

# **THE ROLE OF VITAMIN B COMPLEX AS AN ADJUVANT THERAPY FOR DIABETIC NEPHROPATHY IN PEDIATRIC PATIENTS WITH TYPE 1 DIABETES**

## ***Thesis***

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## ***Submitted By***

**Marwa Zaki Ibrahim**

*BSc of Pharmacy and Pharmaceutical Science (2012),  
Teaching Assistant in Clinical Pharmacy Department,  
Ahram Canadian University*

## ***Under The Supervision of***

**Prof. Mamdouh Ahmed Zaki**

*Professor of Clinical Pharmacy,  
Faculty of Pharmacy, Ahram Canadian University*

**Prof. Manal Hamed El- Hamamsy**

*Professor of Clinical Pharmacy,  
Faculty of Pharmacy, Ain Shams University*

**Prof. Nancy Samir El-barbary**

*Professor of Pediatrics,  
Faculty of Medicine, Ain Shams University*

***Ain Shams University***

***Faculty of Pharmacy***

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## *List of Abbreviations*

<b>Abb.</b>	<b>Full term</b>
<i>ACE</i> .....	<i>Angiotensin-converting enzyme inhibitors</i>
<i>ACR</i> .....	<i>Albumin / creatinine ratio</i>
<i>ADA</i> .....	<i>American Diabetes Association</i>
<i>AER</i> .....	<i>Albumin excretion rates</i>
<i>AGEs</i> .....	<i>Advanced glycation end products</i>
<i><math>\alpha</math>-KDH</i> .....	<i><math>\alpha</math>-ketoglutarate dehydrogenase</i>
<i>ARBs</i> .....	<i>Angiotensin II receptor blockers</i>
<i>ATP</i> .....	<i>Adenosine triphosphate</i>
<i>BMI</i> .....	<i>Body mass index</i>
<i>CKD</i> .....	<i>Chronic kidney disease</i>
<i>CoA</i> .....	<i>Conversion of methylmalonyl coenzyme A</i>
<i>CVD</i> .....	<i>Cardiovascular Disease</i>
<i>CysC</i> .....	<i>Cystatin C</i>
<i>DAG</i> .....	<i>Diacylglycerol</i>
<i>DCCT</i> .....	<i>Diabetes Control and Complications Trial</i>
<i>DKA</i> .....	<i>Diabetic ketoacidosis</i>
<i>DM</i> .....	<i>Diabetes mellitus</i>
<i>DN</i> .....	<i>Diabetic Nephropathy</i>
<i>EDIC</i> .....	<i>Epidemiology of Diabetes Interventions and Complications</i>
<i>ESRD</i> .....	<i>End stage renal disease</i>
<i>GABA</i> .....	<i><math>\gamma</math>- aminobutyric acid</i>
<i>GAD</i> .....	<i>Glutamic acid decarboxylase</i>
<i>GAD-65</i> .....	<i>Glutamate decarboxylase-65</i>
<i>GAPDH</i> .....	<i>Glyceraldehyde-3 phosphate dehydrogenase (</i>
<i>GDF-15</i> .....	<i>growth differentiation factor-15</i>
<i>GDM</i> .....	<i>Gestational diabetes mellitus</i>
<i>GFR</i> .....	<i>Glomerular filtration rate</i>

## *List of Abbreviations (cont...)*

<b>Abb.</b>	<b>Full term</b>
<i>GSH</i> .....	<i>Reduced glutathione</i>
<i>GSSG</i> .....	<i>Oxidized glutathione;</i>
<i>HbA1c</i> .....	<i>Hemoglobin A1c</i>
<i>HCC</i> .....	<i>Human Cys C</i>
<i>HIV</i> .....	<i>Human immunodeficiency virus</i>
<i>IDF</i> .....	<i>International Diabetes Federation</i>
<i>IF</i> .....	<i>Intrinsic factor</i>
<i>IgA</i> .....	<i>Immunoglobulin A</i>
<i>KDOQI</i> .....	<i>Kidney Disease Outcomes Quality Initiative</i>
<i>KIM</i> .....	<i>Kidney injury molecule</i>
<i>LADA</i> .....	<i>Latent autoimmune diabetes in adults</i>
<i>LDH</i> .....	<i>Lactic dehydrogenase;</i>
<i>MCV</i> .....	<i>Mean cell volume</i>
<i>MMA</i> .....	<i>Methylmalonic acid</i>
<i>MODY</i> .....	<i>Maturity-onset diabetes of the young</i>
<i>NAG</i> .....	<i>N-acetyl-b-D-glucosaminidase</i>
<i>NGAL</i> .....	<i>Neutrophil gelatinase-associated lipocalin</i>
<i>NKF</i> .....	<i>National Kidney Foundation</i>
<i>NMDA</i> .....	<i>N-methyl-D-aspartate</i>
<i>PARP</i> .....	<i>Poly (ADP-ribose) polymerase</i>
<i>PCA</i> .....	<i>Parietal cell antibodies</i>
<i>PDH</i> .....	<i>Pyruvate-dehydrogenase;</i>
<i>PKC</i> .....	<i>Protein kinase C</i>
<i>RAAS</i> .....	<i>Renin-angiotensin-aldosterone system</i>
<i>ROS</i> .....	<i>Reactive oxygen species</i>
<i>T1DM</i> .....	<i>Type 1 diabetes mellitus</i>
<i>T2DM</i> .....	<i>Type 2 diabetes mellitus</i>

