ISSN 2347-6893

Study of serum 25-hydroxyvitamin D in critically ill patients with acute kidney injury

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ABSTRACT

Acute renal failure (ARF) has traditionally been defined as the abrupt loss of kidney function that results in retention of urea and other nitrogenous waste products and dysregulation of extracellular volume and electrolytes **(1).** 25(OH)D deficiency prior to hospital admission might be linked to acute kidney injury in a critically ill patient population **(2).**

Eighty patients were selected from ICU of Ahmed Maher Teaching Hospital, and informed consent was obtained from all patients. This study was approved ethically by the local authority of the hospital and the patients were concented to do this study. The selected patients were subjected to**:** history taking, full clinical examination, laboratory investigations, serum 25-hydroxyvitamin D, blood urea and serum creatinine, eGFR, CBC,serum calcium,serum phosphorus, lipid profile, serum albumin, fasting and 2h postprandial blood sugar and urine analysis.

There was significant difference between groups on regard age (AKI group was 58.2±10.6 and non AKI group 65.1±11.3). There was significant association between mortality and AKI as 20% of AKI group died while no one in other group died. There was significant association between 25 (OH)D deficiency and AKI as 75% of AKI group had 25 (OH)D deficiency while other group hadn't any one. There was significant association between mortality and 25 (OH)D deficiency as 26.7% of 25 (OH)D deficiency group died while no one in other group died. There was significant association between 25 (OH)D deficiency and AKI as 100% of 25 (OH)D deficiency had AKI while 7.7% only of other group had AKI. There was significant association between AKI and level of 25 (OH)D and kappa for agreement was 0.95. 25 (OH)D was a high validity tool for detection of AKI. There was significant association between mortality and level of 25 (OH)D and kappa for agreement was 0.84. 25 (OH)D was high validity tool for detection of mortality. GFR<90 , UTI, DM, high level of serum creatinine and high level of blood urea were significant risk factors for AKI and 25 (OH)D deficiency was a highly significant risk factors for AKI. AF, GFR<90 , high level of creatinine and high level of urea were significant risk factors for mortality and 25 (OH)D deficiency was highly significant risk factors for mortality

Deficiency of 25-hydroxyvitamin D is a significant predictor of acute kidney injury and mortality in a critically ill patient population.

Academic Discipline And Sub-Discipline

Internal medicine

SUBJECT CLASSIFICATION

Nephrology

TYPE (METHOD/APPROACH*)*

Cohort study

Keywords

Vitamin D; acute kidney injury.

Council for Innovative Research

Peer Review Research Publishing System

Journal: Journal of Advances in Biology

Vol. 6, No. 1

editorsjab@gmail.com , editor@cirjab.com

ISSN 2347-6893

1.0 INTRODUCTION

Acute renal failure (ARF) has traditionally been defined as the abrupt loss of kidney function that results in the retention of urea and other nitrogenous waste products and dysregulation of extracellular volume and electrolytes **(1).**

The causes of acute kidney injury are commonly categorized into prerenal, intrinsic, and postrenal. Prerenal causes of AKI ("pre-renal azotemia") are those that decrease effective blood flow to the kidney. Intrinsic AKI can be due to damage to the glomeruli, renal tubules, or interstitium. Common causes of each are glomerulonephritis, acute tubular necrosis (ATN), acute interstitial nephritis (AIN) and tumor lysis syndrome**.** Postrenal AKI is a consequence of urinary tract obstruction. This may be related to benign prostatic hyperplasia, kidney stones, obstructed urinary catheter, bladder stone, bladder, ureteral or renal malignancy acute Kidney Failure Symptoms **(3).**

The following symptoms may occur with acute kidney failure. Some people have no symptoms, at least in the early stages. The symptoms may be very subtle. The deterioration of renal function may be discovered by a measured decrease in urine output. Often, it is diagnosed on the basis of blood tests for substances normally eliminated by the kidney: urea and creatinine. Both tests have their disadvantages. For instance, it takes about 24 hours for the creatinine level to rise, even if both kidneys have ceased to function. A number of alternative markers has been proposed (such as NGAL, 11KIM-1, IL18 and cystatin C), but none are currently established enough to replace creatinine as a marker of renal function. Sodium and potassium, two electrolytes that are commonly deranged in people with acute kidney injury, are typically measured together with urea and creatinine **(4).**

Rifle criteria consists of three graded levels of injury (Risk, Injury, and Failure) based upon either the magnitude of elevation in serum creatinine or urine output, and two outcome measures (Loss and End-stage renal disease) **(5).**

The management of AKI hinges on identification and treatment of the underlying cause. In addition to treatment of the underlying disorder, management of AKI routinely includes the avoidance of substances that are toxic to the kidneys, called nephrotoxins. These include NSAIDs such as ibuprofen, iodinated contrasts such as those used for CT scans, many antibiotics such as gentamicin, and a range of other substances **(6)**.

