



Prevalence and Age-Related Association of Abnormal Endocrine Changes among Women with Menstrual Disorder

**Faizah Mughal^{1*}, Ashok Kumar², Jai Dev Maheshwari³, Ali Nawaz Bijarani⁴,
Tayyaba Kazmi¹ and Ruqaya Nangrejo^{5,6}**

¹Department of Biochemistry, Baqai Medical University Karachi, Pakistan.

²Department of Anatomy, Shaheed Mohtarma Benazir Bhutto Medical College Lyari, Karachi, Pakistan.

³Department of Community Medicine, Shaheed Mohtarma Benazir Bhutto Medical College Lyari, Karachi, Pakistan.

⁴Department of Pharmacology, Shaheed Mohtarma Benazir Bhutto Medical College Lyari, Karachi, Pakistan.

⁵Department of Anatomy, Baqai Medical University Karachi, Pakistan.

⁶Department of Physiology, Baqai Medical University Karachi, Pakistan.

Authors' contributions

This work was carried out in collaboration among all authors. Author FM planned the study, as well as the protocol and initial draught of the paper, as well as the sample and statistical analysis. The final drafting and literature searches were handled by the authors AK and JDM. Author ANB contributed to the manuscript's creation. Authors TK and RN finished up all of the final settings and assisted with the statistical analysis. All authors read and approved the final manuscript.

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ABSTRACT

Background: The menstrual cycle describes the healthy reproductive system of the women which is controlled by different hormones.

Aim: The goal of the study is to evaluate the prevalence of irregular menstruation in different endocrine changes and to identify their association with the age of women in reproductive life.

Methodology: It was a cross-sectional study conducted on women attending the gynecological clinic of Karachi from March 2019 to June 2019. Of the 165 women with different hormonal changes 100 presented with menstrual cycle abnormality.

Results: Among the women with menstrual irregularities 51% women presented with insulin resistance, 23% with hyperandrogenism, 19% with hypothyroidism and 7% hyperprolactinemia. Age-related association was observed in menstrual irregularities women with insulin resistant and hyperandrogenism.

Conclusion: Menstrual cycle is a physiological process, any irregularities in cycle can be caused by even minimal hormonal imbalance. As a result, it is critical to address endocrine abnormalities in order to improve women's reproductive health.

Keywords: Menstrual disorder; insulin resistance; hypothyroidism; hyperandrogenism; hyperprolactinemia; endocrine; hormone.

1. INTRODUCTION

Menstruation cycle function is characterized by a multifaceted endocrine axis that regulates the ovaries and the endometrium plus it also reflects the women's reproductive system's underlying hormonal milieu [1,2]. The Menstrual abnormalities are among the most common medical conditions affecting women of reproductive age. It is prevalent in both developed and underdeveloped countries [3,4]. In a district of Pakistan, the prevalence of menstrual disorders among women of reproductive age was found to be 26.07% [5].

The hormonal system plays an important role in the rhythmicity of the monthly cycle. Endocrine imbalance, polycystic ovary syndrome (PCOS), infections, malignancy, trauma, certain medicines, and obesity are all important causes of menstrual irregularities [6].

The endocrine abnormalities can contribute to the development of a variety of medical conditions, including infertility, heart disease, and type 2 diabetes [7].

Furthermore, the progression of menstrual cycle irregularities over extended periods of time can lead in the onset of menopause at a younger age. Previous research has linked premature menopause to an increased risk of heart disease and osteoporosis [8].

Menstrual problems are common in insulin-resistant women. They present in a variety of ways, ranging from amenorrhea to oligomenorrhea to menometrorrhagia. During menstruation, the basal levels of ovarian steroid hormones, estrogen, and progesterone usually begins to increase during the follicular phase and eventually peak during the luteal phase.

The hormone progesterone that specifically increases during the luteal phase makes the body cells more insulin resistant. Also, Hyperinsulinemia appears to work in conjunction with pituitary gonadotropins to stimulate ovarian theca cell androgen production, complicating insulin resistance, resulting in menstrual cycle disruptions and lower fertility rates [9-11].

It is also well known that elevated androgen levels disrupt the menstrual cycle in women who do not have clinical hyperandrogenism. The dysregulation of hormone in the hypothalamic-pituitary-gonadal (HPG) axis, results in raised androgens and estrogens levels; hypersecretion of luteinizing hormone (LH); and decreased follicle stimulating hormone (FSH) synthesis in females eventually causing menstrual abnormalities [12,13].

