Renal artery stenosis and mean platelet volume

Muhammet Raşit Sayın, Nesimi Yavuz, Turgut Karabağ, Mehmet Ali Çetiner[1], İbrahim İlker Öz, Orhan Alper Güngördük[2], Mustafa Aydın*

Departments of Cardiology and *Radiology, Faculty of Medicine, Bülent Ecevit University; Zonguldak-*Turkey*
[1]Department of Cardiology, Karadeniz Ereğli State Hospital; Zonguldak-*Turkey*
[2]Department of Cardiology, Çaka Vatan Hospital; Kahramanmaraş-*Turkey*

ABSTRACT

Objective: Increased mean platelet volume (MPV) has been reported in various atherosclerotic diseases. The aim of our study was to investigate the relationship between the atherosclerotic renal artery stenosis (ARAS) and various hematological parameters including MPV.

Methods: This study was performed with a retrospective review of the angiographic images of patients who underwent renal angiography at Bülent Ecevit University catheter laboratory between January 2004 and December 2009. The patients were trichotomized into three groups based on the presence and severity of renal artery stenosis (RAS). Group 1 included patients with a critical RAS (33 patients; 18 female (F), 15 male (M); mean age 61.6±11.5 years), group 2 consisted of patients with non-critical RAS (26 patients; 15 F, 11 M; mean age 58.1±11.3 years), and group 3 was composed of patients without RAS (69 patients; 38 F, 31 M; mean age 53.5±11.9 years). Demographic data, complete blood count, and biochemical parameters were compared between the groups.

Results: Comparison of the hematological parameters revealed that MPV and platelet distribution width were significantly higher in group 1 than in group 2 and 3 (8.96±0.99 fL versus 8.35±0.76 fL, 8.31±0.79 fL, respectively; p=0.001; 16.53±0.58% versus 16.19±0.56%, 16.29±0.53%, respectively; p=0.04).

Conclusion: MPV levels are higher in patients with ARAS. Considering both the effect of platelets on atherosclerosis and their close association with other risk factors, MPV level may be an important factor in pathogenesis of ARAS. *(Anatol J Cardiol 2016; 16: 197-201)*

Keywords: mean platelet volume, platelet, renal artery stenosis, atherosclerosis, complete blood count

Introduction

Renal artery stenosis (RAS) is a common peripheral vascular disease that may be present in 10%–40% of patients undergoing cardiac catheterization (1). Its prevalence increases with aging, and it is particularly more common in those who have hypertension (HT) and renal failure (2, 3). Although ischemic stenosis of renal arteries is a relatively uncommon vascular disease, renal artery ischemia may overlap with other clinical syndromes. Despite the fact that various conditions may lead to RAS, atherosclerosis is the leading cause in many patients. Atherosclerosis typically affects relatively older people and those who present with HT and renal insufficiency (4). In addition to the conventional risk factors, non-conventional risk factors, such as a low apolipoprotein A-1 level, high fibrinogen, high-sensitive C-reactive protein, and homocysteine levels, have been linked to RAS (5, 6).

It is known that platelets may be closely associated with inflammation (7) and its role in onset, progression, and complications of atherosclerotic lesions has been demonstrated (7). Mean platelet volume (MPV) is a potential marker of platelet reactivity, which has been shown by some previous studies to be one of the most important parameters of various systemic disorders (8). Increased systemic platelet activation and MPV has been reported in various atherosclerotic diseases including carotid artery disease (9) and transplant vasculopathy (10) in addition to coronary artery disease (CAD) (11, 12). To the best of our knowledge, however, it is yet unclear if there is a relationship between RAS and MPV or other hematological parameters. The aim of our study was to investigate the relationship between the atherosclerotic renal artery stenosis (ARAS) and various hematological parameters including MPV in the first place.