The myriad causes of intrinsic AKI require specific therapies. For example, intrinsic AKI due to Wegener's granulomatosis may respond to steroid medication. Toxin-induced prerenal AKI often responds to discontinuation of the offending agent, such as aminoglycoside, penicillin, NSAIDs, or paracetamol. If the cause is obstruction of the urinary tract, relief of the obstruction (with a nephrostomy or urinary catheter) may be necessary **(7).**

The use of diuretics such as furosemide, is widespread and sometimes convenient in ameliorating fluid overload, and is not associated with higher mortality (risk of death) **(8).**

Renal replacement therapy, such as with hemodialysis, may be instituted in some cases of AKI . Acute kidney injury (AKI) is common in hospitalised patients, especially in those who are critically ill **(9).**

Vitamin D is a group of fat-soluble secosteroids responsible for intestinal absorption of calcium and phosphate. In humans, the most important related compounds of vitamin D are vitamin D2 (ergocalciferol) and vitamin D (Cholecalciferol). Vitamin D3 and vitamin D2 are unique as they constitute what we know as vitamin D and can be ingested from the diet and/or supplements. The body can also synthesize vitamin D (from cholesterol) when sun exposure is adequate **(10).**

In the liver vitamin D is converted to calcidiol, which is also known as calcifediol (INN), 25-hydroxycholecalciferol, or 25-hydroxyvitamin D — abbreviated 25(OH)D3; and which is the specific vitamin D3 metabolite that is measured in serum to determine a person's vitamin D3 status. Part of the calcidiol is converted by the kidneys to calcitirol, the biologically active form of vitamin D Calcitriol circulates as a hormone in the blood, regulating the concentration of calcium and phosphate in the blood stream and promoting the healthy growth and remodeling of bone. Calcidiol is also converted to calcitriol outside of the kidneys for other purposes, such as the proliferation, differentiation and apoptosis of cells; calcitriol also affects neuromuscular function and inflammation **(11).**

25(OH)D deficiency prior to hospital admission might be linked to acute kidney injury in a critically ill patient population **(2).**

Potential mechanisms of how a deficiency in vitamin D could predispose individuals to increased risk of acute renal failure include dysregulation of the immune system, predisposing patients to sepsis, endothelial dysfunction and prevention of healing of renal ischemia-reperfusion injury. Toll-like receptors and the renin-angiotensin-aldosterone system are mediators of vitamin D effects **(12)**.

2.0 AIM OF THE WORK

The aim of this work is to study serum 25-hydroxyvitamin D level as a predictor of acute kidney injury in the critically ill patients.

3.0 MATERIAL AND METHODS

Our study is a cohort study which is conducted on eighty patients over 6 months from December 2013 to May 2014 selected from ICU of Ahmed Maher Teaching Hospital in Cairo, and informed consent was obtained from all patients.

Patients who received hemodialysis prior to hospitalization or critical care admission were excluded. patients who did not have serum creatinine drawn prior to hospital admission were identified and excluded.The patients were divided according to the presence or absence of acute kidney injury into:

ISSN 2347-6893

1-AKI group: 20 patients (9 females and 11 males) with mean age 58.2±10.6 years.

2-Non AKI group:60 patients (29 females and 31 males) with mean age 65.1±11.3 years.

And according to the presence or absence of 25-OH-D3 deficiency into:

1 Non 25 (OH)D Deficiency group: 65 patients (31 females and 34 males) with mean age 64.8±11.5 years.

2- 25 (OH)D Deficiency group: : 15 patients (7 females and 8 males) with mean age 58.8±10.8 years.

