



TO STUDY CORRELATION BETWEEN LEVEL OF PROLACTIN AND UTERINE LEIOMYOMA

Obstetrics & Gynaecology

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KEYWORDS

Uterine leiomyoma is the most common benign uterine tumor. It is monoclonal tumor of the smooth muscle cells of the uterus. An estimated incidence of leiomyoma is 20%-40% in women during their reproductive years including symptomatic and asymptomatic conditions (1). The reported incidence ranges from 30% to 70% in premenopausal women and the tumor grows at an average rate of 1.2cm per 2.5 years (2). Fortunately most of the leiomyomas remain asymptomatic. The incidence of symptomatic leiomyomas is about 3%. Symptoms include menstrual disturbances which affects 30% of women, pressure symptoms, pregnancy related problems, and infertility. Uterine myomas, especially submucosal myomas are associated with adverse reproductive outcomes (6).

Prolactin, a 198-amino-acid polypeptide secreted by the anterior pituitary lactotroph, is the primary trophic factor responsible for the synthesis of milk by the breast. Several forms of this hormone, which are named according to their size and bioactivity, are normally secreted (11). Prolactin is also secreted by the extra-pituitary sites as uterus, colon etc. There is an important role of Prolactin hormone for initiating many types of tumors in reproductive and also in non-reproductive tissues which may be due to local excretion or accumulation. Prolactin mediates this function by interacting with type-1 cytokine receptors and signals through Janus Kinase, signal transducers, and activators of transcription (JAK/STAT) pathways. It can act on myometrium as a growth hormone in the form of autocrine and paracrine hormone. Although, it is isolated as a pituitary hormone, Prolactin is expressed in other tissues including uterine leiomyoma.

PRL level may be used as a monitor for detecting an early development of myoma tumor or for assessing the efficiency of treatment. Taking into consideration PRL as vigorous contributor in tumorigenesis; should motivate and support the expansion of novel treatments aimed at decreasing PRL production or by blocking its receptors (7). Treatment of myoma depends on symptoms, patient's age, fertility status, previous obstetric performance, and the location and size of the myoma. Because the tumors are hormonally dependent, develop during reproductive period, and are suppressed by menopause, current medical treatments involve mainly hormonal manipulations. Studies have shown the presence of estrogen and progesterone receptors with higher concentrations in myomas than in the surrounding endometrium (12, 13). Progesterone seems to have a dual effect on myomas by altering local growth factors. It is suggested that one effect of progesterone is to stimulate myoma cell growth and survival by increasing epidermal growth factor (EGF) and Bcl-2 protein expression, as well as by decreasing tumor necrosis factor (TNF) alpha, expression in those cells; the second effect is to inhibit expression in uterine myoma cells.

AIMS AND OBJECTIVES

1. To diagnose Uterine Leiomyoma, and to confirm their size, site, and number.
2. To find the level of serum Prolactin in patients of Leiomyoma.
3. To establish the relation between the size and number of Leiomyoma to the level of serum Prolactin.

MATERIAL AND METHOD

The present study was done in Swaroop Rani Nehru Hospital and

Kamla Nehru Memorial Hospital, Department of Obstetrics and Gynecology, PRAYAGRAJ on 100 patient over a period of 1 year (JULY 2019-JUNE 2020)

INCLUSION CRITERIA

All women between the age of 20-50 years who presented to SRN and KMNH gynaecology outpatient department with leiomyoma uterus, whether symptomatic or asymptomatic and had no apparent cause of hyperprolactinemia were included in the study.

EXCLUSION CRITERIA

1. Prolactinoma
2. Physiological hyper secretion such as pregnancy
3. Acromegaly
4. Hypothyroidism
5. Chronic liver failure
6. Cirrhosis
7. Epilepsy
8. Some drugs as Calcium channel blockers
9. Suspected adenomyosis
10. Any other uterine pathology such as polyp, endometriosis etc.
11. Hormonal therapy within 3 months
12. Any malignancy

ASSESSMENT OF THE SIZE, NUMBER AND LOCATION OF LEIOMYOMA

Ultrasonography was done using Gevoluson E8 and Siemens S200Acuson ultrasound units using transabdominal (3.5–5.0 mHz) and transvaginal (5.0–7.0 mHz) ultrasound probes. In USG the uterus and adenexa were examined systematically and Leiomyomas were recorded only if their maximum diameter was at least 0.5cm and could be visualized in all the three planes. Each individual Leiomyoma was measured with their 3 perpendicular diameters (sagittal, longitudinal, and transverse). Volume was calculated by the ellipsoid method with the formula $V = 0.5233(D1 \times D2 \times D3)$. The location of all the fibroids was noted.