The network of gonadotropins (such as luteinizing hormone (LH) and follicle-stimulating hormone (FSH)) and sex steroid hormones (such as estrogens and progesterone), affecting menstruation are key components of the hypothalamic-pituitary-gonadal axis [14]. This system is connected to the hypothalamic-pituitary-thyroid axis that regulates thyroid function. Therefore, thyroid dysfunction is another endocrine abnormality that has been identified as an indicator of menstrual irregularity [15].

Hyperprolactinemia is widely known hormonal disorder that can be physiological, pathological, or idiopathic. The main physiological effect of hyperprolactinemia is the suppression of pulsatile GnRH. The main symptoms of the ailments differ significantly depending on the patient's age and gender. It frequently causes gonadal dysfunction in women, including ovulatory dysfunction, menstrual irregularity and galactorrhea [16].

As previously discussed, menstrual cycle is influenced by a number of hormones. Anovulation is characterized by irregular menstrual cycles, which are associated by reduced ovarian steroid secretion and production [17,18]. Functional hypothalamic amenorrhea, which is associated with reduced gonadotropin-releasing hormone secretion and hypothalamic–pituitary–adrenal (HPA) axis dysregulation, is the most common cause of menstruation irregularity. The presence of these hormonal issues may contribute to the development of a variety of chronic diseases such as infertility, heart disease, and type 2 diabetes [19].

The Objectives of the study are:

- To evaluate the prevalence of irregular menstruation in different hormonal disruption
- To clarify the association between endocrine changes causing irregular menstruation with the age of women in reproductive life.

2. METHODOLOGY

A cross-sectional study was performed on women attending the gynecological clinic of Karachi from March 2019 to June 2019. It was conducted on women of reproductive age ranging from 20 to 45 years. The sample size was calculated using an open epi sample calculation (95 percent CL) and the sampling technique was non-probability convenient sampling.

The participants were interviewed on an individual basis after providing informed consent, with their privacy respected and to reduce influence from other people.

The study recruited the participation of 165 women with different hormonal changes. The information was obtained in both English and Urdu, however the Performa was completed in English. A data collection form was based on age and biochemical profile including Fasting Insulin, Hyperandrogenism, Hypothyroidism and Hyperprolactinemia in patients with presence or absence menstrual cycle irregularities.

The presence abnormal menstruation was defined as a menstrual cycle length of less than 21 days or more than 35 days, or more than four days variation between cycles, was used to assess menstrual irregularity.

The biochemical parameters studied were chosen based on a predefined laboratory endocrine profile. Values of the parameters were compared to normal reference ranges established in laboratory using standardized guidelines.

2.1 Statistical Analysis

SPSS version 20 was used to analyze the data. The categorical variable was represented as frequencies and percentages. The Chi Square statistics was used for testing relationships between categorical variables. A p -value of <0.05 was considered statistically significant.

3. RESULTS

A total of 165 women in their reproductive years with different endocrine abnormalities participated in the study by visiting a gynecological clinic at a hospital in Karachi. The age range of women was between 20-45 years. Out of the 165 women, 100 i.e. 60% of them had menstrual irregularities.

Out of 100 women with menstrual irregularities, 51 % presented with insulin resistance 23% had hyperandrogenism, 19% had hypothyroidism and finally 7% presented with hyperprolactinemia (Fig. 1).

3.1 Association of Age with Endocrine Abnormalities - Chi Square

3.1.1 Insulin resistant

71 women were diagnosed with insulin resistance, 51 (71%) of whom had menstrual irregularities, and maximum women who were insulin resistant with menstrual irregularities were between the ages of 26 to 30. Furthermore, a significant association between age and insulin resistance was discovered ($p=0.034$) as mentioned in Table 1.

3.1.2 Hyperandrogenism

Among the 42 women with hyperandrogenism, 23 (54.7%) presented with menstruation abnormality. Most of the women with the hyperandrogenism were in the age range of 20 to 25 years. Moreover, there was significant association found between age and hyperandrogenism ($p=0.029$) as mentioned in Table 1.