Methods

The patients and the demographic variables

This study was performed with a retrospective review of the angiographic images of 163 patients who underwent renal angiography for suspected uncontrolled HT, signs of secondary HT suggestive of ARAS, and severe HT during coronary angiography performed for a suspicion and/or signs of ischemic heart disease at catheter laboratory in Bülent Ecevit University, Faculty of Medicine, Department of Cardiology between January 2004 and December 2009. The exclusion criteria were

Address for Correspondence: Dr. Muhammet Raşit Sayın, Bülent Ecevit Üniversitesi Tıp Fakültesi, Kardiyoloji Anabilim Dalı, Kozlu 67600, Zonguldak-*Türkiye*
Phone: +90 372 261 21 62 Fax: +90 372 261 01 55 E-mail: sayinmr@mynet.com
Accepted Date: 28.04.2015 **Available Online Date:** 18.06.2015

DOI:10.5152/AnatolJCardiol.2015.6102

as follows: acute coronary syndrome; hematological, oncological, or inflammatory disorder; white blood cell (WBC) count >10400 mm^3; hemoglobin level <10 g/dL; history of a cardiac valve disease or a cardiac valve operation; using any anticoagulant drug; ejection fraction <40%; renal insufficiency; liver or thyroid dysfunction; thrombocytopenia or thrombocytosis; and RAS not having the characteristics of an ARAS (as in the case of fibromuscular dysplasia). After exclusion of patients with the above mentioned exclusion criteria (3 patients with thrombocytopenia, 2 with a previous history of cancer, 10 with an elevated WBC count, 6 with thyroid dysfunction, 3 with fibromuscular dysplasia, 2 on anticoagulant therapy, 3 with anemia, 3 with acute coronary syndrome, and 3 with chronic renal failure) remaining 128 patients [71 females (F) and 57 males (M); mean age 56.5±12.1 years] were included in the study. All patients were hypertensive and 117 patients underwent coronary angiography while the remaining 11 did not.

Demographic characteristics were recorded, including diabetes mellitus (DM), HT, hyperlipidemia (HL), smoking history, and a family history of CAD. The following criteria were required to consider a patient hypertensive: having a history of HT; being on an antihypertensive therapy; or having a systolic blood pressure equal to or greater than 140 mm Hg and/or a diastolic blood pressure equal to or greater than 90 mm Hg, both of which were recorded after taking the mean value of two measurements from each arm. The criteria of being DM included having a previous history of diabetes and/or having a fasting glucose equal to or greater than 126 mg/dL. The patients were said to have HL when they had a fasting total cholesterol, low-density lipoprotein, and triglyceride level of ≥200 mg/dL, ≥160 mg/dL, and ≥200 mg/dL, respectively; and/or they were taking antihyperlipidemic agents. The family history of CAD was determined by the presence of a male first-degree relative younger than 55 years or a female first-degree relative younger than 65 years with a CAD history or sudden cardiac death.

Transthoracic echocardiography was performed with Vivid 5 echocardiography device (GE, Horten, Norway) using a 2.4 MHz phased array transducer. Simpson's rule was used to calculate left ventricular ejection fraction. The local ethics committee approved the study.

Analysis of the hematological parameters

Platelet indices were measured in blood samples drawn into collecting tubes containing tripotassium ethylenediaminetetraacetic acid (7.2 mg). All samples were analyzed by an automated blood counter (Beckman Coulter LH 780 Analyzer, Miami, FL, USA) within 1 h of collection.

Angiography

Coronary angiography (Integris BH 5000; Philips, Amsterdam, the Netherlands) was carried out with standard Judkin's technique using the femoral artery as the arterial entry point. The renal angiograms were obtained by injecting 20 cc contrast agent after the origin of each renal artery was seated with a pigtail catheter with multiple side holes. Coronary and renal angiograms were evaluated by two separate operators who were unaware of the clinical characteristics of the patients. The lesions causing coronary or renal artery stenosis above 50% were considered critical and below 50% were accepted as non-critical. Interobserver variability was within acceptable limits.

The patients were trichotomized into three groups based on the presence and severity of RAS. Group 1 included patients with a critical RAS (33 patients, 18 F, 15 M; mean age 61.6±11.5 years), group 2 comprised the patients with non-critical RAS (26 patients, 15 F, 11 M; mean age 58.1±11.3 years), and group 3 was composed of the patients without RAS (69 patients, 38 F, 31 M; mean age 53.5±11.9 years).

Statistical analysis

All statistical analyses were performed using Statistical Package for the Social Sciences for Windows version 18.0 (Chicago, IL, USA). Shapiro–Wilk test was run to test if data met parametric test assumptions. Continuous variables were presented as mean ± standard deviation. One-way analysis of variance (ANOVA) was used for comparison of parametric variables and Kruskal–Wallis analysis of variance for non-parametric variables in three groups followed by a Tukey's HSD and Dunn's posthoc analysis. The difference between the two groups was analyzed with a two-sample unpaired t-test when parametric test assumptions were met. Categorical variables were compared with the chi-square test. Pearson's correlation analysis was performed to examine the relationship between continuous variables and outcomes. A p value less than 0.05 was considered statistically significant.

