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Research Article

Abnormal Menstrual Chart Patterns, Their Treatment and Fertility Outcome Among Women with Hormonal Infertility at Bugando Medical Centre, Mwanza, Tanzania

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Abstract

Background: Infertility is a global public health issue, affecting one in six individuals at some point in their lives. Menstrual cycle patterns serve as indicators of reproductive health, and tracking these patterns is a simple, noninvasive, and cost-effective method that all women should consider. This study aimed to analyze menstrual chart patterns, associated clinical profiles, interventions and fertility changes among women with hormone-related infertility at Bugando Medical Centre. *Methods*: A prospective longitudinal study that involved 230 women with hormonal infertility aged 18-44 years, was carried out at Bugando Medical Centre from March 2023 to March 2024. A pretested data collection tool was used. Mothers were instructed to chart their menstrual cycle biomarkers. Basic hormonal profiles were investigated. Data analysis was done according to the objectives using STATA version 15 and Pearson's Chi^2 test or Fisher's Exact test was used to measure the association between menstrual patterns and clinical profiles. The significance level was determined at p-value <0.05. *Results:* The mean age of the participants was 32.2 ± 5.7 years. The years of infertility ranged from 1 to 20 with a median age of 4 [IQR=2–7] years. Participants with normal HbA1c conceived more than those with abnormal HbA1c; 34.7 % (41/118) versus 22.3 % (25/112), (p-value 0.037), while those with normal thyroid function 31.1% (61/196) conceived more compared to those with thyroid dysfunction 14.7% (5/34) (p-value 0.035). At the end of three months, most of them were ovulating. Among those who ovulated 28.7% conceived within three months. *Conclusion:* Answers to infertility are hidden within the menstrual cycle patterns. Menstrual cycle charting and lifestyle changes should be incorporated as tools in managing women with infertility.

Keywords

Menstrual Patterns, Basic Hormonal Profile, Lifestyle Changes, and Infertility

1. Introduction

Infertility affects many people in their lifetime and one in every 6 people have infertility globally and 17.5% estimates the lifetime prevalence of infertility [1]. It is a disease of either the male or female reproductive system defined by the failure to achieve pregnancy after 12 months or more of regular unprotected sexual intercourse [2]. Ovulation disorders which

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commonly present as menstrual disturbance are the cause of infertility in around 25% of couples [3]. The hormonal balance that regulates ovulation influences the entire body and the presence of normal ovulatory cycles is a good indicator of a woman's overall health [4]. The most common causes of menstrual irregularities associated with ovulatory dysfunctions are hormonal abnormalities which can be hypothalamic, pituitary, thyroid, adrenal, ovarian, or metabolic disorders [4]. Ovulation is a sign of health and irregular or absent ovulation is a marker for general health and a variety of possibilities of diseases in women [4]. Fertility awareness is a valuable tool that enables women to recognize their health status. Many times the answers to infertility lie hidden within these patterns. Identifying the biological fertile window by peak mucus as clear, slippery, or stretchy mucus related to estrogen) yielded 96% sensitivity and improved specificity [5]. The estradiol has a logarithmic increase from baseline of approximately 1.5 times per day for five consecutive days to reach the estrogen peak occurring 24 to 36 hours before ovulation occurs [6]. Charting menstrual patterns is a simple, noninvasive, inexpensive tool each woman should embrace. Thyroid hormones do influence ovulation by acting upon folliculogenesis and steroidogenesis at the ovarian level and also by affecting sex hormone binding globulin (SHBG) and gonadotropin-releasing hormone (GnRH) secretion [4]. Hyper secretion of prolactin leads to inhibition of GnRH secretion and diminishes GnRH receptor response to GnRH, together with a decline in luteinizing hormone (LH) pulse frequency and amplitude [7]. Obesity causes infertility through various pathways, including impaired ovarian follicular development, qualitative and quantitative development of the oocyte, fertilization, embryo development, and implantation [8]. Hyperinsulinemia affects granulosa cells and theca cells. Due to hyperinsulinemia, luteinizing hormone induces early response on granulosa cells of small follicles and causes premature differentiation of theca cells, causing anovulation [9]. At the hypothalamus, insulin resistance leads to a decline in GnRH neurons activity hence a diminished release of GnRH, LH, and follicular stimulating hormone (FSH). The effectiveness of cervical mucus patterns enables women to recognize their fertile and infertile periods, ovarian response to hormones, and timing of ovulation. Menstrual or mucus secretion patterns help to identify ovarian dysfunctions such as an ovulatory cycle, long and short cycles, and unluteinized cycles. However, despite the known values of the menstrual patterns in determining abnormal menstrual cycles and their relationship with the underlying hormonal condition in women with infertility, they are rarely used as an effective primary tool in managing women with infertility. Some of the clinical factors and basic hormonal profiles that are related to ovulation dysfunction are missed during patient evaluation. The evidence gathered in this study will enlighten the medical practitioners on how to manage patients with hormonal infertility in a simple, noninvasive, and inexpensive way.

