hypocalcemia

Although there are innovative and emerging signs and phe-

nomena for ECG diagnosis of hypocalcemia, some physicians still rely on traditional ECG findings for the diagnosis of hypocalcemia (Figure 1). The prolongation of the QT interval is an essential ECG finding in hypocalcemia. But, the prolongation of the QT interval was a common, non-specific, and principal ECG finding of hypocalcemia in the past. It may predispose to lethal ventricular arrhythmias. The subsequent decreased myocardial contractility can cause CHF, cardiomyopathy (CMP), hypotension, and angina. Ventricular arrhythmias and CMP may be reversible with management [91][92]. The QTc prolongation is essentially relevant to the prolongation of the ST segment [93]. Although ventricular arrhythmias are infrequent, AF has been reported. Torsades de pointes (TdP) may happen, but it is less prevalent than with hypokalemia or hypomagnesemia [93] [94]. Hypocalcemia extends phase 2 of AP [95] with the effect regulated via the rate of change of serum Ca^{+2} levels and activity of the myocytic Ca^{+2} channels [94] by the rate of change of EC Ca^{+2} , all of which impact the QT interval [95]. Elongation of the QTc interval is relevant to early after repolarizations and precipitated arrhythmias. Hypocalcemia prolongs the duration of the plateau of the cardiac action potential. Because hypocalcemia does not affect phase 3 of an action potential, T waves are generally uncommon [96]. However, cases of severe hypocalcemia decrease the T-wave amplitude, flattening of the T-wave, terminal T-wave inversion (TWI), and deeply TWI [98]. ST-segment elevation has also been associated, though rarely, with hypocalcemia [99]. Acute anteroseptal the on the ECG with no associated subsequent MI was reported with hypocalcemia [100] [101]. Hypocalcemia-associated ST segment elevation, mimicking an AMI or T wave abnormalities, is rarely reported [102]. Coronary artery spasm is interpreted theory [103] [104]. QT interval prolongation is parallel to the degree of hypocalcemia. However, the QTc hardly overrides 140% of the normal value [102]. The discrepancy of QTc prolongation due to hypocalcaemia suggests rate dependency between iCa^{+2} and QTc. This ECG finding may present a clinical dilemma [94]. Associated hypomagnesemia can precipitate the ECG changes of hypocalcemia [105]. Cases of TdP due to hypocalcaemia usually had additional QT prolongation confounders [105]. There is no recurrence of TdP after normalization of serum Ca^{+2} [106]. (See ECG tracings as a clinical example for the prolongation of the QT interval in hypocalcemia (Figures 2 and 3).

5. New Signs and Phenomena of Hypocalcemia

It is worth mentioning that there are innovative and emerging signs and phenomena for ECG diagnosis of hypocalcemia. They include: Wavy triple electrocardiographic sign (Yasser's sign), Wavy double electrocardiographic sign (Yasser's sign), and Movable-weaning off an electrocardiographic phenome-

non in hypocalcemia (MWOP or changeable phenomenon or Yasser's phenomenon of hypocalcemia).

5.1. Wavy Triple an Electrocardiographic Sign (Yasser's Sign)

In November 06, 2019, Elsayed et al (2019) [107] studied 37 cases of both manifested and latent hypocalcemia and subsequent discovered a "Wavy triple an ECG sign (WTS or Yasser's sign)". Elsayed concluded that the WTS (Yasser's sign) is a new diagnostic sign seen in 97.3% (36 cases) of hypocalcemia. Wavy triple, an electrocardiographic sign, is a novel, specific diagnostic ECG sign for hypocalcemia if compared with the old traditional non-specific ECG signs. Dramatic improvement of both clinical manifestation and the new ECG sign simultaneously after calcium replacement. The analysis for this sign in the author's interpretations is 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 an isoelectric ST-segment in the third one. 4. The elevated beat is either accompanied by ST-segment elevation (STE) or just an elevated beat above the isoelectric line. 5. Also, the depressed beat is either associated with ST-segment depression (STD) or just a depressing beat below the isoelectric line. 6. The configuration for depressions, elevations, and isoelectricities of the ST segment for the subsequent three beats is variable from case to case. So, this arrangement is non-conditional. 7. Mostly, there is no participation among the involved leads. The author intended that it is not conditionally included in the special coronary artery for the affected leads [107]. (Figures 5). (See ECG tracings as a clinical example for the WTS, Figures 1, 4, 5, 7A, and 7B). Elsayed et al (2020) reported a serial independent different case report indicating a WTS (Yasser's sign) with variable and complex association. So, he reported a case of WTS (Yasser's sign) in hypocalcemia with a tented T-wave and chronic renal failure (CRF) [108]. Elsayed et al (2021) reported a case of phenytoin-induced WTS (Yasser's sign) and hypocalcemia in a young epileptic patient [109]. On May 28, 2021, Elsayed et al (2021) [110] studied 27-case report series aimed to clarify the effect of the management of diabetic ketoacidosis (DKA) on both hypocalcemia and ECG WTS or Yasser's sign. Elsayed concluded that the WTS (Yasser's sign) and hypocalcemia are commonly seen in DKA. Dramatic spontaneous improvement of both WTS (Yasser's sign) and hypocalcemia simultaneously after the management of DKA in most cases [110]. Elsayed et al (2021) reported a case of COVID-19 Pneumonia with atrial fibrillation (AF), coronary artery spasm (CAS), and WTS (Yasser's sign) [111]. He (2021) reported a case of nodular COVID-19 pneumonia with WTS or Yasser's sign and Movable phenomenon (MWOP) [112]. Elsayed et al (2022) reported a case of Camel-hump T-wave,

Tee-Pee sign, and Wavy triple sign (Yasser's sign) with hypocalcemia and hyperkalemia in Covid-19 pneumonia with lacunar infarction [113]. He (2023) reported a case of false angina and mimic MI in Wavy triple sign (Yasser's sign) of hypocalcemia with later mild COVID-19 pneumonia [114]. Elsayed et al (2023) reported a case of severe COVID-19 pneumonia in Parkinson's disease with mental retardation and WTS (Yasser's sign) [115]. He (2023) reported a case of nitroglycerine and furosemide in hypertensive pulmonary edema with WTS (Yasser's sign), Tee-Pee sign, and Camel-hump T-wave in suspected COVID pneumonia [116]. Elsayed et al (2023) reported a case of Zavras-Kounis Type I syndrome, anaphylaxis, WDS, and WTS post-ceftriaxone [117]. He reported a case of WTS (Yasser's sign) accelerated the hypocalcemic convulsive diagnosis in generalized convulsions with CRF and stones [118]. Elsayed et al. reported a case of COVID-19 pneumonia, Non-ST elevation myocardial infarction, QRS fragmentation, and electrocardiographic Wavy triple or Yasser's sign in Hodgkin lymphoma [119]. He reported a case of AMI with transient LBBB, AF with pre-excitation, high lateral CAS, and WTS (Yasser's sign) post-COVID-19 pneumonia in a senile female patient [120]. Elsayed et al. reported a case QTc prolongation, epiglottitis, WTS, WDS (Yasser's signs), and Spike sign post-COVID pneumonia in a mitral valve prolapse (MVP) [121]. He reported a case of Kounis syndrome with syncope, WTS (Yasser's sign), WDS (Yasser's sign), and possible pulmonary embolism after the AstraZeneca ChAdOx1 nCoV-19 vaccine in elderly [122]. Elsayed et al. reported a case of sildenafil-induced allergic angina in an elderly patient with intertwining sinus arrhythmia, WTS, WDS (Yasser's signs), and mild COVID infection [123]. He reported a case of Kounis-Zavras syndrome after diclofenac potassium with intertwining first-degree heart block, WTS, WDS (Yasser's signs), and Triphasic Yasser's stressor syndrome post-CABG [124]. Elsayed et al. reported a case of tramadol-induced MI, hypertensive pulmonary edema, WTS (Yasser's sign), ventricular fibrillation, and SCD with possible serotonin syndrome in a heavy-smoking patient [125]. In a study of 43 cases of Movable-Weaning off an electrocardiographic phenomenon in hypocalcemia (MWOP or Changeable phenomenon or Yasser's phenomenon of hypocalcemia), the WTS was a positive and triple sign in 95.35% (41 cases), but it was combined with both WTS and WDS in 4.65% (2 cases) [126]. (For more details, see Table 2).

