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Association Between Hemoglobin and Glomerular Filtration Rate in Children with Chronic Kidney Disease after Protein RDA Intervention

Dr. Afsana Khanom[1*], Lt Col Dr. Maksuda Khanom[2], Dr. Nazrin Hossain Moury[3]

[1]Consultant, NICU & Pediatrics, Sajida Hospital, Dhaka, Bangladesh
[2]Classified specialist, Department of Radiology & Imaging, Combined Military Hospital (CMH), Chattogram, Bangladesh.
[3]Assistant Professor, Department of Community Medicine, Dhaka National Medical College & Hospital, Dhaka, Bangladesh

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***Corresponding author:** Dr. Afsana Khanom
Consultant, NICU & Pediatrics, Sajida Hospital, Dhaka, Bangladesh

Abstract **Original Research Article**

Background: Chronic kidney disease (CKD) in children is frequently accompanied by anemia and a progressive decline in glomerular filtration rate (GFR), both of which contribute to disease burden and poor outcomes. Nutritional interventions, particularly protein intake aligned with recommended daily allowance (RDA), may influence renal function and hematological status. This study aimed to evaluate the association between hemoglobin (Hb) and GFR in children with CKD following RDA-based protein intervention. ***Methods:*** This clinical trial was conducted at Dhaka Shishu Hospital from January 2016 to December 2017. Thirty children aged 2–18 years with CKD stages II–V (non-dialysis) were included. Participants received RDA-level protein intake according to WHO guidelines and were followed for six months. Hb and GFR were measured at baseline and after intervention by protein RDA at 3 months and 6 months. Statistical analysis was performed using paired t-tests and Pearson correlation in SPSS version 22, with significance set at $p \leq 0.05$. ***Results:*** Among 30 patients, the mean age was 8.10± 3.7 years, with a male predominance (70%). The majority (53.3%) were in the 6 to 10 years age group. At baseline, 53.3% had mild anemia, 33.3% moderate and 13.3% severe anemia. Mean Hb increased significantly from 9.44± 2.08 g/dL at baseline to 10.98 ± 1.33 g/dL at six months (p less than 0.001). Mean GFR improved from 34.3± 17.5 to 42.4± 24.4 mL/min/1.73m^2 (p less than 0.001). After six months of RDA protein intervention, Hb was found to have a highly significant positive correlation with GFR (r = 0.736, p less than 0.001). ***Conclusion:*** RDA protein intake significantly improves both hemoglobin levels and GFR in children with CKD. The strong positive correlation between Hb and GFR after intervention suggests that nutritional optimization may beneficially influence both erythropoiesis and renal function simultaneously.

Keywords: Chronic kidney disease, children, hemoglobin, glomerular filtration rate, RDA protein, anemia.

INTRODUCTION

Chronic kidney disease (CKD) in children represents a progressive and irreversible decline in renal function that ultimately leads to end-stage renal disease if untreated. It is defined by persistent structural or functional abnormalities of the kidney or a reduction in glomerular filtration rate (GFR) below 60 mL/min/1.73m² for more than three months [1]. Pediatric CKD is particularly challenging because it affects growth, neurodevelopment and long-term survival, often resulting in lifelong morbidity when progression is not controlled [2].

Anemia is one of the most frequent complications of CKD in children and is primarily driven by reduced erythropoietin production, iron dysregulation and shortened red cell survival due to uremic toxins [3]. Several studies have demonstrated a close relationship between declining GFR and worsening hemoglobin levels, highlighting anemia as both a marker and consequence of CKD progression [4]. Koshy and Geary reported that lower GFR is consistently associated with lower hemoglobin concentrations in pediatric CKD populations [5].

The pathophysiology of CKD progression is strongly influenced by glomerular hyperfiltration, intraglomerular hypertension and progressive nephron loss. Brenner's hyperfiltration hypothesis suggests that dietary protein intake can modulate intraglomerular pressure and thereby influence renal disease progression [6]. High protein intake increases renal hemodynamic load, whereas controlled protein intake may reduce hyperfiltration and slow nephron damage [7].

Nutritional management is therefore a key component in pediatric CKD care. The WHO recommends protein intake at the level of RDA (approximately 0.8 g/kg/day in non-dialysis CKD) to maintain metabolic balance while avoiding excessive renal burden [8]. Adequate energy intake with controlled protein levels has been shown to stabilize renal function and support growth in children with CKD [9].

