PLATELET INDICES IN NEWLY DIAGNOSED PATIENTS OF MYOCARDIAL INFARCTION.

by Zain Ul Abideen

FILE	17393-67468-1-RV.DOC (92.5K)		
TIME SUBMITTED	06-FEB-2017 04:25PM	WORD COUNT	3685
SUBMISSION ID	767139225	CHARACTER COUNT	19969

PLATELET INDICES IN NEWLY DIAGNOSED PATIENTS OF MYOCARDIAL INFARCTION.

Principal Author

Dr. Zain ul Abideen,

MBBS, M.Phil. (Physiology)

38

Assistant Professor, Department of Physiology, KMU Institute of Medical Sciences, (KIMS) Kohat.

e.mail address: drzain5151&gmail.com

Co-Authors:

1. Dr. Farzana Salman, MBBS, M.Phil. Physiology, Associate Professor, Physiology Department, Peshawar Medical College, Peshawar.(Supervisor)
2. Dr. Robina Usman, MBBS, M.Phil. (Physiology), Associate Professor, Physiology Departemnt, Peshawar Medical College, Peshawar.
3. Dr. Najmush Shakireen, MBBS. MO Health Department,KPK.
4. Dr. Adnan Mahmood Gul, MBBS, MD (Cardiology), Associate Professor, Department of Cardiology, LRH, Peshawar. Co-supervisor)

PLATELET INDICES IN NEWLY DIAGNOSED PATIENTS OF MYOCARDIAL INFARCTION

ABSTRACT:

BACKGROUND: Inappropriate platelet activation plays a prime role in increasing risk of heart disease. There is no accepted ideal measure of platelet activation that would indicate a state of high risk. Evaluation of platelet indices as indicator of their activity could be useful in prediction and prognosis of coronary events

AIMS AND OBJECTS:

The objectives of the present study were:

To find out the role of platelet indices in newly diagnosed patients of myocardial infarction and compare it with normal individuals..

MATERIAL AND METHODS:

In this study the platelet indices were measured in 100 newly diagnosed patients of acute myocardial infarction (AMI) admitted in cardiology unit, Lady Reading Hospital Peshawar and were compared with 100 normal subjects. There were 85 males and 15 females in cases and 75 males and 25 females in control group. The mean age in cases was 50.87±11.02 and 42.31±12.09 in control group. Two ml of venous blood of each subject was collected in K3-EDTA tubes. Platelet indices were assayed by using Sysmex KX-21, Japan auto-analyzer in Clinical Laboratory, Lady Reading Hospital, Peshawar within 10-20 minutes of collection of blood. The data was analyzed by using SPSS version 20.

RESULTS: Platelets count was significantly decreased (233 x10 ^{9}/L) in patients as compared to controls (291.27x10 ^{9}/L) (P <0.001). Mean platelets volume (MPV) was

10.99±1.34 fl in cases as compared to control where it was 9.21±0.98 fl. Platelets distribution width (PDW) was 14.17±2.14 fl in cases as compared to controls where it was 12.36±1.86 fl. Platelets large cell ratio (P-LCR) was 28.21±7.84 in cases as compared to controls where it was 22.83±6.85%. All the three aforementioned platelet indices were significantly higher in cases as compared to controls (P< 0.001).

CONCLUSION: Platelet indices are significantly increased in newly diagnosed cases of MI. Evaluation of platelets indices is simplest, less expensive and easily available parameter to predict patients at higher risk for acute coronary event.

Keywords – Myocardial infarction, MPV, PDW, P-LCR

PLATELET INDICES IN NEWLY DIAGNOSED PATIENTS OF MYOCARDIAL INFARCTION.

