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HEMATOLOGICAL CHARACTERISTICS OF SECONDARY POLYCYTHEMIA ASSOCIATED WITH CHRONIC HYPOXIA

Subreena Akhtar
Research Scholar
Rayat Bahra University (Usahs), Mohali, Punjab
Sabreenajan98267@Gmail.Com
Maroofa Altaf
Research Scholar
Mr. K. S. Rana
Associate Professor
Department Of Medical Laboratory Sciences

ABSTRACT

Secondary polycythemia is a compensatory response of the hematology to chronic hypoxia, which is marked by the presence of increased red blood cell mass and the high level of hemoglobin and hematocrit. The objective of the current cross-sectional study, which was conducted in the hospital, was to determine the hematological features and etiology of secondary polycythemia in patients with chronic hypoxia. Clinical evaluation and hematological analysis were done on 100 adult patients in whom hypoxic conditions were reported. The findings showed a moderate to high level of hemoglobin and hematocrit level in a majority of the patients, with a range of hemoglobin levels of between 18.0-19.9 g/dL and a range of hematocrit of over 55%. The most prevalent underlying condition was chronic obstructive pulmonary disease then obstructive sleep apnea and other hypoxia-related conditions. The percentage of patients brought with the symptoms of hyperviscosity such as headache, dizziness, and thrombotic events were noted. The results not only demonstrate the adaptive flexibility of erythrocytosis in chronic hypoxia but also emphasize identification and management of underlying hypoxic disorders early in life as a way of preventing complications related to the occurrence of high blood viscosity.

Keywords: *Secondary Polycythemia, Chronic Hypoxia, Hemoglobin, Hematocrit, Erythropoietin, Hyperviscosity.*

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1. INTRODUCTION

Polycythemia is a hematological disorder that is identified by excessive mass of the red blood cells resulting in the increase of the concentration of hemoglobin and hematocrit. According to the underlying etiology, polycythemia is categorized in general as either primary or secondary. Primary polycythemia or polycythemia vera is a myeloproliferative disease caused by intrinsically abnormal functions of hematopoietic stem cells. Conversely, secondary polycythemia occurs as a physiological reaction or pathological process to elevated levels of erythropoietin production that is usually stimulated by chronic hypoxia. Other disorders like chronic obstructive lung disease (COPD), cyanotic congenital heart disease, extended stay at elevated altitudes and sleep-disordered breathing are often related with long-term hypoxic situations that provoke erythrocytosis.

Persistent hypoxia triggers renal peritubular interstitial cells to secrete more erythropoietin, which is one of the primary regulators of red blood cells production. The increase in the level of erythropoietin increases erythropoiesis in the bone marrow leading to increased red cell mass to help in the enhancement of tissue oxygenation. Despite the adaptive role played by this compensatory mechanism, chronic erythrocytosis may cause elevation of blood viscosity, dysfunction of the microcirculation, and thrombotic and cerebrovascular events. Thus the precise diagnosis of secondary polycythemia is only achievable through a proper knowledge of the hematological properties of secondary polycythemia, a proper distinction between the two entities i.e. secondary and primary myeloproliferative disorders and the formulation of suitable treatment strategies aimed at both treatment of underlying hypoxic source and prevention of related complications.

1.1 Research Objectives

- To assess the hematological characteristics of secondary polycythemia associated with chronic hypoxia by evaluating hemoglobin and hematocrit levels among affected patients.
- To identify and analyze the major etiological factors contributing to chronic hypoxia leading to secondary polycythemia, with special emphasis on chronic pulmonary disorders.

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- To evaluate the occurrence of hyperviscosity-related clinical manifestations in patients with secondary polycythemia and their association with elevated hematological parameters.

