Reprint from The Review of DIABETIC STUDIES Vol 19 No 3 2023

The Review of DIABETIC STUDIES

RESEARCH

The Role of Vitamins B Complex in the Management of Diabetic Peripheral Neuropathy: an Electrophysiological Study

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Manuscript Submitted October 19, 2023; Resubmitted December 19, 2023; Accepted December 22, 2023

■ Abstract

Background: Diabetic neuropathy has an increasingly challenging clinician due to limited available therapeutic remedies, including vitamins, minerals, herbal remedies, and physical therapy. **Aim:** To evaluate the effect of vitamin B complex on diabetic peripheral neuropathy (DPNP) by assessment of nerve conductive study. **Methods:** Fifty diabetic patients with signs and symptoms of diabetic symmetrical peripheral neuropathy (DSPNP) enrolled in the study. A nerve conductive study (NCS) was done for all patients, according to the result of the NCS the patients were divided into 2 groups, group one include 36 patients with mild to moderate DSPNP, and group two consisted of 14 patients with severe DSPNP, both groups received vitamins B for 3 months. NCS was repeated every month of treatment for 3 successive months. **Results:** In a mild and moderate group there is a significant improvement in nerve conductive studies ($p<0.001$), while in severe group patients there was no such improvement. **Conclusion:** The present study demonstrated that vitamin B complex has a beneficial effect on mild to moderate cases of patients with DPNP.

Keywords: Diabetic Peripheral Neuropathy, Vitamin B Complex, Nerve Conductive Study.

1. Introduction

Hyperglycemia is a recurring metabolic condition known as diabetes mellitus (DM). It could be caused by an inability to produce enough insulin, a resistance to the peripheral effects of insulin, or both. Numerous organ systems can be damaged by chronic hyperglycemia, which can lead to incapacitating complications. Retinopathy, nephropathy, and neuropathy are the most common ones [1]. The international diabetes federation estimated that 425 million people had diabetes globally in 2017, and that number will rise to 628 million by 2045 as the disease's epidemiology has reached global proportions [2].

Diabetic peripheral neuropathy (DPNP) is a complication of both type I and type II diabetes mellitus [3] and is the most common diabetic neuropathy, expected to be in 47% of diabetics patients when diagnosed by nerve conductive study [4]. It has been estimated that at least half of patients with DM will develop DPNP in their life, and almost 20% presenting with neuropathic-related pains [5, 6]. The most frequent peripheral neuropathy in diabetes individuals is distal symmetrical polyneuropathy (DSPN) [7]. Diagnosis is challenging due to the wide variety of presentations and the fact that over 50% of diabetic peripheral neuropathies have no symptoms [8, 9].

Despite that the pathogenesis of DPNP is not well understood, most of the studies that focus on oxidative stress (OS) have concluded that it is the primary factor that contributes to the aetiology of DM and its complications [10-12]. Vitamin B12 deficiency has been associated with important neurological pathology, mainly peripheral neuropathy [13, 14]. It is also accompanied by the onset of diabetic neuropathy. The deficiency of vitamin B12 in patients with DPNP could be caused by the use of antidiabetic drugs such as metformin [15, 16]. Although ongoing efforts have been made in recent years to find a cure for DPNP, including the use of aldose reductase, tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors (SNRI), some anticonvulsants, opioid analgesics, diabetic neuropathy remains a persistent clinical challenge that is challenging to treat in many patients, and frequently the efforts become limited due to the different efficacy of these drugs [17], several of these medications were either unsuccessful or only somewhat beneficial at treating DPNP [4]. Additionally, many treatments lack enough evidence and frequently have undesirable side effects that restrict their therapeutic utility [18]. Therefore, individuals with diabetes who have neuropathies that are difficult or intractable to treat need more therapy alternatives. The current work's objective is to assess how vitamin B complex affects diabetic DPNP using nerve conductive experiments.

2. Subjects and Methods

The study had approval from the regional research scientific and ethics committee of Ninevah college of medicine and was performed during the period between the 1st of December 2021 to the 30th of April 2022 in the Al-Wafaa centre of diabetes management and research, and from the main diabetic private clinics in Mosul city.

