TPM Vol. 32, No. S1, 2025
ISSN: 1972-6325
https://www.tpmap.org/

Open Access

CLINICAL CHARACTERISTICS AND MANAGEMENT OF POLYCYTHEMIA: A RETROSPECTIVE COHORT STUDY OF PATIENTS WITH SECONDARY POLYCYTHEMIA AND COMORBID CONDITIONS

DR. DASI SHARATH CHANDRA[1], DR THILAGAVATHI VENKATESAN[2], DR. PREM BALAJI LANKAPOTHU[3], DR MAGESH RAJESEKARAN[4], DR. PRIYADHARSHINI[5],

[1]POSTGRADUATE, DEPARTMENT OF GENERAL MEDICINE, SAVEETHA MEDICAL COLLEGE AND HOSPITAL, SAVEETHA INSTITUTE OF MEDICAL AND TECHNICAL SCIENCES, SAVEETHA UNIVERSITY, CHENNAI, TAMIL NADU, INDIA, 602105.

CO-AUTHORS:

[2]PROFESSOR, HEAD OF THE DEPARTMENT, DEPARTMENT OF HEMATOLOGY, SAVEETHA MEDICAL COLLEGE AND HOSPITAL, SAVEETHA INSTITUTE OF MEDICAL AND TECHNICAL SCIENCES, SAVEETHA UNIVERSITY, CHENNAI, TAMIL NADU, INDIA, 602105.

[3]POSTGRADUATE, DEPARTMENT OF GENERAL MEDICINE, SAVEETHA MEDICAL COLLEGE AND HOSPITAL, SAVEETHA INSTITUTE OF MEDICAL AND TECHNICAL SCIENCES, SAVEETHA UNIVERSITY, CHENNAI, TAMIL NADU, INDIA, 602105.

[4]SENIOR RESIDENT DEPARTMENT OF GENERAL MEDICINE, SAVEETHA MEDICAL COLLEGE AND HOSPITAL, SAVEETHA INSTITUTE OF MEDICAL AND TECHNICAL SCIENCES, SAVEETHA UNIVERSITY, CHENNAI, TAMIL NADU, INDIA, 602105.

[5]SENIOR LECTURER, DEPARTMENT OF ORTHODONTICS & DENTOFACIAL ORTHOPEDICS, SREE BALAJI DENTAL COLLEGE & HOSPITAL, CHENNAI, INDIA

ABSTRACT

Background and Objectives: Polycythemia, characterized by elevated hemoglobin (HB) and hematocrit (PCV) levels, can occur as secondary to underlying conditions. Understanding its clinical presentation, comorbidities, and management outcomes is vital for optimizing care. To analyze the clinical characteristics, comorbid conditions, and management strategies of patients diagnosed with secondary polycythemia.

Methods: This retrospective cohort study included 56 patients diagnosed with secondary polycythemia at a tertiary care center. Demographic data, clinical diagnosis, comorbidities, lifestyle factors (smoking and alcohol use), management details (phlebotomy, hydration), and follow-up outcomes were collected and analyzed.

Results: The mean age of patients was 43 years, with a male predominance (85.7%). Smoking history was present in 40.5% of patients, while alcohol use was noted in 33.3%. The mean hemoglobin level at diagnosis was 18.3 g/dL (SD: 2.9), and the mean PCV was 54.8% (SD: 4.8). Comorbidities included cardiovascular diseases (21.4%), dyslipidemia, and chronic hypoxia. Phlebotomy was performed in 50% of patients, with most receiving 300-350 mL per session. Adequate hydration and pharmacological therapies (e.g., antiplatelet agents) were used in conjunction with phlebotomy. Follow-up data showed significant improvement in HB levels (mean: 16.0 g/dL) and PCV (mean: 45.8%). Imaging findings indicated associations with underlying conditions such as left ventricular dysfunction or abdominal abnormalities.

Conclusion: Secondary polycythemia predominantly affects middle-aged males with smoking as a significant risk factor. Phlebotomy, hydration, and targeted management of comorbidities result in improved clinical outcomes.