5.2. Wavy Double an Electrocardiographic Sign (WDS or Yasser's Sign)

In November 06, 2019, Elsayed et al (2019) [107] studied 37 cases of both manifested and latent hypocalcemia and subsequently discovered a single case of Wavy double an ECG sign (Yasser's sign) in 2.7%. So, there are only two affected beats, but not the three like-Wavy triple sign [107]. Elsayed also reported a serial independent different case report indi-

cating a WDS (Yasser's sign) with variable and complex association. So, he reported a case of hypocalcemia-induced Camel-hump T-wave, Tee-Pee sign, WDS (Yasser's sign), and bradycardia in a car painter of a complex dilemma. [127]. A wavy double ECG sign was also prescribed in hypocalcemia, which is mostly seen with either tachycardia or bradycardia [107] [126] [127]. Elsayed concluded that the dramatic disappearance of the Wavy double sign of hypocalcemia (Yasser's sign) and bradycardia meant that all these signs and findings were lonely due to severe hypocalcemia [127]. In a study of 43 cases of MWOP in hypocalcemia (Changeable phenomenon or Yasser's phenomenon of hypocalcemia), the wavy triple sign is positive and triple sign in 95.35% (41 cases), but it is combined with both WDS and WTS in 4.65% (2 cases) [126]. Elsayed reported a case of Zavras-Kounis Type I syndrome, anaphylaxis, WDS, and WTS post-ceftriaxone [117]. He reported a case of QTc prolongation, epiglottitis, Wavy triple sign, Wavy double sign (Yasser's signs), and Spike sign post-COVID pneumonia in a mitral valve prolapse [121]. He reported a case of Kounis syndrome with syncope, WTS (Yasser's sign), WDS (Yasser's sign), and possible pulmonary embolism after the AstraZeneca ChAdOx1 nCoV-19 vaccine in an elderly [122]. Elsayed reported a case of sildenafil-induced allergic angina in an elderly patient with intertwining sinus arrhythmia, WTS, WDS (Yasser's signs), and mild COVID infection [123]. He reported a case of Kounis-Zavras syndrome after diclofenac potassium with intertwining first-degree heart block, WTS, WDS (Yasser's signs), and Triphasic Yasser's stressor syndrome post-CABG [124]. (For more details, see Table 3). See ECG tracings as a clinical example for the WDS, Figures 1, 2, 3, 6, and 7A).

5.3. Movable-Weaning off an Electrocardiographic Phenomenon in Hypocalcemia (MWOP or Changeable Phenomenon or Yasser's Phenomenon of Hypocalcemia)

On 04 January 2021, Elsayed et al (2021) [126] studied 43 cases of hypocalcemia with the target being both WTS and WDS (Yasser's signs). Manifested or latent tetany were fundamental cases and subsequently discovered a Movable-Weaning off an ECG Phenomenon in Hypocalcemia (MWOP or Changeable Phenomenon or Yasser's Phenomenon of Hypocalcemia)". Elsayed concluded that the MWOP in hypocalcemia (changeable phenomenon or Yasser's phenomenon of hypocalcemia) is defined according to the author's opinion in the study as a novel ECG phenomenon characterized by serial dynamic changes present in all cases of either WTS and WDS (Yasser signs) of hypocalcemia. Movable-weaning off an electrocardiographic phenomenon is a guide for both WTS and WDS (Yasser signs) of hypocalcemia. Don't be angry if the staring ECG or the last one was normal. He classified the patterns of MWOP into: regressive (30.23%), weaning-off (20.93%), progressive (13.95%), changeable (13.95%), variable: 4.56%, reversed (4.56%), re-

gressive characteristic (2.33%), unknown (2.33%), reversed with progression (2.33%) changeable with regression, (2.33%), and intermittent with regression (2.33%) [126]. Elsayed reported a serial independent different case report indicating a WTS (Yasser's sign) with variable and complex association. So, he reported a case of an elderly COVID-19 pneumonic patient with both Graded phenomenon and MWOP or Yasser's phenomena in a surgical severe aortic stenosis [128]. Elsayed reported a case of a COVID-19 extensive bilateral pneumonia, variants ischemic heart disease (IHD), and MWOP of hypocalcemia or Yasser's phenomenon [129]. He reported a case of COVID-19 pneumonia with RBBB, MWOP, and S1S2S3 syndrome in a diabetic, hypertensive, and stented IHD [130]. Elsayed reported a case of mimic high lateral MI in chest tetany with mirror ECG change, MWOP (Yasser's phenomenon), and coronary spasm [131]. He reported a case of nodular COVID-19 pneumonia with WTS or Yasser's sign and MWOP [112]. Elsayed reported a case of acute pericarditis with MWOP (Yasser's phenomenon) and variant T-wave in the underlying repolarization pattern [132]. He reported a case of lacunar infarction with MWOP (Yasser's phenomenon), hypertensive emergency, mild pneumonia, and associated Brugada syndrome post-COVID-vaccination [133]. (For more details, see Table 3). (See ECG tracings as a clinical example for the MWOP, Figures 1, and 7A-C).

6. Hypocalcemia and Hypercalcemia, factors affecting and mechanisms

Indeed, several processes, hormones, and receptors are implicated in the mechanisms of both hypocalcemia and hypercalcemia. Intestinal absorption, bone turnover with Ca^{+2} exchange in the bone, and renal reabsorption are the three main implicated processes in Ca^{+2} homeostasis [1] [2]. PTH, calcitriol or 1,25(OH)₂D (the most active form of vitamin D), calcitonin, and serum iCa^{+2} are the hormonal regulators of the above three processes. However, PTH receptor (PTHrP), vitamin D receptor (VDR), calcitonin receptor, and calcium-sensing receptor (CaSR) are the essential receptors for this hormonal regulation [134] [135]. PTHrP is the classical PTH receptor, which is expressed at high levels in bone and kidneys. There are two types of PTHrP; type 1 receptor (PTH1R) for PTH, and type 2 receptor, or parathyroid hormone-related peptide (PTHrP) is a G protein-coupled receptor that is highly expressed in bone and kidney. It mediates in these tissues the PTH-dependent regulation of Ca^{+2} homeostasis. The PTH1R also mediates the paracrine actions of PTHrP, which play a particularly vital role in the process of endochondral bone formation [135] [136]. These essential functions involve the PTH1R in certain genetic diseases of skeletal development, Ca^{+2} homeostasis, and the potential utility of PTH in treating osteoporosis [135]. Both the receptor and its peptide ligands

results in a receptor-ligand interaction process through the use of site-directed mutagenesis and photoaffinity cross-linking methods. This interaction process could enable the development of the therapeutic value of novel PTH receptor ligands in treating osteoporosis and hypercalcemia [135]. PTH1R has been shown to interact with sodium-hydrogen exchange regulatory cofactor 2 and $\text{Na}^{+1}\text{H}^{+1}$ antiporter 3 regulator 1 [137]. Defects in PTH1R are established causes of Jansen's metaphyseal chondrodysplasia (JMC) and chondrodysplasia Blomstrand type (BOCD), as well as enchondromatosis and essential failure of dental eruption [138]. The PTHrP receptor and the calcitonin receptor regulates Ca^{+2} ion homeostasis through mediate activating action of their physiological ligands by activating two different effectors, adenylyl cyclase and phospholipase C [135] [136].

