Original Article

DOI: 10.7860/JCDR/2026/79098.22414

Effect of Therapeutic Phlebotomy on the Haematological Parameters in Polycythaemia Cases: A Cross-sectional Study from a Tertiary Blood Centre in Southern India

Transfusion Medicine Section

PADMINI CHITRADURGA VIJAYASARATHY[1], HAROON ADONI[2], BRILSEE SIMEON[3]

ABSTRACT

Introduction: Therapeutic phlebotomy involves the controlled removal of blood from a patient to reduce complications in polycythemia, in which 300 to 400 mL of blood is removed. Polycythaemia is a condition characterised by an increase in red cell mass and is commonly seen secondary to smoking, Chronic Obstructive Pulmonary Disease (COPD), congenital heart disease and polycythaemia vera. Patients with polycythaemia have an increased risk of thrombotic events such as stroke, coronary artery disease and deep vein thrombosis compared with normal individuals.

Aim: To evaluate the effect of therapeutic phlebotomy on haematologic parameters in cases of polycythemia.

Materials and Methods: This was a retrospective, cross-sectional study conducted in the Department of Transfusion Medicine, ESIC Medical College and PGIMSR, Bengaluru, Karnataka, India,, for a period of one year from January 2024 to December 2024. A total of 186 therapeutic phlebotomy procedures were recorded for polycythemia, involving 104 patients during the study period who were included in the study. Polycythaemia was defined as Haemoglobin (Hb)>16.5 g/dL and Haematocrit (Hct)>48%. All data were collected in Microsoft Excel. Prephlebotomy haematologic values such as Hb and Hct were recorded for all patients. Status of Janus Kinase 2 (JAK2) mutation analysis was recorded from departmental archives when available. Categorical variables were expressed as counts and percentages; continuous variables were expressed as means, medians and ranges. The Pearson's correlation coefficient was used to correlate pre- and post-phlebotomy Hb and Hct values. A paired t-test was used to determine whether the drop in Hb and Hct was statistically significant. A p-value <0.05 was considered statistically significant.

Results: The study included 104 cases and showed male predominance with a male-to-female ratio of 51:1. The patients ranged in age from 23 to 73 years, with a mean age of 47 years. The average fall in Hb was 1.2 g/dL and the average fall in Hct was 3.6 percentage points after a single session of therapeutic phlebotomy (approximately 350 mL). The post-phlebotomy drop in Hb of ≥1 g/dL was observed in 81 (77.8%) patients, while 23 (22.1%) patients showed a drop < 1 g/dL. It was noted that 36 (34.6%) patients underwent multiple repeated sessions of therapeutic phlebotomy within eight weeks to bring Hb and Hct to the normal range.

Conclusion: Therapeutic phlebotomy, involving removal of 300-400 mL of blood, can reduce Hb by about 1 g/dL and is recommended in polycythaemia to reduce the risk of arterial and venous thrombotic events. Polycythemia, irrespective of the cause, should be treated with aspirin in addition to therapeutic phlebotomy to maintain Hct below 45%.

