

Colloid Oncotic Pressure in Children with Nephrotic Syndrome

by

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Abstract

To evaluate the correlation between plasma protein concentration and colloid oncotic pressure (COP) and their influence on clinical symptom of edema, we studied 30 children with nephrotic syndrome (NS). Total plasma protein concentration (TP), albumin, globulin and COP were measured in all patients in edema forming state (EF) and in steady state phase (SS), except for COP, only 16 samples in SS phase.

COP, TP, plasma albumin and globulin contents in EF group were 8.7 ± 2.7 mmHg, 4.07 ± 0.68 g/dl; 2.57 ± 0.50 g/dl and 1.51 ± 0.32 g/dl, respectively. In SS group these figures rose significantly to 16.7 ± 3.9 mmHg for COP; 5.70 ± 0.99 g/dl for TP; 3.46 ± 0.52 g/dl and 2.06 ± 0.56 g/dl for plasma albumin and globulin, respectively. We also found the high correlation both between COP and albumin content ($r = +0.58$; $P < 0.01$) and between COP and TP ($r = +0.54$; $P < 0.01$).

A strong negative correlation was also found between COP and the degree of edema ($r = -0.55$; $P < 0.01$). On the other hand a very low grade correlation was noticed between plasma albumin content and the degree of edema ($r = -0.26$; $P < 0.05$) and no correlation at all was found between edema and TP ($r = -0.19$; $P > 0.05$).

We conclude that COP has the highest correlation with plasma protein concentration and the degree of edema, and can be used as a diagnostic tool. It is even more sensitive and simple compared with the TP or albumin content determination.

Introduction

The importance of plasma protein concentration to maintain blood volume has already been known for some years. It was first discovered by Starling in 1896 but this finding was applied clinically nearly 80 years afterwards. The principal oncologically active protein is albumin and account for 67 - 75% of the normal COP. Globulins and fibrinogen account for most of the remaining oncologically active proteins (Weil et al., 1979).

The normal range of COP in healthy person was 21 to 25 mmHg (Weil et al., 1974). The clinical application of COP hitherto is still limited to the emergency cases hospitalized in intensive ward as

reported by Hassan et al. in 1986. Although the role of COP on the formation of edema in nephrotic syndrome was very important, literature study on this field is very limited and even in children the study has never been conducted so far. We assume that measurement of COP reflects plasma protein concentration and can be used as a diagnostic guide on patient with nephrotic syndrome. The purpose of this study is therefore to get a basic data of COP in children with nephrotic syndrome and its relation with the clinical symptoms of edema, and some laboratory findings, especially TP, plasma albumin and globulin contents.

Materials and Methods

This study was conducted on patients with nephrotic syndrome hospitalized at the Pediatric Ward DR. Cipto Mangunkusumo General Hospital Jakarta from August 1, 1985 to July 31, 1986. The diagnosis of nephrotic syndrome was based on heavy proteinuria (40 mg/m²/hour or more) associated either with edema or hypoalbuminemia (less than 2.5 g/dl) or both. The gradation of edema was calculated from the difference of body weight of the patients between the edema forming state (EF) state and the steady state phase (SS). This difference was recorded in percent of body weight compared with the steady state body weight. EF state and the SS were defined according to the definition proposed by Bohlin and Berg (1984). The colloid oncotic pressure, TP, albumin and

globulin measurements were done twice during the proteinuric phase, firstly during EF and secondly in the SS phase. All patients were treated with prednisone according to the scheme proposed by ISKDC (1979).

Diuretics or plasma infusion was given when necessary. COP was measured with Knauer Oncometer (Wissenschaft Geratebau, Berlin) using 0.3 ml of heparinized plasma. Plasma proteins (albumin and globulin) were measured with Cobas Bio diagnostic apparatus. The data was collected manually and grouped in tabulation form consisted of mean (X) and standard deviation (SD). Statistical analysis was done using the Student's t-test and linear regression to evaluate the correlation between the groups of investigation.

Results

During the study period there were 59 patients admitted with the diagnosis of nephrotic syndrome, but only 30 cases were suitable for investigation. The remaining 29 cases were excluded due to the inadequacy of laboratory data. The basic line data were shown on table 1. There were 23 boys and 7 girls aged 1½ to 14 years.

