



Research article

A prospective observational study to identify the etiology and clinical significance of thrombocytosis

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ABSTRACT

In a tertiary care hospital, a total of 185 individuals with thrombocytosis with a platelet count of more than 450,000/ μ l were studied prospectively for clinical significance and aetiology. The most prevalent causes of thrombocytosis were an infection. Reactive thrombocytosis (97.84%) was shown to be the most prevalent cause of an increased platelet counts in the current research whereas spurious thrombocytosis was found in (2.16%). In our research, we found no evidence of a significant influence of food patterns and antiplatelet medications on platelet count. Platelet count was shown to be higher in a greater percentage of male participants, as well as in patients with existing co-morbidities. The presence of a high platelet count during a routine blood test has medical and clinical implications.

Keywords: Thrombocytosis, Platelets, Etiology, Clinical significance, Infections.

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INTRODUCTION

Platelets are tiny blood cell fragments that cause blood to clot in response to bleeding. The platelet count of a healthy person ranges from 150,000 to 450,000/ μ l of blood. An increased platelet count is defined as the presence of more platelets in the blood than is usual. Thrombocytosis is a condition in which the body generates an abnormally large number of platelets.^[1] Thrombocytosis is defined as a platelet count that exceeds a predetermined upper limit of normal, which might range from 350,000/ μ l to 600,000/ μ l depending on the laboratory or medical reference. The most frequent normal cutoff is 450,000/ μ l^[2].

In hospitalized patients, abnormal platelet counts have been related to a greater risk of mortality.^[2,3] While an increase in platelet count is seldom connected with a medical emergency, it can occasionally result in life-threatening complications including blood clotting, hemorrhage, or stroke. According to studies done in the general population excluding critically hospitalized patients, abnormal platelet counts may be a predictor of underlying morbidities.^[3] Platelets engaged in life-threatening situations that need hospitalization might indicate a poor prognosis.

Thrombocytopenia and thrombocytosis are seen in 7% of all people hospitalized to the hospital for a short length of time, according to research.^[4] Furthermore, an increased platelet count is a common occurrence in 1.5 percent to 2.2 percent of persons over 40 who visit their primary care physician.^[5] In the absence of disease,

the platelet count remains steady; however, it may decline with age.^[6]

Both clinical practice and research laboratories rely on platelet counts. A platelet function issue or a numerical deficit might be the source of the clinical bleed. As long as the platelet count is more than 20,000/ mm^3 , medical symptoms are typically minor and restricted to simple bruising. When the platelet count drops below 10,000/ mm^3 , the risk of life-threatening bleeding, such as cerebral hemorrhage or gastrointestinal bleeding, increases dramatically^[7-8]. Platelet production is enhanced as a result of faulty bone marrow stem cells in autonomous thrombocytosis (Primary thrombocythemia). It is generally inherited, although genetic alterations may play a role in this condition^[9]. Essential thrombocythemia is a kind of thrombocythemia that develops without any blood cell abnormalities. Reactive thrombocytosis (Secondary thrombocytosis) is a frequent cause of an increased platelet value that is generally a physiologic reaction to a concomitant inflammatory illness or surgery. It's a self-contained state that ends when the coexisting one does^[10-11].

Many researches on the etiology of thrombocytosis in children have been published, however local published data for adult patients is sparse. The goal of this study was to find out the most common underlying causes of thrombocytosis in our adult population^[12].

MATERIAL AND METHOD

The study has been conducted in Parul Sevashram, a 750-bed tertiary care teaching Hospital. After taking prior consent from patients, the data has been collected from all medical notes, including progress charts, nursing documents, consultations sheets, discharge files, vital signs charts, laboratory investigations reports, radiographic images, and pathologic data. The Institutional Ethics Committee on Human Research – Parul University (PU-IECHR) authorized the protocol (PUIECHR/PIMSR/00/081734/3007), and whole research was conducted at Parul Sevashram Hospital.

Identification of subjects

We looked for adult patients between the ages of 18 and 65 who had a platelet count of more than 450000/ μ l of blood and were hospitalized to either the medicine or surgery departments between November 2020 and February 2021. If a patient experienced multiple episode of thrombocytosis over the time, only the event with the higher platelet count was noted. During the research period, all patients who satisfied the criteria were enrolled. The data from 185 patients were examined in total.

