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The correlations of some hematological factors in pediatrics chronic renal diseases

Eman A. Muhsin and Nibal Kh. Mousa

Iraq Ministry of Science and Technology, Baghdad, Iraq.

Abstract

Six hematological factors were measured and statistically analyzed to detect the significant correlation between them within two pediatrics sick groups with the most occurred chronic kidney diseases (CKD). They were 36 patients with nephrotic syndrome (NS) and 26 patient with chronic renal failure (CRF) at the age range 1-12 years of both genders from three pediatrics hospitals in Baghdad. The control group consisted of 26 healthy children at the same age range of sick groups and of both genders. The measured factors were: urea, creatinine, Interleukin-6, Erythropoietin, packed cell volume and hemoglobin. The results showed that there was a significant correlation between urea and creatinine in the control group only, referred to intact renal function. Also, there was a significant correlation between erythropoietin and each of interleukin-6, packed cell volume, and hemoglobin in the nephrotic syndrome group. Finally, there was a high significant correlation between packed cell volume and hemoglobin in both sick groups as well as controls.

Key words: Chronic kidney diseases, Hematological factors, correlations, Pediatrics, Baghdad.

Introduction

Chronic kidney disease (CKD) is a worldwide public health problem, it is defined as renal failure due to structural or functional causes that persist for more than three months. There is a growing incidence that the pediatrics CKD progresses towards end stage renal disease (ESRD) (Burg *et al*., 2006). In childhood, nephrotic syndrome (NS) and chronic renal failure (CRF) are the most important CKD, and if not treated, it will result in death (Bagga and Mantana, 2005). The etiologies of CKD in childhood are related to the age of the child at the time the kidney disease occurs. Congenital and obstructive abnormalities are the most common causes between birth and 10 years of age. After age 10, acquired diseases become more prevalent. The progression to end-stage kidney failure varies. CKD generally develops to end-stage renal disease (ESRD) as renal functions are affected (Kliegman *et al*., 2006).

In Iraq, genitourinary system disease were the seventh causes of mortality rate in children under five years old (1.95%) and the sixth cause for infants (1.6%) for 2004-2005 (Hameed, 2008), while it was 4.4% in the period of 1993-2002 in the study of Al-Naaimi (2006). Through in-depth analysis report of Iraqi child and maternal mortality survey 1999, the death incidence due to urogenital system disease was mostly in children between 1-5 years old (WHO, 2005). The most common among conditions, the category labeled "Diseases of the Genitourinary System" was UTI, followed by nephrotic syndrome. Renal failure ranked third in frequency (Al-Naaimi, 2006). The clinical picture includes anemia, abnormalities in renal function (Burg *et al*., 2006) and wide variety of immunological abnormalities (Ece *et al*., 1999). Moreover, some references (Azhir *et al*., 2006; Mong *et al*., 2007) reported an association between anemia and inflammation.

Anemia is a major complication of CKD and ESRD in children that can frequently develop (Staples *et al*., 2009). It results from erythropoietin (Epo) deficiency due to its decreased production from kidneys (Azhir *et al*., 2006). Epo is probably not only hematopoietic factor but also a cytokine produced mainly in the kidneys (Prutchi Sagiv *et al*., 2006).

Among proinflammatory cytokines, interleukin-6 (IL-6) is reported to have a central role in the pathophysiological process in patients with renal disease. A range of cells secretes it. Its activities range from the control of the immune response to the involvement in the pathological states (Kindt *et al*., 2007).

This study was carried out to determined six hematological factors and statistically analyzed to detect the significant correlation between them within two pediatrics sick groups with the most occurred chronic kidney diseases (CKD).

Materials and Methods

Study groups: The pediatrics patients were 26 of CRF and 36 of NS at the age of 1 to 12 years of both genders, who were outpatients and inpatients in the dialysis unit in Al-Kadimiya pediatric hospital, Al-Mansour pediatrics teaching hospital and Child's central teaching hospital. The control group consisted of 26 children of both genders and at the same age range of the study groups.

Blood samples: Five ml of venous blood were obtained from each child in the study and control group and distributed in suitable containers (Plain tubes and capillary tubes) according to the use in different tests. Eppendroff tubes were used for serum storage at -20°C after centrifugation at 3000 rpm for 10 minutes (Polnay *et al*., 2006).

Assay procedure: The biochemical (urae and creatinine) and immunological parameters (interleukin-6 and erythropoietin) of each of the studied groups were measured according to the directions of the manufacturing companies (blood urea kit (BioMérieux), erythropoietin (Epo) ELISA kit(DRG/U.S.A), interleukin-6 (IL-6) ELISA kit (Immunotech/ France), serum creatinine kit (Randox/ U.K). The anemia parameter, including packed cell volume (PCV) and hempglobin (Hb), were measured and calculated according to (Tergeon, 1988) and by using the equation of Connor *et al*. (1994):

Hb (g/dl) = (PCV (L/L)-1) / 3

Statistical analysis: Data were translated into a computerized database structure. Statistical analysis was computer assisted using SPSS (Statistical Package for Social Sciences) 2008, version 17. The charts were done by using curve estimation system (the quadratic mode). The statistical significance of association between two variables within the same group was assessed by Chi-square. LSD was used in comparison between two different groups. p-value less than 0.05 was considered statistically significant.

Results and Discussion

After the data were statistically computed, they were analyzed and there was many correlations between some entire factors in each study group.

