INSIGHTS-JOURNAL OF
HEALTH AND REHABILITATION

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

THE EFFICACY OF HORMONAL THERAPY IN EARLY MENOPAUSE

Original Research

Shazia Awan[1]*, Sanobar Baloch[2], Naheed Parveen[3]
[1]Associate professor, Gu1 LUMHS, Pakistan.
[2]Associate Professor Indus Medical College & University of Moderen Sciences Tando Mohd Khan, Pakistan.
[3]Professor of Obgyn Dept, Lumhs Jamshoro, Pakistan.
Corresponding Author: Shazia Awan, Associate professor, Gu1 LUMHS, Pakistan, Shaziaasad38@gmail.com
Acknowledgement: The authors gratefully acknowledge the support of Liaquat University Hospital staff and study participants.

Conflict of Interest: None
Grant Support & Financial Support: None

ABSTRACT

Background: Early menopause, defined as the cessation of menstruation before the age of 45, is associated with an increased risk of vasomotor symptoms, osteoporosis, and cardiovascular disease. Hormonal therapy (HT) is the cornerstone of management, yet localized data regarding its efficacy and safety among Pakistani women remain limited.

Objective: To evaluate the efficacy of hormonal therapy in the management of early menopause among women treated at Liaquat University Hospital, Hyderabad.

Methods: A prospective cohort study was conducted over six months involving 73 women aged 40–45 years diagnosed with early menopause. Participants were prescribed either estrogen therapy (ET) or combined estrogen-progestin therapy (EPT) and monitored at 1, 3, and 6 months. Primary outcomes included symptom severity (Menopause Rating Scale), quality of life (Menopause-specific Quality of Life Questionnaire), bone mineral density (DEXA), lipid profiles, and therapy adherence. Data were analyzed using SPSS v21.0 with significance set at $p \leq 0.05$.

Results: At baseline, 42.5% of participants had severe symptoms, which decreased to 4.1% at six months. Mean MenQOL scores improved from 4.2 to 1.6. BMD improved from –2.1 to –1.8, while total cholesterol and LDL levels reduced by 21 and 18 mg/dL respectively. EPT showed slightly greater symptom relief compared to ET. Adherence exceeded 90% in most participants, with only mild, self-limiting adverse effects reported.

Conclusion: Hormonal therapy significantly improved menopausal symptoms, quality of life, and early indicators of bone and cardiovascular health in women with early menopause. It remains a safe and effective intervention when individualized and initiated appropriately.

Keywords: Adherence, Bone Density, Cardiovascular Health, Estrogen Replacement Therapy, Hormone Therapy, Menopause, Menopause Rating Scale, Quality of Life.

INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

INTRODUCTION

Menopause is a physiological milestone marking the cessation of menstrual cycles, typically occurring between the ages of 45 and 55. However, a subset of women—approximately 1%—experience menopause before the age of 40, a condition clinically recognized as premature ovarian insufficiency (POI), and before 45 years as early menopause (1). This earlier-than-expected hormonal transition brings with it not only the classic vasomotor symptoms such as hot flashes, sleep disturbances, and vaginal dryness, but also heightened long-term risks for osteoporosis, cardiovascular disease, cognitive decline, and decreased quality of life (2). Hormonal therapy (HT), consisting primarily of estrogen with or without progestin, remains the cornerstone of symptomatic relief and has shown proven benefits in improving bone mineral density and reducing vasomotor symptoms (3). Despite international consensus on the benefits of HT for symptomatic management, its application remains nuanced due to the well-documented risks such as thromboembolic events, stroke, gallbladder disease, and hormone-dependent cancers, especially when initiated late or continued long-term (4). However, literature increasingly supports the hypothesis that initiating HT closer to the onset of menopause, particularly in cases of early menopause, may tilt the benefit-risk ratio in favor of therapy (5). In such cases, continuing HT until the average age of natural menopause—around 51 years—can help mitigate the prolonged hypoestrogenic state that contributes to systemic deterioration (6).