Sources of data collection

We gathered information such as demographics, vital signs, and laboratory results, along with predisposing conditions, primary complaints, and previous medication history. Temperature, red blood cell, palpitations, white blood cell and platelet counts were all measured on the same day. We also kept track of any culture data that was available, as well as therapies and patient outcomes. To check the etiology of elevated platelet counts in patient, we looked at discharge instructions and clinical reports, including regular progress comments, hematology interviews, and communicable diseases evaluations. Patients were divided into three groups: those with primary, secondary and spurious thrombocytosis. [13-16]

Statistical analysis

A Microsoft Excel database was used to store the information. The percentage of individuals with each thrombocytosis etiology was determined (primary, spurious and secondary infectious).

RESULT

Demographic Characteristics of Patients

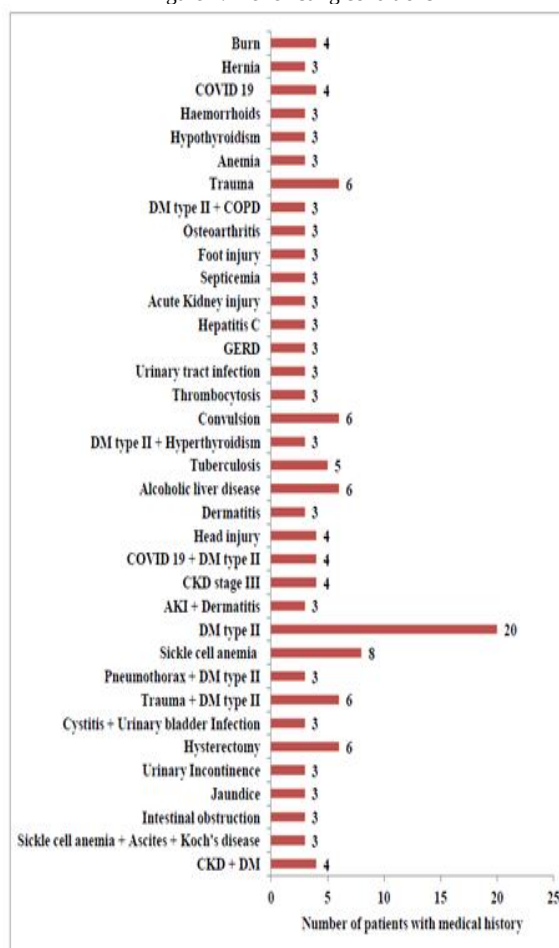
Of 185 participants, 106 were male (57%); and 79 females (43%); the mean age was 44 with standard deviation 14. The majority of patients were in the age groups 46-52 (18%) and 60-67 (18%), with 31 (17%) individuals in the age range 39-45. 110 (59%) of the 185 individuals had addictive social behaviors, with 28 (25.45%) of them being alcoholics, followed by smokers (19.09%). The social addiction habit was discovered in the age groups of 60-67 (17.31%) and 18-24 (16.36%). A total of 153 (82.70%) of the 185 participants had a medical history, with 20 (13.07%) of them having DM type II, followed by Sickle cell anemia (5.22%). During

the study, 92 (49.72%) patients in the medicine department were discovered to have thrombocytosis [(5.43%) had CKD, followed by diabetic foot ulcer (4.35%), DM type II (4.35%), C3 C4 disc compression (4.35%), and UTI (4.35%)]. In the surgical department, 93 (50.28%) patients [(13.99%) had diabetic foot ulcers, followed by fracture (11.84%), renal calculi (7.53%), and non-diabetic foot ulcer (7.53%)] were found to have the same condition.

