

Analysis of Therapeutic Phlebotomy in Patients of Polycythemia: A Single Center Study

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ABSTRACT

Introduction: Polycythemia is increased red cell mass according to age and sex of the individual. It could be primary (Polycythemia Vera), or secondary, due to chronic hypoxia or increased erythropoietic drive. Polycythemia is managed with therapeutic phlebotomy along with treating the underlying cause if determined. Phlebotomy of one unit whole blood should result in fall of Hb of at least 1g/dl. This study was conducted to see the effect of phlebotomy on fall in Hb level.

Different parameters which can affect Hb levels in polycythemia patients, like age, JAK-2 mutation status and underlying cause were also studied.

Methodology: A cross sectional study was conducted at blood bank of Pakistan Atomic Energy Commission (PAEC) General Hospital, Islamabad Pakistan January 2020 to December 2020. Data were collected from 121 patients of Polycythemia vera who reported in blood bank for phlebotomy.

Results: The average pre phlebotomy hemoglobin of the patients was 17.45g/dl, which dropped to 15.97g/dl after phlebotomy. In total, 89 (73.5%) patients who underwent phlebotomy had a fall in Hb of greater than or equal to 1g/dl, while in 32 (26.4%) patients, Hb drop was less than 1g/dl. One hundred and five patients underwent multiple therapeutic phlebotomies to maintain their hemoglobin within normal range.

Conclusion: This study has shown that there is fall in Hb as result of recommended phlebotomy leading to relief in symptoms due to Polycythemia. Phlebotomy is the basis of treating polycythemia, although in secondary polycythemia the underlying cause should also be diagnosed and treated.

Key Words: Polycythemia, phlebotomy, Hemoglobin.

Authors' Contribution:

^{1,2}Conception; Literature research; manuscript design and drafting; ^{2,3} Critical analysis and manuscript review; ^{1,4} Data analysis; Manuscript Editing.

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Introduction

Polycythemia is one of the Myeloproliferative disorders characterized by increased red cell mass according to the age and gender of the individual. Polycythemia can be due to hematopoietic clonal expansion, in which case it is designated as polycythemia vera (PV)¹ or due to any secondary

cause such as smoking, chronic heart disease, hypertension, chronic obstructive pulmonary disease², which result in hypoxia, known as secondary polycythemia.

PV is most common type of myeloproliferative neoplasms (MPNs).³ It is a hematopoietic disorder due to clonal expansion of erythroid precursors, leading to an increase in hemoglobin and red cell

mass. In PV erythroid precursors are either hypersensitive to erythropoietin or proliferate independent of erythropoietin stimulus. In most of these cases, one of the three driver mutations is positive i.e. *JAK2*, *CALR* or *MPL*, among them *JAK2* is most common mutation.⁴ The patients may present with vague symptoms like fatigue and pruritis with or without splenomegaly. Total leukocyte count and platelet counts are also increased in many cases. PV can transform into acute myeloid leukemia or myelodysplastic syndrome.⁵ Although the incidence rate is low, but if it occurs it may lead to life threatening consequences. The time from the progression of PV to leukemia is highly variable and can range from a few years up to more than 20 years.⁶

Both types of polycythemia result in symptoms of hyperviscosity, such as headache, erythromelalgia and visual disturbances. Polycythemia also carries a risk of thrombotic complications such as coronary artery disease, stroke, and deep vein thrombosis. The risk of thrombotic complications is much higher in patients with PV than those with any secondary cause of polycythemia.⁷ Secondary polycythemia develops due to several causes, including hypoxic drive that leads to increased release of erythropoietin, thus resulting in increase in red cell mass. The causative agents include high altitude, smoking, hypertension, cyanotic heart disease, chronic respiratory disorders, glomerulonephritis and renal cyst. A renal tumor leading to spurious erythropoietin release or any other erythropoietin releasing tumor also causes polycythemia.⁸ Polycythemia occurs in both genders and in any age group; however, the incidents are reported more in elderly individuals. A study conducted on 1545 patients of polycythemia vera showed that the median age at the time of diagnosis was 61 years.⁹ Different studies have shown that polycythemia occurs more commonly in men. However thrombotic complications are not specifically associated with either gender.¹⁰

The treatment in both primary and secondary polycythemia is directed at reducing hematocrit to <45.¹¹ This results in improvement in constitutional symptoms as well as a decrease in thrombotic episodes. However, it is equally essential to determine any underlying secondary cause of the disease before starting the treatment. If any secondary cause is found it is necessary to treat the cause for proper management of polycythemia. A decline in hematocrit is achieved through therapeutic phlebotomy. Phlebotomies are usually performed at various interval till target hematocrit is achieved. The phlebotomy may be performed after a gap of several weeks, depending on the initial level of hematocrit and the fall in Hb.