INTRODUCTION:

Platelets are non nucleated cells present in the circulation which are the fragments of cytoplasm derived from megakaryocytes in the bone marrow.[1] These un-activated platelets are discoid in shape.[2]

It has been shown that the physiological agonists of platelets (such as thrombin, collagen, thromboxane-A_2, Adenosine diphosphate, adrenaline and serotonin) interact with the specific receptors present on the membrane of platelets and induces the platelet activation leading to change in shape and aggregation which are the key factors in platelet adhesion with the exposed collagen of sub-endothelium and formation of thrombus.[3] Therefore platelets have been shown to play an important role in the pathogenesis of acute coronary syndrome.[4]

It has been shown that the function of platelets has got a relation with their size. Large sized platelets are more active (metabolically and enzymatically) as compared to the normal sized platelets.[5]

Higher mean platelet volume (MPV) has been correlated with slowing of blood flow in the coronary vessels and has also been reported to increase in the unstable angina and myocardial infarction.[6, 7]

High MPV after acute ischemic cerebro-vascular event has also been found to be correlated with bad outcome (higher risk of recurrent stroke).[8, 9,]

Some research workers have reported that MPV is a risk factor for myocardial infarction, but not for the prevalence of coronary artery disease. [10, 11]

In a follow up study, MPV has shown to anticipate recurrent MI and death, measured at six months after acute MI.[12]

Dundar et al found in his longitudinal study that MPV is higher in pre-eclampsia as compared to their normotensive counterparts[13].

Platelet indices has also been used and shown to be one of the markers to see the disease activity as well as to see the response to treatment in rheumatoid arthritis along with other conventional markers.[14]

MPV and PDW have been measured in Diabetics having micro and macro vascular complications and were found to play significant role in categorizing these patients on this basis [15, 16.]

In a study carried out in USA, elevated MPV has been found as a strong predictor as well as having prognostic value after percutaneous coronary intervention similar to that of troponin used for the patients having acute coronary syndrome.[17]

Besides diagnostic value of platelet indices, Rechcinski et al, have shown that MPV, PDW and P-LCR are important independent prognostic factors for mortality in patients after MI (long term mortality) and hence platelet volume indices provide valuable contribution to identification of high risk patients.[18]

Majority of the aforementioned studies on platelet indices have been carried out in western population and few in Asian population in different diseases as diagnostic as well as prognostic markers.

In Pakistan Zuberi et al have carried out a study on platelet indices in diabetic patients. [19] No such study so far to my knowledge has been carried out on patients of myocardial infarction in Pakistan.

AIMS AND OBJECTS:

The aims and objective of the present study were:

1. To find out the platelet indices in newly diagnosed patients of myocardial infarction and compare it with normal individuals of nearly the same age group.
2. To see if the platelet indices can be used for prediction of MI as risk factors.

MATERIAL AND METHODS:

Study Design: It was a case control study

Sample size and venue: There were 100 cases and100 control of either sex included in the study.

Patients were selected from Cardiology unit Lady Reading Hospital, Peshawar at the time of admission as emergency and controls of nearly the same age group were selected from normal healthy subjects.

Sampling technique: Convenient sampling.

Duration of study: 06 months

Inclusion Criteria:

Newly diagnosed cases of acute MI, admitted in coronary care unit (CCU) of Lady Reading Hospital Peshawar were included in the study.

The following WHO criteria were used to diagnose the cases. [21]

"A patient was diagnosed having MI if two (probable) or three (definite) of the following criteria were satisfied:

1. Clinical history of ischemic type chest pain lasting for more than 20 minutes
2. Changes in serial ECG tracings
3. Rise and fall of serum cardiac biomarkers"

Exclusion Criteria:

Known cases of Diabetes mellitus, coronary artery disease, old MI, bleeding and platelet disorders and also the patients already receiving antiplatelet drugs or anti coagulants.

Data collection procedure:

Patient's data was recorded on specially designed History proforma for the study.

Ethical consideration:

Approval of the Ethical & Research Committee of Peshawar Medical College was obtained.

Consent of the cases and control subjects was obtained from all individuals on specially designed consent Proforma

METHODOLOGY :

Specially designed study History Proforma was completed for all subjects.

Blood sample was obtained from patients in K3- EDTA tube at the time of admission in cardiology unit, Lady Reading Hospital Peshawar. Blood sample was taken immediately to the Laboratory of the hospital for analysis within 15-20 minutes so that the volume of platelet is not influenced by EDTA.

Platelet indices

The following platelet indices were assayed by using Hematology Auto-analyzer (Sysmex KX-21), Sysmex Japan, in Pathology Department Lady Reading Hospital, Peshawar.