2. Materials and Methods

A cross section study that involved 230 women with hormonal infertility, aged 18 to 44 years was carried out at Bugando Medical Centre (BMC) in Tanzania from March 2023 to March 2024. Objectives were identifying the menstrual cycle chart patterns, their associated clinical profile in women with hormonal-related infertility, changes in cycle patterns and fertility outcomes. Women with hormonal infertility were explained about the purpose of the study, those who voluntarily agreed to consent and met the eligibility criteria were enrolled in the study. A standardized, pre-tested data collection tool was used to collect the participant's information including; social demographic factors, menstrual cycle patterns, and clinical and hormonal profiles. The fertility education and medical management (FEMM) app was downloaded on their phones, and they were taught how to chart their menstrual cycle biomarkers including menstrual bleeding, cervical mucus, and dryness in the downloaded FEMM application. The data was recorded automatically and analyzed. The researcher met these patients once every month for three consecutive months evaluating their menstrual cycles. Counseling about their condition, and lifestyle behavior change (diet, physical exercises, and medical management) were done monthly for three months consecutively.

Laboratory workups were carried out during the first encounter with the patient, thyroid stimulating hormone, hemoglobin A1c, and prolactin hormone were investigated. The estrogen and the follicle-stimulating hormone were investigated on day three of the menstrual cycle. Medical management was initiated and individualized in which Metformin, Levothyroxine, and Bromocriptine were used to treat insulin insensitivity, hypothyroidism, and hyperprolactinemia respectively.

Data from questionnaires were entered into a computer using Microsoft Excel and exported to STATA version 15 for summarization and analysis. Continuous data were summarized using mean with standard deviation or median with interquartile range depending on their normality in distribution. Categorical data were summarized using frequencies, proportions, and percentages. We used Pearson's Chi-square test or Fisher's Exact test to determine the significant differences in the distribution of menstrual patterns and clinical profiles. A p-value less than 0.05 was regarded to be significant.

3. Results

Social demographic characteristics of the participants

During the study period, 230 women with hormonal infertility were enrolled. Their mean age was 32.2 ±5.7 years. The period of infertility ranged from 1 to 20 years with a median duration of 4 years [IQR 2–7]. The cycle lengths of the study participants ranged from 20 – 90 days and a median cycle length of 30 days [IQR 27 – 37]. The median age at menarche

was 14 years [IQR 13 – 15].

Table 1. *Social demographic characteristics and menstrual patterns of the study participants.*

Patient characteristics	Number (n)	Percent (%)
Age		
<25 years	25	10.8
26-35 years	131	56.9
36-45 years	74	32.2
Parity		
Parity 0	119	51.7
Parity 1	71	30.9
Parity ≥2	40	17.4
Education		
Primary	41	17.8
Secondary	99	43.0
College/University level	90	39.1
Residence		
Mwanza region	162	70.4
Outside Mwanza region	68	29.6
Cycle length 24 -36 days		
Short cycles	38	16.5
Normal cycles	130	56.5
Long cycles	62	27.0
Regularity		
Irregular	122	50.9
Regular	108	49.1
Bleeding duration≥3-≤7		
Hypo menorrhea	4	1.7
Normal	187	81.3
Hypermenorrhea	39	17.0
Heavy bleeding		
No heavy bleeding	175	76.1
Heavy bleeding present	55	24.0
Knowledge of cervical mucus		
Knowledge absent	22	9.6
Knowledge present	208	90.4

Clinical characteristics and hormonal profile of study participants.