Results

The mean age of group 1 was higher than that of the other groups (Table 1). The atherosclerotic risk factors of the groups were presented on Table 1. There were no significant differences between the groups with respect to the presence of atherosclerotic risk factors (Table 1). The medications used by the patients in different groups did not significantly differ (Table 1). Systolic blood pressure, diastolic blood pressure, and heart rate were significantly higher in group 1 than in groups 2 and 3 (Table 1).

Comparison of the hematological variables revealed that MPV and platelet distribution width (PDW) were significantly higher in group 1 than in groups 2 and 3 (8.96±0.99 fL versus 8.35±0.76 fL, 8.31±0.79 fL, respectively; p=0.001; 16.53±0.58% versus 16.19±0.56%, 16.29±0.53%, respectively; p=0.04) (Table 2). Posthoc analyses demonstrated that group 1 and 2 differed from each other significantly with respect to both MPV and platelet distribution width (PDW), while groups 2 and 3 were not significantly different with respect to these parameters. WBC, red cell distribution width, and neutrophil/lymphocyte ratio were also significantly higher in group 1 than the other groups, albeit sta-

Table 1. Clinical characteristics of the groups

	Group 1 (n=33)	Group 2 (n=26)	Group 3 (n=69)	*P*
Age, years	61.58±11.49	58.04±11.33	53.46±11.89	0.004
Male, n	15	11	31	0.967
Diabetes mellitus, n	10	4	16	0.405
Family history of CAD, n	7	5	10	0.669
Hyperlipidemia, n	13	13	30	0.716
Smoking, n	12	9	17	0.397
Critical CAD, n	28	13	35	0.002
Systolic BP, mm Hg	189.79±19.91	172.08±15.38	166.33±16.40	0.001
Diastolic BP, mm Hg	106.03±11.66	100.42±8.41	98.78±7.28	0.001
Heart rate, beat/min	87.88±10.26	85.20±7.26	81.85±10.61	0.016
Drugs				
β-blocker, n	16	12	22	0.340
Ca antagonist, n	12	4	17	0.150
ACE inhibitor, n	8	7	18	0.869
ARB, n	6	6	21	0.188
Diuretics, n	8	11	27	0.120
Antiplatelets, n	10	4	12	0.174
Statin, n	8	7	13	0.648

ACE - angiotensin converting enzyme; ARB - angiotensin receptor blocker; BP - blood pressure; CAD - coronary artery disease

Table 2. Complete blood count parameters of the groups

	Group 1 (n=33)	Group 2 (n=26)	Group 3 (n=69)	*P*
WBC, $x10^3$ mm^3	8.02±1.33	7.47±1.35	7.73±1.50	0.330
RBC, $x10^6$ mm^3	4.57±0.62	4.56±0.48	4.69±0.50	0.141
HG, g/dL	13.44±1.60	13.38±1.65	13.77±1.67	0.473
HCT, %	39.69±4.90	39.43±4.90	40.58±4.77	0.495
MCH, picograms/cell	29.50±2.10	29.43±1.98	29.36±1.71	0.937
MCV, fL	87.02±5.77	86.65±5.48	86.54±4.32	0.898
MCHC, gr/dL	33.90±0.94	33.95±0.66	33.93±0.74	0.961
RDW, %	13.41±0.97	13.38±1.21	13.09±0.87	0.212
PLT, $x10^3$ mm^{-3}	255.00±73.97	248.31±53.07	262.10±46.45	0.542
MPV, fL	8.96±0.99	8.35±0.76	8.31±0.79	0.001
PCT, %	0.23±0.060	0.21±0.05	0.22±0.04	0.286
PDW, %	16.53±0.58	16.19±0.56	16.29±0.53	0.042
Lymphocyte, $x10^3$ mm^{-3}	2.03±0.55	2.13±0.55	2.33±0.88	0.149
Neutrophi, $x10^3$ mm^{-3}	5.11±1.17	4.52±1.17	4.59±1.31	0.101
Neutrophil/ Lymphocyte ratio	2.73±1.14	2.27±0.91	2.27±1.23	0.144