Known cases of type II DM (according to American Diabetes Association Criteria) and is registered in Al-Wafaa Center, and patients from private specialist clinics with signs and symptoms of peripheral neuropathy (paresthesia, a burning sensation, numbness, loss of sensation and muscle cramps) enrolled in the study. To diagnose diabetic peripheral neuropathies, nerve conduction studies (NCS) were carried out using conventional supramaximal percutaneous stimulation (Nemus-2; Italy) of the lower limbs and surface recordings [19]. Three distinct nerves on each side—the Sural, Common Peroneal, and Posterior tibial nerves—were examined for distal latency (DL), compound motor action potential (CMAP), and nerve conductive velocity (NCV). The patients were separated into two groups based on the NCS results; group one consisted of 36 patients with mild to moderate DPNP, while group two consisted of 14 patients with severe DPNP. Vitamin B complex (vitamins B1 100 mg, B6 200 mg, and B12 200 µg) therapy was initiated in both groups for 3 months, and the effectiveness of the treatments was evaluated by repeating NCS every month for 3 consecutive months. The possibility of technical bias was decreased because the same physician used the same machine and industry-standard procedures to administer the NCS.

Statistical analysis: Results were analysed using GraphPad Prism (version 9.3.1). A series of unpaired t-tests were conducted between the before initiation of the therapy and thereafter to identify the statistically significant group at p-value (<0.05).

3. Results

A total of 50 chronic type 2 diabetic patients (age 51.58± 8.81 years with up to 7 years of diabetic diseases) were enrolled in the present study. Most of the enrolled patients were male (Males/Females were 39/11). Most of the patients were within normal BMI and body weight (Table 1).

Table 1: The Demographic Characteristics of Males and Females of the Studied Population.

Demographic Parameters	
Age(in years)	51.58 ± 8.81
Gender No.(%)	M=39 (78%)
	F=11 (22%)
Normal BMI	M =30(60%)
	F =17(34 %)
Overweight	M =2(4 %)
	F =1(2 %)
Duration (in years)	(7.24 ± 3.467)

3.1. The Electrophysiological Test

The data obtained from the electrophysiological test (EPT) for distal latency (DL), compound motor action potential (CMAP) and nerve conductive velocity (NCV) in the distal symmetrical peripheral neuropathy allowed the patients to be staged into Mild to Moderate (36 patients (72%) and severe (14 patients (28%). Electrophysiological test (EPT) has revealed that mild to moderate cases have responded to Vitamin B complex therapy only after 3 months of continuous therapy whereas no statistically significant differences existed across both time points (after 1 or 2 months) of vitamin B complex therapy. EPT of the posterior tibial nerve (PTN) has shown that the DL (ms) significantly reduced (P<0.05) after 3 months (Right, 4.3± 1.1; left, 4.2±1.1) compared to baseline conduction velocity (Right, 5.6 ±1.7; left, 5.5±1.7). The CMAP has significantly increased (P<0.05) after 3 months (Right, 7± 1.1; left, 6.6±1.1) compared to baseline power (Right, 4.1 ±1.3; left, 4.2±1.3). The NCV has shown significantly higher (P<0.05) after 3 months (Right, 36.8±9.4; left, 36±9.4) compared to baseline speed (Right, 28.2 ±5.8; left, 27.2±5.8) (Figure 1).

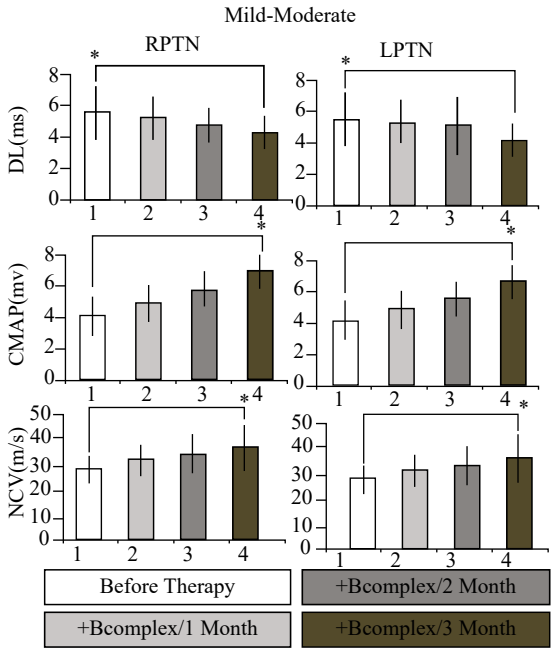

Figure 1: Electrophysiological Study of Posterior Tibial Nerve for Mild and Moderate Cases in Type 2 Diabetic Patients before Vitamin B Complex and after Three Successive Months. RPTN=Right Posterior Tibial Nerve, LPTN=Left Posterior Tibial Nerve DL=Distal Latency in Milliseconds, CMAP=compound Motor Action Potential(in millivolts), NCV=Nerve Conductive Velocity(meter per second). Data Expressed as Mean±SD. *Indicate Significant Differences at p<0.05 Compared to other Group.

