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ORIGINAL ARTICLE

Frequency of folate deficiency in chronic kidney disease patients on maintenance hemodialysis.

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ABSTRACT… Objective: To determine the frequency of folate deficiency in chronic kidney disease patients on maintenance hemodialysis presenting to Nephrology OPD of Khyber Teaching Hospital Peshawar. **Study Design:** Descriptive, Cross sectional. **Period:** 11th January 2021 to 10th July 2021. **Setting:** Department of Outpatient Nephrology, Khyber Teaching Hospital, Peshawar. **Methods:** A total of 142 patients diagnosed with CKD on dialysis sessions were selected for the study in a consecutive sampling manner and observed for folate deficiency. **Results:** The mean age group of our sample was 45.6+ 7.4 years of which 42.2% male patients and 57.8% female patients. The mean duration of dialysis (months) was 9.2+ 5.1 months. Folate deficiency in dialysis patients were recorded in 69.7 % of patients. **Conclusion:** Folate deficiency is very common in our dialysis dependent population. Its deficiency could be due to multiple factors including malnutrition, drugs and dialysis itself. It is important to routinely screen dialysis dependent population for this potentially reversible complication to prevent damage. We recommend further multicenter studies to detect this observation and to form comprehensive guidelines to prevent our patients at risk.

Key words: Acute Complications, Dialysis, Folate Deficiency.

INTRODUCTION

Chronic kidney disease is the end complication of different chronic illnesses including cardiac diseases, diabetes, hypertension, auto-immune conditions, glomerulo-nephritides, congenital diseases and complications caused by drugs.[1,2] Once chronic kidney disease is confirmed, the disease is usually irreversible. Identifying the cause of chronic kidney disease is crucial to improve the survival of the patient by halting the natural progression of the disease.

In initial stages, kidney compensates renal damage by improving renal flow which also causes glomerular hypertension.[3]This glomerular hypertension causes irreversible damage. When the glomerular filtration rate reaches below 10ml/min/1.73m^2, hemodialysis is usually advised. Hemodialysis in itself can cause multiple complications.[4] Folate deficiency is common complication which is usually ignored. Poor appetite and gut malfunction leads to progressive folate deficiency. It can causes resistant anemia and should be promptly addressed to prevent other anemia related complications.[5]

Studies are performed in multiple centers to know the prevalence of the folate deficiency in dialysis dependent population. Many have identified a strong correlation of this complication in dialysis dependent patients, others have found reverse.[6]

Unfortunately limited studies are available in our local population setup to know the frequency of this potentially reversible phenomenon.

The purpose of this study was to evaluate the frequency of folate deficiency observed in our local dialysis dependent population. This will not only help to know the burden of the disease but will also help to identify factors that are closely related to this phenomenon. Correctly

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identifying the potential risk factors will lead to better care of the patients and will improve our healthcare system and increase the confidence and compliance of patients to dialysis schedule.

OBJECTIVE

To determine the frequency of folate deficiency in chronic kidney disease patients on maintenance hemodialysis presenting to nephrology division Khyber Teaching Hospital Peshawar.

METHODS

A descriptive cross-sectional study was conducted after approval from the Hospital Ethical Committee (14/03/2024) and CPSP at the Division of Nephrology, Khyber Teaching Hospital Peshawar. The sample size was 142, determined using a 95% confidence level with a prevalence of 76.47% in CKD patients and a 7% margin of error using the WHO calculator. Non-probability consecutive sampling was employed. The inclusion criteria included all diagnosed CKD patients as defined in the operational definition, aged 18 to 60 years, of both genders, and undergoing regular hemodialysis for more than three months. Exclusion criteria included patients with a history of intestinal resection, recent blood transfusion within the previous two weeks, those already taking chemotherapeutic or immunosuppressive agents, severely malnourished individuals, amputees, paraplegics, those with diagnosed chronic liver disease, and morbidly obese patients (BMI > 35). Written and informed consent about the nature of the study and methods was obtained on a Proforma from each patient who met the inclusion and exclusion criteria. CKD status was confirmed by previous history, medical records, and GFR estimation. A 5 cc blood sample was collected from the peripheral vein of each patient, observing sterile precautions, and immediately sent to the hospital laboratory for measuring RBC folate level, serum creatinine, and blood sugar level, performed by an experienced biochemist. Demographic data including name, age, gender, address, hospital/ward number, and contact number were recorded by the researcher in a Proforma.

