Vitamin A deficiency in chronic kidney disease patients attending a tertiary care hospital

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Abstract

Background: Patients with Chronic kidney Disease are at the risk of developing a deficiency or excess of one or more micronutrients because of inadequate intake, interference of micronutrient absorption either by drug or uremic toxins, altered metabolism or loss or gain during dialysis. This aspect has been poorly explored as far as Vitamin A status is concerned.

Objectives:

- To find out the extent of Vitamin A deficiency in Chronic kidney Disease patients.
- To pinpoint the role of diet in the occurrence of vitamin A deficiency in Chronic kidney Disease patients.

Setting: A Tertiary Care Hospital setup in Northern India.

Subjects: One hundred and seventy five incident cases of Chronic kidney Disease.

Results: Fifty eight (33.14%) subjects had manifestations of vitamin A deficiency. Average vitamin A intake (IU/day) was 944.058±1824.7 which was 39.4% of recommended dietary allowance (RDA). Vitamin A intake of CKD subjects in stage III (1766.0±26.60) was significantly more than those with CKD stage IV (891.84±18.14) and stage V (491.70±860.47). All CKD patients with manifestations of vitamin A deficiency had vitamin A intake less than RDA. Extent of night blindness in subjects belonging to socioeconomic status (SES) very low plus low, lower middle, middle, upper middle and high were 30.30% 28.00%, 25.00%, 12.9% and 9.1%, respectively

Conclusion: Vitamin A deficiency is high in CKD patients primarily due to dietary inadequacy of vitamin A. The findings of the study calls for more in-depth multicentre research to have insight in management of patients of CKD with vitamin A deficiency.

Keywords: Chronic kidney disease, Retinol binding protein, Socioeconomic status, Vitamin A deficiency

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Introduction

Vitamin deficiencies are common in people with advanced renal failure who do not take nutritional supplements[1]. Low dietary intake may be the primary cause and this may be because of anorexia, impaired ability to buy, prepare or ingest foods that are high in nutritional content. Seasonal variations may predispose to deficiency of some vitamins because of reduced access to fresh fruits, vegetables, to dietary protein restrictions. Dietary prescriptions may limit foods which are high in vitamins.

Vitamin A is necessary for vision reproduction, growth, integrity of epithelial tissue for normal immune functions[2,3]. The levels of retinol binding protein 4 (RBP4) are tightly regulated under healthy circumstances. Serum vitamin A concentration are often increased in patients with advanced chronic kidney disease (CKD). Decreased catabolism of RBPs in general and isoforms of RBP 4 in particular in kidney contributes to increase in both forms of RBPs in CKD patients. This may partially explain their elevated plasma concentration in CKD patients. According to a scientific report, levels of RBP4 isoforms were highly increased in CKD patients compare to controls.[4] This is further substantiated by another study reporting significantly increase plasma retinol in patients with chronic renal failure[5].

Situation of CKD patients in Indian context is jeopardized because of the adversities of nutritional care extended to them prior to the development of the disease and during the different stages of the disease. With the advancing stage of CKD serum creatinine level rises and serum vitamin A concentration began to increase with the increase in serum creatinine[4]. In the prevailing situation it seems that there will be no need to provide vitamin A supplements to CKD patients. If the patients of CKD is commonly ingesting vitamin A too less than RDA, supplemental vitamin A up to the RDA can be given[6]. With this background this study was carried out in a tertiary care setup with the following objectives:

- To find out the extent of Vitamin A deficiency in Chronic Kidney Disease patients.

- To pinpoint the role of diet in the occurrence of vitamin A deficiency in Chronic kidney Disease patients.

Materials and Methods

Setting: This study was conducted at the Department of Nephrology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.

Study design: Hospital based cross sectional study was designed for the study.

Study Sample: Clinically stable, non dialysed incident CKD patients from stage II to V from the Department of Nephrology, Sir Sundar Lal Hospital, Banaras Hindu University, Varanasi were considered as study subjects.

Study sample: All the 175 confirmed incident cases of chronic kidney disease attending OPD (twice a week) and indoor cases, from Department of Nephrology of Sir Sunderlal Hospital, BHU, Varanasi were selected as the cases for the study.

Inclusion Criteria: All patients of Chronic Kidney Disease who fulfill following criteria were included in the study.