In Pakistan, the prescription patterns for HT among gynecologists and obstetricians are cautious and often centered around managing acute symptoms rather than long-term preventive care, underscoring a gap in both clinical practice and locally contextualized research (7,8). Furthermore, genetic, lifestyle, and socio-environmental factors unique to the Pakistani population necessitate localized evidence to guide clinical decision-making. Current global guidelines also emphasize individualized treatment approaches, advocating the use of the lowest effective dose for the shortest necessary duration, although early menopause scenarios may require deviation from this model due to differing physiological implications (9). Despite the global body of literature surrounding HT, there is a clear paucity of regional data exploring its efficacy specifically in women with early menopause within the Pakistani healthcare context. This study seeks to address this gap by evaluating the efficacy of hormonal therapy in women diagnosed with early menopause at Liaquat University Hospital, Hyderabad. By monitoring symptom relief, quality of life, bone and cardiovascular health, and any adverse events, the research aims to contribute valuable insights to inform both local clinical practices and broader scientific discourse. The objective of this study is to evaluate the efficacy of hormonal therapy in the management of early menopause among women treated at Liaquat University Hospital, thereby strengthening evidence-based care within the regional healthcare framework.

METHODS

This study was conducted as a prospective cohort study in the Department of Gynecology and Obstetrics at Liaquat University Hospital, Hyderabad, over a period of six months, following formal approval from the institutional review board (IRB). A total of 73 women were included, with the sample size determined using the OpenEpi sample size calculator, based on a 5% estimated prevalence of early menopause (10), a 5% margin of error, and a 95% confidence interval. Non-probability purposive sampling was utilized to recruit eligible participants. Women aged between 40 and 45 years were considered for inclusion, provided they had experienced spontaneous cessation of menstruation for 12 consecutive months without secondary causes. Although 45 years marks the upper boundary of natural menopausal age, the inclusion of women up to age 45 was justified based on biochemical confirmation of early menopause—defined operationally by elevated follicle-stimulating hormone (FSH) levels greater than 40 IU/L on two separate occasions at least one month apart, indicating ovarian insufficiency. This ensured that only those with true early menopause, regardless of being close to the threshold of natural menopause, were included, thereby preserving diagnostic accuracy. Additional inclusion criteria included the willingness to initiate hormonal therapy as part of clinical management. Exclusion criteria encompassed women with surgically or chemically induced menopause, a history of hormone-sensitive malignancies, thromboembolic disorders, uncontrolled hypertension, liver disease, prior use of hormonal therapy for menopause, or those unable to provide informed consent (11).

After obtaining written informed consent, each participant underwent a thorough baseline evaluation that included demographic data, medical history, and menopausal symptom assessment using structured questionnaires. Symptoms such as hot flashes, night sweats, vaginal dryness, and mood disturbances were recorded. Baseline investigations also included bone mineral density (BMD) assessment via dual-energy X-ray absorptiometry (DEXA), as well as measurements of blood pressure and lipid profiles to evaluate cardiovascular health. Hormonal therapy—either estrogen alone or in combination with progesterone—was prescribed based on individual clinical indications by the attending gynecologist. Participants were followed at 1, 3, and 6 months. During each follow-up, menopausal symptoms and quality of life were reassessed using the Menopause Rating Scale and Menopause-Specific Quality of Life Questionnaire. Self-reported adherence to therapy and documentation of any adverse events were also recorded. Bone mineral density

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

was re-evaluated at 6 months, while blood pressure and lipid profiles were reassessed at 3 and 6 months to monitor cardiovascular outcomes. Confidentiality was ensured by anonymizing patient data through coded identifiers and securing digital records with password protection. All data will be retained for five years post-study and subsequently discarded. Data analysis was performed using Microsoft Excel 2016 and SPSS version 21.0. Categorical variables were presented as frequencies and percentages, while continuous variables were summarized as means and standard deviations. Stratification was employed to control for effect modifiers, and chi-square testing was applied post-stratification. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