However, when similar tests were applied for severe PTN cases the improvement was negative. There were no EPT parameter changes associated with vitamin B complex even after 3 months of continuous therapy compared to the levels before therapy (Figure 2).

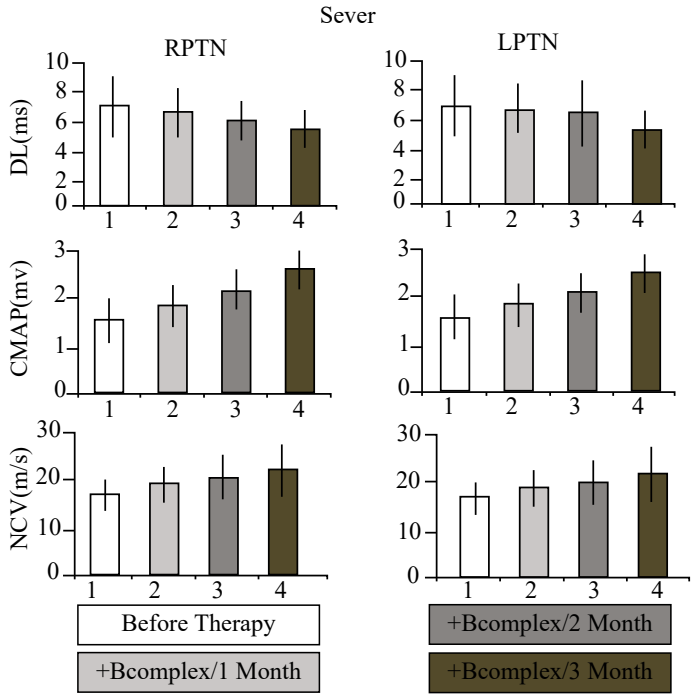

Figure 2: Electrophysiological Study of Posterior Tibial Nerve for Severe Cases in Type 2 Diabetic Patients before Vitamin B Complex and after Three Successive Months. RPTN=Right Posterior Tibial Nerve, LPTN=Left Posterior Tibial Nerve DL=Distal Latency, CMAP=Compound Motor Action Potential, NCV=Nerve Conductive Velocity. Data Expressed as Mean±SD.

EPT of common Peroneal nerves (CPN) has shown that the DL (ms) significantly reduced (P<0.05) after 3 months (Right, 4.4± 1.1; left, 4.3±1) compared to baseline conduction velocity (Right, 5.6 ±1.7; left, 5.7±1.7). The CMAP has significantly increased (P<0.05) after 3 months (Right, 7± 1.1; left, 6.9±1.2) compared to baseline power (Right, 5.1 ±1.3; left, 5.2±1.4). The NCV has shown significantly higher (P<0.05) after 3 months (Right, 36.9±9.4; left, 36±9.2) compared to baseline speed (Right, 29.1 ±5.8; left, 28.2±5.1) (Figure 3).