Data were analyzed using SPSS version 20. Mean and standard deviation (±S.D) were calculated for numerical variables like age, BMI, duration of dialysis, blood pressure, blood sugar level, and RBC folate level. Frequency and percentage were calculated for categorical variables such as gender, diabetes status, access used for dialysis, and folate deficiency. Folate deficiency was stratified among age, gender, duration of dialysis, blood pressure, blood sugar level, and BMI to observe effect modification. Post-stratification chi-square tests were performed, with a P-value of ≤0.05 considered significant. All results were presented in tables.

RESULTS

A total of 142 patients with chronic kidney disease (CKD) undergoing dialysis were included in the study. The age distribution showed that 29.5% (n=42) of the patients were between 15-40 years, while the majority, 70.5% (n=100), were aged over 40-60 years. Regarding gender, 42.2% (n=60) were male and 57.8% (n=82) were female. The duration of dialysis among the patients indicated that 61.9% (n=88) had been on dialysis for less than 12 months, whereas 38.1% (n=54) had been on dialysis for more than 12 months. The BMI distribution revealed that 45.7% (n=65) of the patients had a BMI less than 25 kg/m^2, and 54.3% (n=77) had a BMI greater than 25 kg/m^2. Pre-dialysis blood pressure measurements showed that 63.3% (n=90) had systolic blood pressure less than 140 mmHg, while 36.7% (n=52) had systolic blood pressure greater than 140 mmHg. Blood sugar levels indicated that 87.5% (n=110) of the patients had random blood sugar levels less than 160 mg/dl, whereas 22.5% (n=32) had levels greater than 160 mg/dl (As summarized in Table-I)

In the 15-40 years age group, 45.2% (n=19) had folate deficiency, while 54.8% (n=23) did not. Among those aged over 40-60 years, 80.0% (n=80) had folate deficiency compared to 20.0% (n=20) who did not (p=0.0003). Among males, 75.0% (n=45) had folate deficiency, whereas 25.0% (n=15) did not. For females, 65.8% (n=54) had folate deficiency, and 34.2% (n=28) did not (p=0.24). Patients on dialysis for less than 12 months had a folate deficiency

prevalence of 68.1% (n=60) compared to 31.9% (n=28) who did not. For those on dialysis for more than 12 months, 72.2% (n=39) had folate deficiency compared to 27.8% (n=15) who did not (p=0.6). Among patients with a BMI less than 25 kg/m², 90.7% (n=59) had folate deficiency, while 9.3% (n=6) did not. For those with a BMI greater than 25 kg/m², 51.9% (n=40) had folate deficiency compared to 48.1% (n=37) who did not (p<0.001). For patients with systolic blood pressure less than 140 mmHg, 77.7% (n=70) had folate deficiency compared to 22.3% (n=20) who did not. Among those with systolic blood pressure greater than 140 mmHg, 55.7% (n=29) had folate deficiency compared to 44.3% (n=23) who did not (p=0.005). Patients with blood sugar levels less than 160 mg/dl had a folate deficiency prevalence of 80.0% (n=88) compared to 20.0% (n=22) who did not. For those with blood sugar levels greater than 160 mg/dl, 34.3% (n=11) had folate deficiency compared to 65.7% (n=21) who did not (p<0.001) (as summarized in Table-II).

Characteristic	Frequency	Percent (%)
Age Groups		
15-40 years	42	29.5
>40-60 years	100	70.5
Gender		
Male	60	42.2
Female	82	57.8
Duration of Dialysis		
<12 months	88	61.9
>12 months	54	38.1
BMI		
<25	65	45.7
>25	77	54.3
Blood Pressure		
<140mmHg	90	63.3
>140mmHg	52	36.7
Blood Sugar Level		
<160 mg/dl	110	87.5
>160 mg/dl	32	22.5

Table-I. Demographic and clinical characteristics of the sample (n=142)

Patients Characteristics	Folate Deficiency			P-Value
	Yes	No	Total	
Age Group				0.0003
15-40 years	19 (45.2%)	23 (54.8%)	42	
>40-60 years	80 (80.0%)	20 (20.0%)	100	
Gender				0.24
Male	45 (75.0%)	15 (25.0%)	60	
Female	54 (65.8%)	28 (34.2%)	82	
Duration of Dialysis				0.6
<12 months	60 (68.1%)	28 (31.9%)	88	
>12 months	39 (72.2%)	15 (27.8%)	54	
BMI (kg/m²)				<0.001
<25 kg/m²	59 (90.7%)	6 (9.3%)	65	
>25 kg/m²	40 (51.9%)	37 (48.1%)	77	
Systolic Blood Pressure (mmHg)				0.005
<140 mmHg	70 (77.7%)	20 (22.3%)	90	
>140 mmHg	29 (55.7%)	23 (44.3%)	52	
Blood Sugar Level				<0.001
<160 mg/dl	88 (80.0%)	22 (20.0%)	110	
>160 mg/dl	11 (34.3%)	21 (65.7%)	32	