All included patients were subjected to the following:

Full history taking ,full clinical examination and laboratory investigations**,** serum 25-hydroxyvitamin D3 by DiaSorin 25-OH-D assay, urea and creatinine by automated colorimetric method, eGFR by creatinine clearance test, CBC by automated blood counter, serum calcium by automated colorimetric technique, serum phosphorus by automated colorimetric technique, lipid profile including Serum total cholesterol level by enzymatic colorimetric determination of total cholesterol,serum triglycerides by enzymatic method, high density lipoproteins and low density lipoproteins by Friedman formula, serum albumin by automated colorimetric technique, fasting and 2h postprandial blood sugar by enzymatic method and urine analysis by dipstick and light microscopy.

4.0 MEASUREMENT OF 25-HYDROXYVITAMIN D:

The DiaSorin 25-OH-D assay consists of a two-step procedure. The first procedure involves a rapid extractionof 25-OH-D and other hydroxylated metabolites from serum or plasma with acetonitrile. Following extraction, the treated sample is then assayed using an equilibrium RIA procedure. The RIA method is based on an antibody with specificity to 25-OH-D. The sample, antibody and tracer are incubated for 90 minutes at 20-25°C. Phase separation is accomplished after a 20-minute incubation at 20-25°C with a second antibody precipitating complex. A NSB/addition buffer is added after this incubation prior to centrifugation to aid in reducing nonspecific binding.

Reagents provided in the kit:

25-OH-D calibrators	6 vials / 1ml
25-OH-D NSB/addition buffer	One bottle / 70 ml
25-OH-D antiserum	One bottle / 105 ml
25-OH-D tracer	One vial / 6 ml
25-OH-D DAG precipitating complex	2 vials / 30 ml
25-OH-D controls	2 vials / 1 ml
25-OH-D acetonitrile	2 vials / 15 ml
Number of tests	100

4.1 Storage:

Upon receipt, the kit should b stored at 2-8°C. After opening, store each reagent at 2-8°C until the expiration date on the label. Reagents should not be used past the expiration date. The expiration date of the kit is reported on the external label. Reagents from different batches must not be mixed.

4.2 Specimen collection and preparation:

Fifty microliters of serum (EDTA or heparin) is required for the 25-OH-D extraction; a volume of 150 microliters will permit repeat analysis and provide adequate pipetting volume as well.

Either human serum or plasma may be used in this kit. The anticoagulants EDTA or heparin may be used with this assay. A fasting specimen is recommended, but not required. Blood should be collected aseptically by venipuncture in a 5 or 10 ml evacuated glass tube. Allow the blood to clot at room temperature (15-25°C). Centrifuge for 15 minutes using approximately 760 xg to obtain hemolysis free sera. No additives or preservatives are required to maintain integrity of the sample. All plastics, glassware or other material coming into contact with the specimen should be entirely free of any contamination. Store serum or plasma samples at -20°C or lower. Specimens may be stored in glass or plastic vials, as long as the vials are tightly sealed to prevent desiccation of the sample.

ISSN 2347-6893

4.3 Equipments and materials:

Disposable borosilicate glass tubes, 12 x 75 mm,temperature controlled centrifuge to accommodate 12 x 75 mm tubes, gamma counter capable of counting 125-iodine ,vortex mixer and Pipetting devices.

4.4 Assay procedure:

Allow all reagents and samples to equilibrate to room temperature, set up labeled 12 x 75 mm disposable glass tubes in duplicate according to the scheme of the assay on the last page.Add reagents [total count tubes, non specific Binding tubes (NSB) and calibrators and controls], vortex gently without foaming and incubate for 90 (± 10) minutes at 20-25°C.Add 500 µl of DAG precipitating complex (DAG precipitating complex should be mixed thoroughly before and during use) to all tubes except the total count tubes, mix tubes well and incubate for 20-25 minutes at 20-35°C, add 500 µl of NSB/addition buffer to all tubes except the total count tubes, vortex gently to mix tubes well, use caution when performing this step to avoid splashing due to high liquid volume in tube,centrifuge all tubes for 20 minutes at 20-25°C at 1800 xg, except the total counts,decant the supernatants, except the total count tubes, using a foam rack tube holder or equivalent by inverting the rack into an appropriate waste container, place the inverted rack onto absorbent paper for 2-3 minutes, blot the tubes gently to ensure all liquid is removed, in a gamma scintillation counter, count each tube for a minimum of one minute. Each tube should be counted for a sufficient time to achieve statistical accuracy.

