[a] Endocrinology and Metabolism Laboratory, Universidad Autónoma de Querétaro, Mexico
[b] Medical School, Universidad Autónoma de Querétaro, Mexico
[c] Cellular Biology and Physiology Department, Instituto de Investigaciones Biomédicas, Universidad Nacional Autónoma de México, Mexico
[d] Department of Environmental Toxicology Laboratory, Medical School, Universidad Autónoma de San Luis Potosí, Mexico
[e] Renal Department, Hospital General de Querétaro, Mexico

* Corresponding author.
E-mail address: esabath@yahoo.com (E. Sabath).

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Inflammation in hemodialysis and their correlation with neutrophi-lymphocite ratio and platelet-lymphocyte ratio.☆

Inflamación en hemodiálisis y su correlación con los índices neutrófilos/linfocitos y plaquetas/linfocitos

Dear Editor,

Cardiovascular disease (CD), the leading cause of death in hemodialysis (HD) patients,[1] is closely related to inflammation. C-reactive protein (CRP) and interleukin-6 (IL-6) reflect inflammation and are associated with malnutrition and atherosclerosis.[2]

Platelets are fundamental for hemostasis and also have a role on inflammation and immunity[3] since they interact with the endothelium and cells of innate and acquired immunity.

During the last five years, the platelet/lymphocyte ratio (PLR) and the neutrophil/lymphocyte ratio (NLR)[4] have been proposed as potential markers of inflammation. The NLR is also related to systemic endothelial dysfunction.[5] Both PLR and NLR are easily obtained, however there is not much research relating PLR and NLR with inflammation in HD.

The objectives of the present study were: (1) To compare in 81 patients in HD with inflammation (PCR $\geq$10 mg/l) and 52 patients without inflammation (PCR $\leq$10 mg/l) the values of Hemoglobin (Hb), red cell distribution width (RDW), total lymphocyte count, total platelet count (TPC), mean platelet volume (MPV), PLR and NLR; (2) To analyze these parameters in patients with/without diabetes mellitus type 2 (DM2) and with/without inflammation; and (3) To determine the correlation between PLR and NLR with known biomarkers of inflammation and nutrition (PCR, IL-6, transferrin, ferritin and albumin).

The ethics and research committee approved the study. The study was performed at the Instituto Mexicano del Seguro Social in patients on HD for more that 3 months and between 18 and 79 years of age. The study was prospective, cross-sectional. Clinical history and laboratory tests were performed. Patients with infection or thrombocytopenia were excluded.

Statistical analysis was performed using the SPSS® v. 20 in Spanish. Depending on the data distribution comparisons were made using Student's *t* or *U* of Mann–Whitney, ANOVA or Kruskal–Wallis, Pearson or Spearman. Linear regression analysis was performed to identify independent factors associated to inflammation. We consider a statistically significant difference a $p<0.05$.

A total of 133 patients were included, 51.1% male. The mean age was 45.86 ± 17.7 years, with a mean dialysis vintage of 45.4 ± 38.4 months; body mass index (BMI) 23.9 ± 5 Kt/V of 1.3 ± 0.09. Diabetes mellitus type 2 in 32% and hypertension in 78.9% of the patients. The main causes of end-stage renal disease were unknown (38.3%) and DM2 (32.3%).

The mean NLR was 3.5 (range: 0.28–61.8) and PLR 173.35 ± 98.5 (range: 40.2–778.9).

As compared with patients with PCR <10 mg/l, those with CRP >10 mg/l had increased levels of IL-6 (10.38 [range: 6.8–13.8 pg/ml] vs. 5.73 [range: 3.3–8.1 pg/ml]). The RDW were (15.9 ± 12.2 vs. 14.7 ± 1.7.7%), total leukocytes (6.31 ± 1.75 vs. 5.38 ± 1.56 × 10^3/μl), PLR (189.8 ± 114.4 vs. 149 ± 61, $p<0.05$), NLR (3.53 (range: 0.3–28) vs. 2.41 (range: 0.28–7.58), $p=0.005$), total number of neutrophils (4.0 ± 1.4 vs. 3.1 ± 1.36 × 10^3/μl, $p=0.001$).

The number of lymphocytes and Hb level were comparatively lower in the group with inflammation 1.48 ± 0.77 vs. 1.62 ± 0.93 × 10^3/μl ($p=0.52$) and 9.7 ± 2.2 vs.10.3 ± 2 g/L ($p=0.17$), respectively. The MPV and number of platelets were not significantly different between the two groups.

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Table 1 – Comparison between patients with/without DM2 and with/without inflammation.