1. Serum creatinine level < 6 mg/dl.
2. Clinical and Biochemical evidence of Chronic Renal Failure [Serum Creatinine > 1.5 mg %, Urea > 40 mg/d for $\geq$ 3 months]

Exclusion Criteria:

1. Patients with acute on CKD.
2. Other conditions like malignancy, advance renal disease or any other chronic illness

Ethical clearance: The protocol of the study was approved by the institutional Ethical committee of Institute of Medical Sciences, Banaras Hindu University, Varanasi, and all the patients gave written consent before entering the study.

Tools of the Study

Pretested and predesigned interview schedule was used for assessing sociodemographic characteristics of the study subjects, recording clinical manifestations of vitamin A deficiency and dietary intake of study subjects. Libra weighing machine was used for weight recording. Its accuracy was checked from time to time against known weight. Fully automatic analyzer (RFCL, Flexor-XL) was used to assess creatinine and urea levels of the study subjects.

Techniques of the Study

Socio demographic characteristics of the study subjects was obtained by interviewing them and was recorded on the predesigned and pretested proforma. Weight of each study subject was recorded with the help of libra weighing machine following standard techniques. Their creatinine and urea levels was assessed by fully automatic analyzer (RFCL, Flexor – XL). Glomerular Filtration Rate based on age, weight and creatinine was calculated separately for men and women by using the following formula mentioned below (Cockroft- Gault equation)[7].

$$\text{GFR for men} = \frac{\text{Ht}140 - \text{Age Hx Weight}}{72 \times \text{Creatinine (mg/dl}}$$

$$\text{GFR for women} = \frac{\text{Ht}140 - \text{Age Hx Weight}}{72 \times \text{Creatinine (mg/dl}} \times 0.85$$

The cases with GFR greater or equal to 120mL/min/1.73m^2 were considered as normal

Statistical analysis

Data thus collected was entered in personal computer and statistical analyses were performed using SPSS version 16. Results were shown as mean±SD for quantitative variables under study. Chi square and ANOVA were applied for statistical inference.

Results

The results of the study are given in following subheadings:

1. **Vitamin A deficiency in CKD patients:** Each study subject was clinically examined for manifestations of Vitamin A deficiency and results are given in Table 1. Fifty eight (33.14%) subjects had manifestations of vitamin A deficiency. As much as 21.71% and 8.57% had night blindness and Bitots spot, respectively, whereas both the conditions were present in 2.86% subjects. Manifestations of vitamin A deficiency did not differ significantly in male and female subjects (Table 2). Out of 97 rural subjects, 32 (32.99%) subjects had night blindness (Table 3). Extent of night blindness in subjects from rural area was significantly ($p< 0.01$) more than the subjects of urban area (7.69%) whereas proportions of subjects from rural and urban areas having night blindness plus Bitots spot were similar ($p>0.05$). Extent of night blindness in subjects belonging to socioeconomic status (SES) very low plus low, lower middle, middle, upper middle and high were 30.30% 28.00%, 25.00%, 12.9% and 9.1%, respectively. Bitots spot were present in respective SES categories to the extent of 9.09%, 12.00%, 8.92%, 5.13% and 0.00%. Presence of night blindness and Bitots spot together did not differ significantly in subjects belonging to different categories of SES. Similar pattern prevailed for subjects with either night blindness or Bitots spot (Table 4).
2. **Dietary Vitamin A intake of study subjects:** Average vitamin A intake (IU/day) was 944.058±1824.7 which was 39.4% of recommended dietary allowance (RDA) of vitamin a for Indians (2400 IU/day). Average intake of

vitamin A in different stages of CKD (Table 5) differed significantly ($p<0.05$); Post hoc test revealed that average dietary Vitamin A intake of CKD subjects in stage III (1766.0±26.60) was significantly more than those with CKD stage IV (891.84±18.14) and stage V (491.70±860.47). Average vitamin A intake of CKD patients with manifestations of night blindness, Bitots spot and night blindness + Bitots spot were 210.28±145.49, 204.30±136.84, 245.91±180.58, 111.53±56.67 IU/day respectively. Percentage intake of vitamin A with respect to RDA in respective categories were 8.76 %, 8.51% and 4.64%. Average vitamin A intake in subjects without manifestations of vitamin A in CKD was 1237.75±2053.80 IU/day which was 51.57% of RDA. All CKD patients with manifestations of vitamin A deficiency had vitamin A intake less than RDA. In case of 97 (82.91%) CKD patients without manifestations of vitamin A deficiency vitamin A intake was less than RDA, whereas 20 (17.09%) subjects had vitamin A intake ≥ RDA.