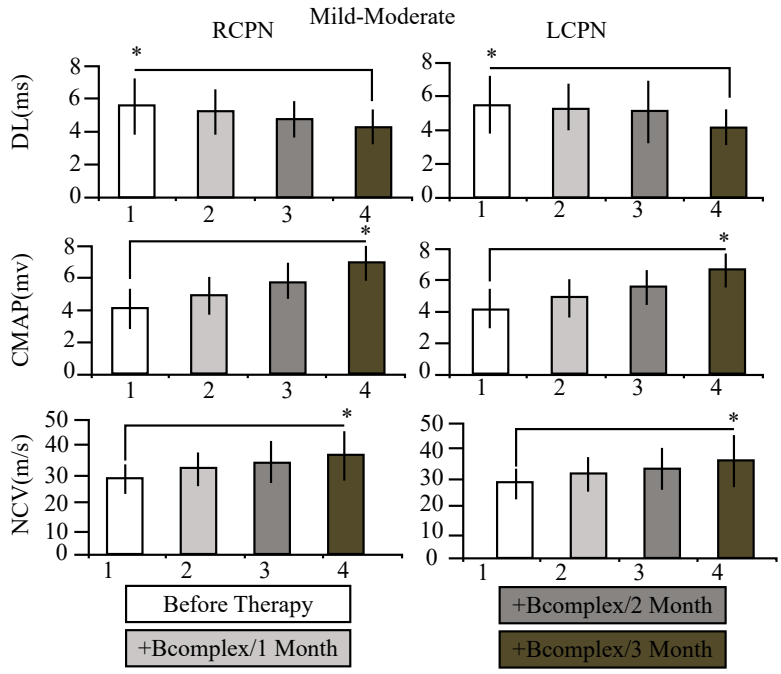

Figure 3: Electrophysiological Study of Common Peroneal Nerves for Mild and Moderate Cases in Type 2 Diabetic Patients before Vitamin B Complex and after Three Successive Months. RCPN=Right Common Peroneal Nerves, LCPN=left Common Peroneal Nerves, DL=Distal Latency, CMAP=Compound Motor Action Potential, NCV=Nerve Conductive Velocity. Data Expressed as Mean±SD. *Indicate Significant Differences at p<0.05 Compared to other Groups.

However, when similar tests were applied for severe CPN cases the improvement was negative. There were no EPT parameter changes associated with vitamin B complex even after 3 months of continuous therapy compared to the levels before therapy (Figure 4).

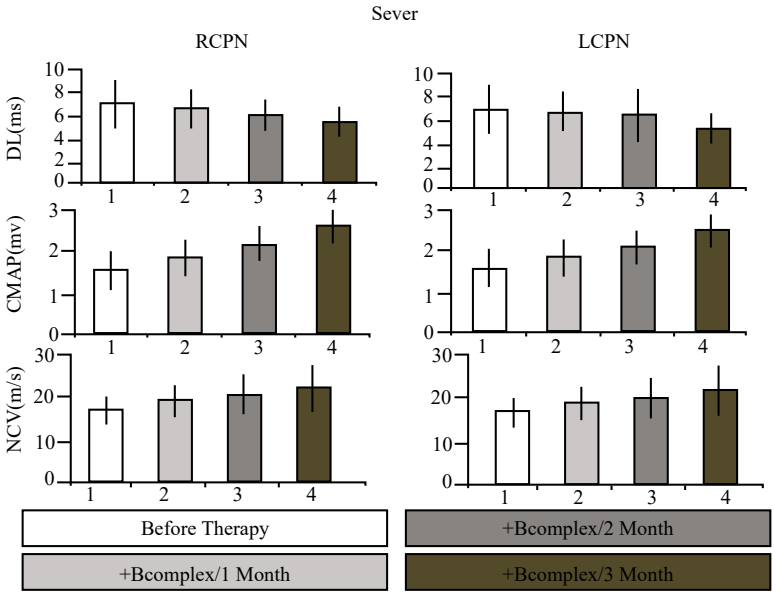

Figure 4: Electrophysiological Study of Common Peroneal Nerves for Severe Cases in Type 2 Diabetic Patients before Vitamin B Complex and after Three Successive Months. RCPN= Right Common Peroneal Nerves, LCPN= Left Common Peroneal Nerves, DL= Distal Latency, CMAP= Compound Motor Action Potential, NCV=Nerve Conductive Velocity. Data Expressed as Mean±SD.

EPT of sural nerve (SN) has shown that the DL (ms) significantly reduced (P<0.05) after 3 months (Right, 4.4± 1.3; left, 3.7±2.2) compared to baseline conduction velocity (Right, 6.9 ±1.1; left, 5.7±3.2). The CMAP has significantly increased (P<0.05) after 3 months (Right, 6.9± 1.4; left, 7±1) compared to baseline power (Right, 3.3 ±1.1; left, 5.4±1.4). The NCV has shown significantly higher (P<0.05) after 3 months (Right, 37±9.4; left, 35.9±8.9) compared to baseline speed (Right, 27 ±5.8; left, 27±7) (Figure 5).