1. "Platelet count,
2. Mean platelet volume (MPV),
3. Platelet distribution width (PDW)
4. Platelet large cell ratio (P-LCR) "

STATISTICAL ANALYSIS.

Data was entered and analyzed by SPSS version 20.

Qualitative variables were analyzed by Chi square test and Quantitative variables were analyzed by independent T test.

P value <0.05 was taken as significant.

Study variables:

Platelet indices were treated as independent variables whereas myocardial Infarction was treated as dependent variable. Other important variables were age, gender and lifestyle.

ODDS RATIO (OR).

Odds ratio (OR) which is a measure of association between an exposure and an outcome was also calculated as OR are most commonly used in case-control studies.

RESULTS:

The cases studied comprised of 100 consecutive patients admitted in Cardiology unit, Lady Reading Hospital, Peshawar who fulfilled the inclusion criteria.

All of them were newly diagnosed patients of myocardial infarction. They were compared with 100 controls of nearly the same age group.

The mean age of cases was 50.87± 11.02 years and the mean age of controls was 42.31 ± 12.09 years (Table – I).

Table -I. Age distribution among Cases and controls

Groups	Mean± SD	Total (n)
Cases	50.87 ± 11.02	100
Controls	42.31 ± 12.09	100

Among gender distribution, 85 of the total cases were males and 15 were females. Among controls, 75 were males and 25 were females. Of the total cases and controls, 160 (80%) were males and 40 (20%) were females. (Table- II)

Table-II: Genders distribution among cases and controls

Gender	CONTROL (n)	CASES (n)	TOTAL
MALE	75	85	160
FEMALE	25	15	40

The mean platelet count in cases was 233.08x10^9/L and in controls it was 291.27x10^9/L. The count in cases was significantly (P<0.001) lower than in controls but was within the normal range. (Table -III).

The mean of the mean platelet volume (MPV) in cases was 10.99 ± 1.34 fl as compared to the controls which was 9.21± 0.98fl. The mean was significantly higher (P<0.001) when compared with controls. (Table -III). Odds ratio (OR) was 5.4 (more than one) with a 95% confidence interval (CI) of (1.44 - 2.10). This confirms that significantly increased MPV is a risk factor for MI.

The mean Platelet distribution width (PDW) in cases was 14.17 ± 2.14fl and in controls it was12.36 ± 1.86fl.The mean PDW was significantly raised (P<0.001) in cases as compared to controls. (Table - III). Odds ratio (OR) was 1.8 (more than one) with a 95% confidence interval (CI) of (1.24 – 2.36). This shows that significantly increased PDW is also a risk factor for MI.

The mean Platelet large cell ratio (P-LCR) in cases was 28.21± 7.84 and it was 22.83 ± 6.85 in controls. It was also statistically significantly higher (P<0.001) in cases as compared to controls. (Table -III).

Table- III. COMPARISON OF PLATELET INDICES AMONG CASES AND CONTROLS

Platelet INDICES	CASES Mean ±SD	CONTROLS Mean ±SD	P-VALUE	95% CI Lower	95% CI Upper
PC x10 ^{9}/L	233.08 ±64.57	291.27 ±70.76	<0.001	-770	-392
MPV (fl)	10.99 ±1.34	9.21 ±0.98	<0.001	1.44	2.10
PDW (fl)	14.17 ±2.14	12.36 ±1.86	<0.001	1.24	2.36
P-LCR (%)	28.21 ±7.84	22.83 ±6.85	<0.001	3.32	7.43

SD=Standard deviation, PC=Platelet count, L=Liter

MPV=Mean platelet volume, PDW=Platelet distribution width

fl =Famto liter, P-LCR= Platelet large cell ratio

CI=confidence interval

DISCUSSION:

Myocardial infarction (MI) is one of the major consequences of thrombotic lesion in coronary artery disease (CAD). Early diagnosis of MI still needs research despite the considerable advancement in the diagnostic parameters [20]. Platelets play a key role in the development and progression of atherosclerosis and its complications, including MI. [21, 22]

Platelet size and its function are interrelated and it has been shown that larger platelets are more reactive than normal platelets. Consequently, larger and hyperactive platelets play a key role in all the consequences of acute thrombotic event in the coronary arteries.[23]