Table 1: Vitamin A deficiency in CKD patients (N=175)

Manifestation of Vitamin A deficiency	Number	Percentage
Night blindness	38	21.71
Bitots spot	15	8.57
Night blindness + Bitots spot	5	2.86
Total	58	33.14

Table 2: Sex wise distribution of manifestation of Vitamin A deficiency

Sex	No	Night Blindness (NB)				Bitots Spot				NB + Bitots Spot			
		Present		Absent		Present		Absent		Present		Absent	
		No	%	No	%	No	%	No	%	No	%	No	%
Male	119	26	21.84	93	78.15	9	7.56	110	92.44	5	4.20	114	95.80
Female	56	12	21.43	44	78.57	6	10.71	50	89.29	0	0.00	56	100.00
Total	175	38	21.71	137	78.29	15	8.57	160	91.43	5	2.86	170	97.14
Test of Significance		$\chi2$= .004; df=1; p=0.95				$\chi2$=0.483; df=1 p=0.49				$\chi2$=2.42; df=1; p= 0.12			

Table 3: Area wise distribution of manifestation of Vitamin A deficiency

Area of residence	No	Night Blindness				Bitots Spot				NB + Bitots Spot			
		Present		Absent		Present		Absent		Present		Absent	
		No	%	No	%	No	%	No	%	No	%	No	%
Rural	97	32	32.99	65	67.01	9	9.28	88	90.72	2	2.06	95	97.94
Urban	78	6	7.69	69	88.46	6	7.69	72	92.31	3	3.85	75	96.15
Total	175	38	21.71	137	78.29	15	8.57	160	91.43	5	2.86	170	97.14
Test of Significance		$\chi2$=15.34; df=1; p=0.00				$\chi2$=0.139; df=1; p=0.709				$\chi2$=0.496; df=1; p=0.481			

Table 4: Socio economic wise distribution of manifestation of Vitamin A deficiency

SES	No	Night Blindness				Bitots Spot				NB + Bitots Spot			
		Present		Absent		Present		Absent		Present		Absent	
		No	%	No	%	No	%	No	%	No	%	No	%
Very Low	15	7	46.67	8	53.33	3	20.00	12	80.00	0	0.00	15	100.00
Low	18	3	16.67	15	83.33	0	0.00	18	100.00	1	5.56	17	94.44
Lower middle	25	7	28.00	18	72.00	3	12.00	22	88.00	3	12.00	22	88.00
Middle	55	14	25.00	41	75.00	5	8.92	50	89.28	0	0.00	56	100.00
Upper Middle	40	5	12.82	35	89.74	2	5.13	38	97.44	0	0.00	39	100.00
High	22	2	9.09	20	90.01	0	0.00	22	100.00	1	5.55	21	95.45
Total	175	38	21.71	137	78.29	15	8.57	160	91.43	5	2.86	170	97.14
Test of Significance		$\chi2$=10.85; df=5; p=0.05				$\chi2$=7.9; df=5; p=0.16				$\chi2$=11.46; df=5; p=0.04			

Table 5: Average intake of Vitamin A according to GFR

Stages of CKD		Dietary Vitamin A Intake (IU/Day)	Test of Significance	
			F value	P value
II	4	2080.0±21.96	0.3.495	0.017
III	27	1766.0±26.60		
IV	96	891.84±18.14		
V	48	491.70±860.47		

Table 6: Dietary Vitamin A Intake and Manifestations of Vitamin A deficiency In CKD Patients:

Subjects	Number	Vitamin A intake Mean ± SD (IU/day)	Intake Less than RDA(2400 IU/Day)
CKD Subjects with manifestation of Vitamin A deficiency	58	210.28±145.49	< 2400 IU = 58
• Night blindness	38	204.30±136.84	< 2400 IU = 38
• Bitots Spot	15	245.91±180.58	< 2400 IU = 15
• Night Blindness + Bitots Spot	5	111.53±56.67	< 2400 IU = 5
CKD Subjects without manifestation of Vitamin A deficiency	117	1237. 75±2053.80	< 2400IU = 97 > 2400IU= 20

