



## "HYPERPROLACTINEMIA: A POTENTIAL FACTOR IN INFERTILITY - INVESTIGATING THE RELATIONSHIP AND IMPLICATIONS".

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### ABSTRACT

Infertility is the inability to establish a clinical pregnancy after 12 months of regular unprotected sexual intercourse. Infertility can be of two types. When a couple has primary infertility, they are unable to conceive after a year without using birth control. However, the couple is unable to conceive after the first child if they have secondary infertility. About 21.9% of Pakistanis suffer from this prevalent issue, with 3.5% primary and 18.5% secondary infertility. Female infertility factors can be divided into the following broad categories polycystic ovary syndrome, hormonal disorders, pelvic inflammatory disease, endometriosis, prolactin deficiency, obesity, ovarian failure, lifestyle factors, and hyperprolactinemia. This study aims to find the relation of hyperprolactinemia with infertile women. It was a cross-sectional study with a sample (convenient) size of 108. This study was conducted from June 2023 to December 2023. The results show that 22.2% of infertile women aged 15 to 25 years, 60.2% of infertile women aged 26 to 35 years, and 17.6% of infertile women aged 36 to 45 years were infertile. Moreover, 79.6% of females had hyperprolactinemia and 20.4% had normal prolactin levels. The study also shows that 60.1% of females had primary infertility 39.9% had secondary infertility. Pearson's Correlation analysis was conducted to see the relationship between infertility and prolactin, PCOS, Blood pressure (BP), and diabetes. There was a significant positive correlation between infertility with prolactin. ( $p < 0.01$ ) and PCOS ( $p < 0.01$ ). The sample consisted of 108 participants for both variables. However, diabetes ( $p = 0.351$ ) and BP ( $p = 0.62$ ) show a nonsignificant negative correlation with infertility types.

**Keywords:** Hyperprolactinemia, infertility, PCOS.

## INTRODUCTION

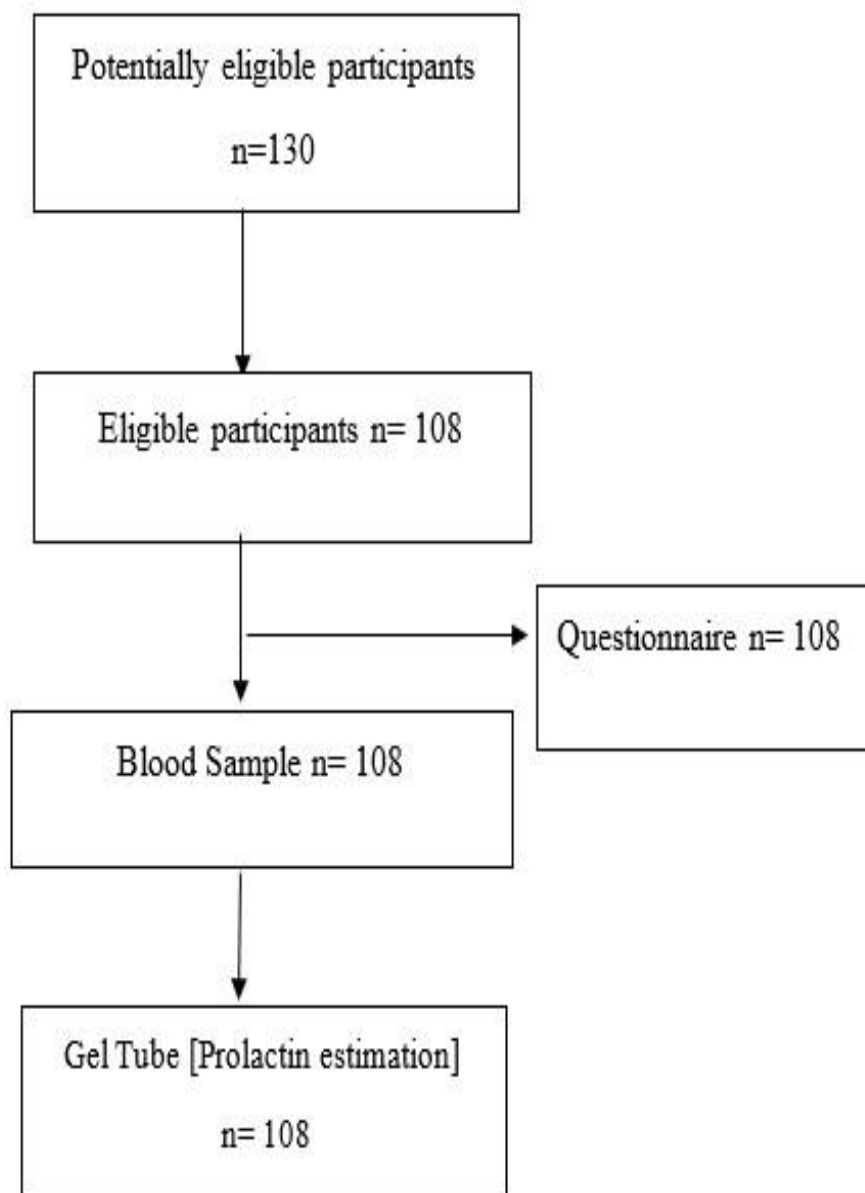
Infertility is a reproductive system disorder. It is the childbearing inability of couples after regular unprotected intercourse for twelve months. (Kumar DP et al., 2009). Globally, 10–15% of couples of reproductive ages are infertile and prevalence varies from country to country (Biennial Report 1992/1993). Infertility can be of two types. When a couple has primary infertility, they are unable to conceive after a year without using birth control. (Thonneau P et al., 1990). However, the couple is unable to conceive after the first child if they have secondary infertility. (Rai R et al., 2006). Pakistan has a frequency of infertility is 21.9%, of which 3.9% is primary infertility and 18.0% is secondary infertility. (Hakim A et al., 2001) Finland's infertility rate is over 10%, whereas Switzerland's is over 17%, 18%, and 21%. The prevalence of infertility among women has been reported to be between 5 and 8% in Norway, 6% in Poland, Romania, the Czech Republic, and Ukraine, while it is higher at >10% in Sweden and Canada. (LUNENFELD et al., 2014) Moreover, the infertility rate is recorded as 4% in Bangladesh, 6% in Nepal, and 4% in Sri Lanka. (Vaessen M et al., 1984)