HCT - hematocrit; HG - hemoglobin; MCH - mean corpuscular hemoglobin; MCHC - mean corpuscular hemoglobin concentration; MCV - mean corpuscular volume; MPV - mean platelet volume; PCT - plateletcrit; PDW - platelet distribution width; PLT - platelet count; RBC - red blood cell count; RDW - red cell distribution width; WBC - white blood cell count

tistically non-significant. The rate of critical CAD was significantly higher in group 1 than in group 2. Correlation analyses revealed that there was significant but weak correlation between MPV, PDW values, and RAS percentage (r=0.23; p=0.008, r=0.26; p<0.05, respectively). However, there was no correlation between MPV, PDW values, and RAS percentage when compared separately for groups 1 and 2.

Discussion

The main findings of our study was that compared with the patients with normal renal arteries or non-critical ARAS, the patients with critical ARAS with multifactorial pathogens had higher MPV and PDW values, and MPV may contribute to ARAS pathogenesis in addition to conventional risk factors in this patient group.

RAS describes RAS limiting normal blood flow and it usually results from a heterogeneous group of factors including atherosclerosis (main factor), fibromuscular dysplasia, vasculitis, extrinsic compression, and radiation (13). Majority of lesions are a result of atherosclerosis (ARAS) that typically involves the ostial and proximal 1/3 parts of the renal artery and usually has a close relationship with the aorta (14). However, segmentary or diffuse intrarenal atherosclerosis may rarely be encountered. We also included stenoses, having the typical characteristics and radiological appearance of an atherosclerotic stenosis and excluded cases with characteristics consistent with fibromuscular dysplasia. Concomitant presence of ARAS and CAD doubles the mortality of patients. Although 90% of cases with ARAS have HT, it is still unclear whether HT is a cause or result of ARAS (15). As any other atherosclerotic disease process, etiological factors for ARAS cannot be considered independent of conventional or novel risk factors. It is already known that the incidence of ARAS increases with aging (16), DM (17), smoking (18), and strong family history (19). In addition, an association between novel risk factors apolipoprotein A-1 (5), fibrinogen, C-reactive protein, and homocysteine levels and ARAS has also been shown (6). MPV is a relatively novel atherosclerotic risk factor that has increasingly drawn attention and many studies have been performed in recent years. Platelet volume has been demonstrated to have an association with other prognostic risk factors such as smoking, DM, obesity, and HT (20). It has been shown that there is a strong link between platelets and inflammation, thrombosis, and atherogenesis. Platelets not only mediate vascular inflammation by releasing various cytokines and chemokines, but they can also be reactivated by substances released by cells attention deficit hyperactivity disorder vessel wall (21). Platelets may attract leucocytes and progenitor cells to the vascular injury site and are capable of releasing pro-inflammatory, angiogenic factors and microparticles to circulation (22). Furthermore, previous studies have shown that platelet factor 4 (14) and other platelet-derived chemokines and growth

factors are present in human atherosclerotic plaques (10, 15). Larger platelets contain more granules and hence exert greater hemostatic, vasomotor, and pro-inflammatory functions. Therefore, increased platelet activation is associated with larger platelet size (23). We also found significantly higher MPV levels in patients with ARAS than in those without ARAS. MPV levels were significantly higher in patients with critical stenosis than in those with non-critical stenosis. Correlation analyses revealed a weak, but significant relationship between MPV and stenosis severity. These findings suggest that a higher MPV level is associated with ARAS.

Bath et al. (24) investigated the platelet volume in two groups of patients at risk of a having ARAS with HT and peripheral vascular disease. They found increased platelet volume in patients with HT and angiographically proven atherosclerotic renal artery disease. They also found correlation between platelet volume and severity of renal artery disease in both groups. In our study, we found increased MPV and PDW values in patients with critical ARAS but not noncritical ARAS similar to that observed in the study of Bath et al. (24). We found weak correlation between MPV values and stenosis severity. The limited number of cases may be the reason of this. We conclude that large platelets are hyperactive, increased platelet volume may contribute to the development of ARAS as stated by Bath et al. (24).

Studies on MPV have pointed MPV as an independent risk factor for atherosclerosis, although its association with other risk factors is already known. Hypertensive patients have been reported to have higher MPV levels (25). Similarly, smokers have been found to have higher MPV levels (26), and hypercholesterolemia has been reported to affect platelet functions such as platelet size, aggregation, and activation (27). In our study, all patients were hypertensive and nearly half of them had HL. Nearly all patients with ARAS have HT. Considering the close association between MPV and HT, we are of the opinion that MPV levels may play an important role in the pathogenesis of ARAS.

