ORIGINAL ARTICLE

SIGNIFICANCE OF C-REACTIVE PROTEIN AND ALBUMIN IN CHRONIC KIDNEY DISEASE PATIENTS

ABDULREHMAN S.,[1] SHEHZAD F.,[2] AZIZ S.,[3] ALI H.[4] AND ZAMEER M.[5]
[1-5]Pathology Department, Children Hospital and AMP; ICH, Lahore – Pakistan

ABSTRACT

Background and Objectives: Chronic kidney disease (CKD) and renal failure (RF) are recognised as significant problems for almost of the last 2 centuries. It is more common in adults than in children. The objective of this study is to determine nutritional status, extant of inflammation and the correlation of CRP an Albumin in chronic kidney disease children.

Methods: In this cross sectional study a total of 78 patients were included out of which 59 (75.6%) were males and 19 (24.4%) were females, with a male to female ratio of 3:1. The average age was 11.8 years with a standard deviation of ± 3.06 years.

Results: Serum CRP levels were high in majority of patients with a mean value of about 21.77 mg/L with a standard deviation of ± 16.44. Serum albumin levels in these patients were found below the normal range giving a mean value of 3.06 g/dl with a standard deviation of ± 1.07.

Conclusion: In chronic kidney disease CRP and albumin are very closely related to each other, as the level of CRP increased the albumin goes on decreasing due to inflammation and decreased synthesis by liver. Low levels of albumin are a marker of poor nutritional status in these children.

Key Words: Chronic kidney disease, C-reactive protein, albumin.

INTRODUCTION

Chronic kidney disease (CKD) and renal failure (RF) are familiar as most of the problems for almost of the previous 2 centuries. Chronic kidney disease has emerged as a grave public health trouble. Scientific and technological improvements throughout the second half of the 20th century provided renal replacement therapy as a life-sustaining choice for the many individuals who otherwise may have died. The collision of these medical advancements has been notable.

Chronic kidney disease is characterized by an irreparable worsening of renal function that slowly leads to end-stage renal disease (ESRD). A set of diverse pathophysiological processes related with atypical kidney occupation and progressive turn down in glomerular filtration rate categorised by kidney hurt or glomerular filtration rate (GFR) <60mL/min/1.73m2 for 3 months or more with remaining glomerular filtration rate (GFR) less than 30%, irrespective of the primary cause.

There are noticeable variations in the commonness and prevalence of CKD in the pediatric people crossways the countries. Just about 80% of RRT (renal replacement therapy) patients globally subsist in Europe, Japan or North America, where all children with ESRD have way in to RRT. In the UK, the occurrence and the numbers of RRT in children from the south Asian population in 2008 were 2.5 and 1.5 times larger than that of the white population aged 0–15 years.[1] In a study from India, the incidence of CKD was resolute 5.3% among all children below 16 year of age.[2]

The principal causes of chronic kidney disease (CKD) in children comprise the following: disruptive uropathy, or dysplastic kidneys, reflux nephropathy, focal segmental glomerulosclerosis as a alternative of childhood nephritic syndrome polycystic kidney disease, autosomal-recessive and autosomal-dominant varieties. The diagnosis of chronic kidney disease depend on definite lab tests, these might be included:

Blood Tests: Blood tests include blood cell counts, electrolyte levels, and renal function tests.

Urine tests, **Chest X-ray:** A diagnostic test that uses unseen electromagnetic energy beams to build images of inner tissues, bones, and organs against film.

Renal Ultrasound (Also Called Sonography): A noninvasive test in which a transducer is approved over the kidney giving sound waves that spring back off the kidney. This sends a depiction of the organ on a record screen. This test is used to establish the size and shape of the kidney, and to discover a mass, kidney calclui, cyst, or other obstacle or abnormalities.

Renal Biopsy: This method involves the exclusion of tissue samples (with a spine or during surgery) from the body for assessment under a microscope.

