Content available at: https://www.ipinnovative.com/open-access-journals

Panacea Journal of Medical Sciences

Journal homepage: http://www.pjms.in/

Original Research Article

Impact of therapeutic phlebotomy on haematological parameters of patients and their clinical outcome

Rashmita Panigrahi[1], Samarendra Satpathy[2], Manu Mangat Marandi[1], Sabita Palai[1]*

[1]*MKCG Medical College, Berhampur, Odisha, India*
[2]*Veer Surendra Sai Institute of Medical Sciences and Research, Sambalpur, Odisha, India*

ARTICLE INFO

Article history:
Received 02-02-2024
Accepted 16-01-2025
Available online 13-03-2025

Keywords:
Erythrocytosis
Polycythaemia
Haemochromatosis haematocrit

ABSTRACT

Background: Phlebotomy, also known as bloodletting or venesection, is a major therapeutic procedure. Currently, there are three main indications for therapeutic phlebotomy i.e., haemochromatosis, polycythaemia vera (PV) and porphyria cutanea tarda (PCT) along with sickle cell disease, some cases of secondary polycythaemia like post renal transplant patient and cyanotic heart disease and hypoxic conditions like chronic lung disease.

Aims and Objective: To evaluate the effect of therapeutic phlebotomy on haematological parameters and also its role in clinical outcome.

Materials and Methods: The study was carried out at Department of Transfusion Medicine with collaboration of Department of Clinical Haematology, SCB MCH, Cuttack from January-2016 to September-2017. This is a prospective study comprising of 55 cases of erythrocytosis, on whom 393 procedures of therapeutic phlebotomy done after scrutinizing the eligibility criteria. There were 393 procedures of phlebotomy conducted over 55 cases.

Results: After 393 procedures, with a mean of 6 procedures for each patient, there was reduction in Hb, Hct, WBC, RBC, TPC ,Ferritin from (18.7± 2.1)gm/dl, (57±6.6)%, (10.5±5.9)$10^3/\mu$l, (6.9±1.8)$10^6/\mu$l, (458.5±312)$10^3/\mu$l, (246.05±84.4)ng/dl to (14.9±1.91)gm/dl, (46.1±4.1)%, (7.35±4.4)$10^3/\mu$l,(5.1±1)$10^6/\mu$l, (304.5±243)$10^3/\mu$l, (195±98.3)ng/dl respectively.

Conclusion: Therapeutic phlebotomy is a cost effective and safe treatment for patients having high haematocrit. In conclusion, the evidence that we have observed, indicates that phlebotomy is safe and provides good efficacy with relatively low costs, so it should be the first line of treatment in the above cases as cytoreductive therapy has serious adverse effects and further studies are needed to improve the treatment guidelines for phlebotomy.

1. Introduction

Phlebotomy, also known as bloodletting or venesection, is a major therapeutic procedure that has been performed by physicians since antiquity up to the present.[1,2] Currently, there are three main indications for therapeutic phlebotomy i.e., haemochromatosis, polycythaemia vera (PV) and porphyria cutanea tarda (PCT)[3] along with sickle cell disease, some cases of secondary polycythaemia like post renal transplant patient and cyanotic heart disease and hypoxic conditions like chronic lung disease.

As per 2016 WHO criteria, PV can be suspected in any person with an increase in haemoglobin level (more than 16.5 g/dL or 16 g/dL in men and women, respectively) and increase in haematocrit level (> 49% in men and >48% in women respectively) or an increase in red blood cell countand JAK2 mutation.[4]

* *Corresponding author*.
E-mail address: khattimithi79@gmail.com (S. Palai).

https://doi.org/10.18231/pjms.v.15.i.1.214-219

Phlebotomy is now considered to be the main stay of treatment in PV. Some studies suggested that haematocrit level should be maintained below 45% to reduce the risk of vascular occlusive episode.[5] Phlebotomy has been used for the treatment of secondary polycythaemia in patients with chronic obstructive pulmonary disease. It results in an improvement of cerebral perfusion as well as sensory and mental function by lowering blood viscosity.[6] Treatment for post-transplant erythrocytosis includes angiotensin-converting enzyme inhibitor or an angiotensin II receptor antagonist, or venesection with a target haematocrit less than 45%.[7] Patients with a cyanotic congenital heart disease, such as Eisenmenger's syndrome or Tetralogy of Fallot, develop erythrocytosis secondary to their cyanosis. In 2008, the American College of Cardiology/American Heart Association published guidelines and recommended performing therapeutic phlebotomy for symptomatic patients with haemoglobin and haematocrit values greater than 20 g/dL and 65%, respectively, while taking care to avoid iron depletion.[8]