Several clinical studies have demonstrated that dietary protein restriction within safe RDA limits can slow CKD progression and improve biochemical parameters such as serum creatinine, urea and phosphate [10]. However, evidence linking nutritional intervention with hematological improvement and its relationship to renal function remains limited in pediatric populations.

Recent findings suggest that anemia in CKD is not only a consequence of erythropoietin deficiency but may also be influenced by metabolic and inflammatory changes associated with declining renal function [11]. As renal function improves or stabilizes, hemoglobin levels may improve due to better erythropoietin responsiveness and reduced toxin accumulation.

In this context, understanding the relationship between hemoglobin and GFR after nutritional intervention is clinically important. If a strong association exists, hemoglobin could serve as a surrogate marker of renal response to dietary therapy. This study therefore focuses on evaluating the correlation between hemoglobin and GFR following an RDA-based protein intervention in children with CKD, aiming to clarify the interplay between renal function improvement and correction of anemia.

Materials & Methods

This was a prospective clinical trial conducted in the Department of Pediatrics, Dhaka Shishu Hospital, Bangladesh Institute of Child Health, over a period of 24 months from January 2016 to December 2017. A total of 30 children aged 2 to 18 years with an established diagnosis of CKD were enrolled after accounting for dropouts from an initial cohort of 38 participants. Eight patients were excluded from final analysis: three withdrew at the first follow-up (three months) and five at the second follow-up (six months).

Selection Criteria

Inclusion Criteria:

- Children aged 2–18 years
- Diagnosed CKD stage II–V (non-dialysis)
- Not on dialysis or renal replacement therapy
- Stable clinical condition for at least 6 months before enrollment
- Informed consent from parents or guardians

Exclusion Criteria:

- Congenital renal anomalies
- Congenital heart disease
- Diabetic nephropathy
- Patients on dialysis
- Renal transplant recipients

Data Collection Procedure

Baseline data were obtained from medical records documenting the six months preceding enrollment, capturing hemoglobin (Hb), random blood sugar (RBS), serum total protein, albumin, cholesterol, electrolytes, calcium, ferritin, parathyroid hormone (PTH) and 24-hour urinary total protein. GFR was estimated using the Schwartz formula, which uses serum creatinine and height. Following enrollment, all participants received RDA of protein according to WHO dietary guidelines, administered under the supervision of a trained pediatric dietitian, along with appropriate iron and calcium supplementation. Anthropometric measurements including weight, height, weight-for-age z-score (WAZ), height-for-age z-score (HAZ) and body mass index (BMI) were recorded at baseline and after intervention by protein RDA at three months and six months. Laboratory investigations were repeated at each time point. Dietary adherence was monitored through telephone follow-ups between visits and three-day dietary recalls were conducted at each follow-up assessment under dietitian supervision.

Ethical Considerations

Ethical approval was obtained from the Institutional Review Board of Dhaka Shishu Hospital. Written informed consent was obtained from parents or guardians. Confidentiality was strictly maintained using coded identifiers. Participants were allowed to withdraw at any stage without affecting clinical care.

Statistical Analysis

Data were analyzed using SPSS version 22. Descriptive statistics were expressed as mean ± standard deviation and frequency percentages. Paired t-tests were used to compare baseline and follow-up variables. Pearson correlation analysis was used to assess the relationship between hemoglobin and GFR. A p-value ≤ 0.05 was considered statistically significant.

Results

The study enrolled 30 children with CKD aged 2 to 18 years. The results are presented sequentially, beginning with patient demographics, followed by anemia profile, longitudinal changes in hemoglobin and GFR and the correlation analysis between Hb and GFR after six months of RDA protein intervention.

Table 1: Age distribution of the study patients (n=30)

Age Group	Frequency (n)	Percentage (%)
≤5 years	8	26.7
6-10 years	16	53.3
> 10 years	6	20
Total	30	100
Mean ± SD	8.10 ± 3.7 years	
Range:	2-16 years	

The age distribution of the study participants is shown in Table 1. The majority of study subjects, 16 (53.3%), were in the age range of 6 to 10 years, followed by 8 (26.7%) subjects aged 5 years or below and 6 (20.0%) respondents older than 10 years. The mean age was 8.10 ± 3.7 years, with a minimum age of 2 years and a maximum of 16 years.