Prolactin hormone is secreted by the anterior pituitary gland's lactotrophic cell. Thyrotropin releases prolactin, which is necessary for its synthesis and secretion. Dopamine and hormone (TRH) regulate lactotroph function. (Bayliss, 2003) Hyperprolactinemia is the term for the condition when nonlactating, non-pregnant women have elevated levels of prolactin hormone in their blood. The primary factor contributing to female infertility is an increase in prolactin levels during a woman's ovulation and menstrual cycles. This occurs as a result of changes in fertility hormones such as luteinizing hormone (LH) and follicle-stimulating hormone (FSH). (Crosignani, 2012). Infertility is caused by hyperprolactinemia by inhibition of GnRH from the hypothalamus. The follicular stimulating hormone (FSH) and luteinizing hormone (LH) are not secreted from the anterior pituitary because of the loss of GnRH secretion. In the follicular phase of the menstrual cycle, ovarian follicular development does not occur because of less amount of FSH. Furthermore, it also decreased estrogen production by the developing follicles. In the absence of an LH surge, the ovarian follicle does not rupture and release a mature ovum it can cause anovulation. The endometrium helps in the fertilization of the egg. The absence of LH can cause poorly developed endometrium. The implantation of an embryo cannot be supported by poorly developed endometrium. (Shibli-Rahhal et al., 2011) The anterior pituitary gland cannot secrete luteinizing hormone (LH) or follicle-stimulating hormone (FSH) when plasma prolactin levels are elevated. This gonadotropin deficiency leads to disruption of the menstrual cycle and a reduction in the release of ovarian estrogen, which in turn causes anovulation and infertility. (Kaiser UB, 2012). The primary hormones involved in the workup of female infertility are thyroid-stimulating hormones (TSH), prolactin (PRL), luteinizing hormone (LH), and follicle-stimulating hormone (FSH). Anovulation and infertility can result from an excess or lack of any of these hormones.

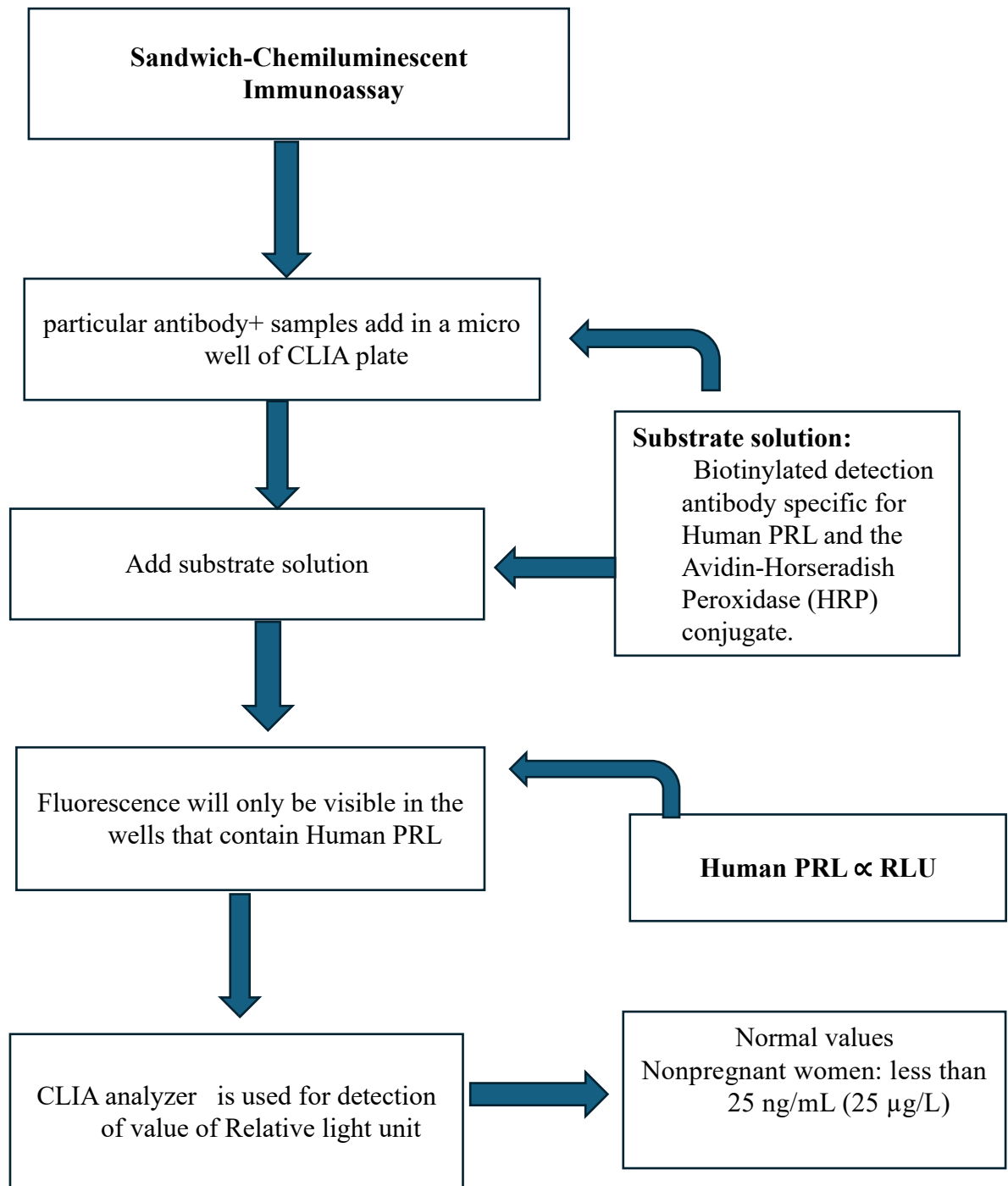
According to Bade Sara & Jakhar's study infertility is caused by a complex interplay of causes, one of which is an imbalance in hormones. The prevalence of hyperprolactinemia in infertile, euthyroid women is assessed in the current investigation. This research revealed that Prolactin levels in serum were  $13.89 \pm 10.03$  ng/ml on average. Thirteen of the 153 subjects or 8.50% of the total, exhibited hyperprolactinemia. In cases of primary infertility, the mean serum prolactin level was  $13.18 \pm 8.485$  ng/ml, whereas in cases of secondary infertility, it was  $17.21 \pm 15.1$  ng/ml. About half (53.85%) of the hyperprolactinemia group and the majority (85%) of the normoprolactinemia group experienced primary infertility. Prolactin levels were favourably connected with marital life duration, infertility, and fasting blood sugar levels. (Bade Sara & Jakhar, 2020). Hence present study was conducted to see the relationship between Hyperprolactinemia and infertility.