The current study aims to stratify data of polycythemic patients based on age, gender, cause, *JAK2* mutation status and fall in hematocrit following phlebotomy.

Methodology

This cross-sectional study was conducted over a period of one year from January, 2020 to December, 2020 at blood bank of Pakistan Atomic Energy Commission (PAEC) General Hospital, Islamabad, Pakistan. Ethical approval was obtained from hospital ethical committee prior to the study. A total of 121 patients diagnosed with polycythemia were selected by purposive sampling. Among total of 121 patients, 116 (95.86%) were male and 6 (4.95%) were female with male to female ratio of 19:1. The mean age of the patients at the time of presentation was 45 years, with a range of 19 to 76 years.

Patients having Hb > 16.5 g/dl and hematocrit > 48 were selected for the study. Hemoglobin and hematocrit were done on peripheral collected in EDTA. All samples were run on hematology analyzer Sysmex XN1000 (Japan). Phlebotomy was done using 17G needle after informed consent and after obtaining vital signs. Patients were counseled about the procedure and were constantly monitored.

Results were entered and analyzed using SPSS version 20.0.

Results

Out of 121 patients, the most common blood group was B positive [47 (39%)], while the least common were O negative and AB negative, with one patient belonging to each blood group (0.8% each), figure 1. The average pre phlebotomy hemoglobin of the patients was 17.45g/dl while post-phlebotomy, hemoglobin was 15.97g/dl. Among all, patients those underwent phlebotomy, 89 (73.5%) had a fall in Hb of greater than or equal to 1g/dl, while in 32 (26.4%) patients, Hb drop was less than 1g/dl. 105 patients out of 121 underwent more than one therapeutic phlebotomies to maintain their hemoglobin and hematocrit within normal range, figure 2.

The patients presented with rise in hemoglobin were also suffering from a number of underlying causes including smoking, cardiac disease, renal or liver disease and chronic obstructive pulmonary disease. Smoking was found to be the cause of secondary polycythemia in 27.27% of the patients, and it was followed by unknown cause in 23.9% patients, figure 3.