Variable	DM2 with CRP >10 mg/l ($n=24$)	DM2 with PCR <10 mg/l ($n=19$)	No DM2 with PCR >10 mg/l ($n=57$)	No DM2 with PCR <10 mg/l ($n=33$)
BMI (kg/m^2)	26.4 ± 6[a]	25.0 ± 6.5	23 ± 4	23.9 ± 1.4
Hb (g/dl)	9.9 ± 2.3	11.1 ± 1.8	9.7 ± 2.2	9.9 ± 1.9
RDW (%)	16.56 ± 2.63[b]	14.9 ± 1.7	15.7 ± 2.0	14.5 ± 1.1
Platelets (10^3/μl)	260.6 ± 77.1[b]	217.1 ± 62.1	223.7 ± 71.5	205.8 ± 72.8
Total lymphocytes (10^3/μl)	1.46 ± 1.1	1.83 ± 1.4	1.48 ± 0.59	1.59 ± 0.5
Total neutrophils (10^3/μl)	4.3 (1.8–8.4)	4 (1.1–6.2)	3.9 (1.3–6.7)	2.7 (0.9–6.75)[c]
NLR	5.06 (0.3–28)[a]	2.99 (0.32–6.9)	2.94 (0.75–7.4)	2.12 (0.28–7.5)
PLR	284.7 ± 175.6[d]	148.1 ± 68.9	167.1 ± 70	149.5 ± 57.9
IL-6 (pg/ml)	14.5 (2.3–54.3)	5.75 (0.6–15.1)	8.76 (0.0–126.6)	5.7 (0.0–56)
Transferrin (mg/dl)	229.4 ± 65.5[e]	264 ± 53	227.8 ± 62.1	229.4 ± 48.5
Ferritin (ng/ml)	233.87 (13–1610)[d]	34.95 (8–163)	82.19 (10–385)	109.7 (8–393)
Albumin (g/dl)	3.65 ± 0.35[d]	3.9 ± 0.36	3.9 ± 0.42	3.8 ± 0.4
Urea (mg/dl)	108.3 ± 43.1	129.9 ± 36.4	111.4 ± 33.8	129.2 ± 46.5
Creatinine (mg/dl)	7.68 ± 2.4[a]	9.2 ± 2.3	10.66 ± 2.8	11.2 ± 2.9

Mean ± SD (standard deviations) are reported, the ranges within brackets.
DM2: type 2 diabetes mellitus; Hb: hemoglobin; IL-6: interleukin 6; BMI: body mass index; NLI: neutrophil/lymphocyte index; PLI: platelet/lymphocyte index; CRP: C-reactive protein; RDW: red cell distribution with.
[a] $p<0.05$ between group 1 with 3 and 4.
[b] $p<0.05$ between groups 1 and 4.
[c] $p<0.0001$, 0.014 and 0.001 of group 4 vs 1, 2 and 3 respectively.
[d] $p<0.05$, between group 1 and the other 3 groups.
[e] $p<0.05$, between groups 2 and 3.

Table 2 – IPR and INR correlations with biomarkers.

		CRP	IL-6	Ferritin	Albumin	RDW	Transferrin
PLR	Correlation	0.236[a]	0.229[b]	0.243[a]	−0.198[a]	0.287[b]	NS
NLR	Correlation	NS	0.237[b]	0.239[b]	NS	0.299[b]	NS

IL-6: interleukin 6; NLR: neutrophil/lymphocyte ratio; PLR: platelet/lymphocyte ratio; NS: not significant; CRP: C-reactive protein; RDW: red cell distribution with.
[a] $p<0.05$ level (bilateral).
[b] $p<0.01$ level (bilateral).

Comparisons of patients with and without DM2 revealed differences in IL-6 ($p=0.001$), NLR ($p=0.02$) and PLR ($p=0.017$), but not in CRP ($p=0.16$). Patients with DM2 showed a higher degree of inflammation; therefore 4 groups of patients were generated according to the presence or absence of DM2 and/or inflammation (Table 1).

Correlation between PLR and NLR (Spearman's) was 0.654, $p=0.0001$. No relationship was found between these ratio and the Hb level or dose of erythropoietin. The rest of the data analysis is shown in Table 2.

The values of PLR correlated significantly (by linear regression) with: IL-6 ($\beta=3.26$; $p=0002$) and ferritin ($\beta=3.15$; $p=0.003$). The NLR correlated with ferritin ($\beta=4.0$; $p=0.0001$) and PLR ($\beta=7.9$; $p=0.0001$).

In HD, a low lymphocyte count and a high neutrophil count are independent predictors of mortality[6]; it is important to note that lymphocyte count in patients with inflammation is lower than 1.5×10^3/μl and this is associated with an increased risk of mortality.[7] Likewise hypoalbuminemia is associated with mortality and it is more frequent in diabetics and patients with inflammation.

The mean values of PLR and NLR were higher than those reported by other authors; the values were particularly elevated in DM2 patients with CRP >10 mg/l, similar to the report by Lou et al.[8]

We found that the correlation between PLR with inflammatory and nutritional parameters was superior than that obtained by NLI; this is similar to what was reported by Turkmen et al.[9]

In conclusion, the PLR and NLR are elevated in HD patients with inflammation; both parameters can be obtained at no additional cost and may be used to identify patients with inflammation.

