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**To cite this article:** Nikolaos Sotirakopoulos, Tilemachos Tsitsios, Maria Stambolidou, George Athanasiou, Maria Peiou, Vassiliki Kokkinou & Konstantinos Mavromatidis (2004) The Red Blood Cell Deformability in Patients Suffering from End Stage Renal Failure on Hemodialysis or Continuous Ambulatory Peritoneal Dialysis, Renal Failure, 26:2, 179-183, DOI: [10.1081/JDI-120038517](https://doi.org/10.1081/JDI-120038517)

**To link to this article:** <https://doi.org/10.1081/JDI-120038517>



Published online: 07 Jul 2009.



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CLINICAL STUDY

## **The Red Blood Cell Deformability in Patients Suffering from End Stage Renal Failure on Hemodialysis or Continuous Ambulatory Peritoneal Dialysis**

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### **ABSTRACT**

Anemia is the main problem for patients suffering from end stage renal disease (ESRD). This study aimed to determine whether the index of rigidity (IR), that shows red blood cells (RBCs) deformability and the possible IR disturbances can provide an explanation about the cause of anemia, in patients undergoing maintenance hemodialysis (HD) or on peritoneal dialysis. The IR was determined in 39 hemodialyzed patients, who were already in dialysis for a period of time ranging from 16 to 120 months (mean  $\pm$  SD =  $41.8 \pm 24.1$ ) (Group A). Furthermore, the IR was measured in 32 patients on continuous ambulatory peritoneal dialysis (CAPD), who were in CAPD for a period of time ranging from 6 to 60 months (mean  $\pm$  SD =  $10.7 \pm 9.9$ ) (Group B). Finally, the IR was determined in 17 normal individuals (group C). The RBCs IR was measured twice in group A (before and after the end of a hemodialysis session) and once in groups B and C. The IR was determined by hemorrheometry (method of filtration), using special equipment. In group A the IR was increased in comparison to the control group (C) ( $17.9 \pm 6.2$  vs.  $10.2 \pm 1.8$ ,  $p < 0.0001$ ). This increase was even higher in the measurement at the end of the hemodialysis session (paired t-test,  $p < 0.0001$ ). The RBCs IR in CAPD patients was significantly lower than that of HD patients ( $12 \pm 3.8$  vs.  $17.9 \pm 6.2$ ,  $p < 0.0001$ ) and was not statistically different from the control group ( $12 \pm 3.8$  vs.  $10.2 \pm 1.8$ ,  $p = 0.068$ ). It is concluded from the study that: 1) in HD patients occur disturbances in the deformability of the RBCs, that are worsened by the hemodialysis session; 2) the index of rigidity of RBCs is

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significantly higher in the HD patients than in CAPD patients; 3) in patients on CAPD, the disturbance of deformability of the RBCs was less in comparison to the control group, which however does not reach the statistically significant levels.

**Key Words:** Red blood cell; RBC deformability; CAPD; Hemodialyzed patients; Hemodialysis; ESRD.

## INTRODUCTION

Anemia is a common clinical and laboratory finding of end stage renal disease (ESRD) patients. The major factor responsible for anemia is the deficient production of erythropoietin (EPO) by the failing kidneys. ESRD patients have a decreased EPO production not relative to the degree of anemia.<sup>[1]</sup> Anemia is also caused in ESRD patients by frequent blood examinations, blood losses from the gastrointestinal tract, iron, B<sub>12</sub> and folate deficiency and by less common factors as aluminium toxicity and hyperparathyroidism.<sup>[2]</sup> The red blood cell (RBC) survival in ESRD patients is shortened<sup>[3]</sup> due to hemolysis, which is partly attributed to an abnormality in the structure of the erythrocyte membrane.<sup>[4]</sup> The present study was conducted to assess the RBC Indice de Rigidite (IR) in patients undergoing hemodialysis and continuous ambulatory peritoneal dialysis (CAPD).

## SUBJECTS–METHODS

The IR of the erythrocytes was assessed in 3 groups of subjects. Group A consisted of 39 hemodialyzed patients (22M, 17F) aged from 27 to 84 years old (median age 59 years), who were undergoing hemodialysis treatment for  $41.8 \pm 24.1$  months (ranging from 16 to 120 months). Group B consisted of 32 CAPD patients (18M, 14F) aged 35 to 92 years (median age 65 years), who were on CAPD treatment for  $10.7 \pm 9.9$  months (ranging from 6 to 60 months). Group C consisted of 17 healthy individuals as control group, aged from 28 to 60 years (median age 46 years).