### Materials & Methods

At Benazir Bhutto Hospital in Rawalpindi, all patients were enrolled between June 2023 and December 2023 with their informed consent. The ethical committee of Abasyn University gave their approval to this study. Patient informed consent was obtained before any data was gathered. This study involved 108 infertile women. In this study, only those female participants were included who had been trying to conceive for more than a year, had not used any form of protection, were living together, and had not taken any infertility medication. The clinical history and demographic data of the patients were to be gathered through structured interviews with informed consent. After questionnaire completion, a gel tube was used to obtain the patient's blood sample (for Prolactin measurement). Estimation of prolactin hormone was done through Chemiluminescent immunoassay test (CLIA). The obtained data was analyzed with SPSS. Statistical analysis included descriptive analysis and Pearson's Correlation to see the relationship between hyperprolactinemia with infertility in women.

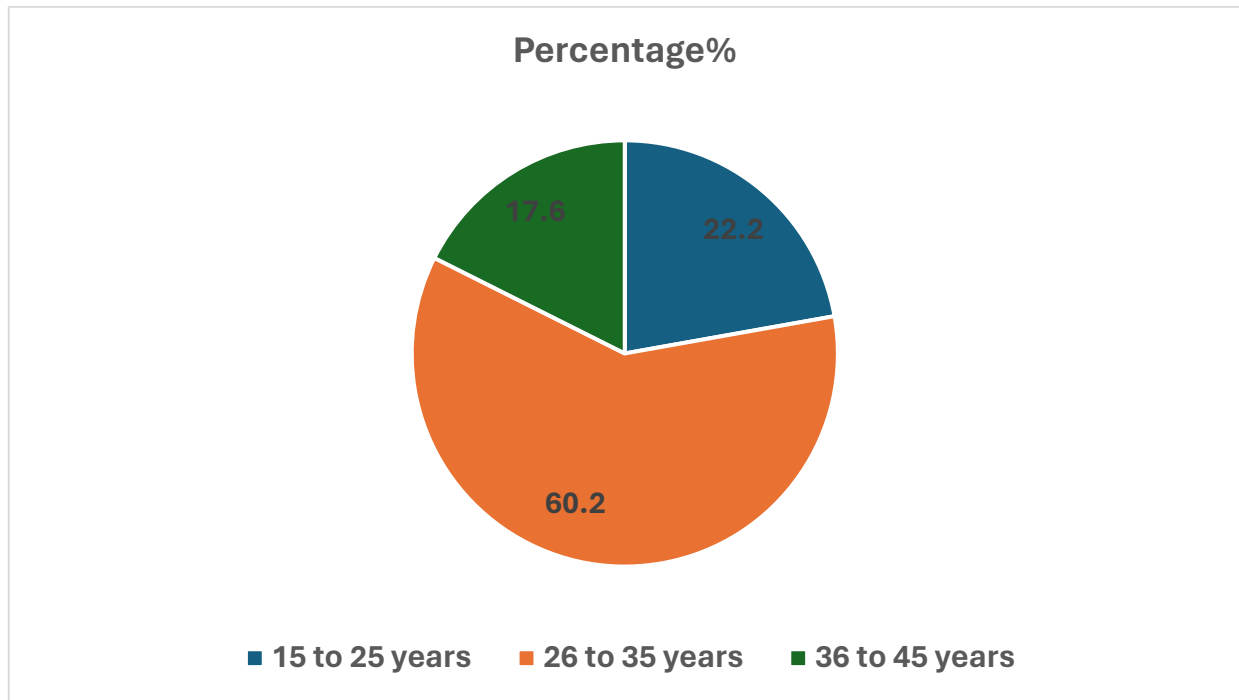


The study was done according to the Declaration of Helsinki principles, informed consent, dignity, autonomy, integrity, privacy, and confidentiality were carefully considered. The tests were performed under the PNCA registered lab and with their guidelines and regulations.