Table 1: Some base line data and laboratory findings in 30 cases of nephrotic syndrome

No.	Age (yrs)	Sex	N/R	Gradation of edema %	CHOL mg/dl	EF			SS		
						COP mmHg	ALB g/dl	TP g/dl	COP mmHg	ALB g/dl	TP g/dl
1	6	F	R	10.9	513	8.7	2.18	3.25	21.6	2.68	4.56
2	4	M	R	10.2	620	9.7	1.92	3.35	16.9	4.12	6.36
3	1.5	M	N	11.6	658	15.4	2.81	4.34	15.6	2.81	4.93
4	2	F	R	21.9	1042	9.6	2.19	3.36	16.6	3.18	4.51
5	5	M	R	14.4	940	8.6	2.48	4.11	10.4	3.46	6.13
6	4	M	N	14.7	487	8.0	2.46	4.33	17.5	4.07	6.93
7	6	M	N	25.9	562	5.7	2.54	3.98	19.6	3.68	5.00
8	7	M	R	32.1	755	7.9	1.87	3.25	13.3	3.71	6.29
9	11	M	N	14.9	672	6.5	3.12	5.38	12.4	2.96	4.91
10	2	F	N	33.5	442	8.1	2.81	4.58	16.4	4.29	7.21
11	7	F	N	8.9	408	12.3	3.08	4.26	21.5	3.19	5.24
12	0	M	N	10.8	719	15.3	2.66	4.52	16.5	2.74	4.72
13	11	M	N	24.3	554	9.8	2.62	3.78	25.6	3.65	5.59
14	8	M	N	11.9	499	8.9	3.27	4.83	17.2	4.14	6.57
15	9	M	N	25.2	484	4.5	2.58	3.92	14.5	3.66	6.62
16	7	M	R	35.3	700	6.1	2.56	4.34	16.1	4.07	6.83
17	5	F	N	20.6	565	8.3	2.06	3.18	X	4.06	6.33
18	7	M	N	14.3	817	9.8	1.98	3.47	X	3.06	4.15
19	7	M	N	14.3	689	8.7	1.82	3.28	X	2.89	4.77

20	14	M	N	13.2	803	7.7	2.54	3.68	X	3.64	5.98
21	4	M	N	24.9	569	6.7	2.14	3.31	X	3.28	5.42
22	5	M	R	20.7	930	4.0	1.78	2.93	X	2.78	3.81
23	2	F	N	11.1	396	7.5	3.38	4.82	X	3.54	5.18
24	5	F	N	23.2	378	9.8	3.38	5.41	X	3.77	6.29
25	9	M	N	7.3	358	13.5	3.34	5.08	X	3.48	5.62
26	12	M	N	27.6	472	6.0	2.24	4.16	X	2.74	4.87
27	12	M	N	15.4	458	4.1	2.24	3.91	X	3.05	5.58
28	6	M	R	16.9	496	7.4	3.47	4.58	X	3.38	4.99
29	9	M	N	24.0	789	8.3	2.96	4.25	X	3.12	4.91
30	3	M	N	20.2	780	12.9	2.43	4.16	X	3.27	4.71

Abbreviations : - COP: Colloid oncotic pressure - F: female case
 - ALB: Albumin content - M: male case
 - TP: Total protein - N: new case
 - X: not done - R: relapse
 - CHOL: Cholesterol - SS: steady state phase
 - EF: Edema forming state

Twenty two patients were studied during their first episode of clinical symptom and the remaining 8 cases were hospitalized in relapsing period. Table 2 showed the results of laboratory investigation including COP, TP, albumin and globulin, both during EF and in SS phase. TP, albumin and globulin were measured in all cases, but only 16 samples for COP examination were available in SS phase. The mean value of COP in EF state was 8.7 ± 2.7 mmHg which ranged from 4 to 15.4 mmHg. The mean

values of TP, albumin, and globulin were 4.07 ± 0.68 g/dl, 2.57 ± 0.50 g/dl and 1.51 ± 0.32 g/dl, respectively. These figures rose significantly ($P < 0.01$) in SS phase. The value of COP rose to 16.7 ± 3.9 g/dl mmHg while the TP, albumin and globulin contents increased to 5.7 ± 0.99 g/dl, 3.46 ± 0.52 g/dl and 2.06 ± 0.56 g/dl, respectively. The value of total plasma cholesterol, on the other hand, did not change significantly ($P > 0.05$).