Table-II. Patients characteristics and folate deficiency in dialysis dependent CKD patients (n=142)

DISCUSSION

Chronic kidney disease is a debilitating illness. It is slowly progressing irreversible renal damage caused by a list of pathologies. Chronic renal failure once diagnosed, cannot be reversed and often leads to multiorgan failure due to nervous system and cardiovascular system involvement. The mortality and morbidity is so high that it is among the leading causes of death worldwide.[9] Exact etiology is not known but multiple factors contributes to the development and progression of chronic kidney disease.[8,9]

Drugs play a contributing role in the pathology and complications of chronic kidney disease worldwide. Due to numerous over the counter medications available worldwide, NSAIDs and proton pump inhibitors along with other conventional medications can cause irreversible renal damage and chronic renal failure. The disease process can only be halted by stopping altogether all medications with potential to damage kidneys. If disease is severe, steroids might help in reversing the renal damage. The scarring in renal tubules and ischemia leads to the development of chronic renal failure.[9,10]

As the glomerular filtration rate of an individual reduces to less than 10ml/min/1.73m^2, the patient becomes symptomatic in the form of volume overload, acidosis, difficult to control hypertention, malnutrition, gut motility disturbances and neuro-psychologic behavior changes. All these become evident during the late stages and the need for renal replacement therapy arises which can reverse the complications. KDIGO guidelines recommend regular screening for complication in both dialysis dependent and non-dialysis dependent patients.[11] The routine investigations include electrolytes and mineral levels including folic acid. The deficiency of folic acid is evident in chronic renal failure patients due to two main reasons.[12]

Folic acid deficiency can be encountered in patients on renal replacement therapy in the form of hemodialysis. It is due to the leak and loss of folic acid during diffusion and convection processes which leads to its deficiency. Second main reason for folic acid deficiency in dialysis individuals is the poor nutritional status due to impaired gut motility and loss of appetite. Whatever the reason, folate deficiency leads to anemia and impaired metabolic processes in hepatic and cardiac tissues.[13]

Study performed in other regions of the world showed that folate deficiency is not uncommon among chronic kidney disease patients.[14] Our study showed that folate deficiency is present in 69.7% of dialysis dependent chronic kidney disease patients.

Multiple associated risk factors and contributing finding related to folate deficiency are also observed. Age is among the top associated factor observed in our study. It is observed in our study that higher age group is vulnerable for folate deficiency (p value <0.05) and ultimately resistant anemia. This finding is also observed in other studies performed in different regions.[14,15]

Gender is not significantly associated with the onset of folate deficiency in dialysis dependent individuals (p value >0.05). Low BMI, however, is strongly associated with the development of folate deficiency (p value <0.05). The reason could be due to poor appetite, malnutrition, protein loss due to diet or renal replacement therapy. This finding is not observed in studies performed worldwide and needs to be validated.[14,15]

On the basis of this discussion and study, one can suggest that all dialysis dependent patients who have low BMI and belong to age group more than 40 year should be thoroughly screened for folate deficiency. They should be examined more frequently and if any cause and risk factor is observed, it must be immediately reversed to prevent long term and irreversible damage. Further studies are definitely needed to find out the reason behind the association of folate deficiency and normal and low blood pressure measurements. It will help to improve patient survival and better health.

CONCLUSION

Frequency of folate deficiency during dialysis

is much greater in our local population. Low BMI and increase age has been identified as an important association related to folate deficiency and require further validation by performing studies on large scale.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Muhammad Waheed Sohail:** Manuscript writing, Data analysis, Final drafting.
2	**Zarak Khan:** Data collection, Proof reading, Critical analysis.
3	**Mavish Arif:** Data collection, Proof reading, Critical analysis.
4	**Aimal Khan:** Data collection, Proof reading, Critical analysis.
5	**Muhammad Israr:** Manuscript writing, Data analysis, Data collection, Final drafting