Corresponding Author: Dr. Farhana Shazad, MBBS, M. Phil (Immunology)
Associate Professor Immunology, Department of Pathology, Children Hospital & ICH
Lahore – Pakistan. Email: farhanashehzad@gmail.com Contact: 0321-4240200

Certain immunological tests might help to make sure the level of inflammation including a variety of cytokine levels and acute phase proteins, of which c-reactive protein is very central and sensitive. C-reactive protein similar to other cytokines also raised in CKD or dialysis patients. The clear-cut cause of inflammation in CKD patients is not clear.[3] C-reactive protein is notably high in CKD patients due to inflammation and due to use of catheterization. The harshness of inflammation can be expected by the serum concentration of CRP.[4]

CRP is also supportive in prognostication and in monitoring treatment in CKD patients, it rose in these patients because CKD is an inflammatory process and pro-inflammatory cytokines are responsible for its increased synthesis. The raised serum levels of CRP reveal the activity of cytokine-mediated (the main cytokines for its production are IL-1, IL-6 and TNF which are proinflammatory and cause an increase in APRs) acute phase course and are approximately proportional to the degree of tissue damage.[5]

In addition, significant evidence has mounted up over several years that malnutrition is related with cardiac co-morbidity, inflammation and deprived endurance in chronic kidney disease patients. Clinical evaluation of malnutrition is mainly commonly done by biochemical markers.[6] Serum albumin is an eminent marker of diet in chronic kidney disease children. Low serum albumin levels possibly will reproduce poor nutrition. Occurrence of an inflammatory response, old age and extent of hydration could also grounds hypoalbuminemia.[7]

There is a considerable association between serum albumin and CRP levels in CKD children, as CRP levels boost up there is a reduction in serum albumin, the reason for this is that as the pro-inflammatory cytokines such as IL-1, IL-6 and TNFα cause an increase in positive APRs in liver they also cause reduction in synthesis of albumin and other negative APRs.[8] CRP and albumin are together acute phase reactants, of which CRP is positive APR (acute phase reactant) while albumin is negative APR. So when the level of one is increasing in inflammation such as CKD the other goes on decreasing and vice versa.[9]

Operational Definition

Chronic kidney disease is characterised by a set of diverse pathological process related with atypical kidney function and progressive turn down in glomerular filtration rate <60mL/min/1.73m² for 3 months or more with remaining glomerular filtration rate less than 30%, irrespective of the primary cause.

Rational of this Study

1. This study purpose guideline as patients with chronic kidney disease show raised levels of CRP which is a prognostic and diagnostic marker for these patients.
2. This study may lead to develop therapeutic measures after assessing the severity of CKD in patients.
3. This study leads to batter prognostic effect in CKD children as the disease is progressive in nature.

Objectives

The objective of this study was to determine the extent of inflammation and the relation of CRP and albumin with each other.

MATERIAL AND METHOD

It is a descriptive hospital based study done at children's hospital Lahore, comprising a total of 78 CKD patients over a period of six months. Sample size is calculated using the following formula:

$$n = \frac{Z^2P(1-P)}{d^2}$$

$$n = \frac{1.96)20.053(1-0.053)}{(0.05)^2}$$

n =78

Where n = sample size
z = statistic for a level of confidence (1.96 for 95% confidence interval)
p = prevalence or proportion taken as 5.3%.[2]
d = precision (5% = 0.05)

The inclusion criteria for the study were as follows: patients younger than 16 year of age, male or female, diagnosed with chronic kidney disease and having dialysis on regular basis since at least last 3 months. Patients were excluded if they were more than 16 year of age, unwilling to participate in this study, clinically unstable, patient those with tumors and other inflammatory conditions like diabetes, rheumatoid arthritis etc. or taking immunosuppressive drugs.

The average age was 11.8 years with a standard deviation of ± 3.06 years (range between 4-6 years). The blood sample of CKD patients were collected using performa and CRP was done by agglutination method giving a mean of about 21.77 with 16.44 ± SD. The normal range for CRP is < 6 mg/L. The measurement of albumin was done with colorimetric assay with end point method on Hitachi MODULAR-P using rerun function. The color intensity is directly proportional to the amount of albumin.

Statistical Analysis

statistical analysis was done with IBM SPSS version 22. All results are given in mean ± SD. The correlation of CRP and Albumin was done using Pearson's correlation test, and a p-value of <0.05 was considered to be significant.

RESULTS

Chronic kidney disease (CKD) and renal failure (RF) are recognised as significant problems for almost of the last 2 centuries. Chronic kidney disease has emerged as a serious public health problem especially in developing countries. A total of 78 patients 59 (75.6%) were males and 19 (24.4%) were females, with a male to female ratio of 3:1 (table 1). The average age was 11.8 years with a standard deviation of ± 3.06 years. The minimum and maximum ages were 4.00 years and 16.00 years respectively. Mostly children were more than 6 years (table 2).