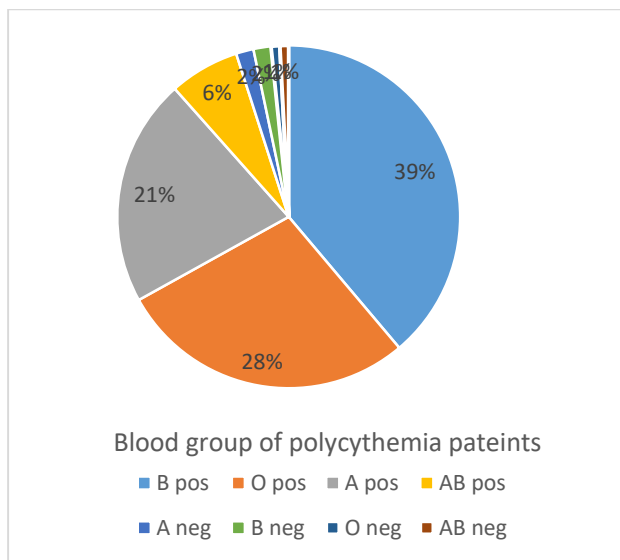


Figure 1: Distribution of blood groups among patients

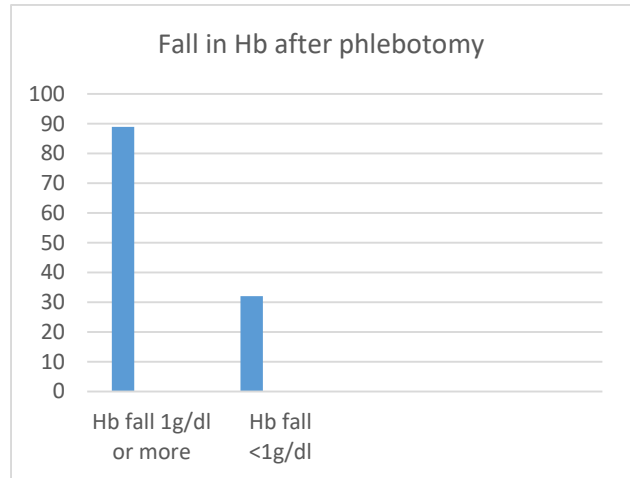


Figure 2: Fall in Hb after phlebotomy

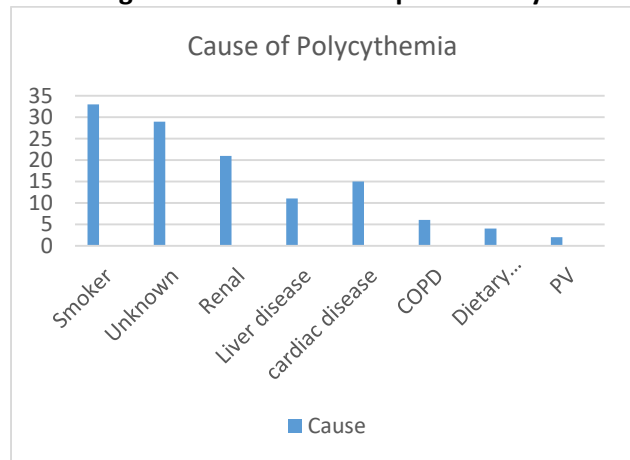


Figure 3: Causes of Polycythemia in study patients

Discussion

The World Health Organization (WHO) defines *JAK2V617F* as a major criterion for the diagnosis of Polycythemia Vera. Other markers include Hb > 16.5 in men and 16 in women, or hematocrit >49% in men and 48% in women, or RBC mass >25% above the mean predicted value.¹² Polycythemic patients present with a variety of symptoms, among which headache is quite common.¹³ Facial plethora is also seen in a large number of patients. Several patients complain of erythromylgia or pruritus. Splenomegaly is seen in a large number of patients with polycythemia vera¹⁴ In the current study, smoking was found to be the most common cause of secondary polycythemia.

The studies have also reported that smokers have increased red cell mass and decreased plasma volume, due to increased carboxyhemoglobin levels which result in hypoxia.¹⁵ A study conducted on 40 healthy individuals and 40 smokers in Taif, Saudi Arabia reported that smoking causes damage to alveolar tissue, resulting in inflammation, as well as injury to vascular tissue which causes leukocytes to increase. Smoking also adversely affects gaseous exchange in the lungs, resulting in hypoxia and leading to an increase in the red cell mass.¹⁶ In our study, *JAK2* mutation status was analyzed to diagnose patients of polycythemia vera, however it was only found positive in 02 patients out of 121. Bases on this finding other patients were evaluated for secondary causes. In 29 patients of study among 121, the cause of polycythemia could not be determined despite conducting all investigations and taking a detailed history. In another study conducted on 231 patients, in 40 patients no cause of polycythemia was detected.¹⁷

Phlebotomy is the mainstay of treatment in polycythemic patients, with an aim to decrease hematocrit to below 45%. Taking in account the hemoglobin, phlebotomy would be considered successful if Hb falls 1g/dl or more after one phlebotomy. Phlebotomy also results in a decrease in blood viscosity that reduces subsequent occurrence of thrombotic events. Studies have also shown that at maintained hematocrit below 45%, the risk of cardiovascular morbidity is decreased. In our study, we recorded the Hemoglobin level of patients before and after phlebotomy. About 73.5% of patients had a fall in Hb of 1g/dl or more, while in 26.4% of patients, a fall in Hb was less than 1g/dl.

Conclusion

A number of factors can lead to an increase in Hb, among them smoking is a very common cause along with other associated illnesses like renal disease, lung disease, cardiac disease and malignancies. Phlebotomy is the basis of treating polycythemia, although in secondary polycythemia

the underlying cause requires further diagnosed and treated accordingly.

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