Table 2 : Statistical analysis of laboratory findings on edema forming and steady state phase

Lab. Investigation	EF			SS			P
	N	X	SD	N	X	SD	
COP (mmHg)	30	8.7	2.9	16	16.7	3.9	0.001
TP (g/dl)	30	4.07	0.68	30	5.70	0.99	0.001
ALB (g/dl)	30	2.57	0.50	30	3.46	0.52	0.001
GLOB (g/dl)	30	1.51	0.32	30	2.06	0.56	0.001
CHOL (mg/dl)	30	634.8	186.4	30	593.2	177.6	0.05

Abbreviations :

- COP : Colloid oncotic pressure
- TP : Total protein
- ALB : Albumin
- GLOB : Globulin
- CHOL : Cholesterol
- EF : Edema
- SS : Steady state phase

In an effort to evaluate the correlation between COP and TP, albumin and globulin contents, the samples from EF group and the SS phase were combined in one group so that there were 46 samples measured simultaneously.

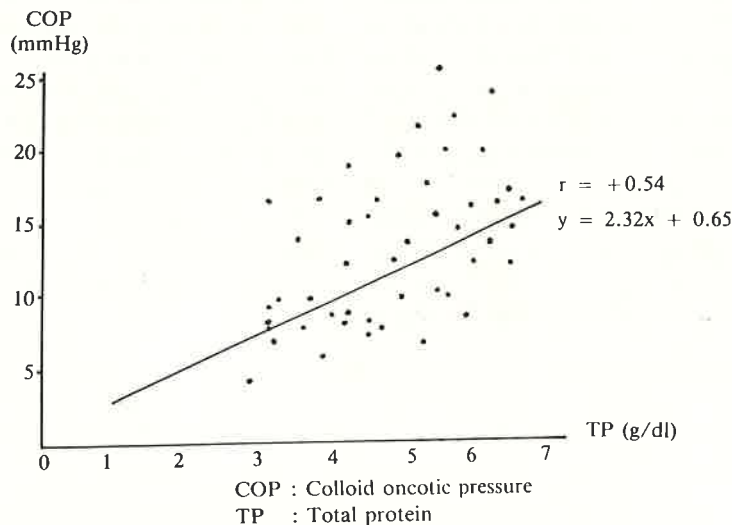


Fig 1. The correlation between COP and TP

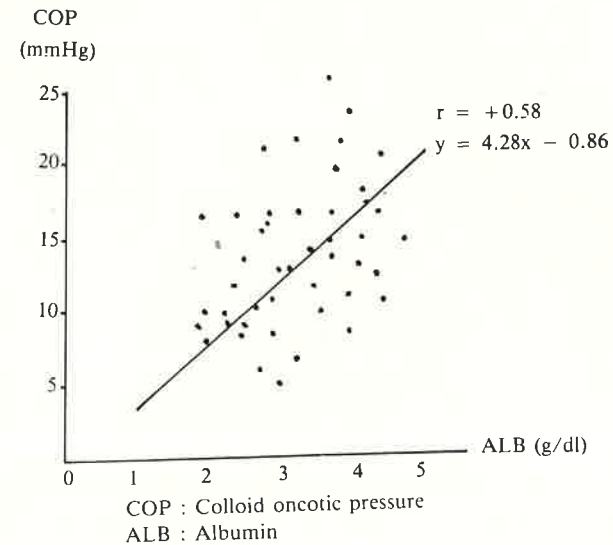


Fig 2. The correlation between COP and albumin content

Figure 1 showed a good correlation between COP and TP ($r = 0.54$; $P < 0.01$). Similar result was also found between COP and albumin contents (fig. 2: $r = 0.58$; $P < 0.01$), but no correlation was observed between COP and globulin ($r = 0.19$; $P > 0.05$).

There was a tendency that the values of COP, TP and albumin contents in the

group of new cases were higher than those of relapse cases. This was shown in table 3, but statistically these differences were not significant ($P > 0.05$). The mean increment of body weight on EF was about 18.6% of the SS body weight. There was a good negative correlation between the value of COP and the severity of edema as shown in figure 3 ($r = -0.55$; $P < 0.01$).