2. LITERATURE REVIEW

Alkhaldy and Assiri (2025) discussed the fact of polycythemia in people, who live at moderate altitudes, and critically assessed the difficulties in screening polycythemia vera in these groups of population. Their research underlined that altitude related chronic hypoxia had a great impact on hemoglobin and hematocrit values and their study tended to simulate some primary polycythemia features. There were the risks of misdiagnosis in case the secondary causes of erythrocytosis were not properly eliminated, which were mentioned by the authors. They found hypoxia due to altitude to have significant contribution in secondary polycythemia and emphasized on the need to undertake thorough clinical and hematological assessment to distinguish between secondary erythrocytosis and myeloprolliferative disorders.

Babakhanlou et al. (2023) has given a comprehensive overview of secondary erythrocytosis with emphasis on its pathophysiology, clinical manifestation and how it can be diagnosed. The authors stated that secondary erythrocytosis was often caused by prolonged hypoxia caused by lung diseases, sleep-disordered breathing, heart diseases, and exposure. Their results emphasized the importance of the elevated production of erythropoietin as the leading pathway to the erythrocytosis in hypoxia. It was also noted in the review that hematological parameters, including a high hemoglobin and hematocrit, were necessary diagnostic features whereas the count of leukocytes and platelets were usually within the normal limits, differentiating between secondary erythrocytotic and primary polycythemia.

Chandra et al. (2025) carried out a retrospective cohort study design to examine the clinical profile and the management approach of patients with secondary polycythemia and comorbid illnesses. The research revealed that the most common underlying causes were chronic respiratory disorders, with a lot of patients having symptoms associated with hyperviscosity such as a headache, dizziness, and thrombotic injuries. According to the authors, there was a trend among

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management options that put more emphasis on the underlying hypoxic state and not on aggressive hematological approaches. They inferred that early comorbid hypoxic disorders and specific treatment had a significant beneficial effect on patients and decreased the likelihood of complications.

Gangaraju et al. (2020) discovered how thrombosis risk is mediated by analyzing the genes controlled by thrombotic, inflammatory, and hypoxia-inducible factor (HIF) in polycythemia vera and essential thrombocythemia. The article stated that hypoxia-related pathways impacted substantially on erythropoiesis and thrombotic risk via changed gene expression. Though the researches mostly concentrated on primary myeloprolliferative disorders, the results of the research were important in understanding the involvement of hypoxia-mediated pathways in elevating blood viscosity and thrombosis. The authors pointed out that hypoxia-related mechanisms dysregulation was a contributing factor to vascular complications and, therefore, provided a biological framework that can be used to interpret hyperviscosity-related risks in secondary polycythemia.

Holopainen et al. (2022) to investigate the connection between sustained hypoxia and erythrocytosis, examined polycythemia in dogs with chronic hypoxic pulmonary disease. It was revealed that chronic respiratory disorders in animals were characterized by significantly high levels of hemoglobin and hematocrit in the compensatory mechanism to hypoxemia over a long period of time. The authors noted that the degree of hypoxia was associated with the levels of polycythemia severity, which supported the adaptive character of erythrocytosis. Even though the study was done in a population of veterians, the results supported similar pathophysiological processes in humans and underscored the universal role of chronic hypoxia in the pathophysiological processes of secondary polycythemia.

Li et al. (2019) considered the relationship between nocturnal oxygen saturation and secondary polycythemia in young obstructive sleep apnea patients. The research found that, lower nocturnal mean oxygen saturation was greatly linked with higher levels of hemoglobin and hematocrit, especially in the male subjects. The authors ended up concluding that intermittent nocturnal hypoxia was a powerful stressor on erythrocytosis as mediated by erythropoietin. Their results

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emphasized the significance of sleep-disordered breathing as a risk factor in the development of secondary polycythemia and the necessity of the early diagnosis and treatment of obstructive sleep apnea in order to avoid the occurrence of hematologic changes caused by hypoxia.

3. MATERIALS AND METHODS

This cross-sectional study entailed 100 patients (patients with secondary polycythemia caused by chronic hypoxia) at this hospital. To determine the etiological factors and the characteristics of the disease, clinical examination and hematological parameters were determined. Analytical statistics was done through descriptive statistics and the data were given in percentages.