Activated large size platelets not only secrete thromboxane A2 and ADP but also directly bind to the circulating fibrinogen, via platelet glycoprotein (GP) IIb /IIIa (integrin). The platelet–fibrinogen–platelet integration initiates the process of platelet aggregation and thus, leads to coronary thrombus formation. These findings suggested that in larger platelets, MPV may be useful marker in patients with ACS.[24]

Automation in the field of hematology analyzers have made it possible to determine the parameters that had not previously been measured or used specially related to platelets and doctors were unaware of their importance because these parameters were not printed or ignored in the reports.[25] These parameters include, "platelet indices (mean platelet volume (MPV), platelet distributing width (PDW), and platelet large cell ratio (P-LCR) " which offer valuable information about the morphology and maturity of platelets. MPV is a measurement of the average size and volume of platelets in blood whereas PDW reflects the variability in the platelets size.[26]

It has been shown by many research workers that the MPV is increased in MI and can be used as an independent risk factor for myocardial infarction in patients having coronary artery disease.[27, 28]

In my study I measured the platelet indices in newly diagnosed patients of MI which is first study of this type in Pakistan. The differences in mean of mean platelet volume (MPV), Platelet distribution width(PDW) and Platelet large cell ratio (PLC-R) between the cases of MI as compared to healthy controls were statistically highly significant (P<0.001) whereas mean platelet count was significantly decreased which might be due to increased rate of platelet expenditure at the site of plaque (atherosclerosis). This also led to walkout of large sized platelets from the bone marrow. These findings are in accordance with the results of other research workers who have conducted nearly the same type of research in different countries of the world and have shown that MPV and PDW can be use as predictors as well as prognostic markers in cases of MI. [29-35].

My data also conclude that the higher MPV and PDW contribute to the prothrombotic state in acute MI and that large sized platelets play a significant role in myocardial infarction as is also pointed out by Abass et al.[28]

The only study which has shown that P-LCR cannot be expressed as marker of platelet reactivity or a risk factor for coronary artery disease is that of Luca GD et al [36] which is contrary to our study in which P-LCR was significantly increased along with other two indices.

CONCLUSION:

Large sized platelets are more active and a risk factor for developing myocardial infarction. Therefore, in these patients, auto-analyzer for measuring platelet indices is more helpful regarding diagnosis and preventive measures.

As platelet indices (MPV, PDW and P-LCR) were significantly raised in newly diagnosed subjects of MI, therefore they can be considered as useful and cheaper early diagnostic markers along with other biomarkers (if available) for acute MI.

As platelet indices are routinely measured by modern hematology auto analyzers and mentioned in the printed results but no attention is paid by the honorable Physicians due to either ignorance of these parameters or intentional deletion of these parameters from printed results by the technicians who are also unaware of the importance of these parameters. Therefore awareness about the importance of these new parameters is important and should be used as diagnostic as well as prognostic factor.

RECOMMENDATIONS:

Awareness about the importance of platelet indices should be created amongst doctors about their importance.

The technicians who are analyzing blood by auto analyzers should also be directed to mention these in the self typed results as they usually ignore them as useless parameters.

It needs further follow up studies in cases of MI to see its prognostic importance after continuation of treatment.

Platelet indices can also be used as routine investigation to assess success of thrombolytic medicine in cases of MI.

It is also recommended that practical applications of platelet indices in other pathological conditions should also be used as diagnostic as well as prognostic markers.

References:

1. Machlus KR; Thon JN; Italiano JE. Interpreting the developmental dance of the megakaryocyte: A review of the cellular and molecular processes mediating platelet formation". British Journal of Hematology 2014; 165 (2): 227–36.
2. Michelson AD, Platelets, 2013, P. 117-118
3. Holmsen H. Physiological functions of platelets. Ann Med. Feb.1989; 21(1):23-30.
4. Grover A, Bahl A, Vijyvergiya R, Kumar RM, Thingan ST. Changing trends of cardiovascular disease in India: implications for prevention based on 2001 census. Indian J Cardiol 2003; 6:59-3.
5. Thompson CB, Jakubowski JA, Quinn PG, Deykin D, Valeri CR. Platelet size as a determinant of platelet function. J Lab Clin Med, 1983; 101: 205- 13.
6. Isik T, Ayhan E, Uyarel H et al. Increased mean platelet volume associated with extent of slow coronary flow. Cardiol J, 2012; 19: 355–362.
7. Pizzuli L, Yang A, Martin JF, Luderitz B. Changes in platelet size and count in unstable angina compared to stable angina and non-cardiac chest pain. Eur Heart J, 1998; 19: 80–84.
8. Greisenegger S, Endler G, Hsieh K, Tentschert S, Mannhalter C, Lalouschek W. Is elevated mean platelet volume associated with a worse Outcome in patients with acute ischemic cerebrovascular events? Stroke, 2004; 35: 1688–1691.