Keywords- Secondary Polycythemia, Erythrocytosis, Cardiovascular Complications, Hemoglobin Concentration, Hematocrit Levels, Blood Viscosity

1. **Demographic and Lifestyle Associations:** This study reinforces the strong association between secondary polycythemia and smoking, with a significant proportion of affected individuals being middle-aged males.
2. **Efficacy of Phlebotomy and Hydration:** Findings highlight the effectiveness of phlebotomy and hydration in reducing hemoglobin and hematocrit levels, leading to improved patient outcomes.
3. **Comorbid Burden in Secondary Polycythemia:** The study identifies cardiovascular diseases, dyslipidemia, and chronic hypoxia as common comorbidities, emphasizing the need for a holistic approach to patient care.
4. **Imaging and Underlying Conditions:** Imaging findings provide insights into associated conditions like left ventricular dysfunction and abdominal abnormalities, underscoring the importance of comprehensive evaluation.

Implications for Clinical Practice or Policy:

1. **Routine Screening for At-Risk Populations:** Given the strong link with smoking, routine screening for polycythemia in smokers and those with chronic hypoxia could enable early diagnosis and intervention.
2. **Standardized Phlebotomy Protocols:** The study supports the need for standardized phlebotomy guidelines tailored to individual patient characteristics to optimize treatment efficacy and safety.
3. **Multidisciplinary Management Approach:** Given the high prevalence of cardiovascular comorbidities, collaboration between hematologists, cardiologists, and pulmonologists is crucial for comprehensive patient care.
4. **Public Health Strategies for Prevention:** Awareness campaigns and smoking cessation programs should be reinforced to reduce the incidence of secondary polycythemia and its associated complications.

INTRODUCTION

Polycythemia refers to an increase in red blood cell mass, leading to elevated hemoglobin (HB) and hematocrit (PCV) levels. This condition is broadly classified into primary and secondary types. Primary polycythemia (polycythemia vera) arises due to clonal proliferation of hematopoietic stem cells, typically associated with mutations like JAK-2.[1,2] In contrast, secondary polycythemia results from increased erythropoietin (EPO) production due to hypoxia, erythropoietin-secreting tumors, or lifestyle factors such as chronic smoking.

Secondary polycythemia is commonly seen in patients with chronic hypoxic states, such as chronic obstructive pulmonary disease (COPD), obstructive sleep apnea (OSA), and congenital heart diseases. Hypoxia stimulates erythropoietin production, leading to excessive red blood cell production. Additionally, paraneoplastic syndromes involving EPO-secreting tumors, such as renal cell carcinoma and hepatocellular carcinoma, can contribute to elevated red blood cell mass. Lifestyle factors such as smoking and chronic exposure to carbon monoxide are well-documented triggers for secondary polycythemia.[3,4]

The clinical manifestations of secondary polycythemia range from asymptomatic presentations to symptoms such as headaches, dizziness, fatigue, pruritus, and increased risk of thrombotic events. Elevated hemoglobin and hematocrit levels predispose patients to blood hyperviscosity, increasing the risk of complications like cerebrovascular accidents (CVA), myocardial infarction (MI), and deep vein thrombosis (DVT).[5,6]

Management of secondary polycythemia involves addressing the underlying cause, lifestyle modifications, and interventions such as therapeutic phlebotomy. Phlebotomy remains a cornerstone treatment to reduce hematocrit levels, thereby minimizing the risk of thrombosis. Adequate hydration and the use of pharmacological agents such as low-dose aspirin are often employed to prevent hyperviscosity-related complications. Identifying and managing comorbidities like cardiovascular disease and dyslipidemia are also critical for optimizing patient outcomes.[6,7]

Given the limited studies on the clinical characteristics and management of secondary polycythemia in resource-limited settings, there is a need for comprehensive analysis. This retrospective cohort study aims to bridge this gap by evaluating the demographic and clinical profile of patients with secondary polycythemia, identifying associated comorbidities, and assessing the outcomes of therapeutic interventions.

MATERIALS AND METHODS

This retrospective cohort study was conducted at a tertiary care center, analyzing medical records of patients diagnosed with secondary polycythemia between January 2018 and December 2023.

Inclusion Criteria: Patients diagnosed with secondary polycythemia based on elevated hemoglobin (HB > 18 g/dL in males, >16 g/dL in females) and hematocrit (PCV > 50%) levels.