One of the main indications for therapeutic phlebotomy is haemochromatosis. A large survey that included 2,851 patients with haemochromatosis to assess the symptoms and the response to therapeutic phlebotomy found that 86% of cases had some or all of their symptoms improved with phlebotomy with an average time for improvement of 39±67 weeks.[9] Therapeutic phlebotomy has long been considered the treatment of choice in most patients with PCT.[10] Phlebotomy decreases the viscosity of blood by reducing the haemoglobin level and thus reduces HbS molecule polymerisation in sickle cell disease.[11] Patients with metabolic syndrome who underwent iron reduction by phlebotomy had statistically significant differences in systolic blood pressure, glucose, HbA1c, HDL cholesterol, iron and ferritin compared to controls ($p<0.001$).[12]

2. Aims and Objective

The aim of the study is to evaluate the effect of therapeutic phlebotomy on haematological parameters and also its role in clinical outcome. The objectives of our study are to

1. To formulate the treatment decisions and guidelines basing on patient condition.
2. Prevent the complication of patients and decrease the mortality rate among the patients.

3. Materials and Methods

The study was conducted in the Phlebotomy section of department of Transfusion Medicine, Sriram Chandra Bhanja (SCB) Medical College &Hospital, Cuttack, Odisha.

3.1. Study design

A prospective study was carried out on patients with erythrocytosis attending the department of Transfusion Medicine for therapeutic phlebotomy being referred from department of Clinical Haematology and Medicine, SCB Medical College &Hospital, Cuttack between January 2016 to September 2017. The study included total 55 no of patients with erythrocytosis meeting the eligibility criteria, on whom 393 therapeutic phlebotomy procedures were performed after their consent The medical history of each patient such as patient's name, age, sex, smoking history were recorded prior to the procedure.

3.2. Inclusion criteria

All the Primary PV cases,Secondary Polycythaemia due to hypoxic conditions such as chronic lung diseases, cyanotic heart diseases, renaltransplant ,Hemochromatosis and Metabolic Syndrome,High serum ferritin level after bone marrow transplant and those who gave consent for enrollment in the study were included in the study.

3.3. Exclusion criteria

Patients of Secondary Polycythaemia due to smoking, high altitude, renal cell carcinoma (RCC), hepatocellular carcinoma, adrenal adenoma, Von-Hippel-Lindau disease, Cushing syndrome, Pheochromocytoma, hypogonadism on testosterone therapy, athletes on anabolic steroid and the patients who neither gave consent to participate in the study and who couldn't be followed up were excluded from the study.

3.4. Sample collection

Five millilitres of venous blood samples were collected in two plain vacutainers and two ethylene di-amine tetra acetic acid (EDTA) vacutainers. EDTA sample was used for complete blood count (CBC), JAK2 mutation (Referral Laboratory). Serum of the patient was tested for Erythropoietin & if required ferritin. Under aseptic condition and local anaesthesia bone marrow aspirate was collected and studied.

3.5. Methods

To begin with, a requisition from the treating physician for venesection (clearly indicating clinical diagnosis, haemoglobin, haematocrit level and JAK2 mutation, serum erythropoietin) was obtained and after that consent of the patient was taken for phlebotomy. Clinical diagnosis of primary polycythaemia was made as per the WHO criteria 2016.

Before the procedure, patient's blood pressure, pulse rate, respiratory rate and temperature, symptoms & signs were recorded. The phlebotomy site mostly cubital fossa was

prepared as per departmental standard operating procedure for phlebotomy.

3.6. Statistical analysis

The Data collected were entered in Microsoft excel spreadsheet and later subjected to statistical analysis using a statistical software SPSS trial version 24.0. Statistical analysis included descriptive statistics of mean and chi-square. Differences were considered significant when $p \leq 0.05$.