Table 3 : Laboratory results of COP, TP and albumin content in the group of new cases and the relapsing episode

Group of patients	N	COP (mmHg)		TP (g/dl)		ALB (g/dl)	
		X	SD	X	SD	X	SD
New cases	22	9.1	2.80	4.24	0.65	2.67	0.45
Relapse	8	7.5	3.59	3.50	0.57	2.28	0.53
P		> 0.05		> 0.05		> 0.05	

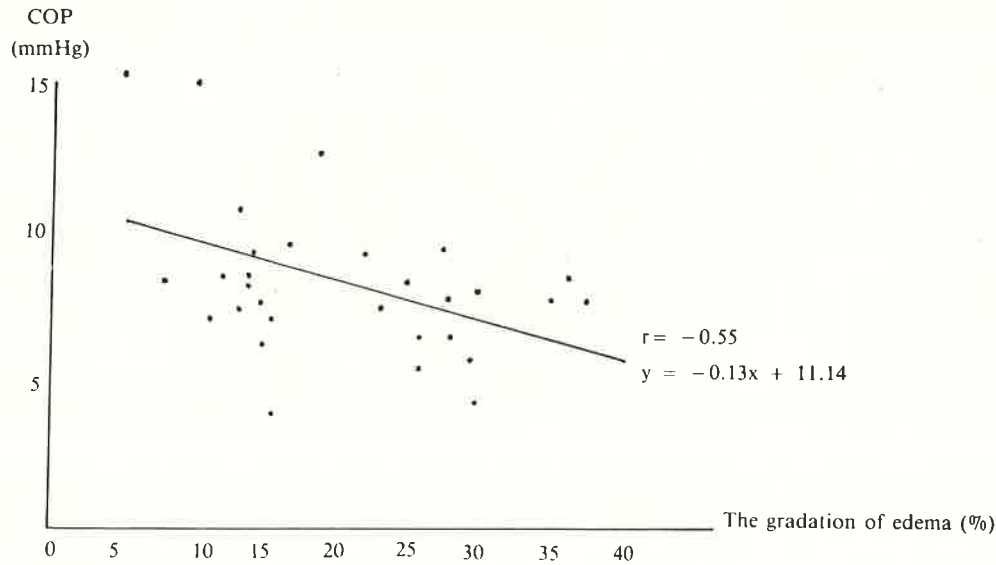


Fig. 3 The correlation between COP and the gradation of edema

On the other hand, only a low grade correlation was noted between plasma albumin and the degree of edema ($r = -0.26$; $P < 0.05$) and no correlation at all ($r = -0.19$; $P > 0.05$) was detected between the degree of edema and TP. We

noticed also the significant difference of COP between the ascitic patients and those cases without ascites as shown in table 4. Similar result was also found for albumin, but not for TP.

Table 4 : Laboratory results of COP, TP and albumin content in the group of ascitic and non ascitic cases

Group of patients	N	COP (mmHg)		TP (g/dl)		ALB (g/dl)	
		X	SD	X	SD	X	SD
Ascites	20	7.4	2.6	3.91	0.70	2.39	0.42
Non ascites	10	9.8	2.7	4.38	0.50	2.81	0.50
P		< 0.05		> 0.05		< 0.05	

Discussion

The mean value of the COP in EF state was 8.7 ± 2.7 mmHg. It means that if we take two standard deviations as the upper border for confidence limit, then the value as high as 14.1 mmHg or lower can be used as a diagnostic criterion for nephrotic syndrome. Koomans et al. (1986) in their study on adult cases found the mean value of 8.6 mmHg which ranged from 6 to 11.9 mmHg.

Our study and Koomans's finding were in confirmity with the investigation of Noddeland et al. (1982), who found that edema in nephrotic patient would appear when the value of COP was 16.5 mmHg or lower.

If we notice the lower value of COP in our study (i.e. 4 mmHg) then we can predict that some of our cases would suffer from pulmonary edema, especially in those cases with a COP below 7 mmHg. This prediction is proposed based on the study of Weil et al. (1978). These authors stated that if the difference between COP and pulmonary artery wedge pressure was 3 mmHg or less, they almost invariably found pulmonary edema. The normal range of pulmonary wedge pressure was 4 to 12 mmHg with the mean value of 8 mmHg (Weil et al., 1979). From these findings we can assume that pulmonary edema will appear when the value of COP decrease to 7 mmHg or less and we must keep in mind the possibility of pulmonary edema on COP below 11 mmHg. Chest X-Ray should be offered to confirm the diagnosis and albumin or plasma infusion is justified when pulmonary edema is really present.