The primary renal disease did not constitute a selection criterion. The duration of the dialysis therapy received by Group A varied from 4 to 4 1/2 hours per session and modified cellulose and hemophan membranes were used throughout the study. The IR was measured by hemorrheometry (filtration method) using a specific apparatus in all three groups. In Group A, IR was measured twice (just before and just after the end of hemodialysis session). In Group B and C the measurement was carried out once. The method used is designed to estimate the time required for the erythrocytes to pass through a pore, one by one. The

measurement is performed under stable temperature and osmolarity conditions as well as pH and hematocrit (Hct) values. The outcome constitutes the IR,<sup>[5]</sup> which is in inverse relation to the erythrocyte flexibility.

## RESULTS

The statistical analysis of the data revealed that the IR was significantly higher in Group A, than in the control Group ( $17.9 \pm 6.2$  vs.  $10.2 \pm 1.8$ ,  $p < 0.0001$ ) and it was even higher in the measurement at the end of the hemodialysis session (paired t-test,  $p < 0.0001$ ) (Tables 1, 3). The IR was significantly lower in CAPD patients compared to the hemodialyzed patients ( $12 \pm 3.8$  vs.  $17.9 \pm 6.2$ ,  $p < 0.0001$ ). No significant differences in IR were found between CAPD patients and controls, even though the values reached the significance limits ( $12 \pm 3.8$  vs.  $10.2 \pm 1.8$ ,  $p = 0.068$ ) (Tables 2, 3).

## DISCUSSION

The erythrocyte deformability is an important parameter, which can influence the microcirculation, as well as the oxygen transfer and release. Lapshina et al. studied the effect of free fatty acids on the structure and properties of erythrocyte membrane and concluded that the fatty acids perturb the lipid bilayer and distort the protein/lipid complementarity of the erythrocyte membrane.<sup>[4]</sup>

The erythrocyte life is reduced in ESRD patients due to hyperparathyroidism, uremic toxins, osmotic trauma, hypersplenism and mechanical trauma. Moreover, it must be noted, that the erythrocyte survival is decreased, by various biochemical and biophysical changes that occur to the red cells, thereby altering the lipidic and phospholipidic components of their membrane. These alterations result in a decreased RBC deformability, which seems to improve by L-carnitine supplementation.<sup>[6–9]</sup> L-carnitine affects the stabilization of the erythrocyte membrane by facilitating the lipid uptake.

Jendryczko et al. investigated the rheological disturbances in 40 hemodialyzed patients (34 of them



**Table 1.** Age of patients (Group A), hemodialysis duration, IR before and after dialysis session.

Patients (22M, 17F)	IR		Age (y)	Duration of haemodialysis (months)
	Before	After		
1	17.99	27.92	67	18
2	15.68	16.44	72	24
3	11.9	31.25	78	18
4	15.78	24.11	78	16
5	10.08	19.29	71	29
6	11.8	41.37	67	17
7	13.88	31.61	57	18
8	35.94	36.84	67	16
9	25.56	34.67	59	24
10	15.78	19.73	79	27
11	34.72	15.27	57	22
12	12.34	16.66	60	84
13	16.33	17.76	65	72
14	23.12	13.49	72	48
15	20.26	20.58	60	60
16	13.19	40	60	60
17	20.58	11.9	55	36
18	17.77	25.65	65	24
19	13.88	25	32	40
20	16.99	30.24	55	36
21	16.71	13.12	38	24
22	19.85	16.14	28	24
23	14.47	21.25	42	60
24	13.23	31.25	38	24
25	12.85	26.38	42	19
26	24.34	22.45	32	60
27	15.43	14.37	65	60
28	18.75	21.8	28	24
29	19.07	23.39	44	18
30	16.66	17.76	84	60
31	12.7	20.3	82	72
32	15.07	21.42	58	40
33	14.19	35.85	55	29
34	13.07	16.87	59	60
35	16.66	15.78	57	72
36	32.74	36.3	38	72
37	21.16	27.5	27	48
38	11.02	38.75	35	48
39	25	33.33	82	120
<b>Mean±SD</b>	<b>17.9±6.2</b>	<b>24.5±8.4</b>	<b>56.7±16.7</b>	<b>41.8±24.1</b>

Statistical analysis: Group A before–Group B, t-test,  $p<0.00001$ ; Group A before–Group C, t-test,  $p<0.00001$ ; Group A before–after the dialysis session, paired t-test,  $p<0.00001$ .

