

# The Association of Erythrocytosis with Uterine Leiomyoma - A tertiary care study

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## ABSTRACT

**Aim:** To study the association of Leiomyoma with size, hemoglobin and red blood cell count.

**Design:** Descriptive cross-sectional study.

**Place and duration of study:** Pathology and Gynecology department, King Edward Medical University (KEMU), Lahore, from December 2018–May 2019.

**Methods:** Both pre- and post-menopausal females of diagnosed cases of Leiomyoma undergoing myomectomy or hysterectomy were recruited in this study after taking informed consent. Data was collected by 2 students. Patients were interviewed using a proforma containing questions on age, marital status, parity/gravidity, presenting complaints, disease character, type of surgical procedure either leiomyomectomy or hysterectomy, complete blood count and biopsy reports. Written consent was obtained from each participant before their involvement in the study. Data was analyzed by SPSS 23. Quantitative variables, like age and size of Leiomyoma were presented as mean  $\pm$ SD. Qualitative variables like marital status, menstrual status either pre-menopausal or post-menopausal and Polycythemia were presented as frequency and percentages.

**Results:** In this study, women who had undergone hysterectomy or myomectomy were between the ages of 20-60 years. 94% of the women were pre-menopausal and 6% were post-menopausal. 86% were married and 14% were unmarried. Those with parity 0 were 20%, parity 1 (12%), 2(26%), 3(14%), 4(10%), 5(12%), 6(6%).

The most common presenting complaint was pain with abnormal uterine bleeding i.e. 40%, 24% presented with pain only and 36% presented with abnormal uterine bleeding only. Leiomyoma between the sizes of 1-5 cm were 14%, 5-10 cm (38%), 10-15 cm (30%) and >15 cm (18%). 60% of the patients had only one Leiomyoma, 12% had 2 and 28% had >2 Leiomyomas. None of the patients suffering from Leiomyoma had increased Hemoglobin. Most of the patients (68%) had normal RBC count i.e., 3.92-5.13 trillion cells/L, 6% had <3.92 and 26% had RBC count >5.13 trillion cells/L. 36% patients had Hematocrit <34% and 64% had normal values of Hematocrit i.e. 34-54%.

**Conclusion:** Leiomyoma may cause Polycythemia as evident by many researches but our study did not provide decisive affirmation of this association showing no significant correlation between Uterine Leiomyoma with Polycythemia in our set-up.

**Keywords:** Leiomyoma, Polycythemia, Hysterectomy, Myomectomy.

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## INTRODUCTION

Uterine Leiomyoma is a very common tumor in pre-menopausal women, the occurrence of which is rare in post-menopausal females and usually describes its malignant potential into Leiomyosarcoma<sup>1</sup>. Pre-menopausal women with Leiomyoma usually present with uterine bleeding/ menorrhagia and hysterectomy is the most common surgical procedure performed for dysfunctional uterine bleeding<sup>2</sup>.

Polycythemia (to be used synonymously as erythrocytosis) is usually seen in association with Uterine Leiomyomas with rise in hemoglobin and hematocrit values. This Leiomyoma induced Erythrocytosis becomes resolved after myomectomy and hysterectomy with normalization of hemoglobin values indicating a complete recovery from Polycythemia and is known as Myomatous Erythrocytosis Syndrome<sup>3</sup>.

Various etiologies have been proposed to elucidate the association between Uterine Leiomyoma and Erythrocytosis, one of which is ectopic erythropoietin production by the tumor itself<sup>4</sup>.

Erythropoietin has been extracted from the cytoplasm of tumor cells and measured by several investigators to determine whether the origin of Polycythemia is Erythropoietin overproduction by tumor cells<sup>5</sup>.

A lot of studies have been conducted to study the association between Uterine Leiomyomas and secondary polycythemia and to determine the etiology of this unique clinical picture but no definite etiology has been confirmed yet to reflect the cause of Polycythemia associated with Uterine Leiomyomas<sup>6</sup>.

There is controversial data regarding the association between these two entities e.g., study conducted by Donnette Simms-Stewart and Horace Fletcher in the University of the West Indies supports the evidence of association between uterine Leiomyoma and Polycythemia while some studies do not provide supportive evidence to confirm this etiology<sup>7</sup>. We want to study and prove or disprove the association between Leiomyomas and Polycythemia in our population.

## METHODOLOGY

This study was a descriptive cross-sectional study, performed with collaboration of pathology and Gynecology & Obstetrics departments at Lady Aitcheson and Lady Wallingdon Hospitals/ King Edward Medical University. This study was conducted from Dec 2018 to May 2019. Ethical

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clearance was obtained from Institutional Review Board of King Edward Medical University, Lahore. 50 patients were included in the study with the help of selective sampling. Both pre- and post-menopausal female patients who had undergone leiomyomectomy or hysterectomy with ages between 15 and 90 years were recruited in this study after taking informed consent. Patients with autolyzed, inadequate or insufficient biopsies and patients, who did not give consent, were excluded from the study. Data was collected by 2 students. Patients were interviewed using a proforma containing questions on age, marital status, parity/gravidity, presenting complaints, disease character, type of surgical procedure either leiomyomectomy or hysterectomy, complete blood count and biopsy reports. Written consent was obtained from each participant before their involvement in the study. Data was analyzed by SPSS 23. Quantitative variables like age and size of Leiomyoma were presented as mean ±SD. Qualitative variables like marital status, menstrual status either pre-menopausal or post-menopausal and Polycythemia were presented as frequency and percentages.