Of the 230 participants, 10.9% (25/230) had signs of hyperprolactinemia (galactorrhea, dry skin, nickel allergy, sweaty hands), while 14.8% (34/230) presented with signs of hypothyroidism (hair loss, scaling of skin and cold intolerance). More than two-thirds of the participants 88.7% (204/230) had signs of glucose insensitivity (acrochordons, acanthosis nigricans and central obesity). In this study 37.7% (89/230) participants had class 1 obesity, 48.7 % (112/230) had HbA1c more than 5.3% and the majority 66.1 % (152/230) had abnormal estrogen levels. Table 2 summarizes the clinical characteristics and hormonal profile of the study participants.

Table 2. *Clinical characteristics and hormonal profile of the study participants.*

Clinical/hormonal characteristics	Number (n)	Percent (%)
Prolactin hormone signs*		
No	205	89.1
Yes	25	10.9
Thyroid hormone **		
No	196	85.2
Yes	34	14.8
*Glucose insensitivity signs****		
No	26	11.3
Yes	204	88.7
Libido		
Reduced	80	34.8
Absent	82	35.7
Normal	68	29.6
Body Mass Index		
Normal (18.5-24.9)	26	11.3
Overweight (25.0-29.9)	67	29.1
Obesity 1 (30.0-34.9)	89	37.7
Obesity 2 (35.0-40)	48	18.7
HbA1c		
Normal (≤5.3%)	118	51.3
High (>5.3%)	112	48.7
TSH		
Normal ranges 0.35-2.5uIU/ml	199	86.5
Abnormal < 0.35 uIU/ml	31	13.5
Prolactin		
Normal (1.4-19ng/ml)	213	92.6
High (>19ng/ml)	17	7.4

Clinical/hormonal characteristics	Number (n)	Percent (%)
Estrogen		
Normal ranges 50-200pg/ml	78	33.9
Abnormal ranges	152	66.1
FSH		
Normal ranges <7mIU/ml	152	66.1
High >7mIU/ml	78	33.9

*Galactorrhea, dry skin, nickel allergy, sweaty hands, **Hair loss, scaling of skin, and cold intolerance ***Acrochordons, acanthosis nigricans, central obesity, hirsutism).

Association between age, hormonal profile, and conception.

There was a significant difference in the distribution of conception age across various groups. Patients aged < 25 years conceived more 56% (14/25) compared to 30.5% for those aged 26-35 and 16.2% (p-value 0.001) those aged 36-44 years. Patients who had normal HbA1c conceived more than those with abnormal HbA1c, 34.8 % (41/118) versus 22.3 % (25/112), (p-value 0.037). Other findings are summarized in Table 3.

Table 3. *Association between age, hormonal profile, and conception.*

Patient characteristics	Conception Yes n (%)	Conception No n (%)	Pearson Chi-square	p-value
Age	-	-		
≤25	14 (56.0)	11(44.0)	14.9578	0.001
26-35	40 (30.5)	91(69.5)		
36-44	12(16.2)	62(83.8)		
Hba1c				
Normal ≤5.3%	41(34.8)	77(65.3)	4.3350	0.037
Abnormal >5.3%	25(22.3)	87(77.7)		
TSH				
Normal	60(30.2)	139(69.9)	1.5278	0.216
Abnormal	6(19.4)	25(80.7)		
Prolactin				
Normal	60(28.2)	153(71.8)	0.3906	0.532
Abnormal	6(35.3)	11(64.7)		
Estrogen				
Normal	27(34.6)	51(65.4)	2.0214	0.155
Abnormal	39(25.7)	113(74.3)		
FSH				
Normal	40(26.3)	112(73.7)	1.2406	0.265
Abnormal	26(33.3)	52(66.7)		

Interventions given to study participants depending on the hormonal changes.