Prolactin was measured using BIO-RAD 680 ELISA microplate reader version 1.7.

OBSERVATION

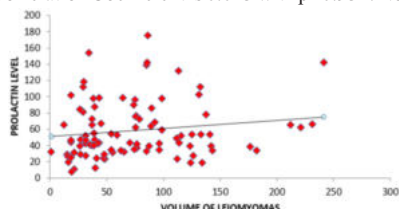
The current study was carried out in the women of reproductive age group of 20 to 50 years with leiomyoma uteri, who presented to the outpatient department or were admitted in the department of Obstetrics and Gynecology of Swaroop Rani Hospital and Kamla Nehru Hospital, Prayagraj over a period of one year.

TABLE 2: Volume of leiomyoma and the level of Prolactin

VOLUME OF LEIOMYOMA (cm ³)	Group 1 (n=45)			Group 2 (n=51)			Total (n=96)		
	NUMBER of Women	PERCENTAGE	PROLACTIN LEVEL	NUMBER of Women	PERCENTAGE	PROLACTIN LEVEL	NUMBER of Women	PERCENTAGE	PROLACTIN LEVEL
<50	30	66.7%	56.37±2.923	10	19.61%	52.73±2.817	40	41.7	55.46±2.86
51-100	10	22.2%	47.30±1.517	20	39.21%	66.70±3.296	30	31.3	60.23±2.94

101-150	5	11.11%	58.12±3.140	15	29.41%	54.65±2.458	20	28.8	55.52±2.5
151-200	-	-	-	2	3.92%	36.30±3.11	2	2.1	36.30±3.11
≥201	-	-	-	4	7.84%	57.67±1.564	4	4.2	57.67±1.564

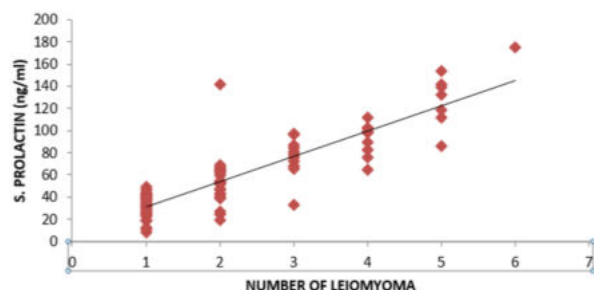
Pearson Correlation Coefficient is 0.013 with $p=0.934$. No Correlation



This table compares the size of the Leiomyomas and the Prolactin level. As it is clearly seen there is no correlation between the volume of Leiomyoma and level of Prolactin in either group. On calculating the Pearson correlation coefficient; the value comes out to be 0.013, and the p value comes out to be 0.934, proving the null hypothesis that there exists no correlation between the size of the leiomyoma and level of Prolactin.

Table 3 Number of Leiomyoma and level of Prolactin

NO. OF FIBROIDS	Group 1 (n=45)		PROLACTIN LEVEL	Group 2 (n=51)		PROLACTIN LEVEL	Total (n=96)		Total Prolactin Level
	Freq.	%		Freq.	%		Freq.	%	
1	20	44.4	35.0±8.2	19	37.3	37.0±7.9	39	40.6	35.9±8.0
2	11	24.4	53.7±7.0	16	31.4	56.0±12.5	27	28.1	55.0±10.5
3	6	13.3	64.7±17.8	6	11.8	64.2±25.3	12	12.5	64.5±20.9
4	4	8.9	80.6±13.8	5	9.8	82.3±10.4	9	9.4	81.5±11.2
5	3	6.7	100.2±13.0	4	7.8	105.4±14.5	7	7.3	103.2±13.0
6	1	2.2	154.0±0	1	2.0	165.1±0	2	2.1	159.5±7.8



Pearson Correlation Coefficient is 0.882 with $p=0.001$. Positive Correlation

The table shows the relation between the number of the fibroids and level of Prolactin in both the groups. It is evident from the above data that level of Prolactin is directly linked the number of fibroids. On calculating the Pearson correlation coefficient and p value which come out to be 0.882 and 0.001 respectively; it is seen that there is a positive correlation between the number of leiomyomas and level of serum Prolactin.

DISCUSSION

In the present study, majority of cases 40 (41.66%) with single or multiple Leiomyoma were of 36- 40 years in both the groups with the mean age range 35.16 ± 6.3 years, most patients i.e. 59 (61.46%) belonged to the urban area which reflects the greater concern of urban population towards health care.