Descriptive statistics like median and interquartile ranges of continuous scale variables like age, haemoglobin, haematocrit, RBC count, WBC count, Platelet count, serum erythropoietin, serum ferritin, systolic blood pressure, diastolic blood pressure, pulse rate was computed.

4. Result

In total, 393 procedures of phlebotomy were conducted over 55 cases. Out of these, 41 (74.5%) cases were of PV, 13(23.6%) cases of secondary polycythaemia and only one case of high serum ferritin secondary to bone marrow transplant. Again, out of these 41 cases of PV, two special conditions were associated with PV, one was pregnancy & other was HIV.

In this study, erythrocytosis was more commonly seen in male in comparison to female (47:7 that was (6.7:1). In PV male to female ratio was 5.9:1 whereas in secondary polycythaemia it was 12:1.As per WHO-2016 guideline of diagnosis of PV, JAK-2 mutation is a minor criterion. In this study there were 30(73%) cases with JAK-2 mutation and 11(27%) cases were without this gene mutation. In this study, serum erythropoietin level was measured in every PV cases. Out of total 41 cases, 44% patients had normal s.epo level,47% patients had low s.epo level and 9% patients had high s.epo level.

The most common cause of secondary erythrocytosis in this study was cyanotic heart disease 5 cases (38%) followed by pulmonary disease 3 cases (23%), post renal transplant 2 cases (15%), medical renal disease, metabolic syndrome and hypertension in young patient each constituting one case (7%).Most of the PV cases belonged to age group of 40- 59years ,18 cases (43%), followed by 20-39years 12 cases (29%), more than 60years 10 cases (24%) and only one case of age group less than 20years. In the secondary erythrocytosis cases group, there was no case above 60 years of age, only 9 cases of 20-39 years age, 3 cases of less than 20years and only one case of age group 40-59.

In the PV cases, 58% belonged to 40-60kg weight group followed by 34 % had more than 60kg and only 7% had less than 40 kg weight. All the 13 cases of the erythrocytosis were equally distributed in these mentioned weight group. In this study population, most of the cases (34.5%) belonged to O blood group, followed by B (32.7%), A (23.6%), AB (7.2%) blood groups.

The presenting laboratory findings of these study population were raised Hb (18.7±2.1), haematocrit (57±6.6), and/or subnormal level of erythropoietin (6.6±9.57) mU/ml. There were 30(73%) cases of PV having JAK-2 mutation and 31(77%) cases with Panmyelosis. [Table 1]

In this study, most common presenting symptom was weakness 51%, followed by headache (49%), pruritus (34%), dizziness (27%), weight loss (17%), breathlessness, joint pain & epigastric pain each 14%, numbness (12%) and myalgia (7%). In present study, about 34 % (17) of cases were found accidentally during a routine check-up. We detected skin plethora in 80% cases, splenomegaly in 73% cases, 70% cases with systolic BP >140mm Hg, 48% cases with high diastolic BP>90, 54% cases with conjunctival plethora and 36% cases of hepatomegaly.

Out of the 393 procedures, only 35 (9%) number of procedures had adverse reaction after phlebotomy. Vasovagal reaction (5.6%) was the most common adverse reaction after phlebotomy followed by hematoma (2.2%), bruise (1.7%) and thrombophlebitis (0.7%). Out of these adverse reactions, 3 patients showed same type of reaction repeatedly.

In this study, vitals of the patient and the presenting Hb & Hct were recorded. The presenting median Hb was 18.7gm/dl (IQR: 2.1), Hct was 57 % (IQR: 6.6), Systolic BP (130±18) mm of Hg, Diastolic BP (88±12) mm of Hg, PR (88±12) per minute. After a single procedure of phlebotomy, the Hb, Hct, Systolic & Diastolic BP, PR was reduced to (17.9±2) gm/dl, (54.2±6.7) %, (124±24) mm of Hg, (84±14) mm of Hg, (82±10) per minute respectively. [Table 2]

In this study we preferred IV fluids in cases of PV having low BP and other complications and in only cyanotic heart disease cases having secondary polycythaemia. Other cases were given oral fluid replacement. No significant changes seen (BP, PR) after removal of one unit of blood.