Keywords: Coronary artery disease, Haematocrit, Therapeutic use

INTRODUCTION

Therapeutic phlebotomy involves the controlled removal of blood from a patient to reduce complications in cases of polycythemia. The term phlebotomy translates literally to lancing (tomia from témno) a vein (fléba from flés), which suggests bloodletting [1]. Approximately 300 to 400 mL of blood is collected in a single blood bag by venipuncture, depending on the patient's condition and the treatment plan. In some cases, multiple sessions may be required to achieve optimal therapeutic effects. Since therapeutic phlebotomy is very similar to blood donation, it can be performed in various settings, such as a ward, a day-care procedure room, a blood center, or an apheresis centre. However, these facilities must be well trained and equipped to collect blood and should be familiar with the mechanics of the procedure [2]. The blood collected cannot be used for allogeneic transfusion because it does not come from a healthy voluntary donor and is also subject to restrictions imposed by blood centre regulatory authorities [2]. The most common adverse effects of therapeutic phlebotomy include bruising, dizziness, fainting, or discomfort at the needle site. Polycythaemia is a type of myeloproliferative neoplasm characterised by an increased red blood cell mass relative to the patient's age and sex [3]. Polycythaemia is defined by an Hb value greater than 16.5 g/dL or Hct>49% in men and Hb>16 g/dL or Hct>48% in women, or a red cell mass greater than 25% of the mean predicted value [3]. Primary polycythaemia is mostly due to polycythaemia vera, with the presence of a JAK2 mutation, while secondary polycythaemia is caused by smoking, chronic lung diseases such as COPD and chronic or congenital heart diseases, all of which result in hypoxia. Polycythaemia leads to hyperviscosity and commonly presents with symptoms such as headache, erythromelalgia and visual disturbances. It also increases the risk of thrombotic complications including stroke, coronary artery disease and deep vein thrombosis [2]. The risk of thrombotic complications is higher in patients with polycythaemia vera than in patients with secondary polycythaemia [4]. The treatment of polycythemia, both primary and secondary, is often directed at reducing Hct to less than 45% [5]. This may readily be achieved with therapeutic phlebotomy. Many studies have been conducted in the past to examine the effect of phlebotomy on iron depletion in cases of haemochromatosis [6-8]. The present study aimed to assess the effect of therapeutic phlebotomy on

haematologic parameters in polycythemia. The principal objective is to examine the therapeutic effects of phlebotomy on haematologic parameters such as Hb and Hct.

MATERIALS AND METHODS

The present study was a retrospective, cross-sectional study conducted in the Department of Transfusion Medicine, ESIC Medical College and PGIMSR, Bengaluru, Karnataka, India, for a period of one year from January 2024 to December 2024.

Sample size: A total of 186 instances of phlebotomy were recorded in the department during the study period, involving 104 patients.

Inclusion and exclusion criteria: Stable patients with clinical conditions associated with elevated Hb and Hct who required therapeutic phlebotomy as part of their treatment were included in the study. Pregnant females and patients with unstable vitals were excluded from the study. The laboratory reference ranges for haemoglobin are 13.0–16.5 g/dL in adult men and 12.0–15.0 g/dL in non pregnant adult women.

The laboratory reference range for Hct is 39–49% in adult men and 36–45% in adult women. The World Health Organisation (WHO) criteria define polycythaemia as Hb>16.5 g/dL and Hct>49% in males and Hb>16 g/dL and Hct>48% in females [9].

Study Procedure

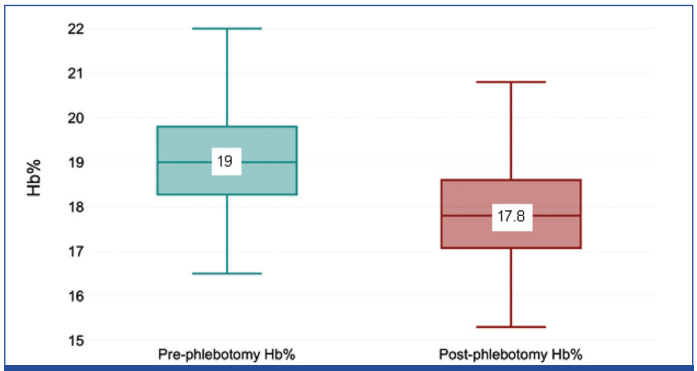
Demographic details, clinical details, prephlebotomy haematologic values, medication history and vitals were checked and recorded in the case files. Therapeutic phlebotomy was performed after obtaining informed consent from the patient. Venipuncture was performed under aseptic precautions using a 16G needle from the median cubital vein of the arm. A single blood bag of 350 mL capacity was used to collect the blood, which was later discarded. All haematological analyses were performed using a haematology analyser, Sysmex XN1000 (Sysmex, Kobe, Japan), in the Department of Pathology. Demographic and clinical information, including prephlebotomy haematologic values, medication history and vital signs, were recorded from each patient's case file. Data on the effect of therapeutic phlebotomy on the haematologic parameters such as Hb and Hct were obtained from the department archives. Status of JAK2 mutation analysis was recorded from the departmental archives wherever available.