The mean value of plasma albumin was 2.57 g/dl. This value is a little bit higher compared to the diagnostic criterion for nephrotic syndrome proposed by ISKDC (1982).

The low value of TP in our study is mainly due to the low value of its main component i.e. plasma albumin since the mean value of plasma globulin did not change significantly from normal value adapted in our hospital (1.3 - 2.7 g/dl; Gandasoebtrata, 1970).

The high values of COP, TP, albumin and globulin during SS phase indicate that each of these parameters play a role in the formation of edema. This phenomenon was also stated by Noddeland et al. (1982). The correlation between COP and plasma albumin is better compared with the correlation between COP and TP. This result is easy to understand because plasma globulin alone as a second component of total protein concentration has no correlation with COP, so that the alteration of COP and albumin is not fully paralell with the alteration of COP and TP. The high correlation found between the COP and the severity of edema as shown in figure 3 again reflects the role of COP in the formation of edema. The significant difference of COP between the ascitic and non ascitic patients also proof it. In contrast to the report of Schreiner (1963), our study failed to show a good correlation between the degree of edema and plasma albumin, eventhough in ascitic patients we still noticed a significantly lower albumin content. It is interesting to know that although the results were statistically not significant, we noticed the tendency that the value of laboratory data found in new cases were higher, compared to the relapsing cases. These differences would probably be more significant if we chose those patients with frequent relapses or those who are steroid resistant.

In summary we can conclude that COP can be used as an alternative parameter to

diagnose patients with nephrotic syndrome. It is even more sensitive and simple compared with the determination of TP or albumin concentration.

REFERENCES

1. BOHLIN, A.B.; BERG, U.: Renal sodium handling in minimal change nephrotic syndrome. *Archs Dis. Childh.* **59**: 825 - 830 (1984).
2. GANDASOEBRATA, R.: Penuntun Laboratorium Klinik, edisi II, 167 - 170 (Dian Rakyat, Jakarta 1970).
3. HASSAN, R.; CHAIR, I.; DARWIS, D.; LATIEF, A.: Colloid oncotic pressure in severe dengue shock syndrome. *Pediatr. Indones.* **26**: 213-219 (1986).
4. KOOMANS, H.H.; GEERS, A.B.; DORHOUT, M.E.J.; KORLANDT, W.: Lowered tissue-fluid oncotic pressure protects the blood volume in the nephrotic syndrome. *Nephron* **42**: 317-322 (1986).
5. NODDELAND, H.; RUSNES, S.; FADNES, H.O.: Interstitial colloid osmotic pressure in patients with hypoproteinaemia. *Acta physiol. scand.* **108**: 6-13 (1982).
6. Report of the International Study of Kidney Disease in Children (ISKDC): Nephrotic syndrome in children: A randomized trial comparing two prednisone regimen in steroid responsive patients who relapse early. *J. Pediat.* **95**: 239-243 (1979).
7. Report of ISKDC: Early identification of frequent relapses among children with minimal change nephrotic syndrome. *J. Pediat.* **101**: 514-518 (1982).
8. SCHREINER, G.E.: The nephrotic syndrome. *Ann. Intern. Med.* **64**: 300-308 (1963).
9. STARLING, E.H.: On absorption of fluid from connective tissue spaces. *J. appl. physiol.* **19**: 312-326 (1896); cited from Weil et al., 1978.
10. WEIL, M.H.; MORISETTE, M.; MICHAELS, S.: Routine plasma colloid osmotic pressure measurements. *Crit. Care Med.* **2**: 229 (1974).
11. WEIL, M.H.; HENNING, R.J.; MORISETTE, M.; MICHAELS, S.: Relationship between colloid osmotic pressure and pulmonary artery wedge pressure in patients with acute cardio-respiratory failure. *Am. J. Med.* **64**: 643-650 (1978).
12. WEIL, M.H.; HENNING, R.J.; PURI, V.K.: Colloid oncotic pressure; clinical significance. *Crit. Care Med.* **7**: 113-116 (1979).