3.1 Study Design

The current research was based on the cross-sectional observational study design because it was a hospital-based study aimed at determining hematological features of secondary polycythemia due to chronic hypoxia. The design was selected to determine the distribution of hematological variables and etiological variables at one time in the sample of the affected.

3.2 Study Setting and Duration

The case study was carried out in the Department of Medicine and Hematology of a tertiary care teaching hospital. The data were collected at a specific time of study, and the patients who came with the characteristic of chronic hypoxia, as well as high hemoglobin or hematocrit concentration, were examined.

3.3 Study Population and Sample Size

The number of patients included in the study was 100 and diagnosed with secondary polycythemia related to chronic hypoxia. The sample was chosen due to the convenience of calculating the percentage, as well as to permit meaningful descriptive statistical analysis of the hematological parameters and clinical features and etiological factors.

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3.4 Inclusion Criteria

The study included patients of the age 18 years and older with the documented presence of chronic hypoxia and the laboratory results that were suggestive of secondary polycythemia. Chronic hypoxia was determined according to clinical examination and other complementary research like oxygen saturation level under normal level. Patients having high hemoglobin and hematocrit levels that are in line with secondary erythrocytosis were only recruited.

3.5 Exclusion Criteria

The exclusion criteria were patients who have a proven diagnosis of primary polycythemia, myeloprolliferative disorders, acute hypoxic conditions, or patients undergoing erythropoietin treatment. Patients having hematological malignancies or acute infections that may affect hematological parameters were also crossed out.

3.6 Data Collection Procedure

Upon informed consent, elaborate clinical history and the corresponding demographic data were taken. Special focus was placed on the determination of the underlying causes of chronic hypoxia including chronic obstructive pulmonary disease, obstructive sleep apnea, cyanotic congenital heart disease, interstitial lung disease and high altitude dwelling. Hyperviscosity clinical symptoms such as headache, dizziness, dyspnea, visual disturbances, and thrombotic were recorded.

3.7 Hematological Assessment

Aseptic venous blood samples were taken and examined with a hematology analyzer with an automated hematological method. Some of the hematological parameters measured were hemoglobin concentration, the hematocrit values and red blood cell indices. These parameters were employed to describe the severity of erythrocytosis and to compare the results of hematology with hypoxic etiologies.

3.8 Statistical Analysis

The analysis of data was performed through descriptive statistics. Hematological parameters, clinical features and etiological factors were also expressed in the form of frequencies and

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percentages. Tables and graphical representations were used to present the findings in order to make findings clear and easy to compare.

4. RESULTS

The study involved 100 patients with secondary polycythemia related to chronic hypoxia so that it was easy to represent them in percentages. Frequencies and percentages were analyzed and used to express Hematological parameters.

Table 1 and Figure 1 show how the patients are distributed according to hemoglobin level among patients with secondary polycythemia which is caused by chronic hypoxia. Among all the 100 patients who were studied, 28 patients (28%) had hemoglobin levels of 16.5 -17.9 g/dl. The highest percentage of 46 (46%) of the patients showed hemoglobin of 18.019.9 g/dL. Also, 26 patients (26%) had significantly higher levels of hemoglobin of 20.0 g/dL or higher. This is clearly illustrated in the graphical representation where patients on the moderate elevation range of hemoglobin are the majority.

Table 1: Distribution of Patients Based on Hemoglobin Levels

Hemoglobin Level (g/dL)	Number of Patients	Percentage (%)
16.5 – 17.9	28	28%
18.0 – 19.9	46	46%
≥ 20.0	26	26%
Total	**100**	**100%**