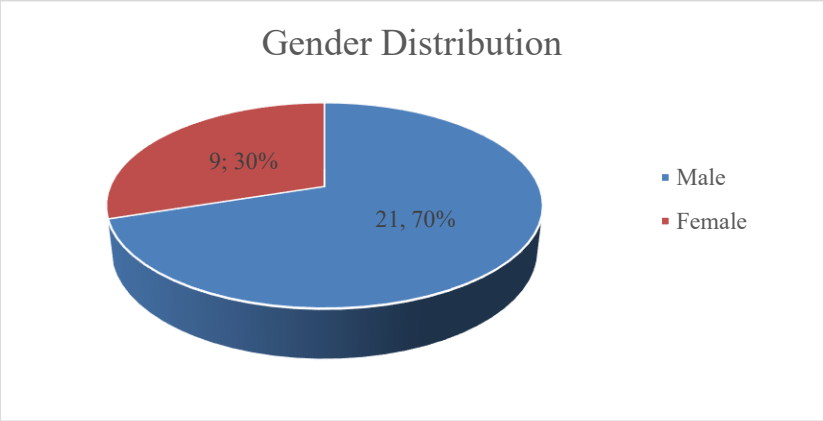

Figure 1: Sex distribution of the study patients (n=30)

Figure 1 presents the sex distribution of the study patients. A clear male predominance was observed, with 21 (70.0%) male patients and 9 (30.0%) female patients. The male-to-female ratio was 2.3:1.

Table 2: Distribution of the study patients by CKD stage (n=30)

CKD Stage	Frequency	Percentage (%)
Stage II	4	13.3
Stage III	11	36.7
Stage IV	10	33.3
Stage V (without dialysis)	5	16.7
Total	30	100

Table 2 presents the distribution of patients by CKD stage. The largest proportion of patients, 11 (36.7%), were classified at CKD stage III, followed by stage IV in 10 (33.3%) patients, stage V (without dialysis) in 5 (16.7%) patients and stage II in 4 (13.3%) patients. This distribution indicates that the majority of participants had moderate to severe renal impairment at the time of enrollment.

Table 3: Distribution of the study patients by anemia status (n=30)

Anemia Severity	Frequency (n)	Percentage (%)
Mild	16	53.3
Moderate	10	33.3
Severe	4	13.3
Total	30	100

The distribution of anemia severity at baseline is shown in Table 3. Mild anemia was the most prevalent category, present in 16 patients (53.3%). Moderate anemia was identified in 10 patients (33.3%) and severe anemia in 4 patients (13.3%). All 30 enrolled children had some degree of anemia at baseline, reflecting the near-universal hematological compromise characteristic of pediatric CKD.

Table 4: Comparison of Hb and GFR before and after RDA of protein intake (n=30)

Variable	Baseline (Before RDA)	After 3 Months	After 6 Months	p-value (Paired t-test)	
				Baseline vs. 3 M	Baseline vs. 6 M
Hb (g/dL)	9.44 ± 2.08	10.36 ± 1.42	10.98 ± 1.33	<0.001	<0.001
GFR (mL/min/1.73m²)	34.3 ± 17.5	38.2 ± 21.15	42.4 ± 24.4	<0.001	<0.001

The temporal changes in mean Hb and mean GFR across the three assessment time points are presented in Table 4. Mean Hb increased from a baseline value of 9.44 ± 2.08 g/dL to 10.36 ± 1.42 g/dL at three months and further to 10.98 ± 1.33 g/dL at six months. Both improvements were statistically significant compared to baseline (p less than 0.001 for both comparisons). Similarly, mean GFR rose from 34.3 ± 17.5 mL/min/1.73m^2 at baseline to 38.2 ± 21.15 mL/min/1.73m2 at three months and 42.4 ± 24.4 mL/min/1.73m^2 at six months, with both improvements reaching statistical significance (p less than 0.001 for both comparisons).