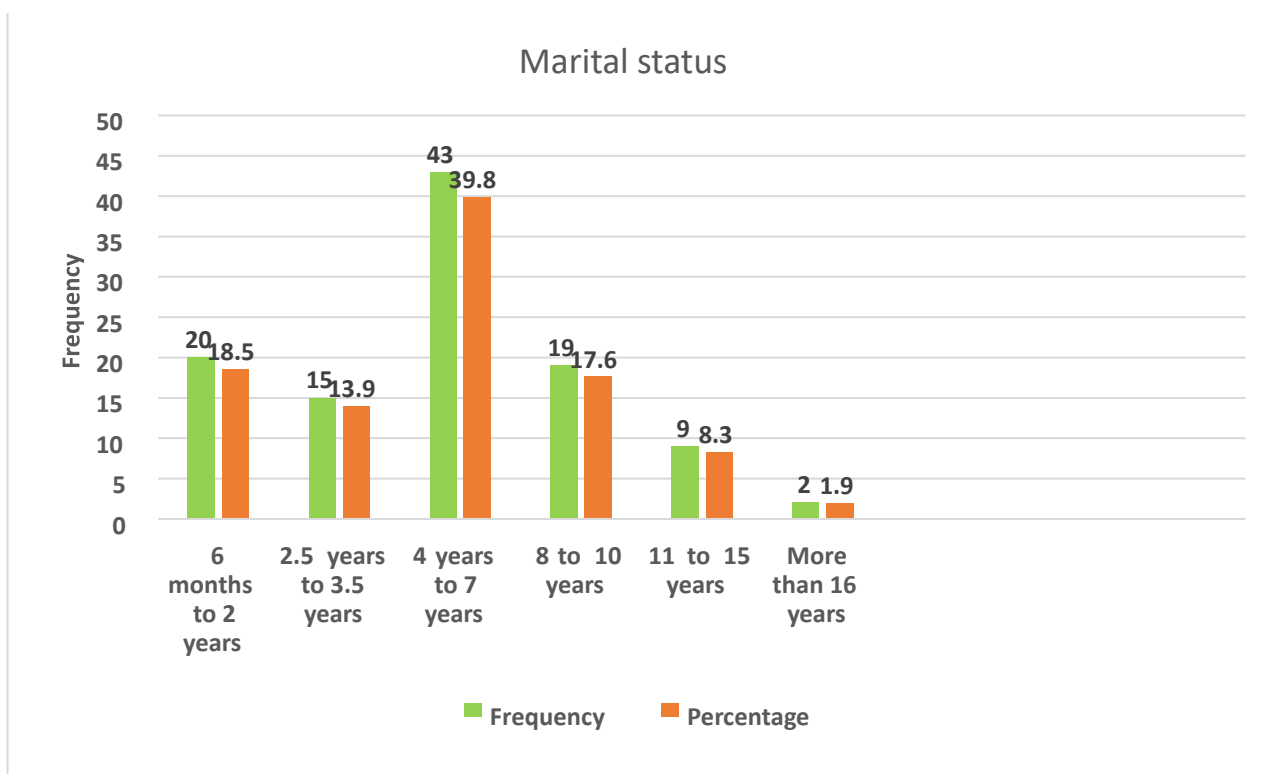


## Results

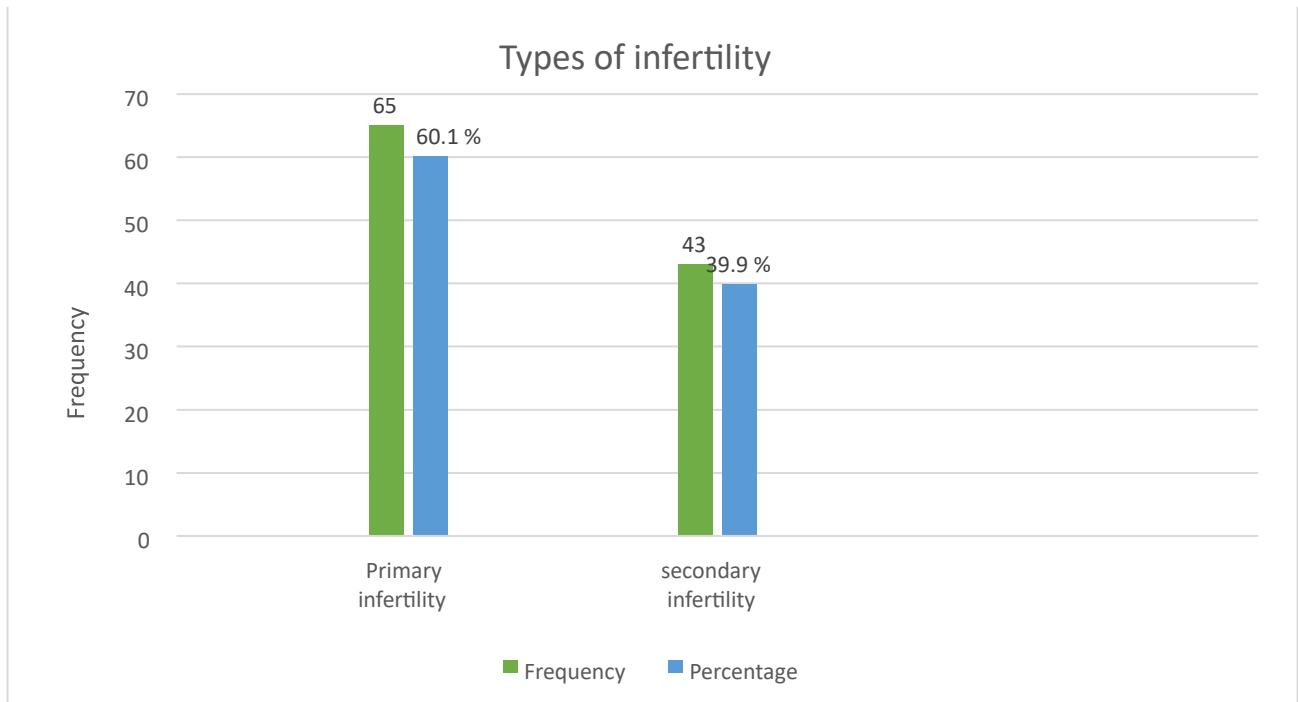
According to this research, the most prevalent age group of infertility is 26 to 35 years which counts 60.2% and 39.8% of women who have been married for four to seven years, primary infertility is highly common in this population. In the population under study, the most prevalent duration of infertility is between six months and two years and that counts 43.5%. Mostly infertile women have menarche before the age of fourteen. According to the current study, obesity, PCOS, and hyperprolactinemia are the most common risk factors for infertility.