A total of 73 participants diagnosed with early menopause were enrolled in the study. The mean age was 42.3 years, with an average BMI of 26.1 kg/m². Mean height and weight were 158.6 cm and 65.4 kg, respectively. Baseline blood pressure readings averaged 128/82 mmHg. Most participants resided in urban areas (61.6%), with the remainder from rural regions (38.4%). The majority fell within the middle socioeconomic class (56.2%), while 13.7% belonged to the upper class and 30.1% to the lower class. A substantial proportion of the cohort was married (83.6%), with 39.7% employed at the time of the study. Family history of osteoporosis and cardiovascular disease was reported in 28.8% and 35.6% of participants, respectively. Educational background varied, with 31.5% having attained higher education, while 12.3% had no formal schooling. At baseline, the mean follicle-stimulating hormone (FSH) level was recorded at 52.8 IU/L. The initial lipid profile showed a mean total cholesterol level of 219 mg/dL, LDL at 142 mg/dL, HDL at 46 mg/dL, and triglycerides at 170 mg/dL. Bone mineral density (BMD), measured using DEXA scanning, averaged −2.1, indicating osteopenia in a significant number of participants. Regarding hormonal therapy, 54.8% of participants received estrogen-progestin therapy (EPT), while 45.2% received estrogen-only therapy (ET). The majority were prescribed standard doses via oral administration. Hormonal therapy was initiated immediately after enrollment and continued throughout the six-month follow-up period.

Baseline evaluation using the Menopause Rating Scale (MRS) revealed that 42.5% of participants fell into the severe category (17–28 score), while 19.2% had very severe symptoms (29–44 score). Over time, a progressive improvement was observed. At one month, the proportion of participants with no or few symptoms (0–4 score) increased from 2 to 8, and further improved to 31 participants by six months. Concurrently, those in the severe and very severe categories reduced to just 3 and 0 participants, respectively, by the end of the study period. Menopause-specific Quality of Life (MenQOL) scores also reflected notable improvement. The average baseline score was 4.2, which reduced to 3.1 at one month, 2.4 at three months, and further to 1.6 at six months, indicating enhanced overall well-being. Adherence to therapy was reported as >90% by 82% of participants at all time points. Adverse effects were minimal, with 9 participants reporting transient nausea or breast tenderness during the initial phase of therapy; no serious adverse events or changes in prescribed medications were recorded. By the third month, lipid profiles showed mild improvement: mean total cholesterol reduced to 204 mg/dL, LDL to 132 mg/dL, HDL increased to 49 mg/dL, and triglycerides decreased to 160 mg/dL. At six months, further favorable shifts were observed with total cholesterol at 198 mg/dL, LDL at 124 mg/dL, HDL at 52 mg/dL, and triglycerides at 148 mg/dL. Similarly, BMD showed a modest improvement with the average score improving from −2.1 at baseline to −1.8 at six months, reflecting positive skeletal response to hormonal therapy.

At the six-month follow-up, stratification by hormonal therapy type revealed meaningful differences in symptom resolution. Among those receiving estrogen-progestin therapy (EPT), 45% (18/40) achieved “no or few symptoms” on the Menopause Rating Scale (MRS), compared to 39.4% (13/33) of those on estrogen therapy (ET) alone. Additionally, none of the participants on EPT remained in the “severe” or “very severe” categories, whereas 4 participants in the ET group (3 severe, 1 very severe) continued to report more intense symptoms. These findings suggest that EPT may offer a slightly more favorable symptom control profile than ET alone by the end of the study period. Adherence to therapy remained high across both groups, with over 90% adherence reported by 81.8% (27/33) of ET users and 80% (32/40) of EPT users at six months. This pattern was consistent throughout earlier follow-ups, showing sustained engagement with treatment. The proportion of participants reporting moderate adherence (70–90%) and low adherence (<70%) remained small and stable over time in both cohorts. Adverse effects were mild and transient across the board, with no serious complications recorded. Nausea was the most reported side effect (ET: 2 cases; EPT: 3 cases), followed by breast tenderness (ET: 3; EPT: 1). Headache and bloating were less common but still noted in both groups. Notably, these symptoms resolved spontaneously or with minor supportive care and did not necessitate discontinuation or alteration of hormonal therapy in any case. These subgroup insights strengthen the overall findings by demonstrating consistent safety and effectiveness of hormonal therapy in early menopause, with EPT showing marginally better outcomes in symptom control.