More than half (62.5%) patients belonged to middle class family who came to seek medical advice and that too when they have symptoms affecting day to day activity.

Most of the subject (97.9%) were married and were second para (32.3%) i.e. had low parity.

Approximately half of the cases (51.0%) had normal body mass index i.e. $18.6-24.99 \text{ kg/m}^2$

More than half (69.8%) cases presented with heavy menstrual bleeding

at the beginning of treatment.

we found that on calculating the Pearson correlation coefficient between the volume of leiomyoma and level of Prolactin levels; the value comes out to be 0.013, and the p value comes out to be 0.934, proving the null hypothesis that there exists no correlation between the size of the leiomyoma and level of Prolactin. This is in accordance with the study done by **Baban et al (2008)** who found no correlation between size and location and level of Prolactin, **Ashraf et al (2018)** found the p value to 0.101, which was insignificant. **Ahmed et al (2019)** also found no correlation between size of the leiomyoma and level of Prolactin.

In this study it was found that a relation between the number of the fibroids and level of Prolactin exists in both the groups. On calculating the Pearson correlation coefficient and p value which come out to be 0.882 and 0.001 respectively showing that there is a positive correlation between the number of leiomyomas and level of serum Prolactin. It is in accordance with the study conducted by **Baban et al (2009)** who found a positive correlation between the level of Prolactin and number of Leiomyoma and **Ahmed et al (2019)** who also arrived at a similar conclusion where the level of Prolactin was $141.78\pm14.37 \text{ ng/ml}$ in case of single Leiomyoma and was as high as $534.1\pm41.75 \text{ ng/ml}$ in patients with 5 Leiomyomas. **Ashraf et al (2018)** found a positive correlation between the level of Prolactin and number of Leiomyoma with a p value of 0.001.

CONCLUSION

1. In the present study, majority of cases 40 (41.66%) with single or multiple Leiomyoma were of 36- 40 years in both the groups with the mean age range 35.16 ± 6.3 years
2. In this study most patients i.e. 59 (61.46%) belonged to the urban area which reflects the greater concern of urban population towards health care.
3. More than half (62.5%) patients belonged to middle class family who came to seek medical advice and that too when they have symptoms affecting day to day activity.
4. Most of the subject (97.9%) were married and were second para (32.3%) i.e. had low parity.
5. Approximately half of the cases (51.0%) had normal body mass index i.e. $18.6-24.99 \text{ kg/m}^2$
6. More than half (69.8%) cases presented with heavy menstrual bleeding at the beginning of treatment.
7. There exists no correlation between the size of the leiomyoma and level of Prolactin.
10. There is a positive correlation between the number of Leiomyomas and level of serum Prolactin.

Thus it was found that, there occurs a strong correlation with the level of Prolactin and presence of Leiomyoma which has a correlation to the number of fibroids. Thus Prolactin can be used as a biochemical marker for the myoma along with other clinical and laboratory findings for diagnosis and to monitor the treatment of Leiomyoma uterus. Though there is still a dearth of research regarding this and a lack of standardized biochemical marker for leiomyoma uterus, hence more research should be conducted to establish laboratory ranges for Prolactin to be used in Leiomyoma uterus.

REFERENCES

1. Levy G, Hill MJ, Plowden TC, Catherino WH, Armstrong AY. Biomarkers in uterine leiomyoma. *Fertil Steril*. 2013;99(4):1146-1152. doi:10.1016/j.fertnstert.2012.10.048.
2. Brun del Re R, del Pozo E, de Grandi P, et al. Prolactin inhibition and suppression of puerperal lactation by a Br-erocryptine (CB 154). A comparison with estrogen. *Obstet Gynecol* 1973;41:884-890.
3. Suh HK, Frantz AG. Size heterogeneity of human Prolactin in plasma and pituitary extracts. *J Clin Endocrinol Metab* 1974;39:928-935.
4. Eglund K, Gillerot S, Casanas- Roux F, et al. Sex steroid receptors in human myometrium and fibroids: changes during menstrual cycle and gonadotropin-releasing hormone treatment. *J Clin Endocrinol Metab* 1998;83(11):4092-4096.
5. Nisolle M, Gillerot S, Casanas-Roux F, et al. Immunohistochemical study of the proliferation index, oestrogen receptors and progesterone receptors A and B in leiomyomata and normal myometrium during the menstrual cycle and under gonadotrophin-releasing hormone agonist therapy. *Hum Reprod*. 1999;14(11):2844-50.