Serum CRP Levels in CKD Patients

Serum CRP levels were high as compare to the normal value which is 6 mg/L in these patients with a mean value of about 21.77 with 16.44 ± SD (Table 3).

Serum Albumin Levels in CKD Patients

Serum albumin levels in these patients were found below normal range giving a mean value of 3.06 with 1.07 ± SD (table 4).

Correlation of CRP and Albumin in CKD Patients

In chronic kidney disease CRP and albumin are very closely related to each other, as the level of CRP increased the albumin goes on decreasing due to inflammation and decreased synthesis by liver. There was a significant correlation between serum albumin and CRP giving a p-value of less than 0.0001 (table 5).

Table 1: *Distribution of male and female patients in study population.*

	Frequency	*Percentage (%)*
Male	59	75.6%
Female	19	24.4%
Total	78	100%

The male to female ratio is 3:1.

Table 2: *Distribution of age in study population.*

Statistics	*Age in Year(s)*
Mean	11.08
Standard deviation	3.06
Minimum	4.00
Maximum	16.00

Majority patients were more than 6 years of age.

Serum CRP levels were raised in CKD patients which is a strong predictive marker for inflammation.

Table 3: *Serum levels of CRP in CKD patients.*

	CRP (mg/L)
Mean	21.77
Standard deviation	16.44

Table 4: *Serum levels of albumin in CKD patients.*

	Albumin (g/dl)
Mean	3.06
Standard deviation	1.07

Low serum albumin levels are indicators of inflammation and albumin loss in urine.

Table 5: *Correlation of CRP and Albumin in CKD patients.*

	r (correlation)	*p-value*
CRP	1	< 0.0001
Albumin	-0.459	<0.0001

A p-value of less than 0.05 is significant and indicates the correlation of two variables significant.

DISCUSSION

Chronic kidney disease has turned into a very grave and lethal health problem in both developed and in developing countries. In adult population there are momentous data is accessible regarding CKD but in children a little is known due to limited resources. Greater part of our study presented after 6 years of age. There was a high proportion of males (M:F ratio 3:1) which is in agreement to the study conducted by S. Jamro et al. Our children had more growth retardation as compared to Belts and Margrath Study. This may be due to delayed diagnosis and more dominance of malnutrition in wide-ranging population of our country.

Albumin is a negative acute-phase immediate protein and its fusion is actively concealed as a part of response to inflammation.[10] Most of the children on dialysis have albumin levels that lie within the typical range. A lot of have albumin levels that lie below normal. Children with normal renal function may drop albumin in the urine. Their body retort by increasing the speed of albumin synthesis, although this reaction is insufficient to regularize serum albumin levels.[11]

Hypoalbuminemia is a familiar marker for morbidity and mortality in CKD population. Lowrie and Lew renowned a linear raise in death rate with waning serum albumin levels at the beginning of dialysis in addition to during the route of preservation of dialysis.[12] Serum albumin concentration is an indicator for nut-

rition, inflammation plasma volume. Serum albumin is commonly considered a dietary marker and has been revealed to predict results in CKD children which is in concordant with a study conducted by Stienman in 2000.[13]

There is rising indication that it may be more associated chronic inflammation than to dietary status. The reported relationship between hypoalbuminemia and death may be due to inflammation more willingly than to poor nutritional ingestion.[14] Therefore hypoalbuminemia is not merely a marker of starvation but also reveals inflammation and co-morbidity, therefore its usual estimation is very vital in CKD children.[15]

CRP protein kindles tissue factor production and neutrophil aggregation. The propensity to coagulation might point to a direct payment of CRP to death. In our study, we generalized that a large part of children had high serum CRP levels (≥ 10 mg/L). The presence of raised CRP in a major number of CKD children prove the survival of chronically activated acute phase reactant.

Current data from CKD children also demonstrated high CRP levels have considerable connection with hypoalbuminemia, undernourishment, increased morbidity and transience in CKD patients[3] which is in agreement with our study. Bergstrom *et al.,* were first to illustrate that raised CRP was a strong interpreter of mortality. Owen and Lowrie in 2001 demonstrated the relationship between CRP and nutritional statistics which is also in agreement with our study.[16]

In ***conclusion*** this study shows that elevated CRP and reduced levels of albumin are the main predictive markers of inflammation in CKD patients. They both are associated with each other and showed a strong relation as the level of CRP increased the albumin goes on decreasing due to the effect of pro-inflammatory cytokines. It is also noted that reduced levels of albumin also a marker for malnutrition.