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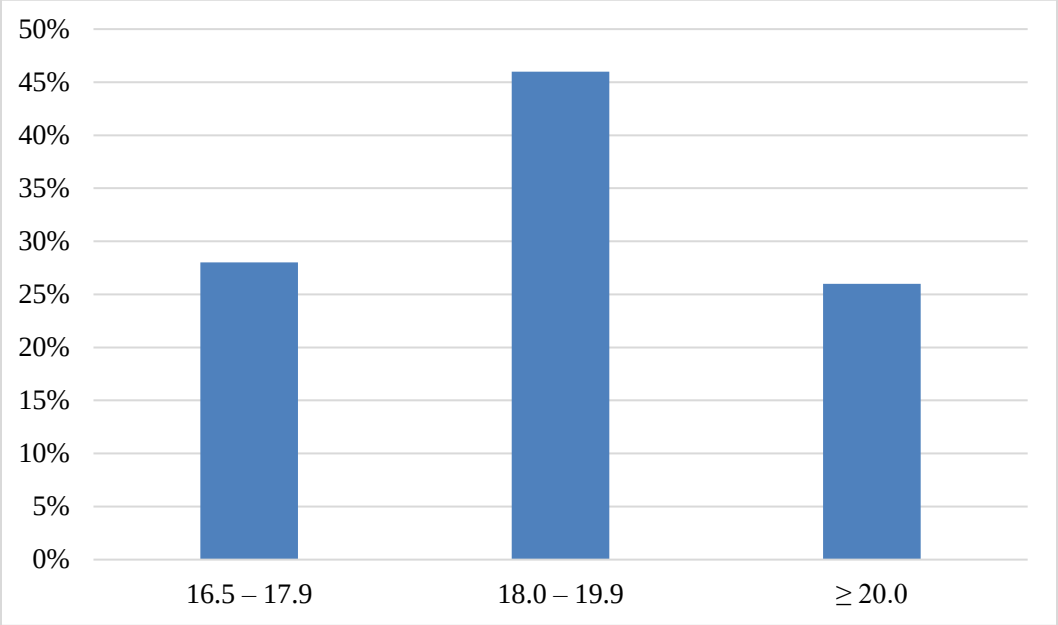

Figure 1: Graphical Representation of Distribution of Patients Based on Hemoglobin Levels

The given distribution demonstrates that most of the patients having chronic hypoxia develop moderate or severe hemoglobin levels increase due to the compensatory effect of the lack of oxygen. The fact that hemoglobin readings are dominated by 18.0-19.9 g/dl is an indication of continuous erythropoietic stimulation, which is facilitated by elevated erythropoietin levels. The availability of a large percentage of patients reporting a hemoglobin level of 20.0g/dL and above indicates the threat of hyperviscosity-affected complications. Such results confirm the typical hematological picture of secondary polycythemia which is differentiated by primary polycythemia as it represents an adaptive as opposed to a myeloprolliferative process.

Table 2 and Figure 2 provide the distribution of the number of patients in the cases of secondary polycythemia in chronic hypoxia. A total of 100 patients were assessed with 34 patients (34%) found to have hematocrit levels ranging between 52 -55. The biggest sample was that of 41 patients (41%) with hematocrit ranging between 56-59. Besides, 25 patients (25%) also had significantly increased hematocrit levels of 60% or higher. The graphical representation shows that there is more patients with moderately to severely increased hematocrit levels.

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Table 2: Distribution of Patients Based on Hematocrit Values

Hematocrit (%)	Number of Patients	Percentage (%)
52 – 55	34	34%
56 – 59	41	41%
≥ 60	25	25%
Total	**100**	**100%**