The vitamin D receptor (VDR, the calcitriol receptor) is a member of the nuclear receptor family of transcription factors. The nuclear receptors of the NR1H and NR1I subgroups include the constitutive androstane receptor, pregnane X receptor, farnesoid X receptors, liver X receptors, and vitamin D receptor. The newly emerging functions of these related receptors are under the control of metabolic pathways, including the metabolism of xenobiotics, bile acids, cholesterol, and calcium. This summarizes the results of structural, pharmacologic, and genetic studies of these receptors. [139]. Calcitriol (1,25-(OH)₂vitamin D₃) binds to VDR, forming a heterodimer with the retinoid-X receptor. The VDR heterodimer sinks in the nucleus and binds to vitamin D-responsive elements (VDRE) in genomic DNA. VDR binding yields expression or transrepression of several specific gene products. VDR is also involved in microRNA-directed post transcriptional mechanisms. When bound to the DR, the active form of vitamin D (1,25(OH)₂D) is a potent regulator of osteoblast transcription [140]. In humans, the vitamin D receptor is encoded by the VDR gene located on chromosome 12q13.11. This result implies that the locus for the clinical disorder vitamin D dependency rickets type II maps on 12q [141]. VDR is expressed in most tissues of the body and regulates transcription of genes involved in intestinal and renal transport of calcium and other minerals [142]. The most natural potent agonist for VDR is calcitriol (1,25(OH)₂D₃), and the vitamin D₂ homologue ercalcitriol (1- α ,25-dihydroergocalciferol) is also a strong activator [143]. The CaSR is a G protein-coupled receptor that regulates PTH secretion in the parathyroid glands. The CaSR senses EC iCa^{+2} in the cases of hypercalcemia, causing a subsequent increase in renal Ca^{+2} excretion (calciuria) and inhibition of PTH secretion [144]. Indeed, there are other hormones that can regulate Ca^{+2} absorption in vivo, such as thyroid hormone, growth hormone (GH)/insulin-like growth factor I (IGF-1), estrogen, and testosterone [142].

Regarding the hypercalcemia, factors affecting, and mecha-

nisms, acute hypercalcemia is a life-threatening and rare condition [145]. It is defined as a Ca^{+2} concentration more than 10.5 mg/dL [146]. Based on the serum Ca^{+2} levels, hypercalcemia is classified as mild (10–12 mg/dL), moderate (12–14 mg/dL), or severe (>14 mg/dL) [147] [148].

Hyperparathyroidism (primary and tertiary), malignancy (PTHrP production, metastasis, ectopic production of PTH, and extrarenal activation of vitamin D), drug-induced (thiazide diuretics, lithium carbonate, calcium, vitamin D, A supplements and antiacids), granulomatous diseases (sarcoidosis, tuberculosis, histoplasmosis, leprosy, coccidioidomycosis, and cryptococcus), genetic disorders (familial hypocalciuric hypercalcemia), and miscellaneous (Hyperthyroidism, Pheochromocytoma, adrenal insufficiency, and immobilization) are suggested causes [146]. Hypercalcemia is reported in up to 30% of patients with malignancy. It is most common in later-stage malignancies [149]. It often occurs late in the course of solid-tumor development and is associated with a poor prognosis [150]. The frequent causes of hypercalcemia are malignancy mediated by parathyroid hormone-related peptide, osteolytic cytokine production, humoral hypercalcemia of malignancy (HCM), osteolytic HCM, ectopic hyperparathyroidism, and vitamin D-secreting lymphomas, and excess 1,25-dihydroxy vitamin D production [148] [149]. Primary hyperparathyroidism and granulomatous diseases are also associated causes [149]. Indeed, more than 90% of hypercalcemic cases are caused by primary hyperparathyroidism (PHPT) or malignancy-induced hypercalcemia. The malignancy is the most common cause of hypercalcemia in hospitalized patients [151–153]. The most common cancer associated with hypercalcemia is multiple myeloma [147]. There are three implicated mechanisms for the pathophysiology of hypercalcemia of malignancy: excessive secretion of parathyroid hormone (PTH)-related protein (PTHrP), bony metastases leading to the release of osteoclast-activating factors, and the production of 1,25-dihydroxy vitamin D (calcitriol) [154]. Structurally, PTHrP is similar to PTH in the first 13 amino acid sequences, so this structural similarity, PTHrP binds to the same receptor as PTH, causing bone resorption, and increased phosphate excretion from the proximal tubules, and calcium reabsorption from the distal tubules in the kidneys [147]. Acute and chronic metabolic acidosis causes hypercalcemia because H^{+2} is buffered in the bone with subsequent release of Ca^{+2} and calcinuria. ICa^{+2} changes by 0.12 mg/dl for each 0.1 change in pH. Inhibition of the Na-KCL cotransporter 2 (NKCC2) in the loop of Henle by loop diuretics enhances Ca^{+2} excretion in the urine [155]. Thiazide diuretics are associated with hypercalcemia and hypocalciuria due to enhanced Ca^{+2} reabsorption in the PT after Na^{+} and H_2O reabsorption due to volume depletion in the DCT [1].

But regarding the hypocalcemia, factors affecting, and mechanisms, hypocalcemia is defined as serum Ca^{+2} of <8.8

mg/dl (2.2 mmol/l or 4.4 mEq/l) [1]. PTH is the main arranger of renal Ca^{+2} reabsorption. Hypocalcemia with a decrease in serum ICa^{+2} inhibits the CaSR in the parathyroid glands and subsequently activates PTH secretion. PTH and calcitriol enhance renal Ca^{+2} reabsorption in the DCT via the active transcellular pathway [156]. So, the function of the CaSR in the parathyroid glands will change PTH secretion based on serum ICa^{+2} concentration. Both Mg^{+2} and Ca^{+2} bind to the CaSR in the parathyroid glands and the kidney. All have a distinct binding site. Mg^{+2} plays a role in PTH modulation by acting on the CaSR [157] [158]. PTH secretion is stimulated in acute hypomagnesemia and suppressed in hypermagnesemia. In severe hypomagnesemia, there is suppression rather than stimulation of PTH secretion and increase PTH resistance in the bone leading to hypocalcemia [159] [160]. Calcitriol is important in hypocalcemia. 25-hydroxyvitamin D [25(OH)D] is produced in the liver and is converted to calcitriol by 1α -hydroxylase [161] [162]. Calcitriol enhances intestinal Ca^{+2} and phosphate absorption in addition to renal Ca^{+2} reabsorption in the DCT [1]. Volume expansion increases urine Na^{+} and Cl^{-} excretion and subsequently decreases renal Ca^{+2} absorption, and the reverse is true in volume contraction. In metabolic alkalosis, bound H^{+2} ions dissociate from albumin, which increases the fraction of albumin available for ionized Ca^{+2} binding. Therefore, metabolic alkalosis leads to hypocalcemia [163]. Metabolic alkalosis also increases Ca^{+2} binding to albumin and decreases ICa^{+2} . Hypocalcemia stimulates PTH release, which increases renal production of calcitriol; both hormones increase serum Ca^{+2} by the mechanism mentioned above [1]. Hypocalcemia due to PTH deficiency is associated with low or low-normal PTH and hyperphosphatemia. But the other causes are associated with high PTH. Vitamin D deficiency, acute pancreatitis, hungry bone syndrome, and Mg^{+2} deficiency cause hypocalcemia with normal or low serum phosphate [164].