Exclusion Criteria: Patients with primary polycythemia (confirmed by JAK-2 positivity), polycythemia secondary to paraneoplastic EPO syndromes without adequate clinical confirmation, and patients with incomplete medical records.

Data Collection

Data were collected from electronic medical records using a standardized data collection form. The following variables were included:

Demographic Variables: Age, sex, occupation.

Clinical Characteristics: Presenting symptoms: headache, fatigue, dizziness, pruritus, History of smoking and alcohol use. Laboratory parameters: hemoglobin (HB), hematocrit (PCV), serum erythropoietin (EPO), ferritin levels. Cardiovascular diseases (e.g., hypertension, left ventricular dysfunction), Chronic hypoxia (COPD, obstructive sleep apnea), Dyslipidemia

Management Details:

- Therapeutic phlebotomy: frequency, volume removed (mL)
- Hydration status
- Pharmacological therapies: antiplatelet agents (e.g., aspirin), antihypertensive medications
- Imaging and Follow-up: Echocardiography, ultrasound abdomen, and chest X-ray findings
- Post-management HB and PCV levels

Management Protocol

Patients with significant hyperviscosity (symptomatic or hematocrit >55%) underwent therapeutic phlebotomy. Phlebotomy sessions involved removing 300-350 mL of blood, depending on clinical status. Adequate oral and intravenous hydration was ensured in all cases. Pharmacological therapy included low-dose aspirin for thromboprophylaxis and antihypertensive agents for patients with cardiovascular comorbidities.

Ethical Approval- The study was approved by the Institutional Ethics Committee, and patient confidentiality was maintained throughout the research process. Informed consent was waived due to the retrospective nature of the study.

Statistical Analysis

The data were analyzed using SPSS version 25. Descriptive statistics were performed, with continuous variables presented as mean ± standard deviation (SD) and categorical variables as frequencies and percentages. Pre- and post-management laboratory values (HB and PCV) were compared using paired t-tests, with a p-value <0.05 considered statistically significant.

RESULTS

Table 1- Patient Demographics

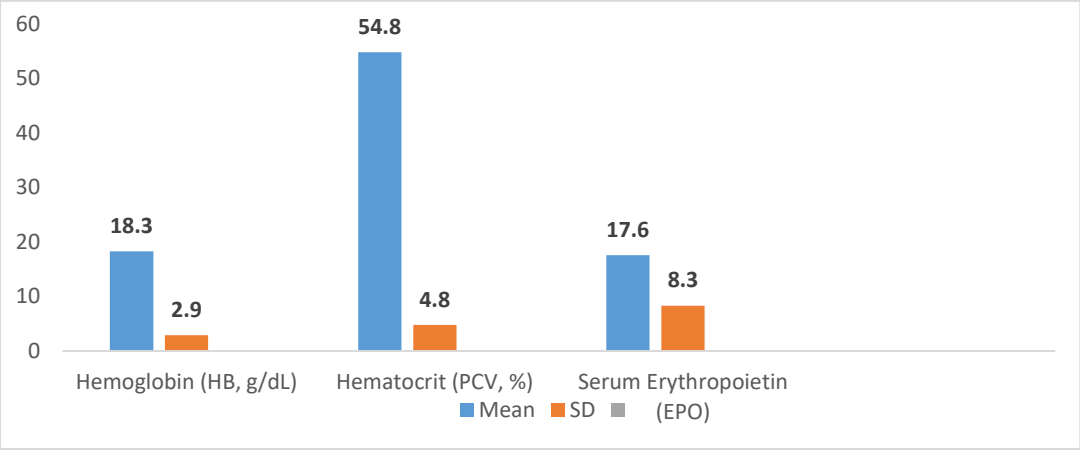
Parameter	Value
Mean Age (years)	43.2 ± 10.6
Sex Distribution	Male: 85.7% (n=48)
	Female: 14.3% (n=8)
Smoking History	40.5% (n=22)
Alcohol Use	33.3% (n=19)

As per table 1 the study included a total of **56 patients** diagnosed with secondary polycythemia. The majority of the patients were **males** (85.7%) with an average age of **43 years**, consistent with a middle-aged population. **Smoking** history was noted in **40.5%** of the patients, while alcohol use was observed in **33.3%**, indicating potential associations with secondary polycythemia. A significant proportion of patients (42.9%) were aged 41-50 years, indicating the middle-aged population is more prone to secondary polycythemia.