9. Bath P, Algert C, Chapman N, Neal B. Association of mean platelet volume with risk of stroke among 3134 individuals with history of cerebrovascular disease. Stroke, 2004; 35: 622–626.
10. Kilicki-Camur N, Demirtunc R, Konuralp C, Eskiser A, Basaran Y. Could mean platelet volume be a predictive marker for acute myocardial infarction? Med Sci Monit, 2005; 11: 387–392.
11. Endler G, Klimesch A, Sunder-Plassmann H et al. Mean platelet volume is an independent risk factor for myocardial infarction but not for coronary artery disease. Br J Haemat, 2002; 117: 399–404.
12. Tekbas E, Kara AF, Ariturk Z et al. Mean platelet volume in predicting short- and long-term morbidity and mortality in patients with or without ST-segment elevation myocardial infarction. Scand J Clin Lab Invest, 2011; 71: 613–619.
13. Dundar O , Yoruk P, Tutuncu L, Erikci AA, Muhcu M, Ergur AR, Atay V, Mungen E. Longitudinal study of platelet size changes in gestation and predictive power of elevated MPV in development of pre-eclampsia. Prenat Diagn. 2008, Nov.28(11):1052-6.
14. Yazici S, Yazici M, Erer B, Calik Y, Ozhan H and Ataoglu S. The Platelet indices in patients with rheumatoid arthritis: Mean platelet volume reflects disease activity. Platelet, 2010;21(2):122-125.
15. Hekimsoy Z , Payzin B, Ornek T, Kandoğan G.Mean platelet volume in Type 2 diabetic patients.J Diabetes Complications. 2004 May-Jun; 18(3):173-6.
16. Jindal S, Gupta S, Gupta R, Kakkar A, Singh HV, Gupta K, Singh S. Platelet indices in diabetes mellitus: indicators of diabetic microvascular complications. Hematology. 2011 Mar; 16(2): 86-9.

17. Goncalves SC, Labinaz M, Le May M, Glover C, Froeschi M, O'Brein E, Shukla D, Ruchin P, Sookur D, Ha A, So D. Usefulness of mean platelet volume as a biomarker for long-term outcomes after percutaneous coronary intervention. Am J Cardiol. 2011 Jan 15; 107(2):204-9.
18. Rechciński T, Jasińska A, Foryś J, Maria Karina KP, Drabik W, Plewka M, Peruga JZ, Kasprzak JD. Prognostic value of platelet indices after acute myocardial infarction treated with primary percutaneous coronary intervention. Cardiology Journal, 2013; 20 (5): 491–498.
19. Zuberi BF, Akhtar N and Afsar S. Comparison of mean platelet volume in patients with diabetes mellitus, impaired fasting glucose and non-diabetic subjects. Singapore Med J 2008:49(2):114-16.
20. Lippi G, Montagnana M, Salvagno GL, Guidi GC. Potential value for new diagnostic markers in the early recognition of acute coronary syndromes, CJEM, 8, 2006, 27–31.
21. Boos CJ, Lip GY. Platelet activation and cardiovascular Outcomes in acute coronary syndromes, J Thromb Haemost, 4, 2006, 2542–2543.
22. Tsiara S, Elisaf M, Jagroop IA, Mikhailidis DP. Platelets as predictors of vascular risk: is there a practical index of platelet Activity, ClinAppl Thromb Hemost, 9, 2003, 177–190.
23. Jesty J, Yin W, Perrotta P, Bluestein D. Platelet activation in a circulating flow loop: combined effects of shear stress and exposure time, Platelets, 14, 2003, 143–149.
24. Kamath S, Blann AD, Lip GY .Platelet activation: assessment and quantification. Eur Heart J 2001; 22:1561–71.