## *List of Abbreviations (cont...)*

<b>Abb.</b>	<b>Full term</b>
<i>TC</i> .....	<i>Transcobalamin</i>
<i>TD</i> .....	<i>Thiamine deficiency</i>
<i>TGF-<math>\beta</math>1</i> .....	<i>Transforming growth factor-beta</i>
<i>TPP</i> .....	<i>Thiamine pyrophosphate</i>
<i>UAE</i> .....	<i>Urinary albumin excretion</i>
<i>WE</i> .....	<i>Wernicke's encephalopathy</i>
<i>YKL-40</i> .....	<i>Chitinase-3-Like Protein 1</i>

## Abstract

**Background and Objectives:** Diabetic nephropathy (DN) is a major microvascular complication of type 1 diabetes mellitus (T1DM). Although with established conventional therapy for glycemic and blood pressure control in patients with DN, and the use of inhibitors of the renin–angiotensin–aldosterone system (RAAS), a significant proportion of diabetic patients develop chronic kidney disease and progress to end-stage renal disease, indicating a need for additional treatments. Evidence for deficiencies of vitamins B1 and B12 in T1DM has been described in several publications. The role of vitamin B supplementation in preventing microvascular complications of diabetes has already been a focus of research for some years. Homocysteine levels are elevated in T1DM patients with DN. Supplementation of folic acid and vitamin B12 is known to reduce homocysteine levels. A combined therapy with vitamin B1 (thiamine) and vitamin B6 (pyridoxine) in patients with type 2 diabetes and nephropathy significantly decreased glycation of nuclear DNA in leukocytes. We studied the role of oral supplementation with vitamin B complex as an adjuvant therapy for diabetic nephropathy in children and adolescents with T1DM and assessed its relation to glycemic control, microalbuminuria and cystatin C as a marker of nephropathy.

**Methods:** This randomized controlled trial included 80 vitamin B12-deficient type 1 diabetic patients with nephropathy, despite oral angiotensin-converting enzyme inhibitors (ACE-Is). Enrolled patients aged 12-18 years with at least 5 years disease duration and glycated hemoglobin (HbA1c)  $\leq 8.5\%$ . Patients were randomly assigned into two groups; one group received oral supplementation with vitamin B complex (Neurorubine<sup>TM</sup> –Forte Lactab<sup>TM</sup> Mepha Pharma Egypt S.A.E manufactured by Medical Union Pharmaceuticals) and the other group did not. Both groups were followed-up for 12 weeks with assessment of FPG, HbA1c, urinary albumin excretion (UAE) and cystatin C.

**Results:** Baseline clinical and laboratory parameters were consistent between vitamin B and no vitamin B groups ( $p > 0.05$ ). After 12 weeks, supplementation with vitamin B complex resulted in significant decrease of fasting blood glucose, HbA1c, total cholesterol, triglycerides, UAE and cystatin C compared with baseline levels ( $p < 0.001$ ) and compared with patients without vitamin B treatment ( $p < 0.001$ ). No adverse reactions due to vitamin B complex were reported. Baseline vitamin B12 was negatively correlated to UAE ( $r = -0.877$ ,  $p = 0.009$ ) and cystatin C ( $r = -0.77$ ,  $p = 0.043$ ) among DN patients with vitamin B adjuvant therapy.

**Conclusions:** Oral supplementation with vitamin B complex for 12 weeks improved glycemic control and renal function. Thus, it could be a safe and effective strategy for treatment of pediatric type 1 diabetic patients with nephropathy.

**Keywords:** Type 1 diabetes, nephropathy, vitamin B complex, cystatin C.