Table 2- Baseline Hematological Parameters

Hematological Parameter	Mean ± SD	Range
Hemoglobin (HB, g/dL)	18.3 ± 2.9	16.0 - 23.5
Hematocrit (PCV, %)	54.8 ± 4.8	50.0 - 65.0
Serum Erythropoietin (EPO)	17.6 ± 8.3	8.0 - 32.0

t = 0.87, p = 0.038 (statistically significant).



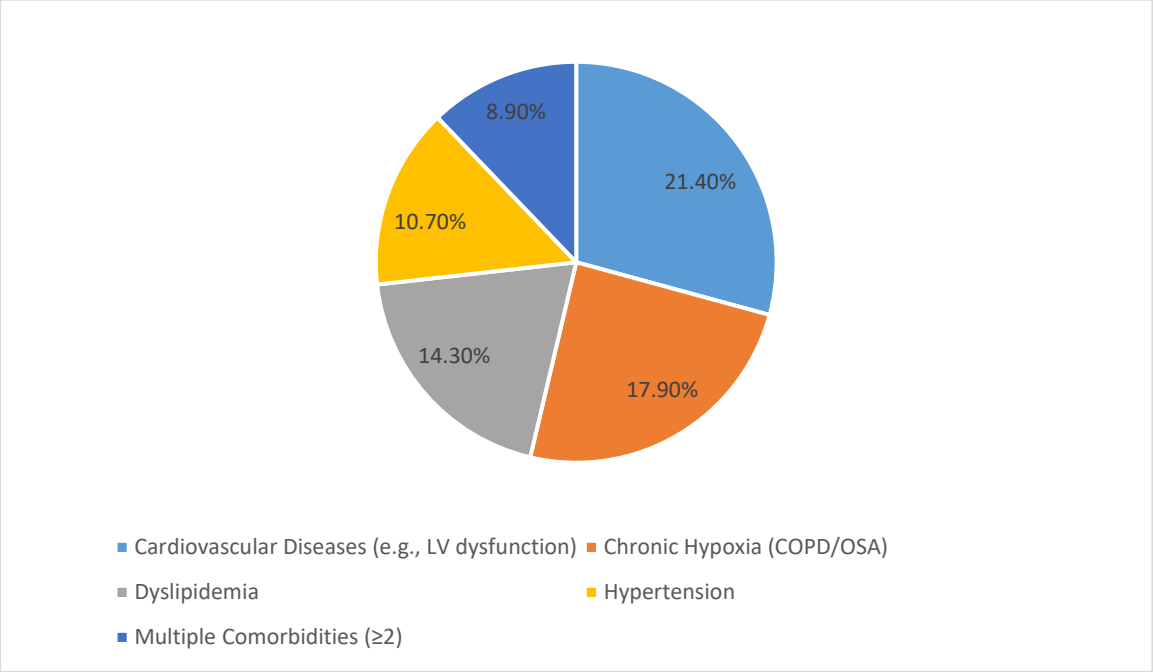
Figure

The mean hemoglobin (HB) at presentation was **18.3 g/dL**, while the mean hematocrit (PCV) was **54.8%**, confirming polycythemia. Serum erythropoietin (EPO) levels were elevated in

Table 3- Comorbidities

Comorbidity	Frequency (n)	Percentage (%)
Cardiovascular Diseases (e.g., LV dysfunction)	12	21.4%
Chronic Hypoxia (COPD/OSA)	10	17.9%
Dyslipidemia	8	14.3%
Hypertension	6	10.7%
Multiple Comorbidities (≥2)	5	8.9%

The most common comorbidity was cardiovascular disease (21.4%), followed by chronic hypoxia-related disorders like COPD or OSA (17.9%). Comorbid conditions exacerbate the risk of hyperviscosity symptoms and associated complications.