PDW is a parameter directly reflecting variability in platelet size (28). The correlation between PDW values and acute coronary syndrome is debatable. Although there are some studies suggesting that it elevates in acute myocardial infarction and unstable angina (29), some other studies have indicated that PDW is not be a risk factor for CAD (28). Rosevear et al. (30) reported higher PDW levels in gestational HT. We found higher PDW values in patients with ARAS than those without ARAS. We also showed a weak correlation between PDW values and blood pressure values and ARAS severity. This demonstrated that PDW values may be higher in patients with ARAS. We think that, with a possible contribution of high blood pressure, higher PDW levels are detectable in patients with ARAS.

Study limitations

The main limitation of our study was its retrospective design. We could not ascertain which outcomes would be achieved by higher MPV levels in patients with ARAS because we did not follow our subjects in a prospective manner. One other limitation of our study was the assessment of atherosclerosis only by visual evaluation of angiographic images. An intravascular ultrasonography examination may have been more appropriate. However, the study center did not possess any intravascular ultrasonography device. One additional limitation of our study was the measurement of platelet count by only an automatic counter. Confirmation of platelet count and density by a peripheral smear may have been more reliable.

Conclusion

In conclusion, MPV levels are higher in patients with ARAS. Considering both the effect of platelets on atherosclerosis and their close association with other risk factors, with HT being in the first place, MPV level may be an important factor in pathogenesis of ARAS.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept - M.R.S., N.Y.; Design - All authors; Supervision - M.A.; Data collection &/or processing - N.Y., O.A.G.; Analysis and/or interpretation - M.R.S., M.A.Ç.; Literature search - N.Y., İ.İ.Ö.; Writing - M.R.S., T.K.; Critical review - All authors.

References

1. Boateng FK, Greco BA. Renal Artery Stenosis: prevalence of, risk factors for, and management of in-stent stenosis. Am J Kidney Dis 2013; 61: 147-60.
2. Hansen KJ, Edwards MS, Craven TE, Cherr GS, Jackson SA, Appel RG, et al. Prevalence of renovascular disease in the elderly: a population-based study. J Vasc Surg 2002; 36: 443-51.
3. Rimmer JM, Gennari FJ. Atherosclerotic renal vascular disease and progressive renal failure. Ann Intern Med 1993; 118: 712-9.
4. Colyer WR, Eltahawy E, Cooper CJ. Renal artery stenosis: optimizing diagnosis and treatment. Prog Cardiovasc Dis 2011; 4: 29-35.
5. Scoble JE, de Takats D, Ostermann ME, Connolly JO, Scott NR, Beeso JA, et al. Lipid profiles in patients with atherosclerotic renal artery stenosis. Nephron 1999; 83: 117-21.
6. Dzielinska Z, Januszewicz A, Demkow M, Makowiecka-Ciesla M, Prejbisz A, Naruszewicz M, et al. Cardiovascular risk factors in hypertensive patients with coronary artery disease and coexisting renal artery stenosis. J Hypertens 2007; 25: 663-70.
7. Gawaz M, Langer H, May AE. Platelets in inflammation and atherogenesis. J Clin Invest 2005; 115: 3378-84.
8. Lancé MD, Sloep M, Henskens YM, Marcus MA. Mean platelet volume as a diagnostic marker for cardiovascular disease: drawbacks of preanalytical conditions and measuring techniques. Clin Appl Thromb Hemost 2012; 18: 561-8.
9. Fateh-Moghadam S, Li Z, Ersel S, Reuter T, Htun P, Plöckinger U, et al. Platelet degranulation is associated with progression of intima-media thickness of the common carotid artery in patients with diabetes mellitus type 2. Arterioscler Thromb Vasc Biol 2005; 25: 1299-303.