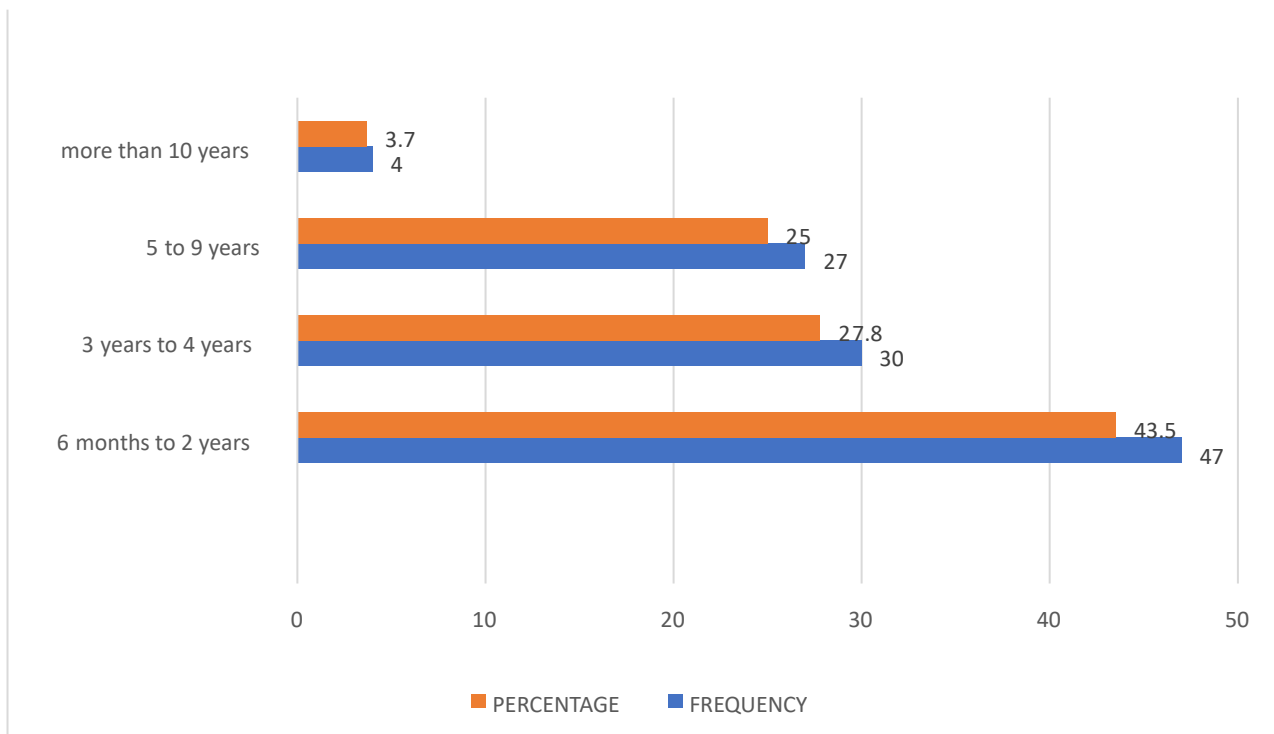
**Figure 1.:** Age of studied Patients. According to the above chart 22.2% of women aged 15 to 25 years, 60.2% of women aged 26 to 35 years, and 17.6% of women aged 36 to 45 years are infertile. The most prevalent age group in infertile studied women is 26 to 35 years.



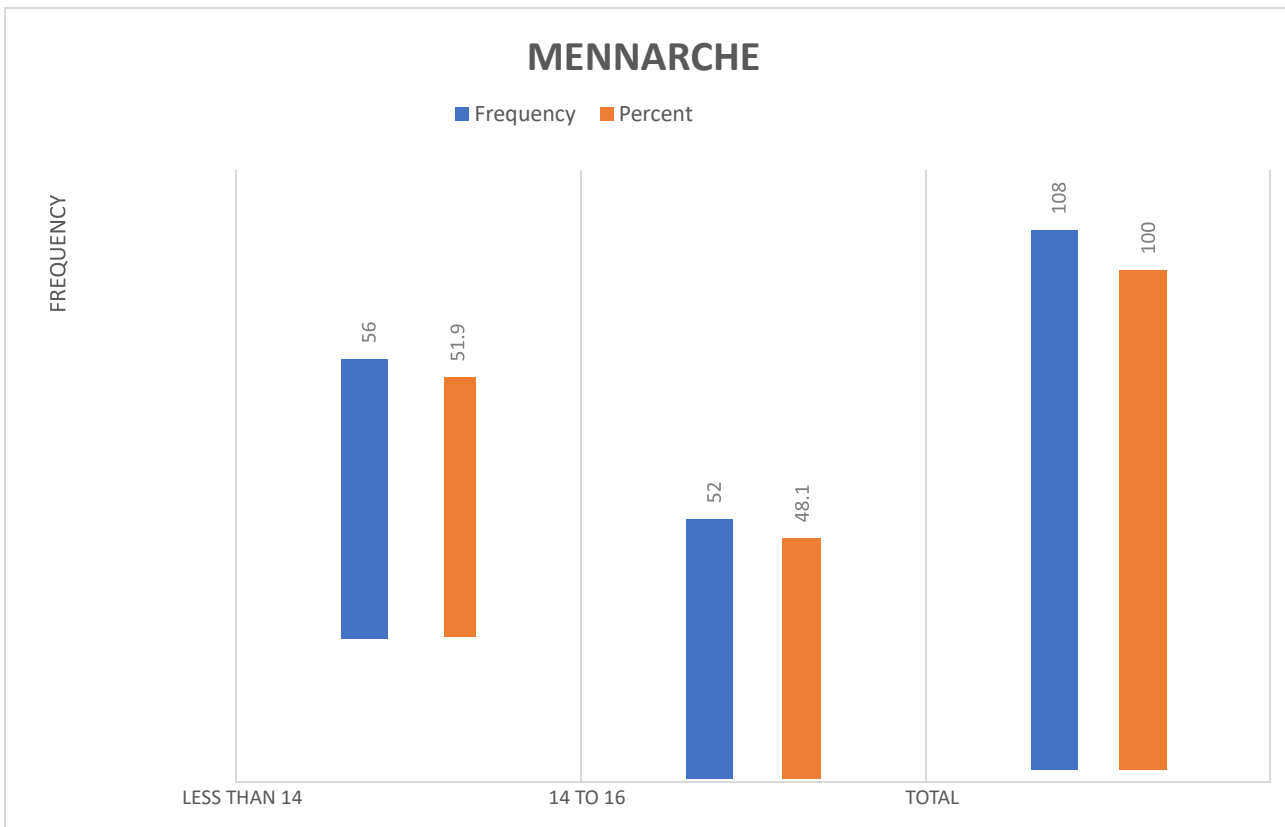
**Figure 2:** Marital of Studied Population. According to this study, 18.5% of women have been married for six months to two years, 13.9% for two years to three years, 39.8% for four to seven years, 17.6% for eight to ten years, 8.3% for eleven to fifteen years, and 1.9% for more than sixteen years.