After 393 procedures, with a mean of 6 procedures for each patient, there was reduction in Hb, Hct, WBC, RBC, TPC ,Ferritin from (18.7± 2.1)gm/dl, (57±6.6)%, $(10.5\pm5.9)10^3/\mu l$, $(6.9\pm1.8)10^6/\mu l$, $(458.5\pm312)10^3/\mu l$, (246.05±84.4)ng/dl to (14.9±1.91)gm/dl, (46.1±4.1)%, $(7.35\pm4.4)10^3/\mu l$,($5.1\pm1)10^6/\mu l$, $(304.5\pm243)10^3/\mu l$, (195±98.3)ng/dl respectively. [Table 3]

After an average 8 procedure of therapeutic phlebotomy in PV cases, the serum ferritin level decreases to lower normal limit, 7 cases developed iron deficiency, which was managed by giving regular folic acid. In this study 7 (17%) cases of PV were having hyper viscosity related complication like thrombosis (3=7.3%), stroke (3=7.3%) and portal hypertension (1=2.4%). All these cases presented with a Hct more than 50%.

Table 1: Laborotary finding of polycythemic cases

Lab parameter	Lab findings
Hb (Median ± IQR)	18.7±2.1
Hct (Median ± IQR)	57±6.6
JAK-2 mutation	30
Panmyelosis	31
Serum Erythropoietin (Median ± IQR) mU/ml	6.6±9.57

Table 2: Effect of therapeutic phlebotomy (one setting) on various parameters in polycythemia vera cases

Parametres	Pre-phlebotomy (median ± iqr)	Post phlebotomy (median ± iqr)	Mean change
Hb(gm/dl)	18.7± 2.1	17.9±2	0.8
Hct (%)	57±6.6	54.2±6.7	2.8
Blood Pressure Systolic	130±18	124±24	4.8
(mm of Hg) Diastolic	88±12	84±14	3.2
Pulse Rate (/min)	88±12	82±10	1.2

Table 3: Effect of therapeutic phlebotomy (multiple setting, average 6 procedures) on various parameters in polycythemia vera cases

Parametres	Pre-phlebotomy (Median ± IQR)	Post phlebotomy (Median ± IQR)
Hb(gm/dl)	18.7± 2.1	14.9±1.9
Hct (%)	57±6.6	46.1±4.1
WBC ($10^3/\mu$l)	10.5±5.9	7.35±4.4
RBC ($10^6/\mu$l)	6.9±1.8	5.1±1
TPC ($10^3/\mu$l)	458.5±312	304.5±243
S. FERRITIN (ng/dl)	246.05±84.4	195±98.3

Table 4: Effect of therapeutic phlebotomy on various parameters in a case of high serum ferritin after bone marrow transplant

Para meters	Pre phlebotomy	Post phlebotomy 1st	Post phlebotomy 2nd
Hb(gm/dl)	10	9.4	9.1
Hct (%)	32	29.2	26.6
Serum Ferritin(ng/ml)	2840	2693	2550
BP (/mm of Hg)	100/70	94/66	98/68
PR(/min)	82	86	84

With a median 6 number of therapeutic phlebotomies, aspirin & hydroxyurea in PV cases, 30 (73.1%) cases achieved the target Hct level. But there was again elevation in the Hct level in 9 (21.9%) cases of PV out of these 30 cases who had achieved the target. 11cases (26.8%) did not attain the target Hct level. In secondary erythrocytosis cases target Hct level was attained in 9 cases (69.2%) but again one case went out of the target Hct>45%. 4cases (30.7%) cases did not achieve the Hct <45%.

The progression of the PV to thrombosis was found in 17% cases, followed by MPN in 5% cases & Myelofibrosis in 5% cases. The symptoms were relieved in 7 cases with achieved target, and 2 cases without achieving target Hct <45. Out of the 4 cases who did not achieve the target Hct level, two cases of cyanotic heart disease patient developed iron deficiency after an average of 10 procedures and they were managed by iron & folic acid one case of TOF died because of congestive cardiac failure (CCF).