Conclusion and Recommendations

The author concluded that there is variability among ancient electrocardiographic (ECG) findings and recent innovative signs and phenomena of hypocalcemia. The ancient ECG findings are non-specific and non-sensitive signs of hypocalcemia. Wavy triple, an electrocardiographic sign, Yasser's sign, Wavy double, an electrocardiographic sign, and Movable-weaning off, an electrocardiographic phenomenon, are recent diagnostic and prognostic hallmarks in hypocalcemia. Wavy triple, an electrocardiographic sign, Yasser's sign, Wavy double, an electrocardiographic sign, and Movable-weaning off, an electrocardiographic phenomenon, are easy, simple electrocardiographic diagnostic, monitoring, and therapeutic signs. Unfortunately, their sensitivity and specificity have not yet been further studied.

Ethical approval and Informed consent

- Both Ethical approval and Informed consent were not considered.

Artificial intelligence (AI)

- Artificial intelligence (AI) was not used in the manuscript construction.

Conflicts of interest

- There are no conflicts of interest.

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Abbreviations

1,25(OH)₂D: 1,25-dihydroxyvitamin D
 AC: Adenyl cyclase
 AF: Atrial fibrillation
 AMI: Acute myocardial infarction
 Ca²⁺: Calcium
 CaSR: Calcium-sensing receptor
 CAS: Coronary artery spasm
 CHF: Congestive heart failure
 CMP: Cardiomyopathy
 CRF: Chronic renal failure
 EC: Extracellular
 CKD: Chronic kidney disease
 CKD-MBD: Chronic kidney disease with mineral bone disorders
 ECF: Extracellular fluid
 ECG: Electrocardiography
 DKA: Diabetic ketoacidosis
 HAp: Hydroxyapatite
 HCO₃⁻¹: Bicarbonate
 HCM: Hypercalcemia of malignancy
 IC: Intracellular
 iCa²⁺: Ionized calcium
 ICH: Intracerebral hemorrhage
 IHD; Ischemic heart disease
 K⁺: Potassium
 Mg²⁺: Magnesium
 MI: Myocardial infarction
 MWOP: Movable-weaning off, an electrocardiographic phenomenon
 PHP: Pseudohypoparathyroidism
 PTH: Parathyroid hormone
 PTH1R: PTHR, type 1 receptor
 PTHR: PTH receptor
 PTHrP: Parathyroid hormone-related peptide
 PO₄⁻³: Phosphate
 RBBB: Right bundle branch block

RT: Renal tubular
 STD: ST-segment depression
 STE: ST-segment elevation
 TdP: Torsades de pointes
 TWI; T-wave inversion
 VDR: Vitamin D receptor
 WDS: Wavy double, an electrocardiographic sign
 WTS: Wavy triple, an electrocardiographic sign

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Table 1 shows the etiologies of hypocalcemia.

Etiology	Some details	Keys
PTH Deficiency (Inadequate PTH production/Hypoparathyroidism)	Postsurgical	This is the most common cause of hypoparathyroidism (about 75% of cases) ^[42]
	Autoimmune	A common hereditary cause is autoimmune polyglandular syndrome type I ^[43]
	Abnormal parathyroid gland development	Such as DiGeorge syndrome, Charge Syndrome, Gracile bone dysplasia, Mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS), and Medium-chain acyl CoA dehydrogenase deficiency I ^[44]
	Parathyroid gland destruction	
	Functional hypoparathyroidism	Such as granulomatous diseases, hemochromatosis, Wilson disease, amyloidosis, aluminum-containing phosphate binders, or irradiation.
High PTH	PTH resistance (pseudohypoparathyroidism) (PHP)	HIV infection ^[45] Mg ⁺² depletion Magnesium excess ^[46] Genetic disorder ^[44]
	Absolute or relative vitamin D deficiency (Inadequate vitamin D)	Nutritional deficiency Lack of sunlight exposure Malabsorption Post-gastric bypass surgery End-stage liver disease
	Chronic kidney disease (CKD) production /Function)	Cirrhosis Chronic kidney disease, Vitamin D-dependent rickets type 1 and type 2 ^[42, 47-49]
	Pseudohypoparathyroidism (PHP)	Secondary hyperparathyroidism ^[42] Genetic disorder ^[44]
Drugs	Antiepileptics: Such as Denosumab ^[50] Cisplatin ^[51] Foscarnet ^[51] Cinacalcet ^[51] Antiepileptics ^[51] Aminoglycosides ^[51] Intravenous bisphosphonate therapy ^[51] Diuretics ^[28] Proton pump inhibitors ^[51]	Drug-related hypocalcemia is usually mild and asymptomatic but may be severe as well ^[51]
Miscellaneous etiologies	Massive blood transfusion of citrated blood	It causes an acute decline in iCa ⁺² ^[52-53]
	Pseudohypocalcemia	Low albumin states ^[42]
	Acidosis/alkalosis	Ionized calcium is increased in severe acidosis due to less albumin binding and vice-versa in severe alkalosis ^[42]
	Acute pancreatitis	
	Severe sepsis and critical illness	Hypocalcemia is part of Ranson's criteria and is associated with poor prognosis ^[54-55]
	Trauma and shock	Impaired PTH secretion, dysregulation of MG ⁺⁺ metabolism, catecholamine release shifting Ca ⁺² IC, and impaired calcitriol secretion are

Etiology	Some details	Keys
	Hypomagnesemia/hypermagnesemia Acute hyperphosphatemia Pregnancy Osteoblastic metastasis Severe COVID-19 infection	suggested potential causative factors ^[55-56] Hypocalcemia is frequently after severe trauma and shock ^[57] Induced PTH resistance ^[42] This is most common when the calcium-phosphate product is greater than 60 mg ² /dL ² ^[58] Hypocalcemia during pregnancy, mainly related to poor diet, hyperemesis gravidarum, or underlying diseases ^[59] Such as prostate cancer. This results from increased calcium uptake into the bones from increased osteoblastic activity ^[60] Hypocalcemia was associated with poor outcome in COVID-19 patients ^[61]

Abbreviations; Ca⁺²: Calcium, CKD: Chronic kidney disease, IC: Intracellular, iCa⁺²: Ionized calcium, Mg⁺²: Magnesium, PTH: Parathyroid hormone

Table 2 shows studies of Wavy triple, an electrocardiographic sign (WTS: Yasser's sign).