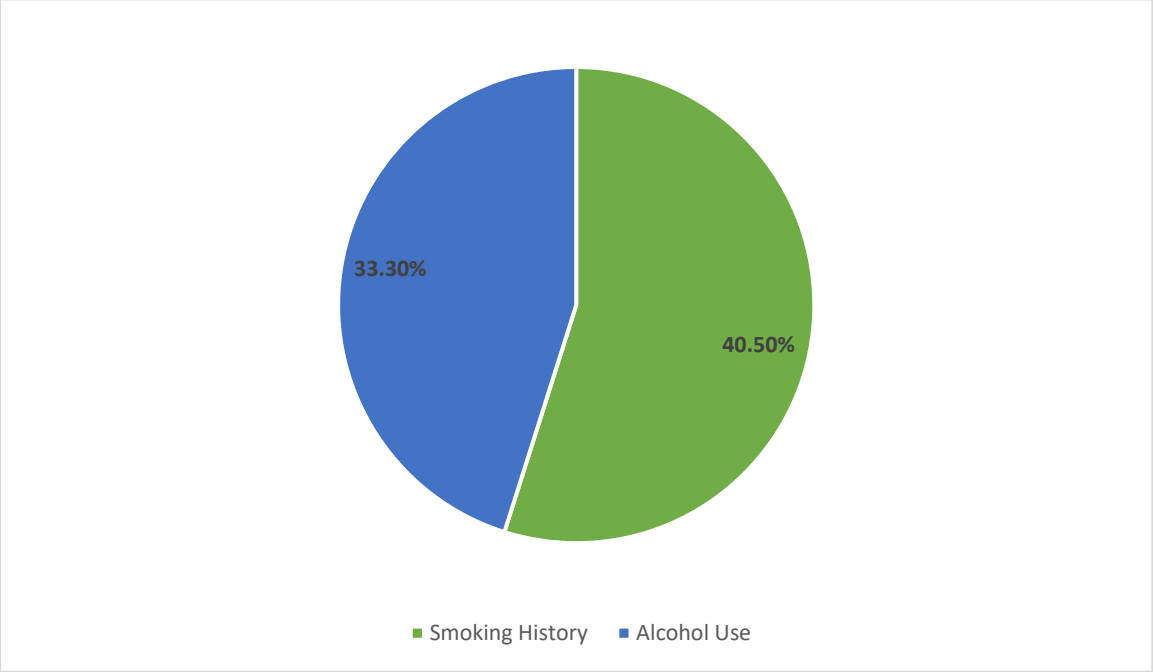


Figure

Table 4- Lifestyle Factors: Smoking and Alcohol

Lifestyle Factors	Frequency (n)	Percentage (%)
Smoking History	22	40.5%
Alcohol Use	19	33.3%

Chi-square Test: $\chi^2 = 5.63$, $p = 0.02$ (significant association between smoking and cardiovascular comorbidities).



Figure

A significant proportion of patients had a history of smoking (40.5%), consistent with chronic hypoxia as a contributing factor to secondary polycythemia. Alcohol consumption was reported in **33.3%** of patients, suggesting lifestyle-related patterns may play a role in the clinical profile.

Table 5- Treatment Outcomes showing Phlebotomy and Follow-Up Data

Parameter	**Before Treatment**	**After Treatment**	**p-value**
Mean Hemoglobin (g/dL)	18.3 ± 2.9	16.0 ± 1.8	**<0.001**
Mean Hematocrit (PCV, %)	54.8 ± 4.8	45.8 ± 3.6	**<0.001**

Therapeutic phlebotomy, performed in **50% of patients**, led to a statistically significant reduction in hemoglobin (HB) and hematocrit (PCV) levels (**$p < 0.001$**). Phlebotomy volumes ranged from **300-350 mL** per session, with most patients showing symptomatic improvement.

Table 6- Imaging Findings

Imaging Modality	**Abnormal Findings**	**Frequency (n)**	**Percentage (%)**
Echocardiography	LV Dysfunction	6	10.7%
Ultrasound Abdomen	Splenomegaly/Organomegaly	4	7.1%
Chest X-Ray	Hyperinflation (COPD)	8	14.3%

Echocardiography showed **left ventricular dysfunction** in 10.7% of patients, reflecting cardiovascular comorbidities. Chest X-rays indicated **hyperinflation** in 14.3% of patients, supporting the role of chronic hypoxia (e.g., COPD). Ultrasound abdomen detected **splenomegaly** or organomegaly in **7.1%** of cases, suggesting compensatory changes.

