بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

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The relationship between serum homocysteine level and cognitive function in elderly patients with chronic kidney disease

Thesis

Submitted in Partial Fulfillment for MD degree in Geriatrics and Gerontology

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Yumna Elgazzar

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List of Abbreviations

Abb.	Full term
%ICV	Percentage of intracranial volume
Aβ	Beta-amyloid plaques
AD	Alzheimer's disease
ADL	Activity of Daily Living
BBB	Blood brain barrier
CDR	Clinical Dementia Rating
CERAD-NB	Consortium to Establish a Registry for Alzheimer's disease neuropsychological battery
CKD	Chronic kidney disease
CVD	Cardiovascular disease
DM	Diabetes Mellitus
DTI	Diffusion tensor imaging
eGFR	Estimated glomerular filtration rate
ELIZA	Enzyme-Linked Immunosorbent Assay
ESRD	End-stage renal disease
FA	Folic Acid
FA	Fractional anisotropy
Hcy	Homocysteine
HHcy	Hyperhomocysteinemia
HTN	Hypertension
MCI	Mild cognitive impairment
MD	Mean diffusivity
MDRD	Modification of Diet in Renal Disease
Met	Methionine
mGluR1	Metabotropic glutamate receptors subtype1
MMSE	Mini Mental State Examination Scores
MOCA	Montreal Cognitive Assessment
MRI	Magnetic resonance imaging

List of Abbreviations Cont...

Abb.	Full term

NAC ..... N-acetylcysteine
NF-KappaB……..Nuclear factor kappa B
NFTs……..Neurofibrillary tangled
NMDA ..... N-methyl-D-aspartate
PTH ..... Parathyroid hormone
RRT .....Renal replacement therapy
SAH……...S-adenosyl homocysteine
SAM……...S-adenosyl methionine
tHcy……...Total plasma homocysteine
VaD..... Vascular dementia
VAT..... Vascular access thrombosis
VISP ..... Vitamin Intervention for Stroke Prevention
VITATOPS ..... Vitamins To Prevent Stroke
VTE..... Venous thromboembolism
WMLs ..... White matter lesions

INTRODUCTION

Patients with chronic kidney disease (CKD) have been found to have cognitive impairment. However, the core features and clinical correlates of the development of cognitive impairment and chronic kidney disease are still unclear. Cognitive impairment was described as an occult burden prevalent in CKD and end-stage renal disease (ESRD) patients. Several studies have suggested its occurrence in earlier stages of kidney disease but unacknowledged as a significant public health burden ***(Etgen et al., 2012; Sarnak, 2013; Heaf, 2017)***.

The *American Journal of Kidney Diseases* added to the evolving story of cognitive impairment in kidney disease by measuring mild and severe cognitive impairment in hemodialysis and peritoneal dialysis patients, this came to a prevalence of cognitive impairment anywhere from 30 to 70% ***(Griva et al., 2010)***.

CKD patients are at higher risk of cognitive decline and even dementia. Investigation of the clinical correlates of cognitive impairment in CKD could potentially result in the identification of treatment targets in order to modify the poor cognitive outcome ***(Tamura et al., 2016).***

Cognitive impairment in CKD is associated with poorer clinical outcomes, including a higher admission rate, a greater duration of hospitalization, more difficulty adhering to

medications, a poorer quality of life and a higher mortality rate ***(Rodriguez-Angarita et al., 2016)***.

Patients with CKD have higher levels of serum homocysteine Hcy than subjects without CKD. Homocysteine is primarily transsulfurated in the kidney and deficiency of this renal transsulfuration contributes to elevation of plasma Hcy ***(Li et al., 2007; Van Guldener et al., 2005).***

Homocysteine is derived from the demethylation of the essential amino acid methionine. Remethylation occurs by two main pathways: the first uses folate and vitamin B12 as cofactors, while the second, transsulfuration, uses vitamin B6 as a cofactor ***(Skovierova et al., 2016)***.

Homocysteine may affect cognitive function through impairing methylation of myelin sheath or the excitotoxic effect of homocysteine metabolites on N-methyl-D-aspartate glutamate receptors which markedly enhances the vulnerability of neurons to oxidative stress and injury ***(Kamat et al., 2013)*** which has emerged as an independent risk factor for several neurodegenerative diseases such as vascular dementia, Alzheimer's disease (AD) and stroke ***(Zhuo et al., 2011).***

Serum homocysteine has been associated with atrophic changes in the brain and is considered a marker for low serum vitamin B12 and folate. Studies have reported raised serum homocysteine, low serum vitamin B12 and low serum folate to