Study	Study Type	Study Population	Intervention	Duration	Positive outcome	Out-	Negative Outcome	Key Findings
Elsayed et al. (2019) ^[107]	Retrospective Observational Study	37 Patients with manifested or latent tetany	ECG	15 months	ECG recovery after Ca+2 administration		Partial ECG recovery in 2.7% (1 case)	WTS in 97.3% (36 cases) WDS in 2.7% (1 case)
Elsayed et al. (2020) ^[108]	Case report	1 Patient with hypocalcemia, WTS, tented T-wave, and CRF	ECG, ABG, O2 inhalation, echocardiography, and Ca+2 injection	24 hours	Dramatic improvement of clinical and ECG WTS after CA++ injection		NA	WTS, CRF, Tented T wave
Elsayed et al. (2021) ^[109]	Case report	1 Patient with phenytoin-induced WTS in a young epileptic	ECG, O2 inhalation, echocardiography, and Ca+2 injection	12 hours	Dramatic improvement of clinical and ECG WTS after Ca+2 injection		NA	Phenytoin-induced WTS in a young epileptic
Elsayed et al. (2021) ^[110]	Retrospective Observational Study	27 patients with WTS in DKA	Standard management of DKA without Ca+2 administration	15 months	Dramatic spontaneous improvement of both WTS and hypocalcemia after the management of DKA		Non-response in 3.7%.	DKA and WTS in ECG

Study	Study Type	Study Population	Intervention	Duration	Positive Outcome	Out- come	Negative Outcome	Key Findings
Elsayed et al. (2021) [111]	Case report	1 Patient with COVID-19 Pneumonia, AF, CAS, and WTS	Chest CT scan, ECG, O2 inhalation, and echocardiography	30 days	Gradual dramatic clinical, ECG, and radiological improvement		NA	COVID-19 Pneumonia, AF, CAS, and WTS
Elsayed et al. (2021) [112]	Case report	1 Patient with nodular COVID-19 pneumonia, WTS, and MWOP	Chest CT scan, ECG, O2 inhalation, and echocardiography	15 days	Dramatic clinical, ECG, and radiological improvement		NA	Nodular COVID-19 pneumonia, WTS, and MWOP
Elsayed et al. (2022) [113]	Case report	1 Patient with Camel-hump T-wave, Tee-Pee sign, WTS, hyperkalemia, COVID-19 pneumonia, and lacunar infarction	Chest CT scan, brain CT scan, ECG, O2 inhalation, and echocardiography	7 days	Dramatic outcome had happened after later management		Initial bad and deterioration outcome	Camel-hump T-wave, Tee-Pee sign, WTS, hyperkalemia, COVID-19 pneumonia, and lacunar infarction
Elsayed et al. (2023) [114]	Case report	1 Patient with false angina and mimic MI, WTS, and later mild COVID-19 pneumonia	ECG, chest CT scan, abdominal US, O2 inhalation, and ABG	40 days	Electrocardiographic and clinical stabilization		NA	False angina and mimic MI, WTS, and later mild COVID-19 pneumonia
Elsayed et al. (2023) [115]	Case report	1 Patient with severe COVID-19 pneumonia, PD, mental retardation, and WTS	ECG, chest CT scan, O2 inhalation, and ABG	30 days	Electrocardiographic and clinical stabilization		She carried a poor prognostic outcome and is indicating a high-risk condition.	Severe COVID-19 pneumonia, PD, mental retardation, and WTS
Elsayed et al. (2023) [116]	Case report	1 Patient with HTN PE, WTS, Tee-Pee sign, Camel-hump T-wave, and COVID pneumonia	Chest CT scan, ECG, and O2 inhalation	10 hours	Good outcomes with dramatic responses		Presence of several remarkable critical risk factors	HTN PE, WTS, Tee-Pee sign, Camel-hump T-wave, and COVID pneumonia

Table 2: Continue

Study	Study Type	Study Population	Intervention	Duration	Positive Outcome	Negative Outcome	Key Findings
Elsayed et al. (2023) [117]	Case report	1 Patient with ZK type I syndrome, anaphylaxis, WDS, and WTS post-ceftriaxone	ECG, O2 inhalation, and echocardiography	12 hours	Dramatic disappearance of ZK type I syndrome, anaphylaxis, and CAS. Complete clinical and ECG recovery	NA	ZK type I syndrome, anaphylaxis, WDS, and WTS post-ceftriaxone
Elsayed et al. (2023) [118]	Case report	1 Patient with WTS, hypocalcemic convulsion, DM, CRF, and stone	ECG, Chest CT, brain CT, abdominal CT, and Ca ⁺² therapy	48 hours	Dramatic improvement of clinical and ECG	NA	WTS accelerate the hypocalcemic convulsive diagnosis in generalized convulsions with CRF and Stones
Elsayed et al. (2023) [119]	Case report	1 Patient with COVID Pneumonia, Non-STEMI, QRS Fragmentation, and WTS in HL	CTPA, ECG, and O2 inhalation	12 hours	Unfortunately, the patient died within 12 hours of management	Bad response and poor outcomes in the presence of numerous remarkable serious risk factors	COVID Pneumonia, Non-STEMI, QRS Fragmentation, and WTS in HL
Elsayed et al. (2023) [120]	Case report	1 Patient with AMI, transient LBBB, AF, WPW syndrome, HL CAS, and WTS post-COVID-19 pneumonia	Chest CT scan, ECG, ABG, O2 inhalation, and echocardiography	5 days	Gradual dramatic clinical, ECG, and radiological improvement	There are constellation prognostic factors	AMI, transient LBBB, AF, WPW syndrome, HL CAS, and WTS post-COVID-19 pneumonia
Elsayed et al. (2024) [121]	Case report	1 Patient with QTc prolongation, epiglottitis, WTS, WDS, and Spike sign post-COVID pneumonia in a MVP	Chest X-ray, ECG, echocardiography, and O2 inhalation	Few days	Dramatic clinical, and ECG improvement	There are serious constellation serious risk factors	QTc prolongation, epiglottitis, WTS, WDS, and Spike sign post-COVID pneumonia in a MVP
Elsayed et al. (2024) [122]	Case report	1 Patient with KZ syndrome, syncope, WTS,	ECG, O2 inhalation, Ca ⁺² IVI, and echocardiography	3 days	Dramatic clinical, and ECG improvement	There are serious constellation serious risk	KZ syndrome, syncope, WTS, WDS, and possible PE after

Study	Study Type	Study Population	Intervention	Duration	Positive Outcome	Negative Outcome	Key Findings
		WDS, and possible PE after AstraZeneca ChAdOx1 nCoV-19 vaccine				factors	AstraZeneca ChAdOx1 nCoV-19 vaccine
Elsayed et al. (2024) [123]	Case report	1 Patient with sildenafil-induced allergic angina in elderly, sinus arrhythmia, WTS, WDS, and mild COVID infection	ECG, O2 inhalation, IV fluids, and echocardiography	3 days	Dramatic clinical, and ECG improvement	NA	Sildenafil-inducing allergic angina in elderly, sinus arrhythmia, WTS, WDS, and mild COVID infection
Elsayed et al. (2024) [124]	Case report	1 Patient with Kounis-Zafras syndrome from diclofenac K ⁺ and novel ECG signs post-CABG	ECG, echocardiography, and O2 inhalation	48 hours	Nearly complete clinical and ECG improvement	There are serious constellation serious risk factors	Kounis-Zafras syndrome from diclofenac K ⁺ and novel ECG signs post-CABG
Elsayed et al. (2024) [125]	Case report	1 Patient with tramadol-induced MI, HTN, PE, WTS, VF, and SCD with possible serotonin syndrome	ECG, O2 inhalation, and streptokinase IVI	Several minutes	Clinical retrograding terminating with sudden death	There are serious constellation serious risk factors.	Tramadol-induced MI, HTN PE, WTS, VF, and SCD with possible serotonin syndrome
Elsayed et al. (2021) [126]	Retrospective Observational Study	43 patients with manifested or latent tetany	Tests for latent tetany, ECG, and Ca ²⁺ administration	24 months	Movable-weaning off an electrocardiographic phenomenon	Variable associated risk factors	Variable changes in WTS and WDS in ECG

Abbreviations; ABG: Arterial blood gases AF: Atrial fibrillation, Ca²⁺: Calcium, CABG: Coronary artery bypass grafting, CAS: Coronary artery spasm, CRF: Chronic renal failure, CKD: Chronic kidney disease, CTPA : CT pulmonary angiography, , DM: Diabetes, ECG: Electrocardiography, DKA: Diabetic ketoacidosis, KZ: Kounis-Zafras syndrome, HL: High lateral, HTN: Hypertension, K⁺: Potassium, LBBB: Left bundle branch block, MI: Myocardial infarction, MVP: Mitral valve prolapse, MWOP: Movable-weaning off, an electrocardiographic phenomenon, NA: Non-available, O2: Oxygen, PD: Parkinson disease, PE: Pulmonary embolism, SCD: Sudden cardiac death, STEMI: ST-segment elevation myocardial infarction, VF: Ventricular fibrillation, WDS: Wavy double, an electrocardiographic sign, WTS: Wavy triple, an electrocardiographic sign

Table 3 shows studies of Wavy double, an electrocardiographic sign (WDS: Yasser's sign).