In this study, there was only one case of high serum ferritin level (>2840 ng/dl) due to post bone marrow transplantation. This was a 9 yr old female child weighing 35kg, having B Positive blood group, had beta thalassemia major. Only 2 therapeutic phlebotomy procedures (weekly once) could be done in this case, she could not be followed up for next procedure. After two procedures the serum ferritin level reduced to 2550ng/dl. [Table 4]

5. Discussion

The incidence of PV in the present study was 2.9 per 1 Lakh, which was similar to Verma S et al.[13] (4.7%) and Ania BJ et al.[14] (1.9 per 1Lakh). There were 13(23.6%) cases of secondary polycythaemia and only one case of high serum ferritin following bone marrow transplant.

In this study, erythrocytosis was more commonly seen in male in comparison to female (6.7:1). In our study, male to female ratio in PV cases was 5.9:1 which was little more (1.2 to 2.2) as compared to Ania BJ et al.,[14] Berlin NI et al.,[4] Modan B et al.[15] where as in secondary polycythaemia it was 12:1. In our study 30(73%) cases had JAK-2 mutation

and 11(27%) cases were without this gene mutation, which is similar to the findings of Sazawal S et al.[16] (82%) and Varma S et al.[13] (81.8%). But Vainchenker W et al.[17] reported higher prevalence of JAK-2 mutation i.e., about 95% in PV cases.

The most common cause of secondary erythrocytosis was cyanotic heart disease 5 cases (38%) followed by pulmonary disease 3 cases (23%), post renal transplant 2 cases (15%), medical renal disease, metabolic syndrome and hypertension in young patient each constituting one case (7%). These conditions are similar as described by McMullin et al.[8] Most of the polycythaemia vera cases were belonging to age group of 40-59years (43% cases) with a median age of 46 year (IQR 22.5) followed by 20-39years (29%), more than 60years (24%) and only one case of age group less than 20years. This finding of median age was less as reported by Berlin NI,[4] Tefferi A (60Years).[18]

The presenting laboratory findings of these study population were raised Hb (18.7±2.1) gm/dl, Haematocrit (57±6.6) %, and/or subnormal level of erythropoietin (6.6±9.57) mU/ml. These findings were similar as reported by Perkins J et al.,[19] London IM et al.[20] Birgegard G et al.[21] There were 30(73%) cases of polycythaemia vera having JAK-2 mutation and 31(77%) cases with Panmyelosis which was similar to Ellis JT et al.[22] There were 33% cases with normal cellularity which was slightly higher than Washerman LR et al. (13%).[23]

In this study, most common presenting symptom was weakness 51%, followed by headache (49%), pruritus (34%), dizziness (27%), weight loss (17%), breathlessness, joint pain & epigastric pain each 14%, numbness (12%) and myalgia (7%) which was similar to the findings by Berlin et al.[4] Skin plethora was detected in 80% cases, splenomegaly in 73% cases, 70% cases with systolic BP >140, 48% cases with high diastolic BP>90, 54% cases with conjunctival plethora and 36% cases of hepatomegaly. All the detected signs were similar with the study of Berlin et al.[4] Vasovagal reaction (5.6%) was the most common adverse reaction after phlebotomy followed by hematoma (2.2%), bruise (1.7%) and thrombophlebitis (0.7%). But Cook LS et al.[3] and Roback J et al.[24] reported that hematoma was the most common adverse reaction after phlebotomy followed by syncope.

In this study 7 (17%) cases of polycythaemia vera were having hyper viscosity related complication like thrombosis (7.3%), stroke (7.3%) and portal hypertension (2.4%). All these cases were presented with a Hct more than 50%. Similarly, Berk et al.[25] reported that risk of thrombosis is more if the Hct is above 50%.