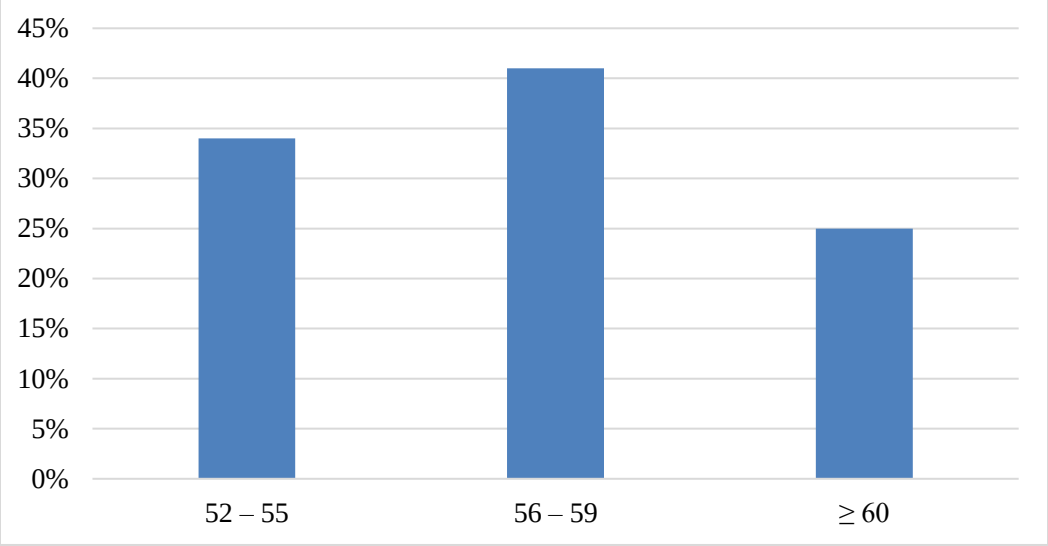

Figure 2: Graphical Representation of Distribution of Patients Based on Hematocrit Values

The hematocrit values are predominantly greater than 55 percent which refers to the fact that there is an enormous growth of the red cell mass as part of the physiological reaction to long-term stress of hypoxia. High hematocrit increases oxygen carrying capacity but also raises blood viscosity and can lead to thrombotic and circulation complications in patients. The observed pattern of distribution favors the compensatory mechanism of erythrocytosis in secondary polycythemia and supports the significance of tracking hematocrit rates in order to inform clinical care and avoid the occurrence of adverse effects of hyperviscosity.

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Table 3 and Figure 3 illustrate etiology of the chronic hypoxia among the study participants who were diagnosed with secondary polycythemia. Chronic obstructive pulmonary disease (COPD) was the most prevalent underlying cause of chronic hypoxia with 38 patients (38%); this out of the 100 patients. Obstructive sleep apnea was found in 22 patients (22%), and cyanotic congenital heart disease played a role in 16 (16%). It was reported that 14 patients (14%), had interstitial lung disease and 10 patients (10%), lived at high altitudes. The graphical representation shows COPD as the biggest etiological factor which is followed by sleep-related and cardiac causes.

Table 3: Etiological Distribution of Chronic Hypoxia Among Study Participants

Cause of Chronic Hypoxia	Number of Patients	Percentage (%)
Chronic Obstructive Pulmonary Disease (COPD)	38	38%
Obstructive Sleep Apnea	22	22%
Cyanotic Congenital Heart Disease	16	16%
Interstitial Lung Disease	14	14%
High-Altitude Residence	10	10%
Total	**100**	**100%**