**Figure 3:** Infertility Types in Studied Patients. This study shows that 60.1% of females had primary infertility and 39.9 had secondary infertility. Primary infertility is most prevalent in this studied population.



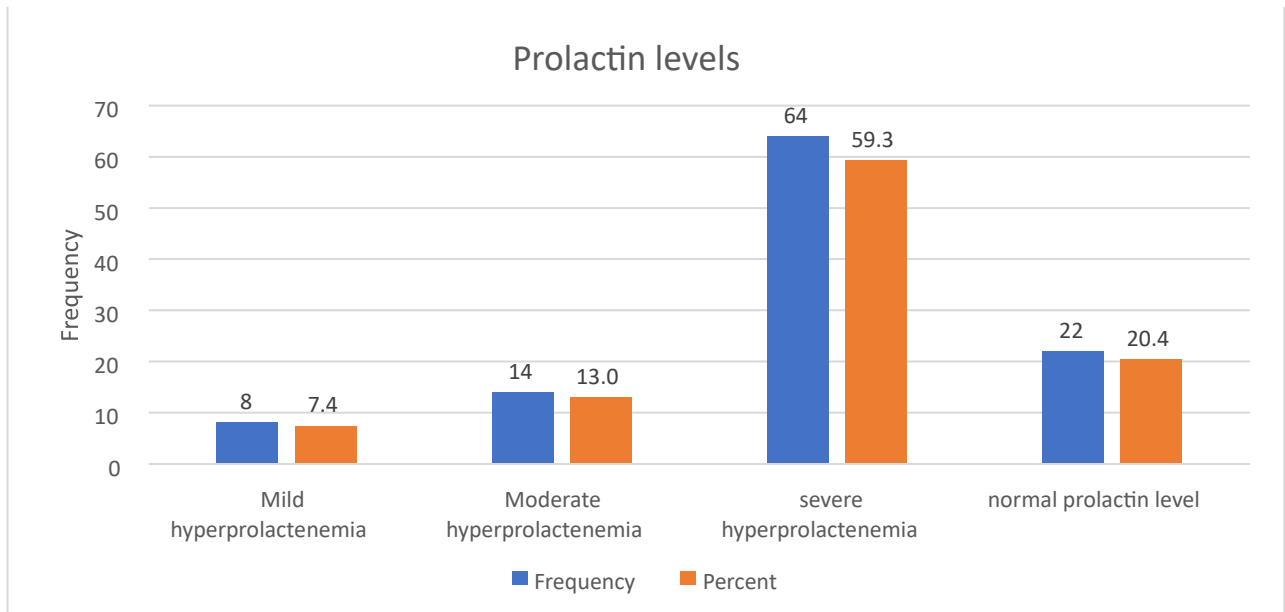
**Figure 4:** Infertility Duration of Studied Patients. Infertility rates among females range from 43.5% between six months and two years, 27.8% between three and four years, 25% between five and nine years, and 3.7% beyond ten years, according to the above chart.



**Figure 5.** Menarche of studied Patients. The above chart demonstrates that 51.9% of females had their menarche between the ages of less than 14 years and 48.1% had their menarche between the ages of 14 and 16.

Risk factors	Frequency	PERCENTAGE
<b>Weight</b>		
Gain	70	64.8%
loss	20	18.5%
normal	18	16.7%
<b>Diabetes</b>		
Yes	3	2.8%
No	105	97.2%
<b>Bp</b>		
Normal	96	88.9%
Hypertensive	5	4.6%
Hypotensive	7	6.5
<b>PCOS</b>		
Yes	<b>97</b>	<b>89.8%</b>
No	11	10.2%