Study	Study Type	Study Population	Intervention	Duration	Positive Outcome	Negative Outcome	Key Findings
Elsayed et al. (2019) [107]	Retrospective Observational Study	37 Patients with manifested or latent tetany	ECG	15 months	ECG recovery after Ca ⁺² administration	Partial ECG recovery in 2.7% (1 case)	WTS in 97.3% (36 cases) WDS in 2.7% (1 case)
Elsayed et al. (2020) [127]	Case report	1 Patient with Hypocalcemia-induced Camel-hump T-wave, Tee-Pee sign, WDS, and Bradycardia in a Carpenter	ECG, ABG, , O2 inhalation, and Ca ⁺² administration	12 hours	Dramatic clinical, and ECG improvement	NA	Hypocalcemia-induced Camel-hump T-wave, Tee-Pee sign, WDS, and Bradycardia in a Carpenter
Elsayed et al. (2021) [126]	Retrospective Observational Study	43 patients with manifested or latent tetany	Tests for latent tetany, ECG, and Ca ⁺² administration	24 months	Movable-weaning off an electrocardiographic phenomenon	Variable associated risk factors	Variable changes in WTS and WDS in ECG
Elsayed et al. (2023) [117]	Case report	1 Patient with ZK type I syndrome, anaphylaxis, WDS, and WTS post-ceftriaxone	ECG, O2 inhalation, and echocardiography	12 hours	Dramatic disappearance of ZK type I syndrome, anaphylaxis, and CAS. Complete clinical and ECG recovery	NA	ZK type I syndrome, anaphylaxis, WDS, and WTS post-ceftriaxone
Elsayed et al. (2024) [121]	Case report	1 Patient with QTc prolongation, epiglottitis, WTS, and Spike sign post-COVID pneumonia in a MVP	Chest X-ray, ECG, echocardiography, and O2 inhalation	Few days	Dramatic clinical, and ECG improvement	There are serious constellation serious risk factors	QTc prolongation, epiglottitis, WTS, WDS, and Spike sign post-COVID pneumonia in a MVP
Elsayed et al. (2024) [122]	Case report	1 Patient with KZ syndrome, syncope, WTS, WDS, and possible PE	ECG, O2 inhalation, CA++ IVI, and echocardiography	3 days	Dramatic clinical, and ECG improvement	There are serious constellation serious risk factors	KZ syndrome, syncope, WTS, WDS, and possible PE after AstraZeneca ChAdOx1 nCoV-19 vaccine

Study	Study Type	Study Population	Intervention	Duration	Positive Outcome	Out-	Negative Outcome	Key Findings
		after Astra-Zeneca ChAdOx1 nCoV-19 vaccine						
Elsayed et al. (2024) [123]	Case report	1 Patient with sildenafil-inducing allergic angina in elderly, sinus arrhythmia, WTS, WDS, and mild COVID infection	ECG, O2 inhalation, IV fluids, and echocardiography	3 days	Dramatic clinical, and ECG improvement	NA		Sildenafil-inducing allergic angina in elderly, sinus arrhythmia, WTS, WDS, and mild COVID infection
Elsayed et al. (2024) [124]	Case report	1 Patient with Kounis-Zafras syndrome from diclofenac K ⁺ and novel ECG signs post-CABG	ECG, echocardiography, and O2 inhalation	48 hours	Nearly complete clinical and ECG improvement		There are serious constellation serious risk factors	Kounis-Zafras syndrome from diclofenac K ⁺ and novel ECG signs post-CABG

Abbreviations; ABG: Arterial blood gases Ca²⁺: Calcium, ECG: Electrocardiography, KZ: Kounis-Zafras syndrome, K⁺: Potassium MVP: Mitral valve prolapse O2: Oxygen, WDS: Wavy double, an electrocardiographic sign, WTS: Wavy triple, an electrocardiographic sign

Table 4 shows the studies of Movable-weaning off an electrocardiographic phenomenon (MWOP) in hypocalcemia.

Study	Study Type	Study Population	Intervention	Duration	Positive Outcome	Out-	Negative Outcome	Key Findings
Elsayed et al. (2021) [126]	Retrospective Observational Study	43 patients with manifested or latent tetany	Tests for latent tetany, ECG, and Ca ²⁺ administration	24 months	MWOP		Variable associated risk factors	Variable changes in WTS and WDS in ECG
Elsayed et al. (2021) [128]	Case report	1 Patient with elderly COVID-19 pneumonic patient with both Graded phenomenon and MWOP in severe aortic stenosis	O2 inhalation, ECG, chest CT scan, and echocardiography	26 days	Gradual dramatic clinical, ECG, and radiological improvement		There are complicated risk factors	Elderly COVID-19 pneumonic patient with both Graded phenomenon and MWOP in severe aortic stenosis

Study	Study Type	Study Population	Intervention	Duration	Positive Outcome	Negative Outcome	Key Findings
Elsayed et al. (2021) [129]	Case report	1 Patient with COVID-19 extensive bilateral pneumonia, variants IHD, and MWOP of hypocalcemia	ECG, chest CT scan, echocardiography, and O2 inhalation	24 days	Nearly complete clinical, radiological, and laboratory improvement	COVID-19 patient is an indicator for severe specific ischemic myocardial insult	COVID-19 extensive bilateral pneumonia, variants IHD, and MWOP of hypocalcemia
Elsayed et al. (2021) [130]	Case report	1 Patient with COVID-19 pneumonia, RBBB, MWOP, and S1S2S3 Pattern in DM, HTN, and stented IHD	Non-contrasted chest CT scan, ECG, O2 inhalation, and echocardiography	15 days	Dramatic of both clinical and radiological improvement	Multiple risks	COVID-19 pneumonia, RBBB, MWOP, and S1S2S3 Pattern in DM, HTN, and stented IHD
Elsayed et al. (2021) [131]	Case report	1 Patient with Mimic HL MI in chest tetany with mirror ECG change, MWOP	ECG, O2 inhalation, IV Ca ⁺² injection, and echocardiography	40 minutes	It signifies the role of O2 in both CAS and tetany. Nearly complete clinical and ECG improvement.	NA	Mimic HL MI in chest tetany with mirror ECG change, Movable phenomenon
Elsayed et al. (2021) [112]	Case report	1 Patient with nodular COVID-19 pneumonia, WTS, and MWOP	Chest CT scan, ECG, O2 inhalation, and echocardiography	15 days	Dramatic clinical, ECG, and radiological improvement	NA	Nodular COVID-19 pneumonia, WTS, and MWOP
Elsayed et al. (2023) [132]	Case report	1 Patient with acute pericarditis with MWOP and variant T-wave in underlying BER	ECG and echocardiography	48 hours	Piecemeal, spectacular clinical and ECG improvements	Serious probable expected outcomes	Acute pericarditis with MWOP and variant T-wave in underlying BER
Elsayed et al. (2023) [133]	Case report	1 Patient with lacunar infarction with MWOP, HTN emergency, mild	Chest CT scan, brain CT scan, ECG, O2 inhalation, and NTG IVI	3 days	Piecemeal spectacular clinical, ECG, and radiological improvement	There are serious remarkable constellation risk factors	Lacunar infarction with MWOP, HTN emergency, mild pneumonia, and Brugada syndrome post-