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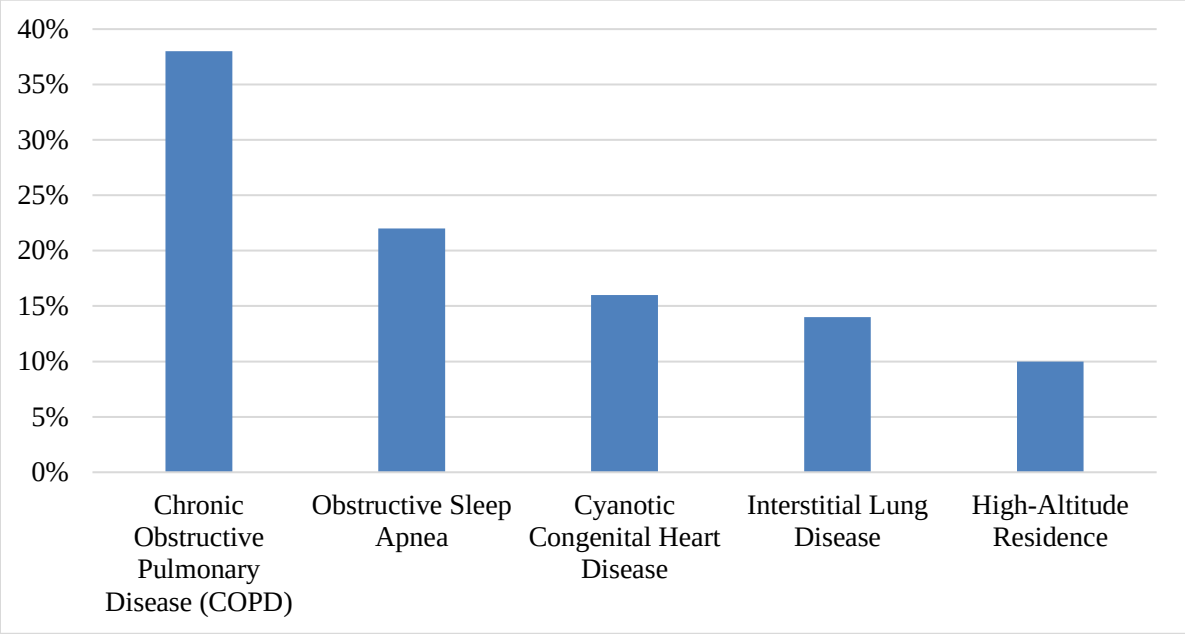

Figure 3: Graphical Representation of Etiological Distribution of Chronic Hypoxia Among Study Participants

The etiological trend identifies chronic pulmonary illnesses as the main causes of persistent hypoxia causing secondary polycythemia. The pre-eminence of COPD accentuates the importance of chronic airflow restriction and deterioration in gas exchange in activating compensatory erythrocytosis. The significant role of obstructive sleep apnea demonstrates the role of the intermittent nocturnal hypoxia as an inductor of higher levels of erythropoietin. Such results highlight the importance of ensuring that underlying hypoxic pathologies are treated to achieve successful management of secondary polycythemia and avoid further development of hyperviscosity-related comorbidities.

The etiological cause of chronic hypoxia among the study participants proves that pulmonary disorders are the most prevalent primary causes contributing to secondary polycythemia. The most common was chronic obstructive pulmonary disease (COPD) and then was obstructive sleep apnea. These disorders can be defined by the presence of protracted or repeated periods of decreased oxygenation underdeveloped ventilation and gas exchange. The given pattern is an

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indication of the prevalence of respiratory etiologies in those patients who had sustained hypoxia with compensatory erythrocytosis.

Table 4: Distribution of Patients Based on Clinical Symptoms of Hyperviscosity

Clinical Symptoms	Number of Patients	Percentage (%)
Asymptomatic	34	34%
Headache & Dizziness	28	28%
Fatigue & Dyspnea	22	22%
Visual Disturbances	10	10%
Thrombotic Events	6	6%
Total	**100**	**100%**