Table 1: Clinical presentations

Clinical Presentation	Percentage
Abdominal pain	35.49%
Difficulty in walking	3.97%
Swelling	9.26%
Weakness	13.97%
Breathlessness	5.53%
Anorexia	2.20%
Oedema	3.09%
Fever	13.67%
Nausea	2.20%
Vomiting	5.29%
Rashes	0.45%
Speaking difficulties	0.45%
Headache	2.65%
Giddiness	1.33%
Body ache	0.45%

Figure 1: Pre-existing conditions



(There's a chance that each patient in the research has a number of pre-existing conditions. Abbreviations: COPD – Chronic obstructive pulmonary disease, DM – Diabetic mellitus, GERD – Gastroesophageal reflux disorder, CKD – Chronic kidney disease, AKI – Acute kidney injury)

Etiology of thrombocytosis

Thrombocytosis was usually secondary; no primary causes of thrombocytosis were found. Post-operative and tissue injury were the most prevalent secondary infection etiologies. Diabetic foot ulcer, non-diabetic foot ulcer, tendon infection, and viral fever were the most prevalent infectious causes of thrombocytosis.

Various bacteria were recovered from infectious disease participants, however, culture data for many of the individuals were not provided. The most often isolated microorganism was *Escherichia coli*. Other frequent bacteria were *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*.

Table 2: Etiology of thrombocytosis in 185 patients

Diagnosis	Percentage
Secondary thrombocytosis	
• Tissue damage	15.46%
• Infection	34.25%
• Anemia	3.31%
• Chronic inflammation and vasculitides	11.60%
• Post-operative	22.09%
• Reaction to certain drugs	1.14%
• Others	12.15%
Primary thrombocytosis	0%
Spurious thrombocytosis	2.16%

Table 3: Incidence of isolated microorganism

Isolated microorganism	Blood	Urine	Percentage
<i>Enterobacter cloacae</i>	0	1	5.51%
<i>Escherichia coli</i>	0	6	33.31%
<i>Staphylococcus aureus</i>	2	0	11.21%
<i>Pseudomonas aeruginosa</i>	4	0	22.21%
<i>Klebsiella pneumoniae</i>	0	3	16.55%
<i>Actinobacterialbaumanni</i>	2	0	11.21%
Total	8	10	100%

Clinical outcome

The underlying etiology of thrombocytosis was cured in the majority of patients, either totally or partially healed.

Only 28 (30.44%) of 92 patients admitted to the medicine department and 53 (56.98%) of 93 patients admitted to the surgery department had complete resolution at discharge; in other words, patients who had their infection surgically managed were more likely to have complete resolution.

DISCUSSION

Thrombocytosis can be caused by several medical conditions, including cancer and infections. Prior to the introduction of electronic blood cell counters, platelet counts were not included in full blood profiles; however, now that platelet counts have been included in routine blood profiles thanks to electronic cell counters, thrombocytosis is more often observed. As a result, a high platelet count has become a serious health problem for many people^[17]. This is a diagnosis that is frequently overlooked. Elevated platelet count is a distinguishing biomarker for several diseases, but it's uncertain if it's a reliable predictor of short-term effects in enrolled individuals. The etiology and clinical relevance of thrombocytosis

were investigated in this study, which included 185 individuals with a platelet count of greater than 450,000/microlitre. Secondary thrombocytosis caused the elevation in 181 (97.84%) of the cases, whereas spurious thrombocytosis caused the increase in 4 individuals. During the research period, no individuals with primary thrombocytosis were reported.

Infection was discovered to be the most common cause of thrombocytosis in this study (35.25%). A diabetic foot ulcer was the most common cause of an increased platelet count related to infection (8.45%). In a few additional investigations, infection was found to be one of the most common causes of thrombocytosis^[7, 13]. Thrombocytosis is a reactive in the majority of cases, according to these studies.^[7, 8, 13, and 14]. The second most common reason given was post-operative complications (22.09%). The most prevalent cause of an increase in platelet counts was renal calculi. In earlier investigations, thrombocytosis induced by surgical or traumatic tissue damage was found to be the most common cause of thrombocytosis.^[9, 11, 15, and 16]. According to Wadenvik H., increased platelet formation following surgery is a major cause of postoperative thrombocytosis.^[18]. Thrombocytopenia and/or bleeding during surgery have both been associated to post-surgery thrombocytosis. After cytotoxic drug therapy, thrombocytosis is thought to be a rebound condition caused by transitory marrow suppression.^[19]. The majority of participants in the study were male (57%). The participants were on average 44 years old, with the bulk of patients falling into the age ranges of 46 to 52 (18%) and 60 to 67 (18%). Almost 153 (82.70%) of the participants have a medical history, with 20 (13.07%) of them having type 2 diabetes and Sickle cell anemia (5.22%).