With a median 6 number of therapeutic phlebotomies, aspirin & Hydroxyurea in polycythaemia vera, 30 (73.1%) cases attended the target Hct level. But there was again elevation in the Hct level in 9 (21.9%) cases of PV after attaining the target level. 11(26.8%) cases did not yet attain the target Hct level 45 %. This finding was similar to the studies of Thomas et al.[26] and Washerman & Gilbert.[27]

The progression of the polycythaemia vera to thrombosis was found in 17% cases which was similar to Najean & Rain et al.,[28] but more than that of Berk et al.(4%).[25] Myelofibrosis was found in 5% cases which is similar to Berk et al.[25] but lesser than Najean & Rain et al (17%) and Lawrence JH et al (25%).[29] MPN was detected in 5% cases which is similar to Najean & Rain et al.[28]

6. Conclusion

Therapeutic phlebotomy is a cost effective and safe treatment for patients having high haematocrit. It also prevents life threating complications by maintaining target haematocrit. Only disadvantage is having milder variety of adverse reactions and development of iron deficiency after multiple procedures. Also, in patients who are presenting with stroke, it cannot decrease the haematocrit suddenly to a target level, as only a small amount of blood can be removed in one procedure. So, in such cases the use of advanced technology like erythrocytapheresis, which can remove larger amount of blood and achieve target haematocrit within a short period of time should be introduced. Only disadvantage of erythrocytapheresis is the cost. Newer technique like hematopoietic stem cell transplant can be used for complete response in PV cases.

However, it is important to make treatment decisions based on each patient's condition and the relevant guidelines for prescribing and implementing phlebotomy. Furthermore, we recommend prioritizing the creation of treatment guidelines with staff and patient education programs for institutions that are seeking to introduce phlebotomy programs. These guidelines should also focus on patient care after the completion of the phlebotomy. In conclusion, the evidence that we have observed, indicates that phlebotomy is safe and provides good efficacy with relatively low costs, so it should be the first line of treatment in the above cases as cytoreductive therapy has serious adverse effects and further studies are needed to improve the treatment guidelines for phlebotomy.

7. Limitation

Three cases could not be traced due to their remote location. Due to economic hindrance, four numbers of cases could not be investigated for JAK2 mutation. Consent could not be obtained in two numbers of PV cases for bone marrow study due to their reluctance. Due to lack of infrastructure, patients with stroke could not be subjected to erythrocytapheresis procedure.

8. Conflict of Interest

None.

9. Source of Funding

None.