Study	Study Type	Study Pop-ulation	Intervention	Duration	Positive Out-come	Negative Outcome	Key Findings
		pneumonia, and Bru-gada syn-drome post-COVID-vac-cination					COVID-vaccina-tion

Abbreviations; ABG: Arterial blood gases, BER: Benign early repolarization, Ca⁺²: Calcium, CAS: Coronary artery spasm, DM: Diabetes, ECG: Electrocardiography, HL: High lateral, HTN: Hypertension, IHD; Ischemic heart disease, KZ: Kounis-Zafras syndrome, K⁺: Potassium, MI: Myocardial infarction, MVP: Mitral valve prolapse, MWOP: Movable-weaning off, an electrocardiographic phenomenon, NTG : Nitroglycerin, O2: Oxygen, RBBB: Right bundle branch block, WDS: Wavy double, an electrocardiographic sign, WTS: Wavy triple, an electrocardiographic sign

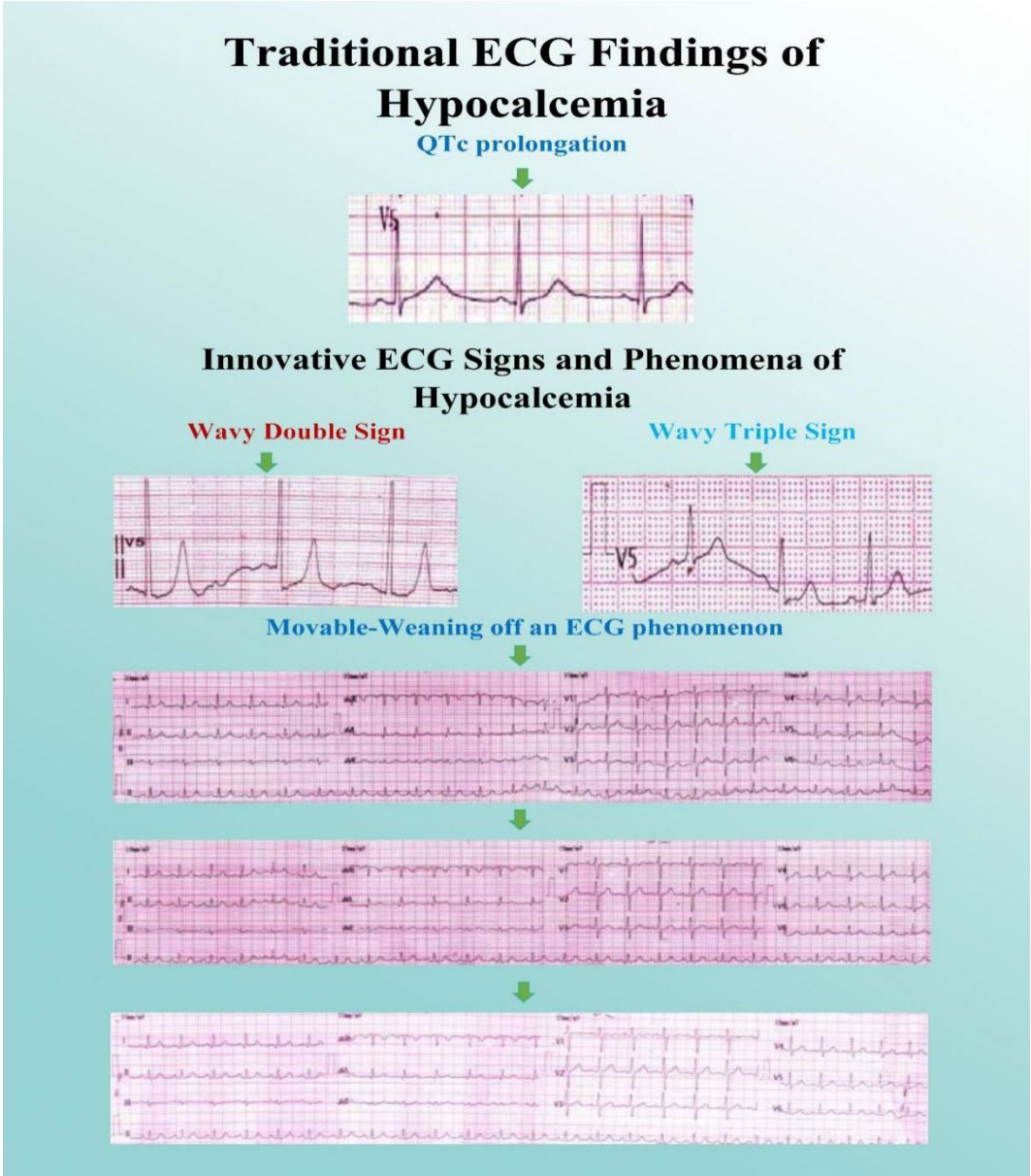


Figure 1 shows a graphical abstract of an innovative signs and phenomena of hypocalcemia

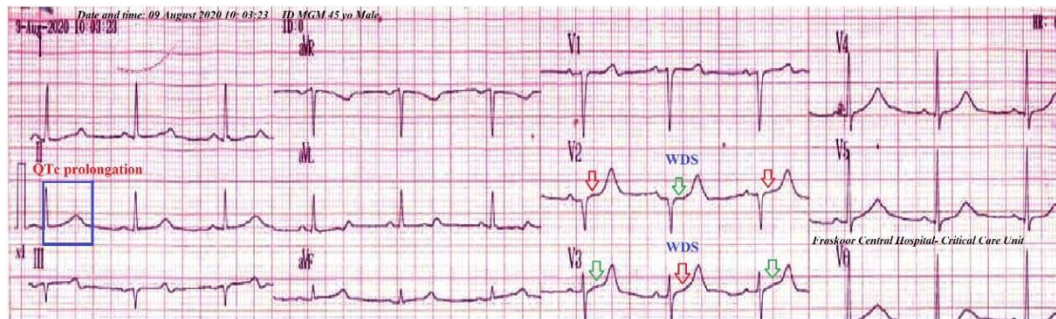


Figure 2 shows prolongation of QTc (blue rectangle) and a Wavy double sign (WDS, red and green arrows in V1-2) in a 45-year-old male teacher presented with tetany.



Figure 3 shows prolongation of QTc (blue golden rectangle), a Wavy triple sign (WTS; red, blue, and green arrows), and a Wavy double sign (WDS; green and blue arrows) in an 18-year-old female presented with tetany.