STATISTICAL ANALYSIS

All data were collected in Microsoft Excel. Categorical variables were expressed as counts and percentages; continuous variables were expressed as means, medians and ranges. The Pearson's correlation coefficient was used to assess the relationship between pre- and post-phlebotomy Hb and Hct values. A paired t-test was performed to determine whether the drop in Hb and Hct was statistically significant. A p-value <0.05 was considered significant. All statistical analyses were conducted using Statistical Package for the Social Sciences (SPSS) software (version 20.0, IBM, USA).

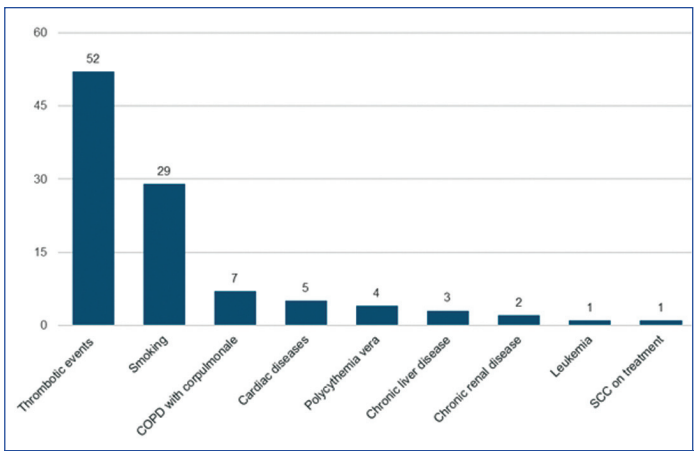
RESULTS

A total of 186 instances of therapeutic phlebotomy were recorded for polycythaemia in the Department of Transfusion Medicine. This included 104 patients who were referred to the department for therapeutic phlebotomy in view of polycythemia. A total of 36 patients (34.6%) of the 104 patients had undergone multiple sessions of therapeutic phlebotomy. The study showed a male predominance with 102 male patients and 2 female patients (M:F=51:1). The patients ranged in age from 23 years to 73 years, with a mean age of 47 years. A single session of therapeutic phlebotomy involved the removal of 350-400 mL of blood. The mean volume of blood removed per session was 326 mL. Secondary polycythaemia was the most common reason, with 100 (96.15%) patients referred for therapeutic phlebotomy. The mean prephlebotomy Hb value was 19.0 g/dL and the mean post-phlebotomy Hb value was 17.8 g/dL. The average fall in Hb after one session of therapeutic phlebotomy was 1.2 g/dL [Table/Fig-1].



[Table/Fig-1]: Boxplot comparing pre and post phlebotomy haemoglobin (gm/dL) value.

The mean prephlebotomy Hct was 58.3% and the mean post-phlebotomy Hct was 54.6%. The average fall in Hct was 3.7 percentage points after a single session of therapeutic phlebotomy. The post-phlebotomy drop in Hb of ≥1 g/dL was noted in 81 (77.9%) patients, while 23 (22.1%) patients showed a drop of <1 g/dL in Hb. Of all study patients, 36 (34.6%) had multiple repeated sessions of therapeutic phlebotomy within eight weeks to bring Hb and Hct values to the normal range. The Pearson's correlation coefficient between prephlebotomy and post-phlebotomy Hb was 0.995 and between prephlebotomy and post-phlebotomy Hct was 0.990, indicating very strong positive linear correlations for both parameters. The paired t-test showed p-values of 0.0003 for Hb and 0.0005 for Hct, both well below 0.05, indicating that the fall in Hb and Hct were statistically significant. A total of 18 cases (17.3%) had JAK2 mutation analysis performed, of which 4 (3.84%) patients were positive for JAK2 mutation. These patients were considered as cases of primary polycythaemia vera and were on recurrent maintenance phlebotomy. A total of 3 (2.88%) cases had the JAK2V617F mutation. A single case (0.96%) had a JAK2 mutation in exon 12. The most common presentation requiring phlebotomy was thrombotic complications, noted in 52 (50.0%) patients. Smoking was the next most common factor, noted in 29 (27.8%) patients. COPD with cor-pulmonale was noted in 7 (6.73%) patients, followed by 5 (4.80%) patients with cardiac disease, including two cases of congenital cyanotic heart disease (Eisenmenger's syndrome). Polycythaemia vera was seen in 4 (3.8%) patients. Chronic liver disease secondary to alcohol intake was noted in 3 (2.88%) patients. History of chronic renal disease was noted in 2 (1.92%) patients. An isolated case each of chronic myeloid leukemia in remission and squamous cell carcinoma on chemo-radiation therapy were referred for phlebotomy for polycythaemia [Table/Fig-2].