Author's Contribution

SA: Did the research, data collection, lab work and manuscript writing. FS: Was the supervisor and corresponding author of data collection, lab work and manuscript writing. SA: Designed and did the statistical analysis. HA: Helped in Sample collection. MZ: Help in various aspects of research process.

REFRENCES

1. Deleau J, Andre JL, Briancon S, Musse JP. Chronic renal failure in children: an epidemiological survey in Lorraine (France) 1975 – 1990. Pediatric Nephrology. 1994 Aug. 1; 8 (4): 472-6.
2. Gulati S, Mittal S, Sharma RK, Gupta A. Etiology and outcome of chronic renal failure in Indian children. Pediatric Nephrology, 1999 Aug. 1; 13 (7): 594-6.
3. Arici M, Walls J. End-stage renal disease, atherosclerosis, and cardiovascular mortality: is C-reactive protein the missing link? Kidney international, 2001 Feb. 1; 59 (2): 407-14.
4. Harris TB, Ferrucci L, Tracy RP, Corti MC, Wacholder S, Ettinger WH, Heimovitz H, Cohen HJ, Wallace R. Associations of elevated interleukin-6 and C-reactive protein levels with mortality in the elderly. The American journal of medicine, 1999 May 31; 106 (5): 506-12.
5. Bensen JT, Langefeld CD, Li L, Mccall CE, Cousart SL, Dryman BN, Freedman BI, Bowden DW. Association of an IL-1A 3′ UTR polymorphism with end-stage renal disease and IL-1α expression. Kidney international, 2003 Apr 30; 63 (4): 1211-9.
6. Stenvinkel P, Barany P, Chung SH, Lindholm B, Heimbürger O. A comparative analysis of nutritional parameters as predictors of outcome in male and female ESRD patients. Nephrology Dialysis Transplantation, 2002 Jul. 1; 17 (7): 1266-74.
7. Heimbürger O, Qureshi AR, Blaner WS, Berglund L, Stenvinkel P. Hand-grip muscle strength, lean body mass, and plasma proteins as markers of nutritional status in patients with chronic renal failure close to start of dialysis therapy. American journal of kidney diseases, 2000 Dec. 31; 36 (6): 1213-25.
8. Zhoul T, Zhan J, Hong S, Hu Z, Fang W, Qin T, Ma Y, Yang Y, He X, Zhao Y, Huang Y. Ratio of C-Reactive Protein/Albumin is An Inflammatory Prognostic Score for Predicting Overall Survival of Patients with Small-cell Lung Cancer. Scientific reports, 2015 Jun. 18; 5.
9. Dashti N, Einollahi N, Nabatchian F, Sarabi MM, Zarebavani M. Significance of albumin and C-reactive protein variations in 300 end stage renal disease patients in Tehran University of Medical Sciences Hospitals during year 2010. Acta Medica Iranica. 2012 Mar. 1; 50 (3): 197.
10. Kaysen GA. Interpretation of plasma protein measurements in end-stage renal disease. Blood purification, 2000; 18 (4): 337-42.
11. Kaysen GA. Biological basis of hypoalbuminemia in ESRD. J Am Sochool of Nephrol. 1998 Sep. (12): 2368-76.
12. Lowrie EG, Lew NL. Death risk in hemodialysis patients: the predictive value of commonly measured variables and an evaluation of death rate differences between facilities. American Journal of Kidney Diseases, 1990 May 31; 15 (5): 458-82.
13. Steinman TI. Serum albumin: its significance in patients with ESRD. In Seminars in dialysis, 2000 Nov. 1 (Vol. 13, No. 6: pp. 404-408). Blackwell Science Inc.
14. Wang AY, Sea MM, Ho ZS, Lui SF, Li PK, Woo J. Evaluation of handgrip strength as a nutritional marker and prognostic indicator in peritoneal dialysis patients. The American journal of clinical nutrition, 2005 Jan. 1; 81 (1): 79-86.
15. Stenvinkel P, Barany P, Chung SH, Lindholm B, Heimbürger O. A comparative analysis of nutritional parameters as predictors of outcome in male and female ESRD patients. Nephrology Dialysis Transplantation. 2002 Jul. 1; 17 (7): 1266-74.