4.5 Stastical analysis

The collected data were tabulated and analyzed using SPSS version 16 soft ware (Spss Inc, Chicago, ILL Company). Categorical data were presented as number and percentages while quantitative data were expressed as mean and standard deviation. Student t test (Student's t-test**,** in statistics, a method of testing hypotheses about the mean of a small sample drawn from a normally distributed population when the population standard deviation is unknown) and Chi square test (X^2) (Chi-square is a statistical test commonly used to compare observed data with data we would expect to obtain according to a specific hypothesis) were used as tests of significance. ROC curve was used to determine cut off values of 25-hydroxyvitamin D with optimum sensitivity and specificity**.(13)**

5.0 RESULTS

There was significant difference between groups regard age as AKI group was 58.2±10.6 and not AKI group 65.1±11.3 but there was no significant difference regard sex between groups (Table1).

Table (1): Age and Sex distribution among AKI patients and non AKI patients

		GROUPS				test	P value
		NoN AKI (n=60)		AKI (n=20)			
Age	Mean ±SD	65.1±11.3		58.2±10.6		2.448	<0.05*
sex	female	29	48.3%	9	45%	>0.05	NS
	male	31	51.7%	11	55%		
Total		60	100%	20	100%		

- P value significan if < 0.05.
- Non-significant (NS) if P value > 0.05.
- Standard deviation(SD).
- (AKI)acute kidney injury.
- (Non AKI)non acute kidney injury group

There was no significant difference between groups regarding clinical and laboratories data except serum creatinine, blood urea, GFR, ALB, FBS, PPBS and 25 (OH)D (Table 2).

ISSN 2347-6893

Table (2): Comparison of clinical and laboratories data between AKI and Non AKI groups

Variable	AKI (n=20) Mean ±SD	NON AKI (n=60) Mean ±SD	test	P value
WT	71.9±6.4	73.6±6.5	-1.059	NS
SBP	159.5±23.6	151.4±26.8	1.198	NS
DBP	100.2±12.4	95.8±14.8	1.195	NS
HR	86.1±9.5	84.6±5.9	0.827	NS
RR	16.9±2.9	16.4±2.3	0.713	NS
HB	10.4±1.1	10.5±0.88	-0.409	NS
TEMP	37.8±0.8	37.5±0.6	1.458	NS
TLC	10.6±3.2	9.6±2.9	1.370	NS
GCS	6.8±2.1	7.3±2.6	-0.776	NS
HCT	42.45±4.1	41.5±4.1	0.800	NS
Creatinine	2.17±0.65	1.07±0.2	10.733	<0.001*
UREA	47.8±10.9	28.5±6.2	9.696	<0.001*
GFR	35.25±12.6	97.5±12.9	-18.780	<0.001*
CA	9.23±0.6	9.1±0.5	0.526	NS
P	3.21±0.5	3.3±0.5	-0.843	NS
ALB	3.09±0.41	3.5±0.4	-3.609	<0.001*
FBS	165±35.2	99±20.3	4.009	<0.001*
PPBS	225.1±71	186.6±64	2.263	<0.05*
LDL	113.6±17.7	110.6±20.3	0.573	NS
HDL	50± 4.1	49±3.2	0.013	NS
TGR	105.15±52.4	111.4±43.9	-0.525	NS
Cholesterol	161.9±51.1	171.3±46.6	-0.764	NS
OHD25	14.8±3.7	25.7±4.8	-19.280	<0.001*

eGFR by creatinine clearance test: Creatinine Clearance = (Cru x V/t) / Crs where serum creatinine concentration (Crs), urine creatine concentration (Cru), and the urine volume (V) collected over a time period (t, usually expressed in minutes).

There wasn't significant association between AKI and co-morbidity except in urinary tract infection and DM as about half of AKI group had UTI while 13.3% of other group had UTI and 50% of AKI group had DM while 23.3% of NON AKI group had DM (Table 3).

ISSN 2347-6893

Table (3): Co-morbidity distribution between groups

Disease	GROUPS				X^2	P value
	Non AKI (n=60)		AKI (n=20)			
HTN	23	38.3%	11	55%	1.7	NS
DM	14	23.3%	10	50%	9.9	<0.001*
Atrial fibrillation	12	20%	7	35%	1.8	NS
IHD	13	21.7%	4	20%	0.02	NS
Smoking	22	36.7%	11	55%	2.08	NS
UTI	8	13.3%	8	40%	6.6	<0.05*
Total	60	100%	20	100%		

There was significant association between mortality and AKI as 20% of AKI group died while no one in other group died (table 4)

Table (4): Mortality distribution between groups

		NON AKI (n=60)		AKI (n=20)		Total	X^2	P value
Mortality	**Survive**	60	100%	16	80%	76	12.6	<0.001*
	Died	0	0%	4	20%	4		

There was significant association between 25 (OH)D deficiency and AKI as 75% of AKI group had 25 (OH)D3 Deficiency while other group hadn't any one (table 5).