[Table/Fig-2]: Causes for polycythaemia in study population.

DISCUSSION

Therapeutic phlebotomy, commonly known as bloodletting, has been practiced since ancient times. There is strong evidence that it remains the most effective treatment for polycythemia. Most available literature on therapeutic phlebotomy focuses on its role in reducing serum iron in haemochromatosis or porphyrin levels in porphyria cutanea tarda. However, studies focusing on the reduction of haemoglobin and its impact in cases of secondary polycythaemia or polycythaemia vera are limited. Specifically, reports detailing changes in Hb and Hct are uncommon. The results of the present study are comparable to those of Noreen N et al., Kulkarni P et al., and Gupta SS et al., [Table/Fig-3] [3,10,11]. Notably, studies by Kulkarni P et al., and Gupta SS et al., reported that all patients experienced a drop in haemoglobin of ≥1 g/dL [10,11]. However, during repeated sessions of therapeutic phlebotomy, the average haemoglobin reduction was found to be less than 1 g/dL between sessions.

Parameters	Present study	Noreen N et al., [3]	Kulkarni P et al., [10]	Gupta SS et al., [11]
Year of study	2024	2020	2023	2024
Study population	104	121	127	159
Mean prephlebotomy haemoglobin (g/dL)	19.0	17.45	19.9	18.5
Mean post-phlebotomy haemoglobin (g/dL)	17.8	15.97	15.7	17.4
Drop in haemoglobin ≥1g/dL	77.9%	73.5%	100%	100%
Most common cause that required therapeutic phlebotomy	Thrombotic events	Smoking	Renal diseases	Polycythaemia under evaluation

[Table/Fig-3]: Comparison of study parameters with similar studies [3,10,11].

Currently, the most common approved indications for therapeutic phlebotomy are polycythaemia vera, haemochromatosis and porphyria cutanea tarda. In both primary and secondary polycythemia, the goal is to reduce Hct to below 45% [5]. This leads to a reduction in the risk of thrombotic events and an improvement in constitutional symptoms. Before starting therapy, it is equally important to identify any underlying secondary causes of polycythaemia [12].

Phlebotomies are typically performed at frequent intervals until the target hematocrit is reached. The adverse effects after therapeutic phlebotomy are similar to those of blood donation. However, because therapeutic phlebotomy is performed more frequently, patients often experience excessive fatigue and dizziness after repeated sessions. There are no set guidelines regarding the optimal regimen or end point of phlebotomy [13].

The word polycythaemia literally translates to poly meaning "many" and cythemia indicating "cells" in the blood [14]. It describes a condition characterised by an abnormal increase in red blood cell mass. Patients with polycythaemia usually present to the outpatient department with nonspecific symptoms that include fatigue, headache, dizziness, pruritus, transient ischemic attacks, or full-blown complications such as stroke.