Discussion

The plasma level of vitamin A are frequently high in CKD[8]. In this situation it is understandable that there is no need of supplementing vitamin A in CKD patients and it is expected that manifestations of vitamin A deficiency will not occur in such patients. Several studies estimating serum vitamin A have not reported manifestations of vitamin A deficiency[4,5]. In contrast to this, one third of the subjects had one of the other manifestations of vitamin A deficiency. One out of ten subjects had Bitots spot which is the pathoglomic sign of vitamin A deficiency. This prevailing situation in CKD patients with respect to vitamin A deficiency clearly reflects that decision of not giving vitamin A supplements to CKD patients is not acceptable on the basis of findings of this study. According to present study gender wise differences did not prevail in subjects with respect to manifestation to vitamin A deficiency. It was obtained from data that there was preponderance of male CKD patients. Gender wise differences in health seeking behavior may reduce the gap in occurrence of vitamin A deficiency.

Although there was not significant difference in terms of presence of Bitots spot with or without night blindness in subjects from rural and urban areas. However, the ratio of night blindness only in urban and rural subjects was 1:4. There has been clear-cut socio economic gradient in presence of night blindness in CKD patients. However no definite pattern was observed for the presence of Bitots spot with or without night blindness in subjects belonging to different socioeconomic status. The existing scenario may be due to variations in serum retinol which was not estimated in this study due to logistic constraint. Serum retinol level is a function of dietary vitamin A intake. Average vitamin A intake of CKD patients has been far from being satisfactory and with advancing stages of CKD, there has been perceptible decline in vitamin A intake by patients of CKD. This is substantiated by the declining trend of average vitamin A intake of CKD patient from stage III to IV and V. It is quite disturbing that in all CKD patients with manifestations of vitamin A deficiency average vitamin A intake has been 10% of RDA. In contrast to this, this was 50% in CKD patients without manifestations of vitamin A deficiency. Thus the management of CKD patient's calls for dietary diversification and supplementation of Vitamin A and therapeutic management in advanced cases of CKD with vitamin A deficiency. In order to evolve a clear cut strategy on this aspect more study are needed in different settings incorporating assessment of serum retinol as well. A prospective study on vitamin A status of CKD patient and development of vitamin A deficiency may provide clear cut insight in the matter.

Conclusion

Vitamin A deficiency was quite high in CKD patients primarily due to dietary inadequacy. Food based approach in management of these patients will be safe but it needs to be evaluated whether such approach alone will be sufficient to restore vitamin A status of CKD patients.

Conflict of interest: None

References

1. Piper C M. Very low protein diet in chronic renal failure: nutrient content and guidelines for supplementation. J Am Diet Assoc. 1985,85:1344-1346.
2. Goodman D S. Vitamin A and retinoids in health and disease. N Engl J Med 1984;16:1023-1031.
3. Napoli JL. Biochemical pathways of retinoid transport, metabolism and signal transduction. Clin Immunol Immunopathol 1996;80: S52- S62.
4. Frey S K, Nagl B, Henze A, Raila J , Schlosser B, Berg T et al. Isoforms of Retinol binding protein 4 (RBP4) are increased in Chronic Disease of the kidney but not of the liver. Lipids and Health and Disease. 2008,7:29.

5. HA T.K.K, Sattar N, Talwar D, Cooney J et al. Abnormal antioxidant vitamin and carotenoid status in chronic renal failure. Q J Med 1996;89:765-769.
6. Cano N, Fiaccadori E, Tesinky P et al. ESPEN guidelines on eternal nutrition: adult renal failure. Clin Nutr (Edinburgh, Scotland) 25:295-310,2006.
7. Gentile M G, Fellin G, Manna G M et al. Vitamin A and retinol binding protein in chronic renal insufficiency. Int J Artif Org 1988;11:403–404.
8. Joel D. Kopple. National Kidney Foundation K/DOQI Clinical Practice Guidelines for Nutrition in Chronic Renal Failure American Journal of Kidney Diseases 2001;37(1),2:S66–S70.