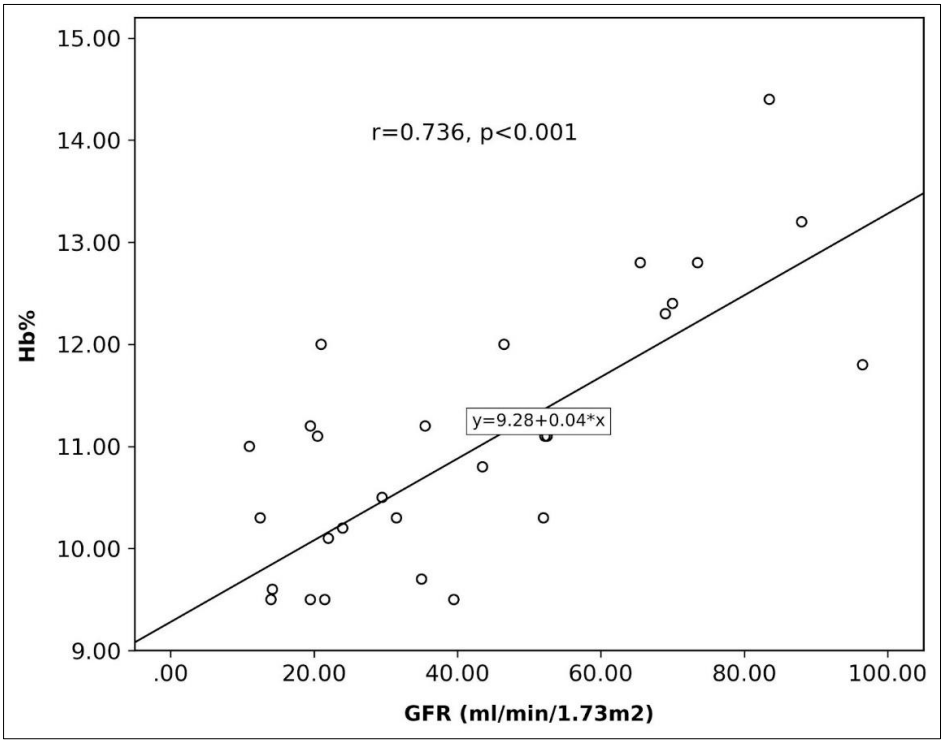

Figure 2: Scatter diagram showing the correlation between Hb% and GFR (ml/min/1.73m^2)

After 6 months of RDA protein intake Hb% was found significantly positive correlation with GFR (r=0.736, p<0.001).

DISCUSSION

This clinical trial examined the association between hemoglobin improvement and GFR changes in children with CKD following a six-month RDA protein intervention. The study found that both Hb and GFR improved significantly over the course of the intervention and that, at the end of six months, the two variables demonstrated a strong positive correlation (r = 0.736, p less than 0.001). These findings contribute meaningfully to the limited body of evidence addressing the hematological and renal functional outcomes of nutritional optimization in pediatric CKD.

The demographic profile of the study population was consistent with what has been reported in comparable studies. The mean age of 8.10 ± 3.7 years and the male predominance (70%) in this cohort resemble patterns documented in other pediatric nephrology studies. Wingen *et al.,* reported a mean patient age of 10.4 years with a predominance of male subjects in a multi-center study of protein restriction in children with CKD [13]. Gupta et al., in a nutritional assessment of CKD children in India, reported a mean age of 9.19 years, with the largest proportion of patients in the 5 to 12 years age group [14]. The similarity in demographic distribution across these different geographical settings suggests a relatively consistent epidemiological pattern of pediatric CKD presentation. The distribution by CKD stage in this study, with the majority of patients in stages III and IV, is also consistent

with observations from Gupta et al., who reported that 40% of their cohort had CKD stage IV or V [14]. This staging profile indicates that most patients enrolled in this study carried a significant burden of renal functional impairment at baseline, making the observed improvements in both Hb and GFR particularly noteworthy.

The prevalence and severity distribution of anemia in this cohort, with 53.3% mild, 33.3% moderate and 13.3% severe anemia at baseline, are concordant with published estimates. Kaspar *et al.,*reported anemia in approximately 45% of children with CKD at the time of cohort entry and noted that EPO production declines progressively with CKD advancement as the peritubular interstitial cells responsible for erythropoietin synthesis are destroyed alongside functional nephron loss [4]. Koshy and Geary demonstrated that lower GFR values are consistently associated with lower hemoglobin concentrations, attributing this pattern to EPO deficiency, shortened erythrocyte lifespan inversely proportional to blood urea nitrogen levels, elevated hepcidin concentrations impairing iron absorption and the direct suppressive effect of uremic toxins on erythroid precursor activity [5]. The finding in the present study that all 30 enrolled patients had anemia at baseline, regardless of CKD stage, underlines the ubiquitous nature of this complication and affirms the pathophysiological reasoning linking renal functional decline with erythropoietic insufficiency.