25. Shattil S.J., Newman P.J. Integrins: dynamic scaffolds for adhesion and signaling in platelets. Blood. 2004; 104(6):1606–1615.

26. Botma J Mogongoa LF Jaftha AD, Janse van Rensburg W. Reference ranges for platelet indices using Sysmex XE -2100 blood analyser, Med Techno Sou Afri, 26(2), 2012, 17-21.

27. Endler G, Klimesch A, Sunder-Plassmann H. Mean Platelet volume is an independent risk factor for myocardial Infarction but not for coronary artery disease. Br J Haematol. 2002; 117:399-404.

28. Abass AE,Yassir T, Saeed Y,Taha1 A, Basheer A, Mubarak E, Zonoon F, Faroog G, Mohammad N. Investigation of platelets count and indices in coronary artery diseases among Sudanese patients . J Dental and Med Sc Jan. 2016; 15(1): 35-38.

29. Ranjith MP, Divyar R, Mehta VK, Krishnan MG, KamaRaj R and Kavishwar A. Significance of platelet volume indices and platelet count in ischemic heart disease. J clin Pathol, Sept 2009; 62(9):830-833.

30. Kilicli-Camur N, Demirtunc R, Konuralp C, Eskiser A, et al. Could mean platelet volume be a predictive marker for acute myocardial infarction. Med Sci Monit 2005; 118: 387-92.

31. Yetkin E. Mean platelet volume not so far from being routine diagnostic and prognostic measurement. Thromb Haemost 2008; 100:3-4.

32. Assiri AS, Jamil AM, Mahfouz AA, Mahmoud ZS, and Ghallab M. Diagnostic importance of platelet parameters in patients with acute coronary syndrome admitted to a tertiary care hospital in southwest region, Saudi Arabia. J Saudi Heart Assoc.2012 Jan; 24(1): 17–21

33. Hamudi Al-Obeidi SR, Ahmedm SH A. Obeid F . Evaluation of Platelet Indices in Patients with Acute Coronary Syndrome. Mustansiriya Medical Journal, June 2013; 12(1): 58-64.

34. Yaghoubi A, Golmohamadi Z, Alizadehasal A, Azarfarin R. Role of platelet parameters and haematological indices in myocardial infarction and unstable angina. JPMA, 2013; 63: 1133-36.

35. Mirzaie AZ, Abolhasaan M, Ahmadineajad B, Panahi M. Platelet count and MPV, routinely measured but ignored parameters use in conjuction with diagnosis of acute coronary syndrome: single study centre in Iranian population, 2010. Med J Islamic Republic of Iran, 2012; 26(1):17-21.

36. Luca GD, Santagostino M, Seeco GG, Cassetti E, Giuliani L, Coppo L, Schaffer A, Fundaliotis A.Platelet Large cell ration and extent of coronary artery disease. J Thrombosis and Thrombolysis 2010, 30: 426-433.

Acknowledgement:

I am thankful to Prof. Taj Ali, Lab Incharge LRH, Peshawar for permission and Senior Technician Niaz Muhammad for their valuable support. I am also gratefull to Dr Zahid Jadoon for his help in statistical analysis.

PLATELET INDICES IN NEWLY DIAGNOSED PATIENTS OF MYOCARDIAL INFARCTION.

ORIGINALITY REPORT

19%	16%	14%	%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	journals.viamedica.pl Internet Source	2%
2	www.haematologica.org Internet Source	2%
3	S Kamath. "Platelet activation: assessment and quantification", European Heart Journal, 09/01/2001 Publication	1%
4	www.pubmedcentral.nih.gov Internet Source	1%
5	www.alliedacademies.org Internet Source	1%
6	www.bcuc.com Internet Source	1%
7	Lippi, Giuseppe Filippozzi, Luca Salvagn. "Increased mean platelet volume in patients with acute coronary syndromes.(Clinical report)", Archives of Pathology & Laboratory Medic, Sept 2009 Issue Publication	1%