Means: The means of the measured hematological factors were as shown in table 1, then the Chi-square test was applied within each study group to detect the significant correlations.

Table (1): The means of the studied hematological factors.

Factors	Groups		
	NS group	CRF group	Control group
Urea	59.5	96.2	29.5
Creatinine	1.85	4.93	0.87
IL-6	75.5	58.2	37.86
Epo	11.86	10.2	16.5
PCV	33.9	26.03	39.5
Hb	10.96	8.38	12.82

The correlation between urea and creatinine: The correlation between serum urea and serum creatinine is represented in table (2). No significant correlation was found in both sick groups, while the correlation in control group was highly significant that explains intact renal function. A significant correlation was found in the normal controls in comparison with renal disease patients in the study of Dhafir *et al*. (1990) and Ismaeel (2004). The urea: creatinine ratio can be useful in determining the cause of renal dysfunction (Lewandrowski, 2002). A linear relationship existed between these two variables in normal subjects. So, this linear relationship may refer to either the two portions of the nephrons (the glomerulus and the tubules) are functioning or their function is impaired (Dhafir *et al*., 1990).

Table (2): Correlation between urea and creatinine.

Correlation	Groups		
	NS group	CRF group	Control group
Chi-square	-0.187	0.071	0.555**
P-value	0.276	0.730	0.003
Sample no.	36	26	26

**Correlation is significant at the (P>0.01)

The correlation between Erythropoietin and IL-6: This correlation was not significant in CRF patients (p-value was 0.923); but it was significant in NS patients (p-value was 0.049). The results are shown in table (3). Those results was similar to Rostaing *et al*. (2001) finding in their study of the cytokines production in CRF patients. They suggested that either the uremic state (significant high levels of blood urea) or the dialysis procedure, or both, might be able to affect on some cytokines but not the other. The significant correlation between IL-6 and Epo in NS children was recorded by Rizk *et al*. (2005). In NS patients, IL-6, in combination with other cytokines, acted on the bone marrow and hematopoiesis. There may be a suppressive effect of high IL-6 concentrations on erythropoiesis, but the reverse occurred in the healthy individuals (Ganong, 1999; Rizk *et al*., 2005). Moreover, some references (Azhir *et al*., 2006; Mong *et al*., 2007) reported an association between anemia and inflammation.

Table (3): Correlation between Epo and IL-6.

Correlation	Groups		
	NS group	CRF group	Control group
Chi-square	-0.331*	0.020	-0.282
P-value	0.049	0.923	0.162
Sample no.	36	26	26

**Correlation is significant at the (P>0.05)

The correlation between erythropoietin and PCV: A highly significant, positive correlation was found between these two parameters in the group of pediatric NS patients (Table 4). No references were obtained about this correlation; except that of Beckman *et al*. (2004) in which no correlation was found. Epo concentrations are related to the hematocrit in an exponential manner. So, when plasma Epo concentrations are low, erythrocytes production from erythroid progenitors is decreased (Yaqub *et al*., 2001). In NS group, the lowest Epo levels may be attributed to the urinary loss (Rizk *et al*., 2005).

Table (4): Correlation between Epo and PCV.

Correlation	Groups		
	NS group	CRF group	Control group
Chi-square	0.687**	0.254	-0.368
P-value	(P<0.001)	0.210	0.064
Sample no.	36	26	26

**Correlation is significant at the (P>0.01)

The correlation between erythropoietin and Hb: A positive significant correlation was found between Epo and Hb in NS group only (Table 5). This is similar to the result of Rizk *et al*. (2005) about NS children. No significant correlation was found in CRF group in this study. These results agreed with many studies (Aikhionbare *et al*., 1987; Chandra *et al*., 1988; Eckardt *et al*., 1990) about CRF pediatric patients. In NS group, the lowest Hb concentration is possibly caused by low levels of Epo in plasma which can result from increased urinary loss in NS (Abras, 1997) or Epo-deficiency which is a primary cause of renal anemia (National Collaborating Centre for Chronic Conditions, 2006).

Table (5): Correlation between Epo and Hb.

Correlation	Groups		
	NS group	CRF group	Control group
Chi-square	0.687**	0.230	-0.369
P-value	(P<0.001)	0.258	0.064
Sample no.	36	26	26

**Correlation is significant at the (P>0.01)

The correlation between PCV and Hb: Table (6) is more likely to show parallel pattern of hematocrits. Hb values were derived from PCV values of each patient by an equation according to Connor *et al*. (1994). In both sick groups, the major cause of anemia in CKD is Epo-deficiency, resulting from its decreased production from the kidneys (Azhir *et al*., 2006). while there was no renal anemia in the healthy children. This was the same results of (Rizk *et al*., 2005; Bolaños *et al*., 2002; Falk *et al*., 2004; Azhir *et al*., 2006).

Table (6): Correlation between PCV and Hb.

Correlation	Groups		
	NS group	CRF group	Control group
Chi-square	1.000**	0.99**	1.000**
P-value	(P<0.001)	(P<0.001)	(P<0.001)
Sample no.	36	26	26

**Correlation is significant at the (P>0.01)

Conclusions

There was a significant correlation between urea and creatinine in the control group only, referred to intact renal function. Also, there was a significant correlation between erythropoietin and each of Interleukin-6, packed cell volume, and hemoglobin in the nephrotic syndrome group. Finally, there was a high significant correlation between packed cell volume and hemoglobin in

both sick groups as well as controls.

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