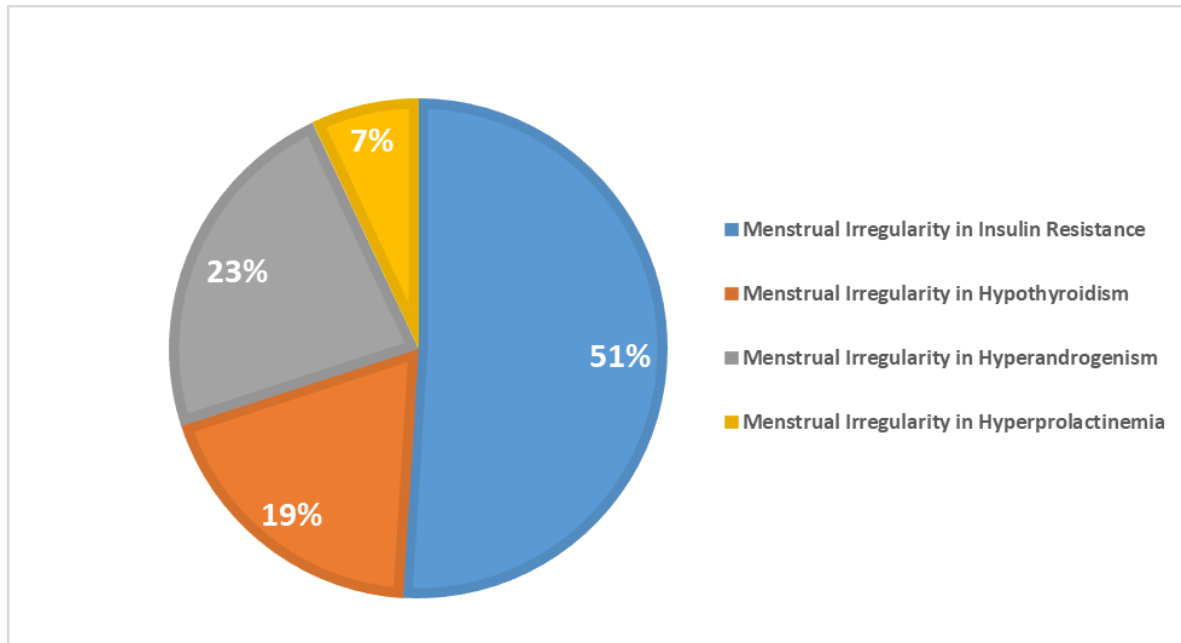


Fig. 1. Prevalence of Menstrual cycle irregularities among women with Hormonal disorders

3.1.3 Thyroidal dysfunction

Menstruation abnormalities were reported by 19 (47.5%) of the 40 women with hypothyroidism. The majority of the women with hypothyroidism were between the ages of 31 and 35. Furthermore, there was no significant relationship found between age and hypothyroidism ($p=0.072$) as stated in Table 1.

3.1.4 Hyperprolactinemia

Menstrual irregularities were noted by 7 (58.3%) of the 12 women with hyperprolactinemia. The large percentage of hyperprolactinemia patients were between the ages of 36 and 40. Besides that, no significant relationship was revealed between age and hyperprolactinemia Table 1.

4. DISCUSSION

The anterior pituitary gland regulates the secretion of important hormones from the endocrine system such as the gonads, thyroid, pancreas and adrenal cortex as well as its abnormalities, can have a significant impact on the normal menstrual cycle [20].

To the best of our knowledge this is the first study that have evaluated the different hormonal imbalances involved in menstrual irregularities.

In the current study, most of the women who visited the clinic with menstrual irregularities were insulin resistant (51%). As a result, it appears that the presence of hyperinsulinemia can signal the advent of menstrual abnormalities in women in the reproductive years. Brower et al. 2013 mentioned the presence of clinically evident menstrual dysfunction can be used to predict the presence and potentially the degree of insulin resistance [21]. Moreover, it was observed by another study that women who are normocyclic and have PCOS have a lower risk of insulin resistance than women with menstrual irregularities [22]. In the same way, Panidis et al. 2013 found amenorrhea as a useful marker of IR, whereas Oligomenorrhea does not indicate more severe IR [23].

Also, our study found a link between age and insulin resistance in women with menstrual irregularities. According to a study conducted by Almassinokiani et al. 2020, there was no statistically substantial relationship between Insulin Resistance and menstrual pattern however, a prominent association was found between age and menstrual irregularity [24].