10. Fateh-Moghadam S, Bocksch W, Ruf A, Dickfeld T, Schartl M, Pogátsa-Murray G, et al. Changes in surface expression of platelet membrane glycoproteins and progression of heart transplant vasculopathy. Circulation 2000; 102: 890-7.
11. Willoughby S, Holmes A, Loscalzo J. Platelets and cardiovascular disease. Eur J Cardiovasc Nurs 2002; 1: 273-88.
12. Nurkalem Z, Alper AT, Orhan AL, Zencirci AE, Sarı I, Erer B, et al. Mean platelet volume in patients with slow coronary flow and its relationship with clinical presentation. Turk Kardiyol Dern Ars 2008; 36: 363-7.
13. Dubel GJ, Murphy TP. The role of percutaneous revascularization for renal artery stenosis. Vasc Med 2008; 13: 141-56.
14. Kaatee R, Beek FJ, Verschuyl EJ, Ven PJ, Beutler JJ, van Schaik JP, et al. Atherosclerotic renal artery stenosis: ostial or truncal? Radiology 1996; 199: 637-40.
15. Conlon PJ, Little MA, Pieper K, Mark DB. Severity of renal vascular disease predicts mortality in patients undergoing coronary angiography. Kidney Int 2001; 60: 1490-7.
16. Coen G, Calabria S, Lai S, Moscaritolo E, Nofroni I, Ronga G, et al. Atherosclerotic ischemic renal disease. Diagnosis and prevalence in an hypertensive and/or uremic elderly population. BMC Nephrol 2003; 4: 2.
17. de Mast Q, Beutler J. The prevalence of atherosclerotic renal artery stenosis in risk groups: a systematic literature review. J Hypertens 2009; 27: 1333-40.
18. Plouin PF, Chatellier G, Darne B, Raynaud A. Blood pressure outcome of angioplasty in atherosclerotic renal artery stenosis: a randomized trial. ESSAI Multicentrique Medicaments vs Angioplastie (EMMA) Study Group. Hypertension 1998; 31: 823-9.
19. Crowley JJ, Santos RM, Peter RH, Puma JA, Schwab SJ, Phillips HR, et al. Progression of renal artery stenosis in patients undergoing cardiac catheterization. Am Heart J 1998; 136: 913-8.
20. Türk U, Tengiz I, Özpelit E, Çelebiler A, Pekel N, Özyurtlu F, et al. The relationship between platelet indices and clinical features of coronary artery disease. Kardiol Pol 2013; 71: 1129-34.
21. Langer HF, Gawaz M. Platelet-vessel wall interactions in atherosclerotic disease. Thromb Haemost 2008; 99: 480-6.
22. Smyth SS, McEver RP, Weyrich AS, Morrell CN, Hoffman MR, Arepally GM, et al. 2009 Platelet Colloquium Participants. Platelet functions beyond hemostasis. J Thromb Haemost 2009; 7: 1759-66.
23. Liuzzo G, Biasucci LM, Gallimore JR, Grillo RL, Rebuzzi AG, Pepys MB, et al. The prognostic value of C-reactive protein and serum amyloid A protein in severe unstable angina. N Engl J Med 1994; 331: 417-24.
24. Bath PM, Missouris CG, Buckenham T, MacGregor GA. Increased platelet volume and platelet mass in patients with atherosclerotic renal artery stenosis. Clin Sci (Lond) 1994; 87: 253-7.
25. Çoban E, Yazıcıoğlu G, Berkant Avcı A, Akçıt F. The mean platelet volume in patients with essential and white coat hypertension. Platelets 2005; 16: 435-8.
26. Varol E, İçli A , Koçyiğit S, Erdoğan D, Özaydın M, Doğan A. Effect of smoking cessation on mean platelet volume. Clin Appl Thromb Hemost 2013; 19: 315-9.
27. Pathansali R, Smith N, Bath P. Altered megakaryocyte-platelet haemostatic axis in hypercholesterolaemia. Platelets 2001; 12: 292-7.
28. De Luca G, Venegoni L, Iorio S, Secco GG, Cassetti E, Verdoia M, et al. Platelet distribution width and the extent of coronary artery disease: results from a large prospective study. Platelets 2010; 21: 508-14.
29. Khandekar MM1, Khurana AS, Deshmukh SD, Kakrani AL, Katdare AD, Inamdar AK. Platelet volume indices in patients with coronary artery disease and acute myocardial infarction: an Indian scenario. J Clin Pathol 2006; 59: 146-9.
30. Rosevear SK, Liggins GC. Platelet dimensions in pregnancy-induced hypertension. N Z Med J 1986; 99: 356-7.

From Prof. Dr. Siber Göksel collections