All study participants were managed individually depending on the cause of the abnormal hormone encountered. Those with abnormal body-mass index (BMI) were managed with Metformin, hypoestrogenic were given Estrogen gel, hyperprolactinemia received Bromocriptine, hypothyroidism with Levothyroxine. All study participants were given integrated iron, cholecalciferol,

avoided starch and sugary diet, managed stress and did physical exercises as shown in table 4.

Table 4. *The interventions given to the study participants.*

INTERVENTIONS	THE USE
METFORMIN	All women with anovulatory irregular cycles, with abnormal body mass index
ESTROGEN GEL	All women with anovulatory cycles (low levels of estrogen of below 50pg/mol).
BROMOCRIPTINE	All women with hyperprolactinemia
LEVOTHYROXINE	All women with hypothyroidism
INTEGRATED IRON	All study participants
CHOLECALCIFEROL	All study participants
LIFESTYLE CHANGES	All study participants were encouraged to take less carbohydrates, sugary foods, to do exercises and manage any stress they have.

Changes in mucus pattern, menstrual bleeding patterns, and fertility outcomes after three months of treatment/interventions

After managing the participants for three months, the majority 85.2% had fertile days of stretchy, slippery, and clear cervical mucus, and 28.7% conceived within the three months. 6.1% had abnormal bleeding patterns. Figure 1 summarizes the three months outcomes of the cycles.

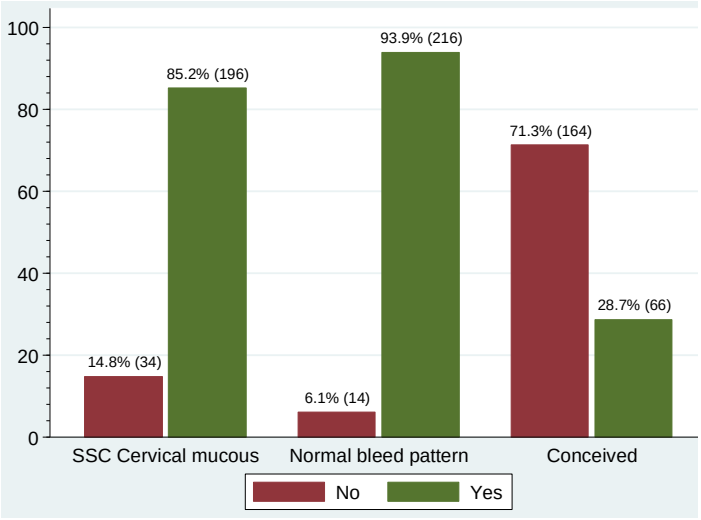

Figure 1. *The changes in mucus patterns, menstrual bleeding patterns, and fertility outcomes in three months of treatment.*

4. Discussion

Menstrual cycle is an important physiological chain of events that lead to conception when regular, functional and in the presence of viable, healthy spermatozoa from a male partner. Menstrual pattern, cervical mucous and hormonal balance are the key to fertility.

4.1. Menstrual Chart Patterns

The median cycle length in this study was 30 days [IQR: 27-37]. Menstrual chart patterns observed during the study period were shorter cycles (16.5%), longer cycles (27.0%), and normal cycles 56.5%. About two-thirds of our participants were not ovulating. Menstrual cycle length (MCL) is primarily determined by the rate and quality of follicular growth and hence the duration of the follicular phase [10]. Regular menstrual cycles may lack ovulation due to hypothalamic adaptations related to nutritional, hormonal, and emotional stressors that women in the population commonly experience [11]. Cycles with normal length are not a guarantee that ovulation will occur. Shorter and longer cycles have been associated with low fecundity rates causing abnormal

menstrual cycle patterns, and thus are expected to be an important predictor of reduced fertility [12]. The study resembles the one done by Sunni Mumford et al 2012 whereby the median cycle length was 28 days [13]. The majority of women (71%) in both cycles were classified in the same cycle length category for both cycles, but 28% of women were classified as having either a short and normal-length cycle or a long and normal-length cycle as well. A very small percentage of women had a short and a long cycle during the study period of (1%). The similarities in these studies are that the population was 18-44 years old and the median length of the menstrual cycle was almost the same. Participants with anovulatory cycles in both studies had normal cycle lengths. The difference is that the participants in the Sunni Mumford et al study had regular menstruating cycles but our participants had infertility.