References

1. Parapia LA. History of bloodletting by phlebotomy. *Br J Haematol*. 2008;143(4):490–5.
2. Schneeberg NG. A twenty-first century perspective on the ancient art of bloodletting. *Trans Stud Coll Physicians Phila*. 2002;24:157–85.
3. Cook LS. Therapeutic phlebotomy: a review of diagnoses and treatment considerations. *J Infus Nurs*. 2010;33(2):81–8.
4. Berlin NI. Diagnosis and classification of the polycythaemias. *Semin Hematol*. 1975;12(4):339–51.
5. Pearson TC, Wetherley-Mein G. Vascular occlusive episodes and venous haematocrit in primary proliferative polycythaemia. *Lancet*. 1978;2(8102):1219–22.
6. Bornstein R, Menon D, York E, Sproule B, Zak C. Effects of venesection on cerebral function in chronic lung disease. *Can J Neurol Sci*. 1980;7(4):293–6.
7. Mcmullin MF, Bareford D, Campbell P, Green AR, Harrison C, Hunt B, et al. Guidelines for the diagnosis, investigation and management of polycythaemia/ erythrocytosis. *Br J Haematol*. 2005;130:174–95.
8. Warnes CA, Williams RG, Bashore TM. ACC/AHA 2008 Guidelines for the Management of Adults With Congenital Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines on the Management of Adults With Congenital Heart Disease): Developed in Collaboration With the American Society of Echocardiography, Heart Rhythm Society, International Society for Adult Congenital Heart Disease, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *Circulation*. 2008;118(23):714–833.
9. Mcdonnell SM, Preston BL, Jewell SA, Barton JC, Edwards CQ, Adams PC, et al. A survey of 2,851 patients with hemochromatosis: symptoms and response to treatment. *Am J Med*. 1999;106(6):619–24.
10. Ramsay CA, Magnus IA, Turnbull A, Baker H. The treatment of porphyria cutanea tarda by venesection. *Q J Med*. 1974;43:1–24.
11. Bouchaïr N, Manigne P, Kanfer A. Prevention of sickle cell crises with multiple phlebotomies. *Arch Pediatr*. 2000;7(3):249–55.
12. Estes JW. George Washington and the doctors: treating America's first superhero. *Med Herit*. 1985;1(1):44–57.
13. Varma S, Naseem MS, Malhotra MP, Binota MJ, Sachdeva MUS, Sood A, et al. MD: Incidence Rates of Myeloproliferative Neoplasms in India- A Hospital Based Study. *Int J Epidemiol*. 2015;44(1):198–9.
14. Ania BJ, Suman VJ, Sobell JL, Codd MB, Silverstein MN, 3rd LM, et al. Trends in the incidence of polycythaemia vera among Olmstead Country, Minnesota, residents, 1935-1989. *Am J Hematol*. 1994;47(2):89–93.
15. Modan B, Kallner H, Zemer D, Yoran C. A note on the increased risk of polycythaemia vera in Jews. *Blood*. 1971;37(2):172–6.
16. Sazawal S, Bajaj J. Prevalence of JAK2V617F mutation in Indian patients with chronic myeloproliferative disorders. *Indian J Med Res*. 2010;132:423–7.
17. Vainchenker W, Delhommeau F, Constantinescu SN, Bernard OA. New mutation and pathogenesis of myeloproliferative neoplasms. *Blood*. 2011;118(7):1723–35.
18. Tefferi A. Polycythemia vera: a comprehensive review and clinical recommendations. *Mayo Clin Proc*. 2003;78(2):174–94.
19. Perkins J, Israuels MC, Wilkinson JF. Polycythaemia vera: clinical studies on a series of 127 patients managed without radiation therapy. *Q J Med*. 1964;33:499–58.
20. London IM, Shemin D. Heme synthesis and red blood cell dynamics in normal humans and in subjects with polycythemia vera, sickle cell anaemia, and pernicious anaemia. *J Biol Chem*. 1949;179(1):463–84.
21. Birgegard G, Wide L. Serum erythropoietin in the diagnosis of polycythemia and after phlebotomy treatment. *Br J Haematol*. 1992;81(4):603–6.
22. Ellis JT, Peterson P, Geller SA. Studies of the bone marrow in polycythemia vera and the evolution of myelofibrosis and second hematologic malignancies. *Semin Hematol*. 1986;23(2):144–55.
23. Wasserman LR, Lawrence JH, Berlin NI, Dobson RL, Estren S. The bone marrow picture in polycythemia vera before and after treatment with radioactive phosphorus. *Acta Med Scand*. 1952;143(6):442–9.
24. Roback J. Technical Manual. 16th ed. Arlington, VA: AABB; 2008.
25. Berk PD, Wasserman LR, Fruchtman SM. Treatment of polycythemia vera: a summary of trials conducted by the Polycythemia Vera Study Group. In: Wasserman LR, Berk PD, Berlin NI, editors. Polycythemia vera and the myeloproliferative disorders. Philadelphia: WB Saunders; 1995. p. 166–94.
26. Thomas DJ, Duboulay GH, Marshall J, Pearson TC, Russell RR, Symon L, et al. Cerebral blood flow in polycythemia. *Lancet*. 1977;2(8030):161–3.
27. Wasserman LR, Gilbert HS. Surgical Bleeding in Polycythaemia Vera. *Ann N Y Acad Sci*. 1964;115:122–8.
28. Najean Y, Rain JD. Treatment of polycythemia vera: use of 32P alone or in combination with maintenance therapy using hydroxyurea in 461 patients greater than 65 years of age. *Blood*. 1997;89(7):2319–27.
29. Lawrence JH, Winchell HS, Donald WG. Leukaemia in polycythemia vera. Relationship to splenic myeloid metaplasia and therapeutic radiation dose. *Ann Intern Med*. 1969;70(4):763–71.

Author's biography

Rashmita Panigrahi, Assistant Professor

Samarendra Satpathy, Assistant Professor

Manu Mangat Marandi, Senior Resident

Sabita Palai, Associate Professor https://orcid.org/0000-0002-4367-8554

Cite this article: Panigrahi R, Satpathy S, Marandi MM, Palai S. Impact of therapeutic phlebotomy on haematological parameters of patients and their clinical outcome. *Panacea J Med Sci* 2025;15(1):214-219.