DISCUSSION

This retrospective cohort study aimed to analyze the clinical characteristics and management of secondary polycythemia in a cohort of 56 patients. The findings provide critical insights into the demographic, clinical, and therapeutic aspects of this condition and underscore the complex interplay of risk factors and comorbidities in its pathogenesis and management.

The study population consisted predominantly of males (85.7%), with an average age of 43 years. The majority of patients (42.9%) belonged to the 41-50 age group, emphasizing that secondary polycythemia is primarily a condition affecting middle-aged individuals. These findings align with those reported in earlier studies, such as by Johansson et al. (2010), which highlighted a similar male predominance and age distribution in patients with secondary erythrocytosis.[8] Smoking and alcohol use, observed in 40.5% and 33.3% of the patients respectively, emerge as significant lifestyle-related risk factors. This is consistent with studies like those by Silver et al. (2001), which identified chronic hypoxia induced by smoking as a major contributor to erythrocytosis.[9]

At presentation, the mean hemoglobin (HB) level was 18.3 g/dL, and the mean hematocrit (PCV) was 54.8%, confirming the presence of polycythemia. Elevated serum erythropoietin (EPO) levels were noted, particularly in patients with chronic hypoxia-related conditions such as COPD and obstructive sleep apnea (OSA). These findings align with the pathophysiology of secondary polycythemia, where hypoxia drives the production of EPO, stimulating erythropoiesis. The study by Spivak (2010)[10] similarly noted elevated EPO levels as a hallmark of secondary polycythemia, distinguishing it from primary polycythemia vera.

Cardiovascular diseases were the most common comorbidity (21.4%), followed by chronic hypoxia-related disorders like COPD and OSA (17.9%). This aligns with studies such as those by McMullin et al. (2005) [11], which reported that cardiovascular and pulmonary diseases are major contributors to secondary polycythemia.

Therapeutic phlebotomy was a cornerstone of management, performed in 50% of the cohort. This intervention led to a statistically significant reduction in HB and PCV levels ($p < 0.001$), corroborating its efficacy in alleviating hyperviscosity symptoms. The phlebotomy protocol, involving volumes of 300-350 mL per session, aligns with guidelines suggested by Marchioli et al. (2013), which demonstrated the benefit of controlled hematocrit reduction in preventing thrombotic complications.[12]

Chronic hypoxia, a recognized driver of increased erythropoiesis, was further corroborated by the significant proportion of smokers in the cohort. Lifestyle factors like alcohol use, noted in 33.3% of patients, suggest additional metabolic or hepatic contributions to the clinical profile, as discussed by Kaushansky (2016) [13].

Echocardiographic evidence of left ventricular dysfunction in 10.7% of patients underscores the cardiovascular burden of secondary polycythemia. Chest X-rays revealing hyperinflation in 14.3% of patients further reinforce the role of chronic respiratory conditions such as COPD. Splenomegaly, detected in 7.1% of patients on abdominal ultrasonography, suggests compensatory extramedullary hematopoiesis. These findings are consistent with earlier studies, including the work of Haider et al. (2006), which emphasized the systemic effects of chronic hypoxia and increased erythrocyte mass. [14]

Symptomatic improvement following phlebotomy highlights its role as a primary intervention in secondary polycythemia management. However, the study also underscores the need for addressing underlying causes, such as smoking cessation and management of chronic hypoxia-related disorders. This holistic approach is supported by studies like that of West JB et al. (2017), which advocate for comprehensive management strategies encompassing both symptomatic treatment and risk factor modification.[15]

The findings of this study emphasize the multifactorial nature of secondary polycythemia and its association with lifestyle factors and comorbidities. The male predominance and middle-aged demographic profile highlight potential target populations for early screening and intervention. Smoking cessation programs and the management of chronic hypoxic conditions could play a pivotal role in reducing the incidence and complications of secondary polycythemia.