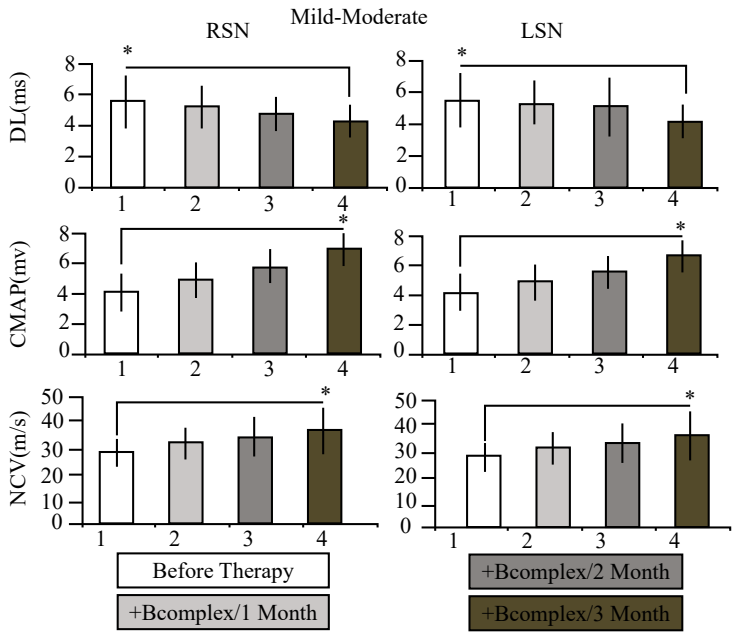

Figure 5: Electrophysiological Study of Sural Nerve for Mild and Moderate Cases in Type 2 Diabetic Patients before Vitamin B Complex and after Three Successive Months. RSN= Right Sural Nerve, LSN= Left Sural Nerve, DL= Distal Latency, CMAP=Compound Motor Action Potential, NCV=Nerve Conductive Velocity. Data Expressed as Mean±SD. *Indicate Significant Differences at p<0.05 Compared to other Groups.

However, when similar tests were applied for severe SN cases the improvement was negative. There were no EPT parameter changes associated with vitamin B complex even after 3 months of continuous therapy compared to the levels before therapy (Figure 6).

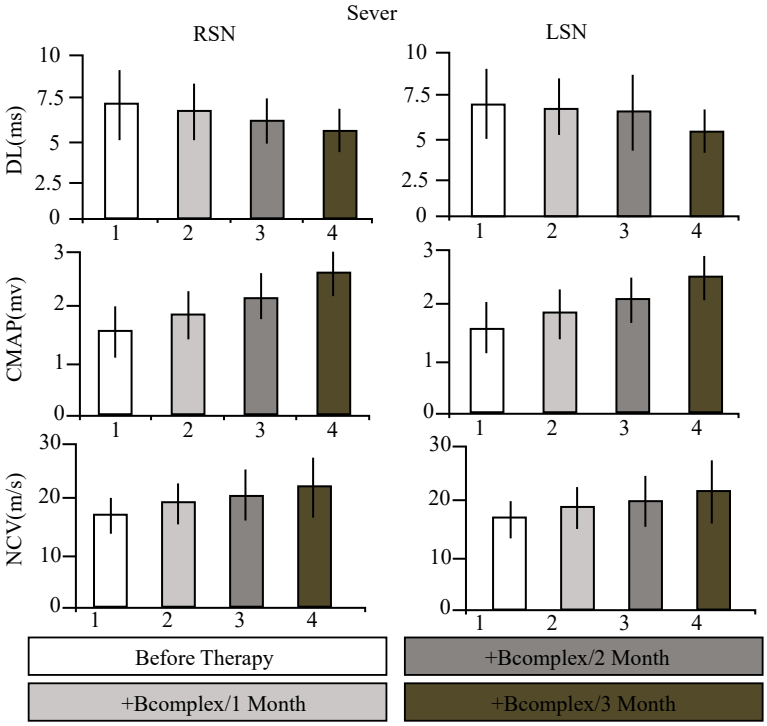

Figure 6: Electrophysiological Study of Sural Nerve for Severe Cases in Type 2 Diabetic Patients before Vitamin B Complex and after Three Successive Months. RSN=Right Sural Nerve, LSN=Left Sural Nerve, DL=Distal Latency, CMAP=Compound Motor Action Potential, NCV=Nerve Conductive Velocity. Data Expressed as Mean±SD.