Table 1. Age-Related association with different endocrine abnormalities

Age (years)	Menstrual Irregularities Present (P) Absent (A)	Insulin Resistance		Hyperandrogenism		Thyroidal dysfunction		Hyperprolactinemia		Total No. of Participants
		P	A	P	A	P	A	P	A	
20-25		14	4	11	2	5	3	1	1	41
26-30		16	3	9	1	5	4	1	1	40
31-35		11	4	2	8	4	7	1	1	38
36-40		8	3	1	7	3	3	3	1	29
41-45		2	6	0	1	2	4	1	1	17
Total		51	20	23	19	19	21	7	5	165
p-value		0.034		0.029		0.072		0.835		

P = Present, A= Absent, p - < 0.05

According to our findings, hyperandrogenism is the second most common cause of menstrual irregularity, affecting 23% of women. Gambineri et al. 2013 discovered contradictory results, with 3.8% of the women suffering from menstrual irregularity and hyperandrogenism, and the difference could be explained by the fact that they evaluated a specific age group of adolescence [25,26]. A research study found a link between hyperandrogenism and menstrual irregularities, hirsutism, and acne, as well as an increased risk of metabolic disorders in women. Furthermore, young women who have irregular periods have higher androgen levels than girls who have regular menstrual cycles [27]. According to the Canadian study, high androgen levels in clinical populations were linked to menstrual irregularities when it was compared to healthy women [28]. Also, Even after excluding women with the most abnormal cycles from the study, the findings revealed significant correlations between testosterone and menstrual irregularities [28].

In the present study, a strong link was found between women's age and hyperandrogenism with menstrual irregularity. We also discovered that the majority of the women were between the ages of 20 and 25 years. Congruently, Panidis et al. 2015 study found that the mean age of women having hyperandrogenism with anovulation was 24.6 ± 6.2 [29].

In our study, 19% of women had hypothyroidism that manifested as menstrual irregularity. Correspondingly, Sharma et al. 2012 discovered that 19% of women with abnormal uterine bleeding had hypothyroidism [30], whereas Manjeera et al. indicated that nearly 28% of females with irregular menstrual cycles had hypothyroidism [31]. Multiple studies have linked menstrual irregularities to thyroid disorders, which can be alleviated by normalising thyroid status; thus, thyroid testing should be done in all patients who have menstrual irregularities [32,33].

Our data did not show a significant relationship between age and menstrual irregularity in women with hypothyroidism. In addition, we discovered that the majority of the women with menstrual aberration with hypothyroidism were between the ages of 31 and 35. In a survey by Padma et al. 2021, patients were drawn from all age groups, ranging from 15 to 45 years old, with the greatest number of patients falling between the

ages of 35 and 45 [34]. Another related research by Charusheela et al. 2001, found that the majority of patients were between the ages of 31 and 40 [35].

In the current study, hyperprolactinemia was found to affect 7% of the women who presented with menstrual irregularities. Besides that, no age related association was observed among these women. Lee et al. discovered that hyperprolactinemia can affect anyone of any age and that its prevalence ranges from 9-17% of women with menstrual problems (such as amenorrhea or polycystic ovary syndrome) [36].

The endocrinological glands (pituitary, thyroid, pancreas, adrenal, and ovaries) are involved in the hormonal regulation of a woman's menstrual cycle. As a result, endocrine disorders are the primary factors of menstrual irregularities in women throughout their reproductive lives. As a result, the current study was designed to assist the community in understanding how various endocrine abnormalities are related to menstrual abnormality. More research is needed to better understand the underlying mechanisms of the link between endocrine disorders and the menstrual cycle.

5. CONCLUSION

The menstrual cycle is a highly regulated physiological process that allows for pregnancy and conception. Menstrual bleeding (menses) is regulated by hypothalamic and pituitary hormones from the beginning of menstruation (menarche) to the end of menstruation (menopause). Even minor changes in hormone levels can cause menstrual cycle irregularities. Therefore, it is important to improve the endocrine abnormalities to improve women reproductive health.

6. LIMITATIONS

It was a single-institute study, and there is a chance of selection bias because we employed a non-probability survey approach.

7. FUTURE RECOMMENDATIONS

More extensive multi-centre are required to verify the findings.

More research is needed to better understand the underlying mechanisms of the link between endocrine disorders and the menstrual cycle.

CONSENT

As per international standard or university standard, respondents' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

The study protocol was performed in accordance with the ethical standards laid down in the Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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