بسم الله الرحمن الرحيم

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Relation of Serum Aluminum Level to Uremic Pruritus in ESRD Patients on Maintenance Hemodialysis

Thesis

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List of Abbreviations

Abb.	Full term
25(OH)D-1-alpha hydroxylase	25 hydroxyvitamin D-1 alpha hydroxylase
ACEIs	Angiotensin converting enzyme inhibitors
ACR	Urinary albumin-creatinine ratio
Al	Aluminum
ARBs	Angiotensin receptor blockers
ATN	Acute tubular necrosis
CaSR	Calcium-sensing receptor
CKD	Chronic kidney disease
CKD-aP	CKD–associated pruritus
CRP	C - reactive protein
CVD	Cardio-vascular diseases
DM	Diabetes mellitus
DOPPS	Dialysis Outcomes and Practice Patterns Study
eGFR	Estimated glomerular filtration rate
ESA	Erythropoiesis-stimulating agents
ESRD	End stage renal disease
FGF-23	Fibroblast growth factor 23
FSGS	Focal segmental glomerulosclerosis
GLA	Gamma-linolenic acid
GN	Glomerulonephritis
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HD	Hemodialysis
HTN	Systemic hypertension
ISS	Itch severity scale
IV	Intravenous
KDIGO	Kidney Disease Improving Global Outcomes
KDOQI	The National Kidney Foundation–Kidney Disease Outcomes Quality Initiative
KDQOL	Kidney Disease Quality of Life
KDQOL-SF	KDQOL -Short Form
NRS	Numeric rating scale
NSAIDs	Non-steroidal anti-inflammatory drug
PCS	Physical component summary
PD	Peritoneal dialysis

Abb.	Full term
PKD	Polycystic kidney disease
PTH	Parathyroid hormone
QoL	Quality of life
RBCs	Red blood cells
rHuEPO	Recombinant human erythropoeitin
RRT	Renal replacement therapy
SCN	Sickle Cell Nephropathy
SGLT-2	Sodium-glucose transporter 2
TSAT	Transferrin saturation
UP	Uremic Pruritus
URR	Urea reduction ratio
UVB	Ultraviolet B
VAS	Visual analogue scale
VRS	Verbal rating scale
WBCs	White blood cells

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INTRODUCTION

Uremic pruritus (UP) is a common symptom in end stage renal disease (ESRD) patients maintained on regular hemodialysis (HD). The pathogenesis of Uremic pruritus is complex.

Aluminum (Al) is a common metal that is toxic to patients undergoing HD and also is a common human allergen which can cause immune reaction. Despite that severe (Al) toxicity in patients on maintenance HD is now uncommon due to the removal of (Al) from water used for dialysis by reverse osmosis and deionization as well as the use of widely available non-aluminum-containing phosphate binders. However, controlling serum (Al) levels remains an important issue for patients on regular HD. The possible sources of aluminum accumulation in patients on regular HD are oral (aluminum-containing phosphate binders and antacids) and injectable medications (calcitriol, vitamins B complex, iron and erythropoietin) that are commonly administered to dialysis patients, and (Al) removal by dialysis is not efficient ***(Tsai et al., 2018).***

Uremic pruritus (UP) is a common and unpleasant symptom in patients with ESRD. It impacts the quality of life and is associated with increased mortality in HD patients ***(Aucella and Gesuete, 2009).***

The prevalence of UP ranges from 42% to 90% ***(Liu et al., 2017)***.

Despite the high prevalence of UP, its pathogenesis is multi-factorial and poorly understood. The main hypotheses of UP include the loss of normal skin function, inflammation, dysregulation of the endogenous opioidergic system and central/peripheral neural systemic dysfunction. Other factors that have also been implicated in the pathogenesis of UP include xerosis, increased parathyroid hormone level, calcium phosphate-containing precipitates, iron deficiency anaemia, hepatitis virus infection and others ***(Chiu et al., 2008).***

(Al) is a toxic metal in humans, and its cumulative effects have been shown to be particularly detrimental to the health of ESRD patients. (Al) is cleared from the blood exclusively by glomerular filtration. Thus, patients with renal failure accumulate (Al) and are the only routine patient group likely to be at risk of (Al) toxicity. (Al) overload results in accumulation principally in the skeleton and the brain and manifests with osteomalacia (resistant to vitamin D therapy), bone and muscle pain, iron-resistant microcytic anaemia, and neurologic abnormalities including speech disorders, encephalopathy and dementia. The (Al) per se only seems to be an issue if given concurrently with sodium citrate which dramatically increases (Al) uptake, and in dialysis patients this leads to very high plasma levels ~2000 μg/L (~75 μmol/L) which

can result in potentially fatal neurological toxicity ***(Sharma et al., 2015).***

The major sources of (Al) in maintenance HD patients are the water used for dialysate solution and Al-containing phosphate binders. Since the 1980s, pretreatment of tap water by reverse osmosis and deionization has significantly reduced the Al concentration in dialysate solution. Also the use of widely available non-aluminum-containing phosphate binders decreased risk of aluminum toxicity. However, controlling serum (Al) levels remains an important issue for patients on regular HD. (Al) removal by dialysis is not efficient, and the possible sources of (Al) accumulation in patients on HD are oral (aluminum-containing phosphate binders and antacids) and injectable medications (calcitriol, vitamins B complex, iron and erythropoietin) that are commonly administered to dialysis patients. The National Kidney Foundation–Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines recommend that the baseline serum (Al) level should be below 20 ng/mL and that (Al) levels and risk for (Al) toxicity should be assessed at least once per year ***(Jaffe et al., 2005).***

Friga et al., **(1997)** demonstrated a positive correlation between serum (Al) levels and UP in 94 long-term HD patients. However, few studies have investigated the association between serum (Al) levels and UP since Friga's study. In particular, the association between serum Al level and UP is uncertain in maintenance HD patients**.**

Aim of the work

To determine the prevalence of serum aluminum level among HD patients.

To assess the relationship between serum aluminum level and uremic pruritus in HD patients.

END STAGE RENAL DISEASE

Chronic kidney disease (CKD) is defined as the presence of kidney damage or an estimated glomerular filtration rate (eGFR) less than 60 ml/min/1.73 m2, persisting for 3 months or more, irrespective of the cause ***(Levin et al., 2013).***

It is a state of progressive loss of kidney function ultimately resulting in the need for renal replacement therapy (RRT) (dialysis or transplantation). Renal damage refers to pathologic abnormalities either suggested by imaging studies or renal biopsy, abnormalities in urinary sediment, or increased urinary albumin excretion rates. The 2012 Kidney Disease Improving Global Outcomes (KDIGO) CKD classification recommends details about the cause of the CKD and classifies into 6 categories based on GFR (G1 to G5 with G3 split into 3a and 3b). It also includes the staging based on three levels of albuminuria (A1, A2, and A3), with each stage of CKD being sub-categorized according to the urinary albumin-creatinine ratio (ACR) in (mg/gm) or (mg/mmol) in an early morning "spot" urine sample ***(Vaidya and Aeddula, 2020).***

The 6 categories include:

- G1: GFR 90 ml/min per 1.73 m2 and above
- G2: GFR 60 to 89 ml/min per 1.73 m2
- G3a: GFR 45 to 59 ml/min per 1.73 m2