Table (5): Association between 25 (OH)D level and AKI

	25 (OH)D level				X^2	P value
	>15		≤15			
NON AKI	60	100%	0	0%	55.3	<0.001*
AKI	5	25%	15	75%		
Total	65	100%	15	100%		

There was no significant difference between groups regarding clinical and laboratories data except creatinine , urea, GFR, ALB, FBS and PPBS (Table 6).

ISSN 2347-6893

Table (6): Comparison of clinical and laboratories date between 25 (OH)D deficiency patients and normal groups

	25 (OH)D ≤15 (15)	**25 (OH)D >15 (65)**	**test**	**P value**
Weight	73.06±6.6	73.2±6.5	-0.112	NS
SBP	157±22.6	152.6±27	0.582	NS
DBP	100±11.3	96.2±14.9	0.916	NS
HR	86.9±10.4	84.5±5.9	1.203	NS
RR	17.2±3.07	16.4±2.3	1.108	NS
HB	10.5±1.2	10.7±0.8	0.008	NS
TEMP	37.8±0.8	37.5±0.6	1.713	NS
TLC	10.7±3.5	9.6±2.9	1.172	NS
GCS	6.53±1.9	7.3±2.5	-1.197	NS
HCT	42.4±4.2	41.6±4.1	0.613	NS
CREAT	2.2±0.6	1.1±0.4	7.886	<0.001*
UREA	48.26±11.5	29.9±8.08	7.260	<0.001*
GFR	35.33±12.3	92.7±21.2	-10.063	<0.001*
CA	9.29±0.6	9.1±0.58	0.902	NS
P	3.18±0.53	3.3±0.53	-0.983	NS
ALB	3.08±0.46	3.49±0.47	-3.012	<0.05*
FBS	166±42	136±21	2.134	<0.05*
PPBS	226.2±63	169.3±45.7	2.689	<0.05*
LDL	117.6±16.8	109.9±20	1.362	NS
HDL	51±6	48±7	1.9	NS
TGR	116.93±51	108.2±44.9	0.662	NS
CHOLEST	178.73±43.7	166.7±48.5	0.873	NS

ISSN 2347-6893

There was significant association between AKI and level of 25 (OH)D p =<0.001 and kappa agreement was 0.95 p=<0.001 (Table 7).

Table (7): Association between 25 (OH)D level and AKI

		AKI				Total	X^2	P value	Kappa Agreement	P value
		-VE		+VE						
OHD25	>22 (-VE)	60	100%	1	5%	61	74.7	<0.001	0.95	<0.001*
	≤22 (+VE)	0	0%	19	95%	19				
Total		60	100%	20	100%	80				

25 (OH)D has highly significant negative correlation with creatinine and urea and highly significant positive correlation with GFR (Table 8).

Table (8): Correlation between 25 (OH)D3 level, serum creatinine ,blood urea and GFR.

		25 (OH)D
Creat	**r**	-0.718
	P	<0.001 *
	N	80
Urea	**r**	-0.704
	P	<0.001 *
	N	80
GFR	**r**	0.824
	P	<0.001 *
	N	80

25 (OH)D has highly significant negative correlation with serum creatinine and blood urea and highly significant positive correlation with GFR .

6.0 DISCUSSION

Renal disease is a worldwide public health problem with an increasing incidence, prevalence, poor outcomes and high cost. Outcomes of renal disease include not only kidney failure but also complications of decreased kidney function **(13)**.

Vitamin D is essential for calcium homeostasis, bone development and remodeling. Vitamin D deficiency has long been recognized as a cause of increased fracture risk associated with rickets in infants and osteomalacia in adults **(10).**

This study illustrated an association between acute kidney injury and preadmission 25(OH) D deficiency. Preadmission 25(OH)D deficiency was a significant predictor of acute kidney injury and remained a significant predictor of acute kidney injury following multivariable adjustments for relevant comorbidities.