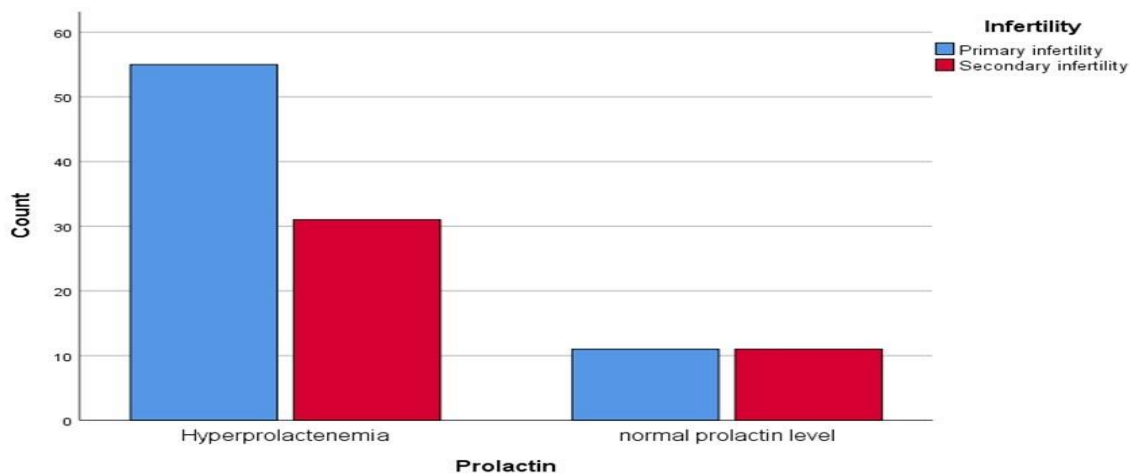
**Table 1:** This table shows the risk factors of infertility. In this study 64.8% of females gained weight, Diabetes and Bp are normal in this studied population of infertile Womens and 89.8% of infertile women had PCOS.



**Figure 6:** Prolactin level of the studied population. This chart shows that 7.4% infertile Womens had mild hyperprolactinemia, 13.0% Womens had moderate hyperprolactinemia, 59.3% Womens had severe hyperprolactinemia and 20.4% females had normal prolactin levels.

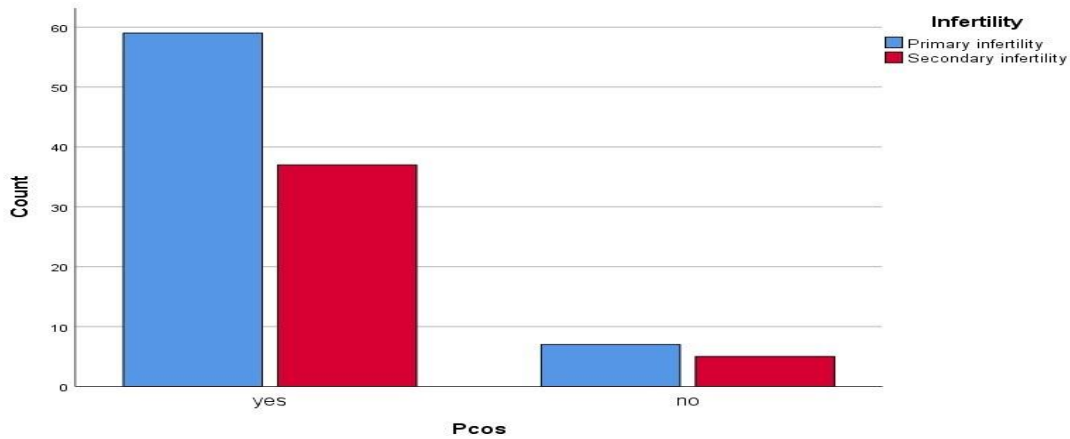
Prolactin	Frequency	Percentage
Hyperprolactinemia	86	79.6
Normal prolactin	22	20.4
Total no	108	100

**Table 2:** Prevalence of hyperprolactinemia in infertile women This table shows that 79.6% of females had hyperprolactinemia and 20.4 % had normal prolactin levels.

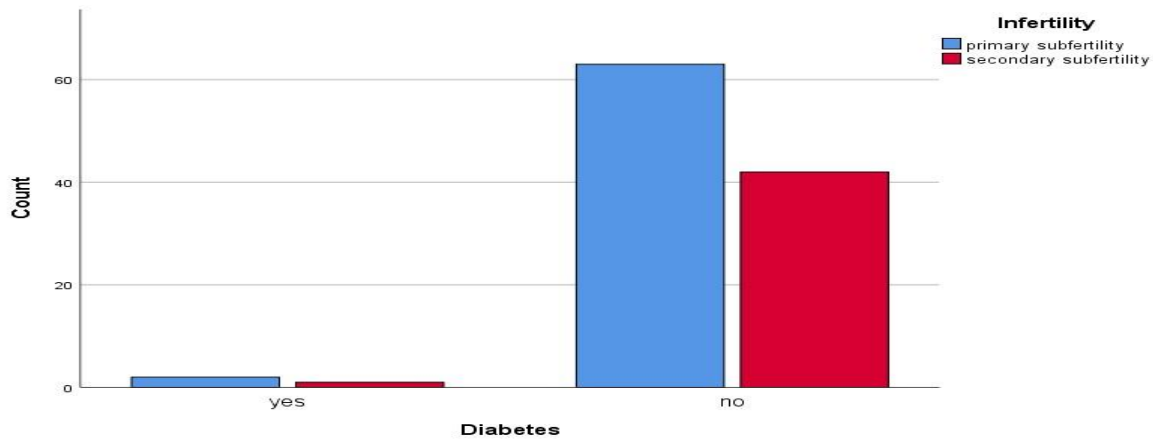


**Figure 7:** Correlation of Infertility with Prolactin. Pearson’s Correlation analysis was conducted to find out the correlation between infertility and prolactin. There was a significant strong correlation between infertility and prolactin. ( $r=0.622^{**}$ ,  $p<0.01$ ) The relationship between these variables was significant at the 0.01 level. The sample consisted of 108 participants for both variables.