8	lib.bioinfo.pl Internet Source	1%
9	Pujol-Moix, Núria, Miquel Vázquez-Santiago, Agnès Morera, Andrey Ziyatdinov, Angel Remacha, Josep F. Nomdedeu, Jordi Fontcuberta, José Manuel Soria, and Juan Carlos Souto. "Genetic determinants of Platelet Large-Cell Ratio, Immature Platelet Fraction, and other platelet-related phenotypes", Thrombosis Research, 2015. Publication	1%
10	Marcus A. Lima. "Thyroid peroxidase expression in diseased human thyroid glands", Endocrine Pathology, 09/1999 Publication	1%
11	content.onlinejacc.org Internet Source	1%
12	anatoljcardiol.com Internet Source	<1%
13	Mahdavi-Zafarghandi, Reza, Behnam Shakiba, Mohammad Reza Keramati, and Mahmoud Tavakkoli. "Platelet volume indices in patients with varicocele", Clinical and Experimental Reproductive Medicine, 2014. Publication	<1%
14	journal.publications.chestnet.org Internet Source	<1%

15	ircrj.com Internet Source	<1%
16	www.ijpbs.com Internet Source	<1%
17	pharmacypractice.org Internet Source	<1%
18	commedtvm.org Internet Source	<1%
19	www.jbiopharm.com Internet Source	<1%
20	bmchematol.biomedcentral.com Internet Source	<1%
21	Shemirani, Amir-Houshang, Béla Nagy, Alajos-Tamas Takáts, Katalin-Szilvia Zsóri, Csilla András, János Kappelmayer, and Zoltán Csiki. "Increased mean platelet volume in primary Raynaud's phenomenon", Platelets, 2012. Publication	<1%
22	www.iapsmupuk.org Internet Source	<1%
23	journalfilter.com Internet Source	<1%
24	en.m.wikipedia.org Internet Source	<1%
	banglajol.info	

25	Internet Source	<1%
26	onlinelibrary.wiley.com Internet Source	<1%
27	67.207.206.99 Internet Source	<1%
28	www.banglajol.info Internet Source	<1%
29	www.ncbi.nlm.nih.gov Internet Source	<1%
30	www.sciepub.com Internet Source	<1%
31	www.umed.lodz.pl Internet Source	<1%
32	ten Berg, Maarten J., Albert Huisman, Patricia M.L.A. van den Bemt, Hanneke den Breeijen, Toine C.G. Egberts, and Wouter W. van Solinge. "Discriminative value of platelet size indices for the identification of the mechanism of chemotherapy-induced thrombocytopenia", Biomarkers, 2011. Publication	<1%
33	Martin, John F., Steen D. Kristensen, Anthony Mathur, Erik L. Grove, and Fizzah A. Choudry. "The causal role of megakaryocyte–platelet hyperactivity in acute coronary syndromes", Nature Reviews	<1%

Cardiology, 2012.
Publication

34	www.termedia.pl Internet Source	<1%
35	ijpbs.net Internet Source	<1%
36	article.sciencepublishinggroup.com Internet Source	<1%
37	academicjournals.org Internet Source	<1%
38	H. CHANDRA. "Role of mean platelet volume as discriminating guide for bone marrow disease in patients with thrombocytopenia", International Journal of Laboratory Hematology, 12/2009 Publication	<1%
39	S. Tsiara. "Platelets as Predictors of Vascular Risk: Is There a Practical Index of Platelet Activity?", Clinical and Applied Thrombosis/Hemostasis, 07/01/2003 Publication	<1%
40	Rechciński, Tomasz; Jasińska, Aleksandra; Foryś, Jakub; Krzemińska-Pakuła, Maria; Wierzbowska-Drabik, Karina; Plewka, Michał; Peruga, Jan Zbigniew and Kasprzak, Jarosław Damian. "Prognostic value of platelet indices after acute myocardial infarction treated with primary percutaneous	<1%

coronary intervention", Cardiology Journal, 2013.
Publication

41	"Poster Abstracts", Nephrology, 5/2008 Publication	<1%
42	"Monday, 3 September 2007", European Heart Journal, 09/02/2007 Publication	<1%

EXCLUDE QUOTES	ON	EXCLUDE MATCHES	OFF
EXCLUDE BIBLIOGRAPHY	ON		