Table 1: Demographics

Variable	Value
Age (years)	42.3 ± 2.1
BMI (kg/m)	26.1 ± 3.4
Height (cm)	158.6 ± 6.7

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

Variable		Value
Weight (kg)		65.4 ± 8.9
Systolic BP (mmHg)		128 ± 10
Diastolic BP (mmHg)		82 ± 6
Residence	Rural	28 (38.4%)
	Urban	45 (61.6%)
Socioeconomic Status	Upper	10 (13.7%)
	Middle	41 (56.2%)
	Lower	22 (30.1%)
Marital Status	Married	61 (83.6%)
	Never Married	3 (4.1%)
	Divorced	5 (6.8%)
	Widowed	4 (5.5%)
Employment Status	Employed	29 (39.7%)
	Unemployed	44 (60.3%)
Family History of Osteoporosis	Yes	21 (28.8%)
	No	52 (71.2%)
Family History of Cardiovascular Disease	Yes	26 (35.6%)
	No	47 (64.4%)
Education Level	No education	9 (12.3%)
	Primary	17 (23.3%)
	Secondary	24 (32.9%)
	Higher	23 (31.5%)

Table 2: MRS Score Categories Over Time

Time Point	No/Few Symptoms (0–4)	Mild (5–8)	Moderate (9-16)	Severe (17–28)	Very Severe (29–44)
Baseline	2	5	21	31	14
1 Month	8	15	28	18	4
3 Months	18	23	20	10	2
6 Months	31	25	14	3	0

Table 3: Mean QOL Score Over Time

Time Point	Mean Score (0–6)
Baseline	4.2
1 Month	3.1
3 Months	2.4
6 Months	1.6

Table 4: Lipid Profile Over Time

Time Point	Total Cholesterol (mg/dL)	LDL (mg/dL)	HDL (mg/dL)	Triglycerides (mg/dL)
Baseline	219	142	46	170
3 Months	204	132	49	160
6 Months	198	124	52	148

Table 5: Bone Mineral Density (DEXA) Over Time

Time Point	BMD (DEXA) Score
Baseline	-2.1
6 Months	-1.8

Table 6: Stratified MRS by HT Type

HT Type	No/Few Symptoms (0-4)	Mild (5-8)	Moderate (9-16)	Severe (17-28)	Very Severe (29-44)
ET (n=33)	13	9	7	3	1
EPT (n=40)	18	16	7	0	0