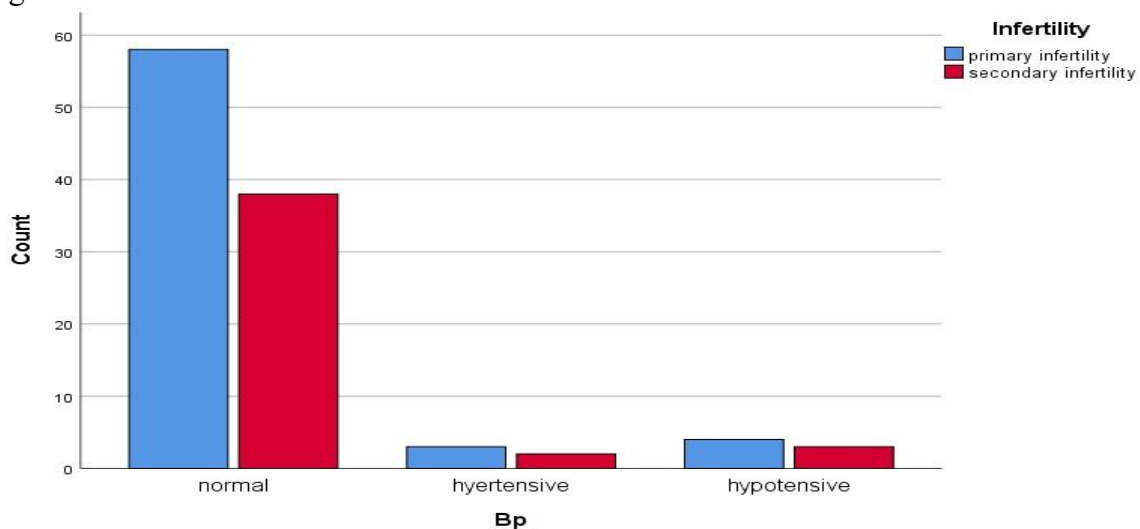




**Figure 8:** Correlation of infertility and PCOS. Pearson’s Correlation reveals a strong -significant positive correlation between infertility type and PCOS. ( $r = 0.414^{**}$ ,  $p < 0.01$ ) The relationship between these variables was significant at the 0.01 level.



**Figure 9:** Correlation of infertility with Diabetes. There was no significant correlation between infertility and diabetes. ( $r = -.091$ ,  $p = .351$ ) Pearson's Correlation analysis was conducted to find out the correlation between infertility and diabetes. The relationship between these variables was significant at the 0.01 level.



**Figure 10:** Correlation of infertility and BP. This correlation analysis revealed no significant relation between these two variables such as infertility and bp. ( $r = .180$ ,  $p = 0.62$ ). The relationship between these variables was significant at the 0.01 level. The sample consisted of 108 participants for both variables.

## **Discussion:**

According to a recent WHO report, a significant portion of the population will experience infertility at some point in their lives. Approximately 1 in 6 adults globally, or 17.5% of the population, suffer from infertility.

The new findings indicate that there is not much regional difference in the incidence of infertility. The rates are similar in high-, middle-, and low-income nations, suggesting that this is a significant worldwide health issue. In high-income nations, the lifetime prevalence was 17.8%, but in low- and middle-income nations, it was 16.5%. (WHO., 2023)

According to the current study that conducted from June 2023 to December 2023 shows that 22.2% of women aged 15 to 25 years, 60.2% of women aged 26 to 35 years, and 17.6% of women aged 36 to 45 years were infertile. Infertility rates among females range from 43.5% between six months and two years, 27.8% between three and four years, 25% between five and nine years, and 3.7% beyond ten years. In this study, 60.1% of females had primary infertility and 39.9% of females had secondary infertility. The study that was conducted in 2016 in OPD of Obstetrics & Gynaecology, Bahawal Victoria Hospital, Bahawalpur shows that an average age of 29.32 + 6.26 years, of which 48% had been infertile for 1–5 years, 27% for 5–10 years, and 25% for longer than 10 years. 63% of cases had primary infertility, while just 37 percent had secondary infertility. Of the 22 cases, 41% had hyperprolactinemia, whereas 59% did not have this morbidity detected. (Chaudhry et al., 2016) According to the results of the 2018 study, the average prolactin level was 31 ng/ml. (range: 2.5–109 ng/ml). Sixty-two (51.7%) of the patients had hyperprolactinemia, while 58 (48.3%) had normal prolactin levels. (Isah et al., 2018) However, this study shows that 79.6% of females had hyperprolactinemia and 20.4 % had normal prolactin levels.

According to the study that was conducted in 2003 it concluded that the patients ranged in age from 20 to 40 (mean age of 28.3 years). Of them, seven (1,68.3%) experienced secondary infertility while thirty-three (31.7%) had primary infertility. 33 (31.7%) of the 104 patients had abnormal plasma prolactin levels. Compared to patients with primary infertility, only 11 patients (10.6%) had abnormal prolactin levels, whereas 22 women (21.1%) had this condition. (Idrisa et al., 2003) According to the results of the current study, the infertile females were aged between 15 to 45. 60.1 % of females had primary infertility and 39.9% had secondary infertility. We had the data of 108 infertile women. Out of 108 infertile women, 86 females had Hyperprolactinemia which counts 79.6 % and 22 females had normal prolactin levels which count 20.4%.

The current study shows that 89.8% of infertile females had PCOS (Polycystic ovary syndrome) and 10.2% of infertile women didn't have PCOS (Polycystic ovary syndrome). A previous study demonstrated that the prevalence of PCOS was 5.8%. 72% of 309 women with PCOS and 16% of 4547 women without PCOS reported being infertile. Women with PCOS had a 15-fold increased risk of infertility. (John et al., 2015)

## **Conclusion :**

The study concludes that hyperprolactinemia and PCOS are major risk factors of infertility. This research indicates a strong correlation between prolactin and PCOS with infertility. Furthermore, no relationship has been discovered between diabetes and BP with infertility. These Diagnostic parameters provide good direction toward treatment.

## **Limitations & Recommendations :**

The sample size of the current was small and it was a cross-sectional type of study. However, we recommend further studies with a larger sample size and cohort type of study because that will be more representative of the population.

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