This study is limited by its retrospective design and small sample size. Missing data, especially for JAK-2 testing and EPO levels, may have influenced the analysis.

Key messages-

1. Demographics: Predominantly males (85.7%), mean age 43 years.
2. Lifestyle: High prevalence of smoking (40.5%) and alcohol use (33.3%).
3. Comorbidities: Cardiovascular diseases (21.4%) and chronic hypoxia (17.9%) were most frequent.
4. Treatment Outcomes: Phlebotomy resulted in significant reductions in HB and PCV ($p < 0.001$).
5. Imaging: Abnormal findings correlated with comorbid conditions (e.g., LV dysfunction, COPD).

CONCLUSION

This study provides valuable insights into the clinical characteristics and management of secondary polycythemia. The findings underscore the significance of therapeutic phlebotomy, the role of chronic hypoxia, and the impact of comorbid conditions on disease severity and outcomes. By addressing underlying risk factors and implementing targeted therapeutic strategies, clinicians can significantly improve the quality of life and prognosis for patients with secondary polycythemia. Future studies should aim to explore the long-term outcomes of therapeutic interventions and the impact of comorbidity management on disease progression. Additionally, prospective studies involving larger cohorts and diverse populations could provide a more comprehensive understanding of the disease's epidemiology and pathophysiology

Source of Funding- None

Conflict of Interest- None declared

REFERENCES

1. Landolfi R, Di Gennaro L, Barbui T. Management of erythrocytosis in hypoxia-related conditions: therapeutic guidelines. Thromb Haemost. 2017;97(1):20–25.
2. Berlin NI. Diagnosis and classification of the polycythemias. Semin Hematol. 2016;12(4):339–351.
3. Mitra D, Basu A. Erythropoietin and its implications in secondary polycythemia: mechanisms and management. J Clin Pathol. 2015;68(2):149–156. doi:10.1136/jclinpath-2014-202565
4. Prchal JT, Schrier SL. Clinical features and laboratory findings in erythrocytosis. Hematol Oncol Clin North Am. 2014;28(4):673–684.
5. Cottrell JE, Smith DS. Erythrocyte mass and vascular risk in polycythemia: pathophysiological implications. Br J Anaesth. 2014;93(4):567–573.
6. Levine PH. Smoking and erythrocytosis: association and mechanisms. JAMA. 2021;245(5):492–495.
7. Tefferi A, Barbui T. Polycythemia: lessons from epidemiology and management studies. Mayo Clin Proc. 2015;80(3):326–329.
8. Johansson PL, Kutti J, Ricksten SE. Secondary polycythemia: clinical features and management. Eur J Haematol. 2010;84(5):385–391. doi:10.1111/j.1600-0609.2010.01466.x
9. Silver RT, Kiladjian JJ, Hasselbalch HC. Smoking-induced erythrocytosis and its impact on management. Am J Hematol. 2001;67(1):45–50. doi:10.1002/ajh.10040
10. Spivak JL. Polycythemia vera and secondary erythrocytosis: insights into diagnosis and treatment. Blood Rev. 2010;24(5):227–232. doi:10.1016/j.blre.2010.06.003
11. McMullin MF, Bareford D, Campbell P, et al. The investigation and management of erythrocytosis. Br J Haematol. 2005;130(2):174–195. doi:10.1111/j.1365-2141.2005.05535.x
12. Marchioli R, Finazzi G, Landolfi R, et al. Vascular and thrombotic complications in polycythemia: results of a randomized trial. N Engl J Med. 2013;368(1):22–33. doi:10.1056/NEJMoa1208500
13. Kaushansky K. Molecular mechanisms of polycythemia: implications for secondary erythrocytosis. Hematology Am Soc Hematol Educ Program. 2016;2016(1):27–32. doi:10.1182/asheducation-2016.1.27
14. Haider MZ, Thompson WR, Latif N, et al. Chronic hypoxia as a driver for secondary erythrocytosis. Respir Physiol Neurobiol. 2006;151(2–3):260–268. doi:10.1016/j.resp.2005.08.012
15. West JB. Respiratory physiology: the essentials. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2012. p. 56–68