The relationship between age, sex, and platelet counts led to the development of modified reference values.

Flegar-Mestric et al. proposed age-dependent platelet count comparison values, observing that participants aged 8–19 years had platelet counts ranging from 178–420 $\times 10^9/L$, while those aged 20–70 years had platelet counts ranging from 158–424 $\times 10^9/L$ ^[19].

Hong et al. also proposed distinct comparison scales for ladies and males, with girls' scales ranging from 122 to 334 $\times 10^9/L$ and males' scales ranging from 111 to 305 $\times 10^9/L$ ^[20]. Females and males have different platelet count reference ranges (137–347 vs. 144–328 $\times 10^9/L$) after sex testing.^[21]

Various bacteria were recovered from infectious disease participants; however, culture data for many of the individuals was not gathered. Table 3 shows that *Escherichia coli* were the most often isolated bacteria. Other frequent bacteria were *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. Various strains of *E. coli* can activate RNA and protein levels, which may impact platelet

bacteria cross communication, according to a research conducted by A.V. Fejes.^[22]

Any inflammatory activity in the blood, such as the presence of bacteria or sepsis, might increase the number of circulating platelets.^[23, 24]

The majority of patients complained of abdominal discomfort (35.49%), followed by weakness (13.97%), and edema (9.26%). Male patients complained of more stomach discomfort (55), swelling (15), weakness (19), and trouble walking than female patients, whereas females complained of higher fever (18). Thrombocytosis typically goes unnoticed, and when it does, it may be linked to underlying medical problems. Weakness, dizziness, chest discomfort, headaches, and numbness of the hands and feet are the most common symptoms. Splenomegaly was found in 61 individuals (32.97%)^[25].

Splenomegaly is prevalent but not always evident in familial thrombocythemia^[26]. During the counselling, it was discovered that around 48 (26%) of patients had used OTC medicine, with nearly 18 (37.54%) using Tab. PCM and 17 (35.41%) taking painkillers. The impact of PCM on platelets has been understudied, and little is known about the impact of NSAIDs and their metabolites on preserved platelets.^[27] PCM has antiplatelet effects and can decrease TxA2 production, according to a few studies^[28-30]. WBC, Neutrophils, RDW-CV, LDH, K⁺, S. Ferritin, SGPT, SGOT, S. Urea, CRP values were found to be higher than normal with increased platelet count, whereas laboratory parameters such as Hemoglobin, Lymphocytes, RBCs, PCV, MCV, MCH, MCHC, Na²⁺, Albumin values were found to be lower than normal with increased platelet count.

In addition, laboratory results such as Mean platelet volume, PT, INR, APTT, S. creatinine, Ca²⁺, Cl⁻, and Globulin were within normal limits. Only 22 (11.90%) of the 185 individuals had been administered antiplatelet medications, the majority of which were Tab Ecosprin 75 mg, with no change in platelet count. Patients with persistent unexplained thrombocytosis, thrombotic disorders, or symptoms associated with primary hematological illnesses should seek medical help.^[31] Based on professional opinion, a repeat FBC may be performed to assess if the thrombocytosis has disappeared or is still present. If a reactive origin is suspected at presentation, repeat tests should be performed to confirm that the thrombocytosis has healed following sufficient therapy.

The main limitation of our study, it was only conducted in a few towns at a single academic center; the results were insufficient to extend to the broader public. There was a reduced intake of cases due to the COVID 19 pandemic, which meant that fewer patients' conditions were evaluated. The model's impact estimates come from

a prospective observational research. As a result, they are more susceptible to biases and confounding, which might have impacted our precision. There was insufficient evidence of follow-up to compare changes in platelet count values. The breadth of the analysis was limited due to time restrictions.