4. Discussion

Despite extensive research, diabetic neuropathy is still a common clinical issue that is challenging to treat in the majority of patients. For diabetic neuropathies, there are various therapy options, however many of them are either ineffective or lose their effectiveness with time. In addition, many drugs have side effects that restrict their therapeutic utility and are poorly tolerated [18]. Additionally, there is no proof that any of the treatments used to treat the symptoms of diabetic peripheral neuropathy, including anticonvulsants, tricyclic antidepressants, opioids, or other analgesics, interfere with the pathogenesis of the condition [12].

In order to treat intractable diabetic neuropathy, new therapy alternatives are required. In this investigation, electrophysiological tests were used to evaluate the effectiveness of vitamins B complex (B1, B6, and B12) in patients with DPNP indications and symptoms. The motor conduction velocity of the peroneal and tibial nerves and the sensory conduction velocity of the sural nerves, both bilaterally, were reported to improve in this study's patients with mild to moderate PNP after treatment. A review of the literature provided limited information about the assessment of vitamin B on diabetic peripheral neuropathy electrophysiologically, the majority of studies assessed their effects by assessment of signs and symptoms of DPNP. According to Stracke *et al.*'s [20] old double-blind, randomized, controlled trial from 1996 [20], neurotropic B vitamins should be the first line of defense in the fight against diabetic polyneuropathy.

Along with improving the patients' subjective paresthesias, improvements in objective metrics were also made, including a reduction in the vibration perception threshold at the second metacarpal and metatarsal bones and an increase in peroneal nerve conduction velocity. The effectiveness of vitamin B12 in treating diabetic neuropathy was the subject of a systematic review conducted in 2005 by Sun *et al.* [21]. Their review found that, in some studies, treatment with combination drugs or vitamin B12 alone appeared to improve symptoms more than electrophysiologic outcomes, and that, in other studies, symptom relief was followed by improvement in objective parameters like vibration perception threshold (VPT) and nerve conduction. In a study done by Farvid *et al.* [22], following 4 months of treatment of type 2 diabetic neuropathy patients, symptoms were significantly reduced in the B complex vitamin-supplemented group as compared to placebo. Other human studies done by Rizvi *et al.* [23] confirmed the usefulness of vitamins B1, B6, and B12 in the management of diabetic neuropathy. For a long time, vitamin B12 has been used to treat pain and is categorised as an analgesic drug that reduces pain and oxidative stress by direct scavenging reactive oxygen free radicals. It is necessary for the metabolism of fatty

acids involved in the maintenance of nerve myelin and increases nerve myelination regeneration [6, 12].

The so-called Wallerian degeneration process is started by the nearby non-nervous cells when a peripheral nerve damage becomes central. The degeneration of axon components is thought to be a critical step in this phenomena, and it starts to happen within a few days after the trauma. The distal stump then perverts as macrophages are brought in to remove myelin and dead cells from the damage site. Additionally, subsequent nerve cell reactions encourage a setting that encourages the regeneration of axons during the ensuing months [24]. Certain B vitamins may help this nerve self - renewal, according to some research. Vitamins B1 (thiamine), B6 (pyridoxine), and B12 in particular (cobalamin). Those are also called "neurotropic" vitamins because of their significant effects in the neurological system [25]. Nerve injury can be a result of acute injury or in cases of chronic courses, such as diabetes. However, nerves are well regenerative, and regeneration is possible until approximately half of the fibers within a nerve are damaged [10, 17, 18]. This may explain the beneficial effect obtained in this study for mild to moderate cases and non-responsive effects for severe cases. The limitation of the present study include a small sample size, the study being a Unicenter study, there was no involvement of the elderly age group in the study, severe cases have shown no response to the therapy, we have no idea about the recurrence of the condition post-therapy.

5. Conclusion

The present study demonstrated that vitamin B complex has a beneficial effect on mild and moderate cases of patients with peripheral diabetic neuropathy, and can be used as an adjunct therapy. Sever cases failed to show improvement using these techniques, alternatively better clinical symptoms could be noticed by clinicians rather than this diagnostic technique.

Acknowledgements

We especially thank Ninevah University and AL-Noor University College for their provided facilities to accomplish this work.

Conflict of Interest Disclosures: The authors declare no conflict of interest.

Funding Statement: Self-Funded

Authors' Contributions: KSA, MIA, and MAA designed and conducted the research; KSA and MIA performed the data management and statistical analyses; KSA and MIA wrote the manuscript. KSA, MIA, and MAA reviewed/edited the manuscript for important intellectual content. KSA, MIA, and MAA read and approved the final manuscript.

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