REFERENCES

1. Collado S, Coll E, Deulofeu R, Guerrero L, Pons M, Cruzado JM, et al. Prevalence of cardiovascular disease in uraemia and relevance of cardiovascular risk factors. Nefrologia. 2010;30:342–8.
2. Kalantar-Zadeh K, Ikizler TA, Block G, Avram MM, Kopple JD. Malnutrition-inflammation complex syndrome in dialysis patients: causes and consequences (Review). Am J Kidney Dis. 2003;42:864–81.

3. Jenne CN, Urrutia R, Kubes P. Platelets: bridging hemostasis, inflammation, and immunity. Int J Lab Hematol. 2013;35:254–61.
4. Okyay GU, Inal S, Oneç K, Er RE, Paşaoğlu O, Paşaoğlu H, et al. Neutrophil to lymphocyte ratio in evaluation of inflammation in patients with chronic kidney disease. Ren Fail. 2013;35:29–36.
5. Martínez-Urbistondo D, Beltrán A, Beloqui O, Huerta A. The neutrophil-to-lymphocyte ratio as a marker of systemic endothelial dysfunction in asymptomatic subjects. Nefrologia. 2016;36:397–403.
6. Reddan DN, Klassen PS, Szczech LA, Coladonato JA, O'Shea S, Owen WF Jr, et al. White blood cells as a novel mortality predictor in haemodialysis patients. Nephrol Dial Transplant. 2003;18:1167–73.
7. Huarte-Loza E, Barril-Cuadrado G, Cebollada-Muro J, Cerezo-Morales S, Coronel-Díaz F, Doñate-Cubells T, et al. Grupo de Consenso de la Sociedad Española de Diálisis y Trasplante Nutrición en pacientes en diálisis. Consenso SEDYT. Dial Traspl. 2006;27:138–61.
8. Lou M, Luo P, Tang R, Peng Y, Yu S, Huang W, et al. Relationship between neutrophil-lymphocyte ratio and insulin resistance in newly diagnosed type 2 diabetes mellitus patients. BMC Endocr Disord. 2015;15:9.
9. Turkmen K, Erdur FM, Ozcicek F, Ozcicek A, Akbas EM, Ozbicer A, et al. Platelet-to-lymphocyte ratio better predicts inflammation than neutrophil-to-lymphocyte ratio in end-stage renal disease patients. Hemodial Int. 2013;17:391–6.

Venice Chávez Valencia[a,c,*], Citlalli Orizaga de la Cruz[a], Oliva Mejía Rodríguez[b], Sergio Gutiérrez Castellanos[a], Francisco Alejandro Lagunas Rangel[c], Martha Eva Viveros Sandoval[c]

[a] *Hospital General Regional No. 1, Instituto Mexicano del Seguro Social (IMSS), Morelia, Michoacán, Mexico*
[b] *Centro de Investigación Biomédica de Michoacán, Morelia, Michoacán, Mexico*
[c] *Universidad Michoacana de San Nicolás de Hidalgo, Facultad de Ciencias Médicas y Biológicas, Maestría en Ciencias de la Salud, Morelia, Michoacán, Mexico*

[*] *Corresponding author.*
E-mail address: drvenicechv@yahoo.com.mx
(V. Chávez Valencia).

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Embolism as a cause of early thrombosis of arteriovenous fistula of hemodialysis patients☆

Embolismo paradójico como causa de trombosis precoz de fístula arteriovenosa para hemodiálisis

Dear Editor,

Thrombosis of the vascular access (CA) is usually due to technical problems and/or small arterial or venous size, obesity, advanced age, diabetes mellitus, female sex and AVF in the wrist.

We present a case, not previously described, of early AVF thrombosis secondary to paradoxical embolism caused by a patent foramen ovale (PFO). He is an 80-year-old man; after 7 years in PD is switched to because of poor dose of dialysis. A left humerus-perforan vein AVF was made that quickly thrombosed at 24 h. During Re-intervention it was observed permeable vessels and a thrombus are detected in the middle third of the humeral artery suggesting an arterial embolism. Thromboembolectomy was successful and anticoagulation was prescribed. The ECG presented sinus rhythm and the echocardiography showed no abnormalities. Transesophageal echocardiography (TEE) is performed, showing PFO with early bubbles after the injection of agitated saline solution. In the descending thoracic aorta, a giant fibrocalcified atherosclerosis plaque with irregularities and thrombotic content occupying 40% of the light was observed.

Thereafter he presented transient cerebrovascular event with loss of intellectual abilities with lower limb chronic small vessel ischemia and injuries suggestive of cholesterol crystals atheroembolism which caused with severe pain, livedo reticularis, cyanotic punctate lesions and cyanosis of the first toe of the left foot with preserved pulses. Then, Sintrom® was discontinued and it was changed to subcutaneous LMWH 60 mg/24 h, aspirin and clopidogrel were added and statins dose was increased to 80 mg daily as recommended by vascular surgery. The patients lost 15 kg in 8 months, albumin 2.1 g/L and CRP was 57 mg/L with severe anemia despite increased EPO. The patient decided to voluntarily stop HD

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