CONCLUSION

Our study concluded that, Reactive thrombocytosis, which can be caused by several acute and chronic underlying diseases, was shown to be the most prevalent cause of an increased platelet count in the current research. A high-quality hematology analyzer is essential for assessing complete blood counts quickly and precisely, but any blood samples that show abnormal results or low platelet counts on analyzers should be manually counted on a peripheral smear. Platelet parameter such as Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW) are additional characteristics provided by analyzers that can help to determine the cause of a low platelet count. The platelet density index (PDW) is a fundamental platelet indicator that increases as platelets become more active. In our research, we found no evidence of a significant influence of food patterns on platelet count.

DECLARATION OF COMPETING INTEREST

The author declares that they have no conflicts of interest.

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REFERENCE

1. Thrombocytosis, 2021. Diseases conditions, thrombocytosis, symptoms-causes, syc-20378315.
2. Marialaura Bonaccio, Augusto Di Castelnuovo, Simona Costanzo, Amalia De Curtis, 2016. Age-sex-specific ranges of platelet count and all-cause mortality prospective findings from the MOLI-SANI study, Blood, 127:1614-1616, doi: 10.1182/blood-01-692814.
3. PJ Vinholt, AM Hvas, H Frederiksen, L Bathum, 2016. Platelet count is associated with cardiovascular disease, cancer and mortality a population-based cohort study, Thrombosis Research, 148, 136-142, doi:jthromres, 08.012.
4. Moulis, Guillaume, Christiansen, Christian Fynbo, Darvalics, Bianka, 2018. Prevalence of thrombocytopenia and thrombocytosis upon acute hospital admission to internal medicine units. A cross-sectional study in Denmark, Eur J Intern Med, 57:34-37, doi: 10.1016/jejim, 08.014.
5. Sarah ER Bailey, Obioha C Ukoumunne, Elizabeth A Shephard and Willie Hamilton, 2017. Clinical relevance of thrombocytosis in primary care a prospective cohort study of cancer incidence using English electronic medical records and cancer registry data, Br J Gen Pract, 67:405-13, doi:103399/bjgp17X691109.
6. Ginevra Biino, Iolanda Santimone, Cosetta Minelli, Rossella Sorice, 2013. Age and sex-related variations in platelet count in Italy a proposal of reference ranges based on 40987 subjects'