The significant improvement in Hb over the intervention period, rising from 9.44 ± 2.08 g/dL at baseline to 10.98 ± 1.33 g/dL at six months (p less than 0.001), occurred in parallel with iron supplementation provided as part of the dietary management protocol. This is consistent with the rationale articulated by Warady et al., who emphasized that CKD children frequently require supplemental parenteral or enteral iron to maintain iron stores, particularly given the role of elevated hepcidin in blunting oral iron bioavailability [3]. The improvement observed in this study, while modest in absolute terms, represents a clinically meaningful shift from the range of moderate anemia toward mild anemia in many patients. The simultaneous improvement in GFR, from 34.3 ± 17.5 to 42.4 ± 24.4 mL/min/1.73m^2, aligns with findings reported by Rizzetto et al., who demonstrated significant improvement in eGFR from 38.70 to 51.1 mL/min/1.73m^2 (p less than 0.001) following a low-protein diet in non-dialysis CKD patients [14]. Although the protein restriction strategy in that study was more aggressive, the directional consistency of the GFR response to protein modulation supports the broader principle that dietary protein management favorably influences glomerular hemodynamics.

The central and most novel finding of this study is the strong positive correlation between Hb and GFR after six months of RDA protein intervention (r = 0.736, p less than 0.001). This correlation, which is considerably stronger than the negative correlation between serum urea and GFR (r = -0.420, p = 0.021) identified in the same dataset, suggests that hemoglobin improvement may be a more sensitive co-varying marker of renal functional recovery in this setting. Several mechanisms may explain this relationship. As protein intake is normalized, the uremic milieu improves, with reductions in serum urea and creatinine reducing the toxic burden on erythroid precursors. Concurrently, as inorganic phosphate levels decline with dietary phosphate restriction embedded within the RDA dietary plan, secondary hyperparathyroidism is attenuated. Elevated PTH has been implicated in erythropoietic suppression and its reduction may contribute to hemoglobin recovery independent of EPO status. King and Levey demonstrated that protein intake modulates renal hemodynamics directly and that reducing protein load decreases hyperfiltration-driven glomerular injury, thereby preserving GFR [15]. The co-improvement of Hb and GFR in this context therefore likely reflects a shared downstream benefit of reduced uremic toxicity rather than a direct causal relationship between hemoglobin and renal filtration capacity.

These findings carry practical implications for the clinical management of pediatric CKD. The data suggest that Hb trend may serve as an accessible, non-invasive indicator of renal functional improvement in children receiving RDA protein therapy. In resource-limited settings where GFR estimation requires laboratory infrastructure, serial hemoglobin monitoring could potentially offer supplementary prognostic information. Furthermore, the observation that both anemia and GFR improved without the growth impairment observed with more aggressive protein restriction strategies reinforces the clinical appropriateness of RDA-guided dietary management as a balanced therapeutic approach. Echten et al., in a study of 56 children with CKD on protein restriction at WHO-recommended safe levels over three years, reported preserved or improved growth indices with no adverse effects on body composition, findings that support the safety of the dietary strategy employed in the present study [16].

Overall, the findings support the hypothesis that RDA-based protein intake not only preserves renal function but also contributes to hematological improvement in children with CKD. The interdependence between hemoglobin and GFR highlights the integrated nature of renal and hematological systems in chronic kidney disease progression.

This study reinforces the importance of nutritional management as a non-pharmacological intervention in pediatric CKD. By maintaining protein intake within recommended levels, it may be possible to

delay disease progression, improve biochemical stability and reduce anemia severity simultaneously.

Limitations of the study

The study was conducted with a small sample size and at a single tertiary care hospital, which may limit the generalizability of the findings. The follow-up period was relatively short (6 months) and longer-term outcomes were not assessed. Dietary adherence was partly dependent on caregiver reporting, which may introduce recall bias.

CONCLUSION

There is a strong positive association between hemoglobin and glomerular filtration rate in children with CKD following RDA-based protein intervention. Improvement in renal function is significantly associated with correction of anemia, indicating that dietary protein management may play a dual role in preserving kidney function and improving hematological status.

Conflicts of interest: There are no conflicts of interest.

Ethical approval: This study approved by the institutional ethical review committee.

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