Our study shows that there was significant difference between AKI and non AKI groups as regard age as AKI group was 58.2±10.6 and non AKI group was 65.1±11.3 but there was no significant difference as regard sex between groups

In contarary to our study, Feest et al.(1993) **(14)** found that acute kidney injury, is frequently encountered in the elderly. The effect of advancing age in decreasing renal reserve and the associated comorbid conditions of elderly patients increase the risk for the development of AKI. Although studies describing the incidence of AKI in this population are difficult to compare because the definitions of AKI vary dramatically from study to study, it is clear that the elderly are at the highest risk for the development of AKI.

In our study we found that there was no significant difference between AKI and non AKI groups regarding clinical and laboratories data except serum creatinine, blod urea, GFR, ALB, FBS, PPBS and 25 (OH)D as blood urea, serum creatinine ,FBS and PPBS were significantly higher in AKI group while , ALB,GFR and 25 (OH)D were significantly lower in AKI group

In agreement with our study a meta-analysis done by Wiedermann CJ et al.(2010) **(15)** provides evidence that hypoalbuminemia is a significant independent predictor both of AKI and of death following AKI development

In agreement with our study a meta-analysis done by Rodrigo Cartin-Ceba et al. (2012) **(16)** demonstrated a significantly increased risk of AKI in critically ill patients with diabetes

In agreement with our study Andrea et al .(2012)**(17)** found that there is an association between acute kidney injury and 25(OH) D deficiency.25(OH)D deficiency was a significant predictor of acute kidney injury and remained a significant predictor of acute kidney injury following multivariable adjustments for relevant comorbidities.

In our study we found that there wasn't significant association between AKI and co-morbidity except in urinary tract infection and DM as about half of AKI group had UTI while 13.3% of other group had UTI and 50% of AKI group had DM while 23.3% of NON AKI group had DM.

In agreement with our study Chiu et al.(2013)**(18)** found that diabetic patients with UTI are at increased risk of superimposed AKI.

There was significant association between mortality and AKI as 20% of AKI group died while no one in other group died (table 4).

There was significant association between 25 (OH)D Deficiency and AKI as 75% of AKI group had 25 (OH)D Deficiency while other group hadn't any one (table 5).

In agreement with our study, Ishir et al.(2010)**(19)** found that deficiency of 25-hydroxyvitamin D is nearly universal among patients with hypoalbuminemia .This may be explained by that hypoalbuminaemia could represent reduced carrying capacity for vitamin D, which largely circulates in protein-bound form However, another possible explanation is that a common disorder predisposes to hypoalbuminemia and vitamin D deficiency. This could represent chronic inflammation, an aspect of many comorbid illnesses.

In agreement with our study, Palomer et al.(2008)(20) found that vitamin D deficiency has been shown to alter insulin synthesis and secretion in both humans and animal models. It has been reported that vitamin D deficiency may predispose to glucose intolerance, altered insulin secretion and type 2 diabetes mellitus.

This can be explained by The presence of vitamin D receptors (VDR) and vitamin D-binding proteins (DBP) in pancreatic tissue and the relationship between certain allelic variations in the VDR and DBP genes with glucose tolerance and insulin secretion have further supported this hypothesis **(20).**

The mechanism of action of vitamin D in type 2 diabetes is thought to be mediated not only through regulation of plasma calcium levels, which regulate insulin synthesis and secretion, but also through a direct action on pancreatic beta-cell function. Therefore, owing to its increasing relevance, this review focuses on the role of vitamin D in the pathogenesis of type 2 diabetes mellitus **(20).**

In our study we found that there was significant association between AKI and level of 25 (OH)D as 95% of patients with serum 25 (OH)D level ≤ 22ng/dl have AKI.

25 (OH)D has highly significant negative correlation with serum creatinine and blood urea and highly significant positive correlation with GFR .

Braun et al. **(2)** showed that vitamin D deficiency prior to hospital admission or at the time of critical care might be associated with increased morbidity and mortality in patients with critical illness. Vitamin D dysfunction might also contribute to common acute complications such as sepsis, organ failure, and systemic inflammatory response syndrome, leading to worse outcomes.

Braun and Christopher **(21)** elucidated the effect of vitamin D on acute kidney injury. They performed 11 years two-center observational study of critically ill patients among whom 25(OH)D was measured within 1 year prior to hospitalization. . They provided clinical evidence of a potential link between vitamin D and acute kidney injury.