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

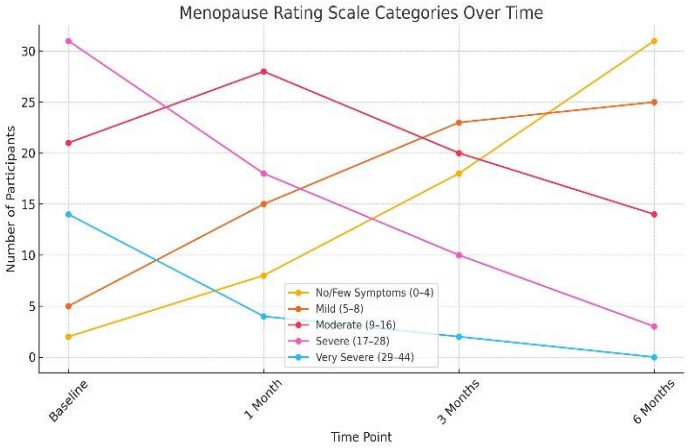

Figure 2 Menopause Rating Categories Over Time

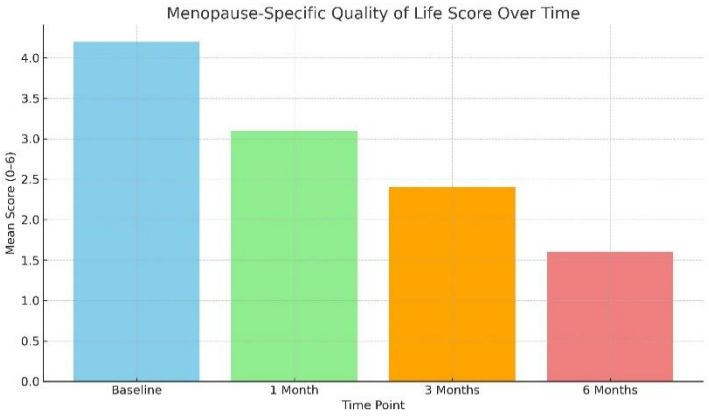

Figure 1 Menopause-Specific Quality of Life Score Over Time

DISCUSSION

The present study aimed to evaluate the efficacy of hormonal therapy (HT) in managing early menopause among women attending Liaquat University Hospital, with a particular focus on symptom relief, quality of life, cardiovascular risk factors, bone health, adherence, and adverse effects. The findings consistently demonstrated significant improvements in symptom severity and menopausal quality of life, with modest yet favorable changes in bone mineral density and lipid profile parameters over six months of treatment. The observed reduction in Menopause Rating Scale (MRS) scores across follow-ups confirms the clinical efficacy of HT in alleviating vasomotor and psychological symptoms of menopause (12,13). By six months, the majority of participants transitioned from moderate-to-severe symptom categories to mild or no symptoms, a trend that supports evidence from recent reviews and trials. A study affirmed that HT is the most effective option for managing vasomotor symptoms and improving quality of life in women younger than 60 or within 10 years of menopause onset (14). This is aligned with the EMAS consensus which emphasizes individualized dosing and early initiation to maximize benefit and minimize risk. Improvement in MenQOL scores further substantiates the effectiveness of HT in enhancing physical, emotional, and sexual well-being (15). The findings are comparable to those reported in a study, which noted that HT significantly improves health-related quality of life, particularly in women presenting with bothersome vasomotor and genitourinary symptoms (16). These improvements appear consistent across both estrogen-only therapy (ET) and combined estrogen-progestin therapy (EPT), although EPT showed a marginally greater reduction in symptom severity in this study.

Cardiovascular parameters, particularly lipid profiles, improved modestly. Total cholesterol and LDL levels showed a steady decline, while HDL increased over time. These findings echo the conclusions of a study which observed similar lipid modulations with HT in menopausal women. However, blood pressure changes were not recorded longitudinally in this study, a notable limitation given its relevance to cardiovascular health. Bone mineral density (BMD), assessed by DEXA scans, showed a minor but clinically relevant improvement over six months. Although short in duration, this finding supports HT's role in osteoporosis prevention in women with early estrogen deficiency, as supported by the EMAS and WHI findings. Adherence to HT was high, with more than 80% of participants maintaining over 90% adherence throughout the study (17,18). The tolerability profile was favorable, with only mild adverse effects such as nausea and breast tenderness, all resolving without intervention. This aligns with findings of other studies, emphasized the improved safety profile of newer HT formulations when initiated appropriately (19-21).

Despite its strengths—including a clearly defined population, structured follow-ups, and validated tools—this study had limitations. The relatively short follow-up period precludes long-term assessment of cardiovascular outcomes and fracture risk. The exclusion of blood pressure data at follow-up, lack of hormonal level monitoring post-treatment, and absence of a control group limit causal inference. Additionally, while both ET and EPT were studied, stratified data on menopausal age, comorbidities, or body mass index in relation to therapy response were not explored, potentially limiting generalizability. Future research should focus on long-term follow-up to capture the extended impact of HT on bone density, cardiovascular events, and breast cancer risk, especially in diverse populations. Additionally, comparisons of different HT formulations, dosages, and administration routes could guide individualized therapy selection. Incorporating patient-centered metrics like satisfaction and preference can also refine treatment algorithms (22). In conclusion, hormonal therapy significantly alleviated menopausal symptoms, enhanced quality of life, and yielded early benefits in bone and cardiovascular health among women with early menopause. With high adherence and minimal adverse effects, HT remains a viable and safe option when initiated at the appropriate time in well-screened individuals.

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

CONCLUSION

This study demonstrates that hormonal therapy is highly effective in managing early menopause by significantly reducing symptom severity, improving quality of life, and providing early benefits to bone and cardiovascular health. With high adherence and minimal adverse effects, HT presents a safe, evidence-based option when initiated appropriately. These findings underscore the importance of individualized, timely intervention to optimize outcomes for women experiencing early menopausal transition.

AUTHOR CONTRIBUTION

Author	Contribution
Shazia Awan*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Sanobar Baloch	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Naheed Parveen	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published