**RESULTS**

In this study, women who had undergone hysterectomy or myomectomy were between the ages of 20-60 years. 94% of the women were pre-menopausal and 6% were post-menopausal. 86% were married and 14% were unmarried. Those with parity 0 were 20%, parity 1(12%), 2(26%), 3(14%), 4(10%), 5(12%), 6(6%). The most common presenting complaint was pain with abnormal uterine bleeding i.e., 40%, 24% presented with pain only and 36% presented with abnormal uterine bleeding only. Leiomyomas between the sizes of 1-5 cm were 14%, 5-10 cm (38%), 10-15cm (30%) and >15cm (18%). 60% of the patients had only one Leiomyoma, 12% had 2 and 28% had >2 Leiomyomas. None of the patients suffering from Leiomyoma had increased Hemoglobin. Most of the patients (68%) had normal RBC count i.e., 3.92-5.13 trillion cells/L, 6% had <3.92 and 26% had RBC count >5.13 trillion cells/L. 36% had Hematocrit <34% and 64% had normal values of Hematocrit i.e., 34-54%. The relation of size of Leiomyoma with Hemoglobin and RBC count is described with the help of the following tables.

Table 1: Relationship of size of Leiomyoma with RBC count.

Size	RBC count (trillion cells/L)			Total
	3.92-5.13 (normal)	LOW <3.92	HIGH >5.13	
1-5	5	0	2	7
5-10	9	3	7	19
10-15	13	0	2	15
>15	7	0	2	9
Total	34	3	13	50

Table 2: Relationship of size of Leiomyoma with hemoglobin.

Size	Hemoglobin (g/dl)		Total
	<11	11-15	
1-5	1	6	7
5-10	9	10	19
10-15	6	9	15
>15	2	7	9
Total	18	32	50

**DISCUSSION**

Leiomyoma is the commonest gynecological tumor in females and a number of literatures have shown its association with Polycythemia in which rapid development of Polycythemia from anemia was a striking feature. Polycythemia is said to be present in females when hemoglobin is above 16.5g/dl, packed cell volume is greater than 48% and RBC count is above 5.13 trillion cells/L<sup>5,8</sup>. Thomson and Marson first proposed the term Myomatus Erythrocytosis Syndrome in 1953<sup>9,10</sup>. Since then various investigations have been done to confirm its etiology e.g., Patel et al. and Kohama et al. proposed the etiology of erythropoietin production by tumor cells, but no definite etiology has been proposed yet<sup>11,12</sup>.

We experienced quite few cases of Uterine Leiomyomas in Lady Aitcheson and Lady Wallingdon hospitals, which were diagnosed with single or multiple Leiomyomas by histopathological techniques after being undergone hysterectomy or myomectomy. Some criteria have been defined to label the cases as Polycythemia e.g. increased hemoglobin, RBC count and Hematocrit values, our study fulfilled the these criteria and collected the values of hemoglobin, RBC count and Hematocrit of the patients with Leiomyoma before their hysterectomies.

Evans et al. stated in their study that incidence of Leiomyoma increases as the woman grows older with highest incidence between 40-60 years<sup>13</sup>. In addition, Shrestha et al. reported a case in which they described Leiomyoma as an estrogen dependant tumor that regresses after menopause<sup>14</sup>. In our study, percentage of females presented with Leiomyoma with age between 25-35 years was the highest, while 6% of our females presented in their postmenopausal age. Parazzini et al. evaluated that parous women have more risk of developing Leiomyoma than nulliparous and this risk decreases with increased parity<sup>15</sup>. In our case, 7% unmarried and 20% married females with parity 0 and 6% with parity 6 presented with Leiomyoma-associated-Polycythemia.

Sabery et al. discussed in their study the presenting complaints which most of the females experienced when they presented with Leiomyoma and these were AUB, pelvic pressure symptoms, menorrhagia, infertility, abortions and preterm labor<sup>(1)</sup>. In our case, 36% of our study population presented with abnormal or heavy uterine bleeding only, 24% presented with pain only and 40% presented with both i.e., pain and bleeding. Association of large and multiple uterine fibroids with Polycythemia has been described in many studies before e.g., Ozsaran et al and Ghaffar et al illustrated the association between large uterine fibroids and Polycythemia<sup>16,17</sup>. On the other hand, as we see in our results, patients; either with single or multiple, small or large Leiomyoma, none presented with Hb >15g/dl or hematocrit >54% and only 26% presented with RBC count >5.13 trillion cells/L.

Despite many studies provide definite evidences to prove the association of Leiomyoma with Erythrocytosis e.g. Hertko et al. highlighted the association of myoma and erythrocytosis and its remission after surgery<sup>18</sup>. In another study, Robb et al. also discussed Leiomyoma and its association with Polycythemia<sup>19</sup>. Similarly, Pollio et al. did experimental study to prove the production of erythropoietin

from the Leiomyoma tissue to elaborate the pathogenesis of its association with erythrocytosis<sup>20</sup>. In our study, no patient with Leiomyoma presented with increased Hb or hematocrit values rather 36% patients had Hb value <11g/dl and only 26% presented with RBC count >5.13 trillion cells/L which could be due to some other underlying cause.

## CONCLUSION

Leiomyoma may cause Polycythemia as evident by many researches but our study did not provide decisive affirmation of this association showing no significant correlation between Uterine Leiomyoma with Polycythemia in our set-up.

**Conflict of interest:** There was no conflict of interest.

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