More than two-thirds of our participants were not ovulating and hence could not conceive. Chronic anovulation is considered a marker of several potential endocrine disturbances. Hambridge H. L. et al in their article, "The influence of sporadic anovulation on hormone levels in ovulatory cycles" observed that reproductive hormone concentrations were lower during anovulatory cycles, and significant reductions were also observed in estradiol levels [14]. This is similar to our study two-thirds of participants had low estrogen levels (below 50 pg/ml).

4.2 Hormonal and Clinical-associated Factors

Half of the participants in this study had abnormal HbA1c levels. Those with normal levels of glycated hemoglobin preconception ovulated and later conceived more than those with abnormal HbA1c compared to those with high levels of glycosylated hemoglobin. Glycosylated hemoglobin (HbA1c) is the most common marker of chronic hyperglycemia and has long been considered the most practical approach used to review long-term glycemic control in diabetic patients. However, in 2010, the American Diabetes Association (ADA) included a glycosylated hemoglobin level as a component of diagnostic criteria for increased risk of diabetes [15]. Hemoglobin A1c helps in identifying a substantial number of women who would otherwise remain undiagnosed in the setting for a normal oral glucose test [16]. However, those with normal HbA1c may be insulin resistant too since HbA1c has a low sensitivity of 30 -35%. A person's weight affects fertility and the majority of our participants had a BMI of 25 and above, indicating overweight and obesity. Obesity is associated with increased menstrual irregularity, ovulatory dysfunction, poor pregnancy outcome, development of insulin resistance, and infertility through the production of signaling molecules by adipokines which have effects on the hypothalamic-pituitary signaling and communication, inhibiting ovulation [17, 18]. Sim KM et al showed that weight loss in overweight and obese women undergoing assisted reproductive technology was achieved by diet, lifestyle changes, a very low-energy diet, and medical interventions and it translated into a significantly increased pregnancy rate [19]. We managed our patients with lifestyle modifications and medications and approximately one-third of our participants conceived within three months. The difference between these two studies was that participants in Sim's study conceived through IVF, and in our study, they conceived naturally.

4.3. Changes in the Cervical Mucus, Menstrual Cycle Patterns and the Fertility Outcomes After Three Months of Treatment

In our study, a substantial number of women experienced positive change in their menstrual cycles after three months of follow-up. Specifically, 85.2% showed improvements in cervical mucus consistency (stretchy, slippery, and clear), 93.9% reported normal bleeding patterns, and 28.7% achieved conception The short-term success was brought about by understanding the menstrual patterns, (biomarkers in each phase of the cycle) lifestyle changes, medical interventions (Metformin, Bromocriptine, Levothyroxine, Cholecalciferol and Integrated iron). A study done by Rene et al points out that self-identification of the biological fertile window by the observation of any type of cervical mucus provides 100% sensitivity and the identification of the biological fertile window by peak mucus (defined as clear, slippery, or stretchy mucus related to estrogen) yielded 96% sensitivity and improved specificity. Our study participants 85.2% had attained fertile days of stretchy, slippery, and clear mucus at the end of the study period. Eun Jin Kim et al reported that there is a significant association between infertility and lifestyle, such as a healthier diet and increased physical activities to improve overall and reproductive health as well as an increase in pregnancy rates [20]. The above interventions in these studies resemble the ones we did for our patients. These interventions helped in upgrading the women's quality of life after achieving back the fertile cervical mucus which helped some of them conceive and also helped women become masters of their bodies. Knowledge about fertility awareness acquired by self-observation of cervical mucus patterns at the vulva is an invaluable tool for women. The identification of medical and environmental causes of abnormal menstrual cycle patterns provides clues to the causes of the most frequent fertility disorders [21].