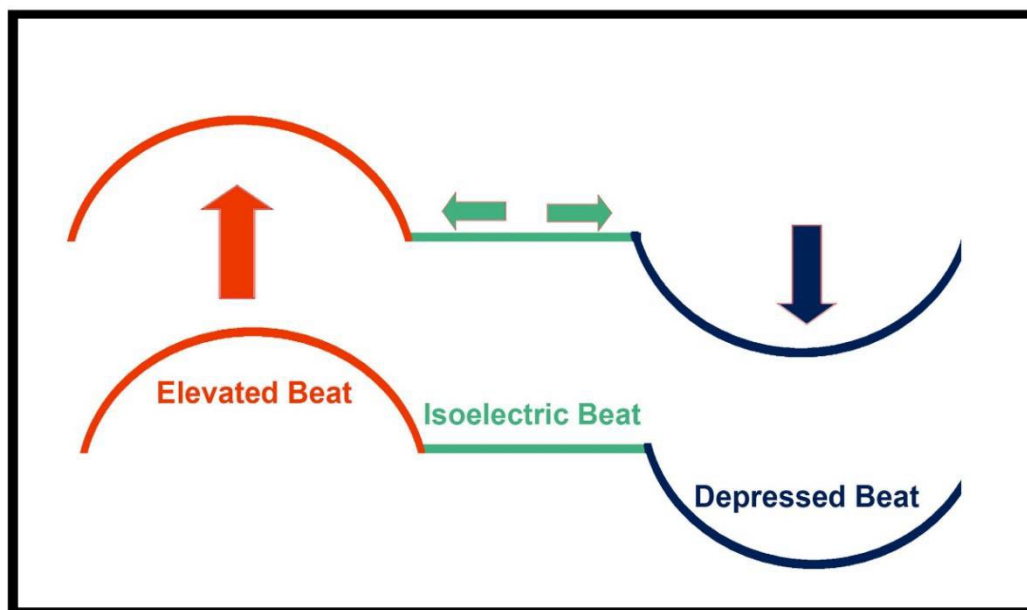


Figure 4 shows the author caricaturing a diagrammatic clarification of a Wavy triple sign.

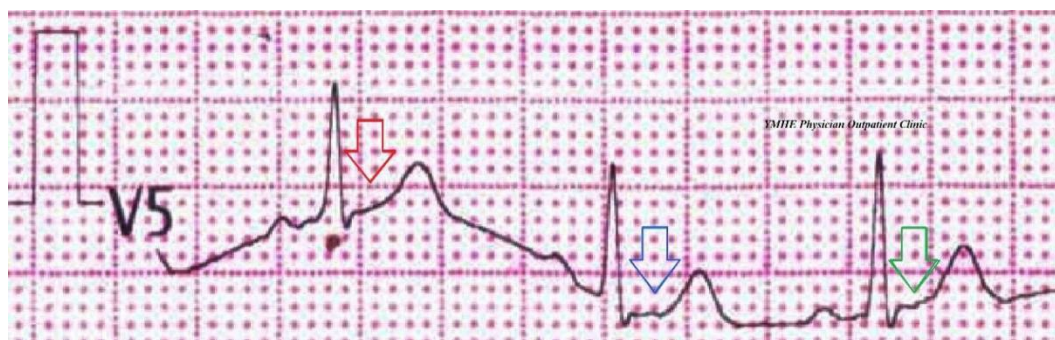


Figure 5 shows a Wavy triple sign (WTS; red, blue, and green arrows) in V5.

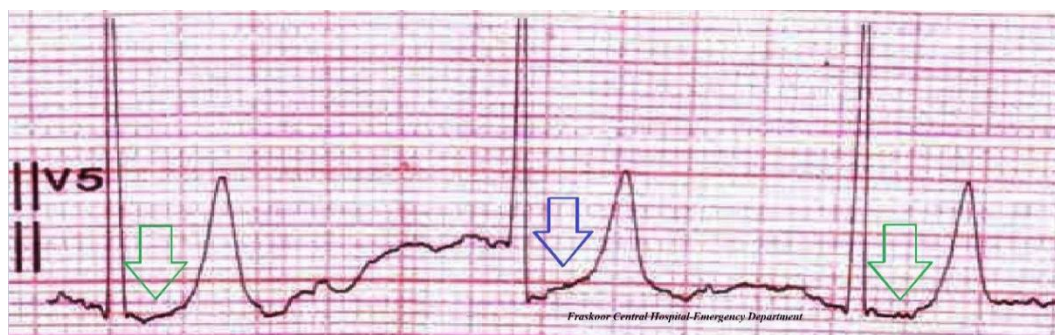
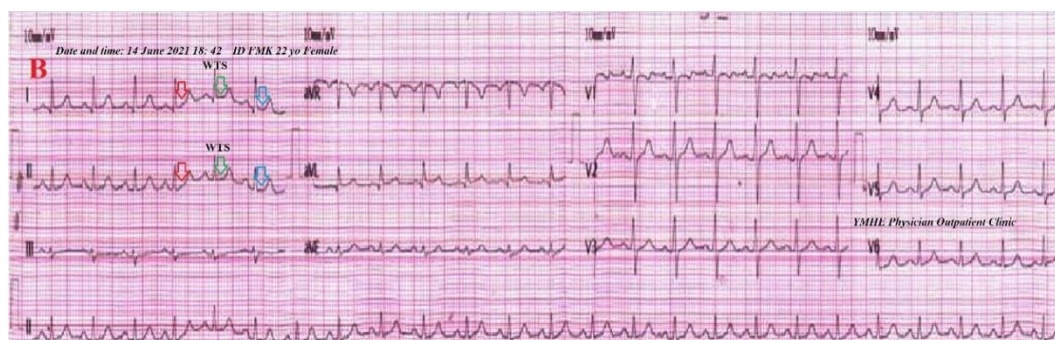
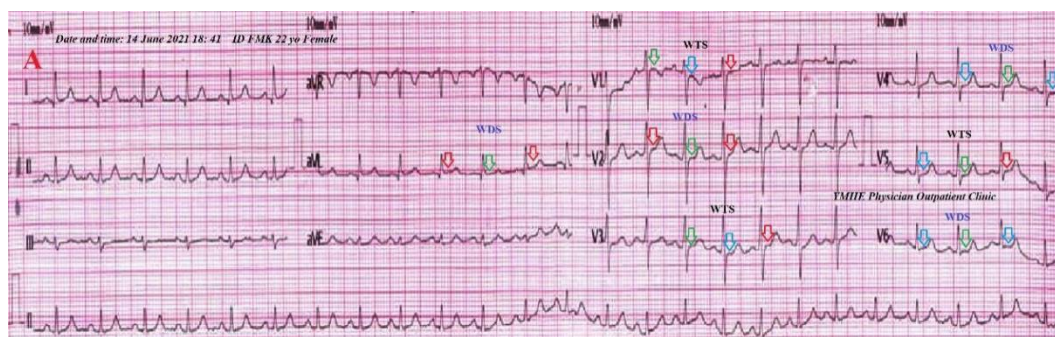


Figure 6 shows a Wavy double sign (WDS; green and blue arrows) in lead II.



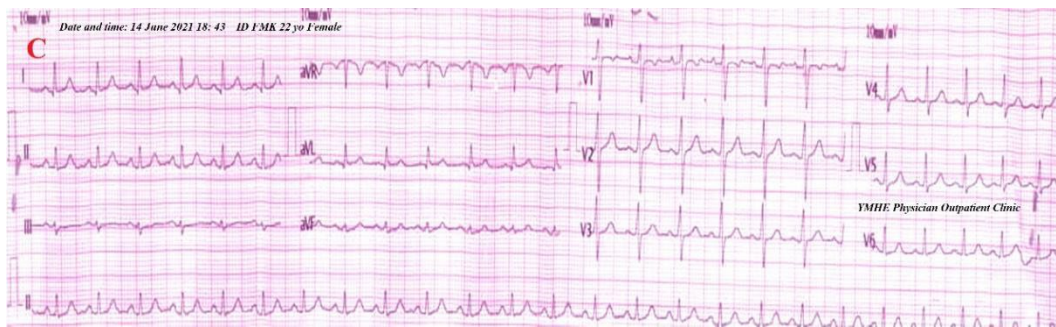


Figure 7 shows Movable-Weaning off an Electrocardiographic Phenomenon in Hypocalcemia, started as a WDS (aVL and V2, V4, and V6) and WTS (V1,-V3 and V5) (A), with lead changes in I, and II leads (B), then shows Movable-Weaning off in (C).