Polycythaemia vera (primary polycythemia) is due to increased proliferation of erythroid progenitor cells secondary to an intrinsic cellular defect. These patients typically have a suppressed or normal Erythropoietin (EPO) level [15]. Polycythaemia vera is a relatively indolent myeloid neoplastic disorder. The dysregulation of the JAK-Signal Transducer and Activator of Transcription (STAT) pathway is the hallmark of myeloproliferative neoplasms, caused by somatic mutations in driver genes including JAK2, Calreticulin (CALR) and Myeloproliferative Leukaemia Protein (MPL). Polycythaemia vera is associated with a somatically acquired mutation in the JAK2 gene, leading to a V617F substitution at the protein level. This mutation dysregulates kinase activity and promotes ligand-independent activation of receptor signalling, resulting in increased erythroid progenitor cells and heightened sensitivity to erythropoietin [16].

The WHO defines JAK2 V617F as a major criterion for the diagnosis of polycythaemia vera. Other markers include Hb values >16.5 g/dL in men and 16 g/dL in women, or Hct >49% in men and 48% in women, or Red Blood Cell (RBC) mass >25% above the mean predicted value [12]. Hence, the first step in evaluating suspected polycythaemia vera should always include screening for the JAK2 V617F mutation. Patients with polycythaemia vera have a higher risk of thrombotic events such as cardiovascular and cerebrovascular complications, arterial and venous thromboembolism. It can progress to myelofibrosis, acute myeloid leukemia/myelodysplastic syndrome [13]. Cytoreductive therapy with hydroxyurea and phlebotomy is now considered the mainstay of treatment for polycythaemia vera. Pure erythrocytosis patients have an isolated elevated RBC mass in the absence of any other precipitating factor.

Secondary polycythaemia encompasses disorders with increased RBC mass secondary to tissue hypoxia or to physiologically inappropriate secretion of the hormone erythropoietin. Factors such as smoking, chronic lung diseases like COPD, cyanotic heart disease, high altitude, renal disease with erythropoietin-secreting tumours and obstructive sleep apnoea are among the most common causes of secondary polycythaemia noted in the Indian population [15]. A detailed history and thorough physical examination are essential to identify the underlying condition causing secondary polycythemia. Therapeutic phlebotomy helps improve cerebral perfusion, as well as sensory and mental function, by lowering the viscosity of the blood. It also improves oxygen consumption without affecting oxygen delivery [15]. It helps by increasing cardiac output, exercise tolerance and reducing the severity of angina pectoris [13]. Patients with cyanotic congenital heart disease, such as Eisenmenger's syndrome or tetralogy of Fallot, develop erythrocytosis secondary to hypoxia, which in these cases is due to cyanosis. The Hct may reach levels as high as 65% with the development of hyperviscosity symptoms [13]. Haemochromatosis is a genetic disorder for which therapeutic phlebotomy is the mainstay of treatment. It is a condition in which excessive iron accumulates, leading to organ damage. Therapeutic phlebotomies are helpful in reducing the iron load; however, not all signs and symptoms are reversible depending on the severity of the condition [14]. Porphyria cutanea tarda is another metabolic disorder for which therapeutic phlebotomy is indicated to reduce accumulated porphyrins. It is caused by uroporphyrinogen decarboxylase deficiency that leads to the accumulation of uroporphyrinogen and carboxylated porphyrins in the liver, plasma, urine and sometimes faeces [13].

Limitation(s)

The present study was conducted in a single tertiary care centre catering to only a portion of the population; robust studies with larger populations may help in establishing standardised protocols for repeated cycles of therapeutic phlebotomy. JAK2 mutation analysis was not available for all cases included in the study.

CONCLUSION(S)

Therapeutic phlebotomy remains the cornerstone of management in both primary and secondary polycythemia, effectively reducing haemoglobin and haematocrit to lower the risk of thrombotic complications. Maintaining Hct levels below 45% is essential and the combined use of aspirin may further enhance the treatment efficacy in cases with thrombotic events. Given its similarity to blood donation, phlebotomy can be safely performed and offers a practical and accessible approach to manage polycythemia.

REFERENCES

[1] Ahmad S, Arora S, Baqar T. Therapeutic phlebotomy revisited: A review. Saudi J Med. 2023;8(4):152-158.
[2] Basavarajegowda A, Kumar S, Srinivas A, Punniakoti S, Sahu SK. Therapeutic phlebotomy as a daycare procedure in the Department of Transfusion Medicine as compared to the admission-based procedure: A qualitative study on patients' perspectives. QAI J Healthc Qual Patient Saf. 2023;4(1):7-11.