REFERENCES

1. Fasero M, Hernández A, Varillas-Delgado D, Coronado PJ. Women with low quality of life by cervantes-short form scale choose menopausal hormone therapy. Eur J Obstet Gynecol Reprod Biol. 2020;252:43-9.
2. Madsen T, Sobel T, Negash S, Allen TS, Stefanick M, Manson J, et al. A Review of Hormone and Non-Hormonal Therapy Options for the Treatment of Menopause. International Journal of Women's Health. 2023;15:825-36.
3. Balan V, Tikhomirova E, Zhuravel A, Titchenko J, Lovygina T. New trends in current menopausal hormone therapy. Gynecology. 2021.
4. Nguyen HH, Milat F, Vincent AJ. New insights into the diagnosis and management of bone health in premature ovarian insufficiency. Climacteric. 2021;24(5):481-90.
5. Samad N, Nguyen HH, Ebeling PR, Milat F. Musculoskeletal Health in Premature Ovarian Insufficiency. Part Two: Bone. Semin Reprod Med. 2020;38(4-05):289-301.
6. Chiarito M, Brunetti G, D'Amato G, Faienza MF. Monitoring and maintaining bone health in patients with Turner syndrome. Expert Rev Endocrinol Metab. 2020;15(6):431-8.
7. Hirsch H, Manson JE. Menopausal symptom management in women with cardiovascular disease or vascular risk factors. Maturitas. 2022;161:1-6.
8. King EM, Prior JC, Pick N, van Schalkwyk J, Kestler M, Tkachuk S, et al. Menopausal hormone therapy for women living with HIV. Lancet HIV. 2021;8(9):e591-e8.
9. Fenton CL, McGauran MJ, Richards AM. Menopausal hormonal therapy in gynaecological cancers: An evidence-based approach for clinical management. Aust N Z J Obstet Gynaecol. 2020;60(6):942-5.
10. Davies HO. A local audit evaluating bone health in patients with functional hypothalamic amenorrhoea secondary to an eating disorder and a review of the application of hormone therapy in this clinical setting. Post Reprod Health. 2024;30(3):182-9.
11. Sundell M, Brynhildsen J, Fredrikson M, Hoffmann M, Spetz Holm AC. Insufficient use of menopausal hormone therapy in Swedish women with early or premature menopause caused by bilateral oophorectomy: a register-based study. Bjog. 2024;131(4):500-7.
12. Palacios S, González SP, Sánchez-Prieto M, Fasero M. Clinical challenges and considerations in pharmacotherapy of osteoporosis due to menopause. Expert Opin Pharmacother. 2024;25(10):1359-72.
13. Levy B, Simon J. A Contemporary View of Menopausal Hormone Therapy. Obstetrics & Gynecology. 2024;144:12-23.
14. Ha J, Park SS, Park S, Yoon JH, Baek KH, Kim HJ, et al. Effects of Hormone Replacement Therapy on Bone Mass After Allogeneic Hematopoietic Stem Cell Transplantation. J Clin Endocrinol Metab. 2020;105(9).
15. Anagnostis P, Bosdou JK, Vaitsi K, Goulis DG, Lambrinoudaki I. Estrogen and bones after menopause: a reappraisal of data and future perspectives. Hormones (Athens). 2021;20(1):13-21.

16. Golezar S, Keshavarz Z, Ramezani Tehrani F, Ebadi A. An exploration of factors affecting the quality of life of women with primary ovarian insufficiency: a qualitative study. BMC Womens Health. 2020;20(1):163.
17. Tomić Naglić D, Mandić A, Zirojević M, Vuković N, Pejaković S, Manojlovic M, et al. Hormone replacement therapy in surgical menopause after gynecological malignancies. Biomol Biomed. 2025;25(4):751-60.
18. Gonçalves CR, Vasconcellos AS, Rodrigues TR, Comin FV, Reis FM. Hormone therapy in women with premature ovarian insufficiency: a systematic review and meta-analysis. Reprod Biomed Online. 2022;44(6):1143-57.
19. Jang JH, Arora N, Kwon JS, Hanley GE. Hormone Therapy Use After Premature Surgical Menopause Based on Prescription Records: A Population-Based Study. J Obstet Gynaecol Can. 2020;42(12):1511-7.
20. Costa GPO, Ferreira-Filho ES, Simoes RDS, Soares-Junior JM, Baracat EC, Maciel GAR. Impact of hormone therapy on the bone density of women with premature ovarian insufficiency: A systematic review. Maturitas. 2023;167:105-12.
21. Li M, Zhu Y, Wei J, Chen L, Chen S, Lai D. The global prevalence of premature ovarian insufficiency: a systematic review and meta-analysis. Climacteric. 2023 Apr;26(2):95-102.
22. Shah N, Tariq H, Khan F, Shah N. Prescribing practices of Hormone Therapy for Menopausal females by OBGYN of Pakistan. Pak J Med Sci. 2023 Jan-Feb;39(1):128-132.