- data, PloS one, 8(1):54289.
7. David H Buss, Alan W Cashell, Michael L O'Connor, Frederick Richards II, 1994. Occurrence, etiology, and clinical significance of extreme thrombocytosis a study of 280 cases, *Am J Med*, 96; 247-53, doi:10.1016/0002-9343(94)90150-3.
 8. Chuncharunee S, Archararit N, Ungkanont A, Jootar S, 2000. Etiology and incidence of thrombotic and hemorrhagic disorder in Thai patients with extreme thrombocytosis, *J Med Assoc Thai*, 83:95-100.
 9. William M. Davis, Alicia OMendez Ross, 1973. Thrombocytosis and thrombocythemia the laboratory and clinical significance of elevated platelet count *Am J Clin Pathol*, 59:243-47, doi:10.1093/ajcp/59.2.243.
 10. M Griesshammer, M Bangerter, T Sauer, R Wennauer, 1999. Aetiology and clinical significance of thrombocytosis analysis of 732 patients with an elevated platelet count, *J Intern Med*, 245(3):295-300.
 11. Robbins G, Barnard DL, 1983. Thrombocytosis and micro thrombocytosis: a clinical evaluation of 372 cases. *Acta Haematol*, 70:175-82, doi:10.1159/000206719.
 12. Dr C. R. Santosh-Kumar, M. D. Yohannan, K. E. Higgy S. A. AL-Mashhadani, 1991. Thrombocytosis in adult's analysis of 777 patients, *J Intern Med*, 229(6):493-495, doi:10.1111/j.1365-2796.tb00383.
 13. Sutor AH, 1995. Thrombocytosis in childhood, *Sem Thromb Hemost*, 21:330-39, doi:10.1055/s-2007-1000654.
 14. Timucin Aydogan, Mehmet Kanbay, Ozlem Allci, Ali Kosar, 2006. Incidence and etiology of thrombocytosis in adult Turkish population, *Platelets*, 17(5): 328331, doi: 10.1080/09537100600746573.
 15. J Hires, JV Dacie, 1996. Persistent post splenectomy thrombocytosis and thromboembolism a consequence of continuing anemia, *Br J Haematol*, 12:44-53, doi:10.1111/j.1365-2141.tb00125.
 16. Christenson JT, Gras PA, Gros Claude A, Simonet F, 1996. Reactive thrombocytosis following coronary artery bypass surgery a possible link to liquid dysfunction, *J Cardiovasc Surg Torino*, 37:491-98.
 17. Hans Wadenvik, Per Ontenwall, Jack Kutti, BO Risberg, 1998. Splenic platelet kinetics and platelet production after major reconstructive vascular surgery, *Acta Med Scand*, 223:147-52, doi:10.1111/j.0954-6820.tb15779.
 18. Alexander Breslow, Richard M Kaufman, Alan RLawsy, 1968. The effect of surgery on the concentration of circulating megakaryocytes and platelets, *Blood*, 32:393401, doi:10.1182/blood.V32.3.393.393.
 19. Z Flegar-Metric, A Nazor, N Jagarinec, 2000. Haematological profile in healthy urban population (8 to 70 years of age) *Collegium antropologicum*, 24(1):185-96.
 20. Jiang Hong, Zhao Min, Pan Bai-shen, Zhang Jie, 2015. Investigation on reference intervals and regional differences of platelet indices in healthy Chinese Han adults, *Journal of clinical laboratory analysis*, 29(1):21-7, Doi: 10.1002/jcla.21721.
 21. D.R. Brummitt, HF Barker, 2000. The determination of a reference range for new platelet parameters produced by the Bayer ADVIA120 full blood count analyzer, *Clinical and laboratory hematology*, 22(2):103-7, doi:10.1046/j.1365-2257.00285.
 22. AV Fejes, MG Best, WA van der Heijden, A Vancura, 2018. Impact of Escherichia coli K12 and O18K1 on human platelet activation, RNAs and proteins, *Sci Rep*, 16145.
 23. MG Alexandrakakis, FH Passam, KPerisinakis, EGanotakis, 2002. Serum pro-inflammatory cytokines and its relationship to clinical parameters in lung cancer patients with reactive thrombocytosis, *Respir Med*, 96:553-558, doi:10.1053/rmed.1328.
 24. Araneda M, Krishnan VHall K, Kalbfleish J, 2001. Reactive and clonal thrombocytosis pro inflammatory and hematopoietic cytokines and acute phase proteins, *South Med J*, 94:417-420.
 25. Thrombocytosis, 2021. Patient care and health information, mayo clinic, diseases-conditions, thrombocytosis symptoms-causes, syc-20.
 26. Pediatric thrombocytosis, 2021. Medscape, medicine, Medscape, article, 959378-overview,
 27. Ben Driver, Denese C Marks, Dianne E van der Wal, 2020. Not all (NSAID and done Effects of nonsteroidal anti-inflammatory drugs and paracetamol intake on platelets, *Res Pract Thromb Haemost*, 4:36-45, doi:10.1002/rth2.12283.
 28. Maria G Sciulli, Francesca Seta, Stefania Tacconelli, Marta L Capone, 2009. Effects of acetaminophen on constitutive and inducible prostanoid biosynthesis in human blood cells, *Br J Pharmacol*, 138:634-41, doi:10.1038/sj.bjp0705078.
 29. Edward Munsterhjelm, Nina M Munsterhjelm, Tomi TNiemi, Olavi Ylikorkala, 2005. Dose-dependent inhibition of platelet function by acetaminophen in healthy volunteers, *Anesthesiology*, 103:712-7, doi:10.1097/00000542-200510000-00009.
 30. Bruce Lages, Harvey JWeis, 1989. Inhibition of human platelet functions in vitro and ex vivo by acetaminophen. *Thromb Res*. 53:603-13, doi:10.1016/0049-3848(89)90150-3.
 31. Abhinav Mathur, Shehan Samaranayake, Neil PF Storrar, Mark AVickers, 2019. Investigating thrombocytosis, *BMJ l4183*, doi: 10.1136/bmj.l4183.

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