[3] Noreen N, Jalil SW, Irfan R, Hanif F. Analysis of therapeutic phlebotomy in patients with polycythemia: A single-center study. J Islamabad Med Dent Coll. 2023;12(3):199-203.
[4] Gordeuk VR, Key NS, Prchal JT. Re-evaluation of hematocrit as a determinant of thrombotic risk in erythrocytosis. Haematologica. 2019;104(4):653.
[5] Teofili L, Valentini CG, Rossi E, De Stefano V. Indications and use of therapeutic phlebotomy in polycythemia vera: Which role for erythrocytapheresis? Leukemia. 2019;33(1):279-281.
[6] Dhiman Y, Khatiwada B, Raturi M, Gaur DS. Therapeutic phlebotomy: A continuously evolving primeval remedy—five-year experience and review from a tertiary healthcare center in India. Indian J Hematol Blood Transfus. 2025;20:1-1.
[7] Zheng L, Wang J, Shu Q, Xu H. Observation of the therapeutic effect of regular bloodletting therapy on hemochromatosis and nursing practice in liver disease outpatient department. Open J Nurs. 2025;15:211-218.
[8] Barton JC, Bottomley SS. Iron deficiency due to excessive therapeutic phlebotomy in hemochromatosis. Am J Hematol. 2000;65(3):223-226.
[9] Tefferi A, Barbui T. Polycythemia vera: 2024 update on diagnosis, risk-stratification, and management. Am J Hematol. 2023;98(9):1465-1487.
[10] Kulkarni P, Bandivadekar S, Gupta S, Thakare V, Reza M, Miriam R. Retrospective audit of therapeutic phlebotomy for assessment of indications and its efficacy in tertiary care teaching hospital Navi-Mumbai. Int J Med Public Health. 2024;14(4):1112-1115.
[11] Gupta SS, Dhote SW, Lad S, Dey DR. A study of indications, clinical applications, and effects of therapeutic phlebotomy at a tertiary care hospital Navi Mumbai. Glob J Transfus Med. 2024;9:126-129.
[12] Murugesan M, Das S, Shastry S. Effect of therapeutic phlebotomy on plasma volume in polycythemia patients. Glob J Transfus Med. 2018;3(2):117-120.
[13] Assi TB, Baz E. Current applications of therapeutic phlebotomy. Blood Transfus. 2014;12(Suppl 1):S75-S83.
[14] Prchal JT. Molecular biology of polycythemias. Intern Med. 2001;40(8):681-687.
[15] Haider MZ, Anwer F. Secondary polycythemia. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.
[16] Grenier JM, El Nemer W, De Grandis M. Red blood cell contribution to thrombosis in polycythemia vera and essential thrombocythemia. Int J Mol Sci. 2024;25(3):1417.

PARTICULARS OF CONTRIBUTORS:
1. Senior Resident, Department of Pathology, ESIC Medical College and Postgraduate Institute of Medical Sciences and Research, Bengaluru, Karnataka, India.
2. Senior Resident, Department of Pathology, ESIC Medical College and Postgraduate Institute of Medical Sciences and Research, Bengaluru, Karnataka, India.
3. Associate Professor, Department of Transfusion Medicine, ESIC Medical College and Postgraduate Institute of Medical Sciences and Research, Bengaluru, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Brilsee Simeon,
Associate Professor, Department of Transfusion Medicine, ESIC Medical College and Postgraduate Institute of Medical Sciences and Research, Bengaluru-560010, Karnataka, India.
E-mail: brilsee1976@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 19, 2025
- Manual Googling: Jul 11, 2025
- iThenticate Software: Jul 14, 2025 (15%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? No
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Mar 04, 2025**
Date of Peer Review: **Jun 05, 2025**
Date of Acceptance: **Jul 17, 2025**
Date of Publishing: **Feb 01, 2026**