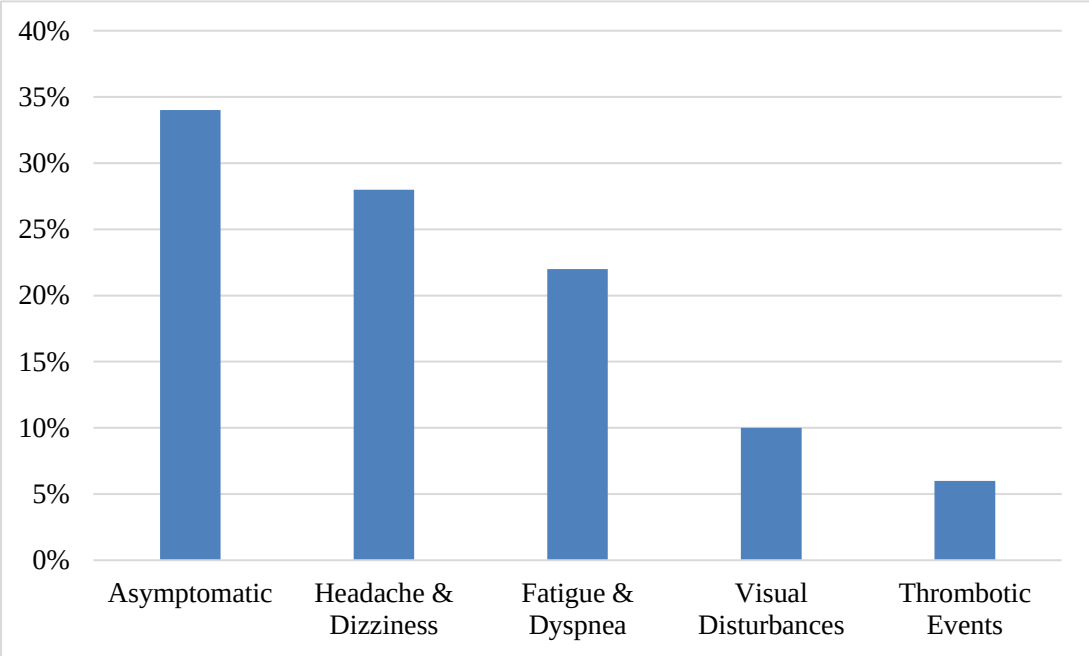

Figure 4: Graphical Representation of Distribution of Patients Based on Clinical Symptoms of Hyperviscosity

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The preeminence of COPD emphasizes how the effects of chronic airflow restriction and chronic hypoxemia provoke the production of red blood cells mediated by erythropoietin. The important role of the obstructive sleep apnea highlights the importance of intermittent hypoxia of the night in the provocation of the process of erythropoietic. All these results highlight that proper management of the underlying hypoxic disorders is essential in the control of secondary polycythemia and prevention of the secondary complications of a high blood viscosity like thrombotic events.

5. DISCUSSION

The study indicates that secondary polycythemia linked with the chronic hypoxic condition is typified by a compensatory rise in the levels of hemoglobin and hematocrit. Moderate to severe increase of these parameters were observed in the majority of patients and indicated an increased erythropoiesis due to prolonged hypoxemia. High hematocrit of more than 55% means that there is an excess of red cell mass that is beneficial in the transportation of oxygen except that it predisposes the patients to hyperviscosity related complications, such as thrombotic events. The hematological pattern of the case in point supports the adaptive character of secondary polycythemia and separates it out of the primary myeloproliferative disorders.

Chronic pulmonary diseases especially chronic obstructive pulmonary disease became the main etiological causes, then there were obstructive sleep apnea and other hypoxic disorders. These disorders also cause long-lasting or periodic hypoxia, which results into high production of erythropoietin and erythrocytosis. The symptoms of hyperviscosity exhibited in some of the patients underscore the need to diagnose and manage this condition early. The management of hypoxic condition underlying the case is the foundation of the treatment to avoid complications and enhance clinical outcomes.

6. CONCLUSION

The current paper emphasizes that the predominant features of secondary polycythemia in chronic hypoxia includes large increases in the levels of hemoglobin and hematocrit as a physiological compensatory mechanism to enhance tissue oxygenation. The most prevalent etiological

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determinants were found to be chronic pulmonary disorders, especially chronic obstructive pulmonary disease, followed by obstructive sleep apnea and any other citation that is related to sustained or intermittent hypoxia. Despite increasing oxygen-carrying capacity, continually high levels of hematocrit elevate the blood viscosity and thus can lead to hyperviscosity-related complications such as thrombotic events. The results underline the need of a thorough clinical assessment and frequent hematological surveillance of patients with persistent hypoxia. Preventing complications and enhancing the general clinical outcome in patients with secondary polycythemia depends on the early detection and proper treatment of the underlying hypoxic disorder as opposed to aggressive hematological intervention.

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