4.4. Limitations

This study was carried out at the tertiary hospital and on a special group of patients (infertility) hence the data obtained may not represent the general population. Hormonal levels and body mass index were not checked when the patients started to ovulate. We used HbA1c as a test to diagnose metabolic disorders while Hba1c sensitivity is low; about 30 to 35%. We failed to do pooled TSH, T3, and prolactin levels. This is due to the high cost of these investigations. We

also did not report on patients with polycystic ovarian syndrome.

5. Conclusion

Women with infertility endure years of pain, surgeries, doctor's appointments, and dead ends before they know why they are not able to conceive and even before the right management begins.

In general, this study indicated that many women with infertility had anovulatory menstrual cycles. Abnormal levels of HbA1c, prolactin, thyroid hormones and obesity were associated with infertility in this study. Menstrual cycle charting, hormonal management, and lifestyle changes made these participants ovulate and later conceive.

6. Recommendations

Menstrual cycle charting patterns and basic hormonal profiles should be incorporated as one of the tools in managing women with infertility.

Signs and symptoms of abnormal insulin, thyroid, and prolactin levels to be accessed during physical and systemic examination.

Women with infertility should be encouraged to adopt lifestyle changes (nutrition and physical exercises) and health-promoting behavior to maintain health and succeed in fertility. They should be encouraged to seek early medical interventions once they notice any abnormalities in their cycle patterns.

Abbreviations

ADA	Association of Diabetes of America
BMC	Bugando Medical Centre
FSH	Follicular Stimulating Hormone
GnRH	Gonadotropin Releasing Hormone
IQR	Inter-quartile Range
LH	Lutenizing Hormone
MCL	Menstrual Cycle Length
SHBG	Sex Hormone Binding Globulin
SSC	Stretchy Slippery and Clear
TSH	Thyroid Stimulating Hormone

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Authors Contribution

Albert Kihunrwa: Conceptualization, Data curation, Formal Analysis, Methodology, Supervision, Writing – review & editing

Juliet Macharia: Conceptualization, Data curation, Formal Analysis, Methodology, Validation, Writing – original draft

Dismas Matovelo: Conceptualization, Data curation, Project administration, Supervision, Validation, Visualization, Writing – review & editing

Adolfine Hokororo: Conceptualization, Data curation, Formal Analysis, Methodology, Supervision, Writing – original draft, Writing – review & editing

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Availability of Data and Material

The data set used and analyzed during the current study are available from the corresponding author on request.

Ethical Approval

Ethical clearance and permission to conduct this study were sought from the joint CUHAS/BMC Research Ethics and Review Committee, and research clearance certificate number CREC/658/2023 was granted. All enrolled study participants voluntarily signed an informed consent to participate in this study after being explained the objectives of the study.

Consent for Publication

Written informed consent to publish these study findings was obtained from the patients, copies of which are available for review by the Editor-in-chief of this journal. Additionally, consent was sought and granted by the Catholic University of Health and Allied Sciences Directorate of Research and Publication to publish this work. A copy of the clearance document is also available for review by the Editor-in-Chief of this journal.

Conflict of Interest

The authors declare no conflicts of interest.

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Research Fields

Albert Kihunrwa: Hypertensive disorders of pregnancy, preeclampsia, Materno-fetal medicine, Female Infertility, role of Prolactin hormone, Family planning and contraception, religion perspective, Quality of health care in pregnancy.

Juliet Macharia: Female infertility, role of insulin hormone, Female infertility, Role of prolactin and thyroid hormones, Maternal sepsis in low income resources, Menstrual patterns in reproductive women, Fertility education and medical management in women with subfertility.

Dismas Matovelo: Maternal Health, Reproductive Health, Gender & Equity, Health systems, Operational and Clinical Research.

Adolfine Hokororo: Maternal and Child health, Adolescent Sexual and Reproductive Health, Newborn Health, Congenital infections, Infectious Diseases.