7.0 CONCLUSION

Deficiency of 25-hydroxyvitamin D is a significant predictor of acute kidney injury and mortality in critically ill patient population.

8.0 ACKNOWLEDGMENTS: Staff members of Ahmed Maher taching hospital and Menufia Faculty of Medicine

REFERENCES

(1) Mehta RL,Chertow GM. (2003):Acute renal failure definition and classification :time for change ?Am Soc Nephrol ;14(8)2178.

(2) Braun A, Gibbons FK, Litonjua AA, et al. (2012): low serum 25-hydroxyvitamin D at critical care initiation is associated with increased mortality. Crit Care Med; 40(1):63–72.

(3) Jim Cassidy,Donanld bissett,Roy A. J.Spence,Mranda Payne (2010) :Oxford Handbook of Oncology Oxford University Press. P.706.

(4) Papadakis MA,Mcphee SJ. (2008) : Current Medical Diagnosis and Treatment. McGraw-Hill Professional.ISBN 0-07-159124-9.

(5) Mehta RL, Kellum JA, Shah SV, et al. (2007) : Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury". Critical Care (London, England) 11 (2): R31

(6) Palevsky PM, Zhang JH, O'Connor TZ, et al. (2008)*:* Intensity of renal support in critically ill patients with acute kidney injury". The New England Journal of Medicine 359 (1): 7–20.

(7) Holmes CL, Walley KR . (2003) :Bad medicine: low-dose dopamine in the ICU. *Chest* 123 (4): 1266–75.

(8) Uchino S, Doig GS, Bellomo R, et al. (2004): Diuretics and mortality in acute renal failure". Crit. Care Med. 32 (8): 1669–77.

(9) BAGSHAW SM, DELANEY A, HAASE M, ET AL (2007): Loop diuretics in the management of acute renal failure: a systematic review and meta-analysis. Crit Care Resusc; 9(1):60-8.

(10) Holick MF (2007): Vitamin D deficiency. N Engl J Med; 357:266–281

(11) Norman AW (2008): From vitamin D to hormone D: Fundamentals of the vitamin D endocrine system essential for good health. Am J Clin Nutr; 88:491S–499S.

(12) Levey SA, Coresh J, Balk E, et al.(2003): National kidney foundation practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Ann. Intern. Med; 139(2):137-147.

(13) -Holick MF (2009): Vitamin D Status: Measurement, Interpretation, and Clinical Application, Annals of Epidemiology, Feb; 19(2):73-8.

(14) Feest TJ, Round A, Hamad S (1993): Incidence of severe acute renal failure inadults: results of a community-based study. BMJ 306: 481–483.

(15) Wiedermann CJ, Wiedermann W, Joannidis M (2010): Hypoalbuminemia and acute kidney injury: a meta-analysis of observational clinical studies. Intensive Care Med.;36(10):1657-65.

(16) RodrigoCartinCeba, MarkosKashiouris, MariaPlataki (2012):Risk Factors for Development of Acute Kidney Injury in Critically Ill Patients: A Systematic Review and Meta-Analysis of Observational StudiesVolume 2012 Article ID 691013, 15 pages

(17) Andrea B. Braun, MD; Augusto A. Litonjua, MD, (2012): Association of low serum 25-hydroxyvitamin D levels and acute kidney injury in the critically ill. Crit Care Med Vol. 40, No. 12.

(18) Chiu PF, Huang CH, Liou HH, Wu CL, Wang SC, Chang CC.(2013): Long-term renal outcomes of episodic urinary tract infection in diabetic patients J Diabetes Complications.;27(1):41-3.

(19) Ishir Bhan, Sherri-Ann M. Burnett-Bowie,Jun Ye, Marcello Tonelli, and Ravi Thadhani (2010):Clinical Measures Identify Vitamin D Deficiency in Dialysis. Clin J Am Soc Nephrol.; 5(3): 460–467.

(20) Palomer X, González-Clemente JM, Blanco-Vaca F, Mauricio D (2008): Role of vitamin D in the pathogenesis of type 2 diabetes mellitus. Diabetes Obes Metab.;10(3):185-97.

(21) Braun AB and Christopher KB. (2013): Vitamin D in acute kidney injury. Inflamm Allergy Drug Targets; 12(4): 262-72.