suffering from hypertension and proteinuria). They examined whether the blood rheological disturbances are related to the lipid composition (cholesterol, phospholipids) of the RBC membrane. The results showed that the cholesterol/phospholipids ratio was significantly higher in the blood samples taken after dialysis than the ratio in the blood samples taken before the session ( $2.48\pm0.14$  vs.  $2.08\pm0.19$ ). In addition, a significant

correlation was found between membrane's cholesterol/phospholipids ratio and the serum's LDL-cholesterol levels.<sup>[10]</sup>

Peuchant et al. examined the fragility, the deformability and the lipid composition of the erythrocyte membranes in 22 dialyzed patients (before and after the dialysis session) and in the control group. They concluded that deformability was not affected by the

**Table 2.** Age of Group B patients, duration of CAPD and IR of RBC.

Patients (18M, 14F)	IR	Age	Duration of CAPD (months)
1	10.83	65	15
2	13.28	43	14
3	13.2	73	14
4	10.93	73	10
5	12.5	73	9
6	9.13	85	9
7	12.5	71	8
8	12.3	72	7
9	10.9	92	6
10	14.28	68	6
11	13.63	65	6
12	10	53	6
13	12.5	60	60
14	7.3	60	9
15	23	64	6
16	24	53	8
17	11.66	47	6
18	8	39	7
19	11.66	57	6
20	9.37	80	6
21	12.7	80	6
22	10.83	80	6
23	18	35	6
24	11.6	73	6
25	14.28	67	6
26	10.98	58	6
27	7.03	78	12
28	10	59	8
29	8.5	58	12
30	10.2	71	24
31	8.8	52	18
32	10.3	63	13
<b>Mean±SD</b>	<b>12.0±3.8</b>	<b>64.6±13.3</b>	<b>10.7±9.9</b>

Statistical analysis: Group B–Group C, t-test,  $p=0.068$  (NS).

dialysis session, in contradiction of our data that revealed an increase to IR. Nevertheless the osmotic resistance to hemolysis was increased significantly after the dialysis session ( $p<0.001$ ).<sup>[11]</sup> Other researchers<sup>[10]</sup> also concluded that the lipid composition of the erythrocyte membranes was altered during dialysis, presented a notable increase in cholesterol and a different phospholipids distribution.<sup>[10]</sup> This acute effect of dialysis on the membrane's lipid composition is probably related to the erythrocyte alterations mentioned above.<sup>[11]</sup>

Shand et al. investigated the blood viscosity (hemorrheology) in hemodialyzed patients, considering it as the major factor, which influences the rate of blood

flow, and is connected to the vascular diseases. They concluded that the main effect of hemodialysis was an increase in Hct related to an increase in blood viscosity and to infirm changes in RBC deformability.<sup>[12]</sup> Novak et al. examined the RBC filtration parameters in 82 predialysis patients with chronic renal failure and 50 healthy controls. They found that the RBC deformability was increased in uremic patients and improved considerably after hemodialysis initiation.<sup>[13]</sup> Moreover, other factors seem to interfere to RBC deformability. Icardi et al. studied the RBC deformability in patients on conventional dialysis treatment with cuprophane membranes. They observed that the RBC membrane showed defects and decreased deformability, which was improved after r-HuEPO administration.<sup>[14]</sup> On the contrary Macdougall et al. measured the RBC deformability in hemodialyzed patients before and after treatment with r-HuEPO. The results showed RBC deformability similar to healthy controls and noted no change after r-HuEPO supplementation.<sup>[15]</sup> In our previous studies, it was found that L-carnitine administration improves the RBC deformability in hemodialyzed patients<sup>[8]</sup> and in CAPD patients.<sup>[9]</sup>

Finally, it is concluded that: 1) The erythrocytes IR is significantly higher in hemodialyzed patients in comparison to CAPD patients, 2) the disturbances of RBC deformability are worsened after hemodialysis session and 3) a disturbance in RBC deformability is

**Table 3.** Age and IR of Group C individuals (controls).

Patients (8M, 9F)	IR	Age
1	7.23	52
2	9.27	35
3	13.23	60
4	13.19	55
5	10	36
6	8.75	45
7	11.25	38
8	8.55	28
9	8.59	47
10	11.76	44
11	10.15	33
12	9.02	42
13	8.33	54
14	10.29	48
15	10.29	47
16	12.28	59
17	11.25	46
<b>Mean±SD</b>	<b>10.2±1.8</b>	<b>45.2±9.2</b>



noticed in CAPD patients in comparison to healthy controls, but it is not statistically significant.

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