



Determination of risk factors for osteopenic changes in women pregnant using assisted reproductive technologies

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Abstract. The study aimed to investigate the factors that influence the risk of osteopenic changes in women who became pregnant with the help of assisted reproductive technologies. The study involved 150 women aged 25-40 who became pregnant after in vitro fertilisation, intrauterine insemination and oocyte donation. Bone mineral density was assessed by ultrasound densitometry in the distal forearm at the early (8-12 weeks) and late (32-36 weeks) stages of pregnancy. The T-score values showed a significant decrease in the third trimester in all groups, the largest – in patients who became pregnant due to oocyte donation (-1.3 ± 0.3 in the distal forearm). An analysis of socio-demographic characteristics revealed that age over 35, low physical activity, vitamin D and calcium deficiency, and bad habits such as smoking and excessive caffeine consumption significantly increased the risk of developing osteopenic changes. Women with regular consumption of dairy products, calcium supplements and a normal level of physical activity had significantly better bone mineral density. Biochemical markers confirmed higher levels of calcium, magnesium and vitamin D in the oocyte donation group, while the intrauterine insemination group demonstrated a deficiency of these elements and increased markers of bone resorption. The hormonal profile also had a significant impact on bone health: high oestrogen levels in the oocyte donation group were associated with less severe osteopenic changes, while elevated parathyroid hormone levels in the intrauterine insemination group contributed to increased bone loss. Patients with the highest levels of prolactin had better bone mineral density preservation due to the positive effect of this hormone on calcium metabolism. The findings emphasise the need for comprehensive monitoring of bone health in women who have become pregnant using assisted reproductive technologies

Keywords: bone density; biochemical markers; hormonal profile; intrauterine insemination; oocyte donation

INTRODUCTION

Assisted reproductive technologies are a significant achievement of modern medicine, overcoming infertility and providing the possibility of having a child in patients with reproductive disorders. However, pregnancy resulting from the use of such methods is accompanied by significant changes in a woman's physiological and metabolic state. Bone tissue is a particularly vulnerable system during this period, as it changes due to the body's increased need for

calcium and other minerals. Women who have become pregnant through in vitro fertilisation, intrauterine insemination or oocyte donation may face an increased risk of osteopenic changes due to the specifics of their hormonal and metabolic background. The study of factors affecting the state of bone tissue in such patients is an urgent task.

The hormonal profile is crucial for maintaining bone health. O. Deinichenko *et al.* [1] studied the effect of oes-

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trogen on bone mineral density in women who became pregnant through oocyte donation. They found that high levels of oestrogen slowed bone loss. The impact of mineral metabolism on bone health is also an important factor. A. Tsymbal & Y. Kotlova [2] analysed the mineral composition of blood in pregnant women and found that calcium and vitamin D deficiency significantly increases the risk of osteopenic changes. The authors emphasised that regular consumption of calcium-containing foods and food supplements has a positive effect on mineral density.

Physical activity is also substantial in maintaining bone health. L. Zhytnik *et al.* [3] demonstrated that pregnant women who exercise regularly have higher bone mineral density than those who are sedentary. Biochemical markers of bone resorption are an important tool for assessing bone health. J.E. Stern *et al.* [4] demonstrated that high levels of C-telopeptides correlate with intense bone loss in pregnant women.

Psychosocial and demographic factors also significantly affect the risk of osteopenic changes. Y. Wang *et al.* [5] demonstrated that women over 35 years of age who have bad habits, such as smoking or excessive caffeine consumption, are prone to a significant decrease in bone mineral density. The authors noted that social factors, such as access to good nutrition, are also substantial in the prevention of osteopenia, but they did not address the hormonal and metabolic characteristics of women who became pregnant using assisting technology. The impact of physiological stress on bone metabolism was investigated by B.M. Nørgård *et al.* [6], noting that elevated cortisol levels during pregnancy can contribute to a decrease in mineral density. Their study confirmed the importance of controlling stress factors. M.E. Graham *et al.* [7] highlighted the correlation between prolactin levels and the preservation of bone mineral density. The study demonstrated that high levels of this hormone positively affect calcium metabolism. The hormonal balance and its effect on calcium metabolism were studied by B. Sun *et al.* [8], noting that elevated levels of parathyroid hormone increase bone resorption. The authors emphasised that women with endocrine disorders during pregnancy need careful monitoring.

Hormonal, metabolic, and social factors are significant in maintaining bone health in pregnant women, especially those who become pregnant through assisted reproductive technologies. However, existing studies do not provide a comprehensive analysis of these aspects in this category of patients. In particular, the effect of oestrogen on bone mineral density was considered without considering concomitant changes in prolactin, parathyroid hormone and cortisol levels, which also affect calcium metabolism. In addition, although a correlation between calcium and vitamin D deficiency and the risk of osteopenic changes was established, the specifics of mineral metabolism in women after *in vitro* fertilisation remain understudied.

Thus, there is a need for a more detailed study of the complex impact of hormonal, metabolic and socio-demographic factors on bone health in women who became pregnant using reproductive technologies. The study aimed to determine the main risk factors for the development of osteopenic changes in women who became pregnant with the help of assisted reproductive technologies, incorporating the influence of hormonal, metabolic and

socio-demographic context. The objectives of the study included assessing bone mineral density at different stages of pregnancy, analysing the impact of hormonal profiles, and developing recommendations for the prevention of osteopenic changes in this group of patients.

✦ MATERIALS AND METHODS

The study was conducted in 2024 at the Kyiv Perinatal Centre [9], a municipal non-profit enterprise (MNE), involving 150 women aged 25 to 40 who became pregnant with the help of assisted reproductive technologies (ART). The types of ART used in the patients included *in vitro* fertilisation (IVF) (57 women), intrauterine insemination (IUI) (45 women) and oocyte donation (48 women). The inclusion criteria were confirmed pregnancy obtained through ART, absence of diagnosed bone diseases or endocrine disorders, and voluntary consent to participate. Patients with existing chronic metabolic disorders or systemic diseases that could affect bone metabolism were excluded from the study. To determine bone mineral density (BMD), ultrasound densitometry of the forearm was performed using the OsteoSys SONOST 3000 apparatus (OsteoSys, South Korea). The study was conducted in two stages: in the first trimester of pregnancy (8-12 weeks) and in the third trimester (32-36 weeks). The measurements were performed in the distal forearm, which was used to detect early osteopenic changes and assess their dynamics during pregnancy.

Additionally, a questionnaire was administered to patients to collect data on risk factors for osteopenic changes. The questionnaire consisted of several sections. The socio-demographic section collected data on age, level of education, place of residence (urban or rural) and occupation. Reproductive history included information about the duration of fertility treatment, the number of previous ART attempts, the number of embryos transferred, the success of previous pregnancies, and complications. Dietary habits were assessed based on the consumption of dairy products, calcium supplements, vitamin D, and diet during pregnancy. Physical activity level was determined by the frequency and duration of activities such as walking, yoga or swimming. A separate section of the questionnaire was devoted to bad habits, including smoking, alcohol consumption, and excessive caffeine consumption. Stress levels were assessed subjectively on a scale from 0 to 10, and the availability of psychological support was also considered. All participants in the study participated voluntarily after providing informed consent, and the confidentiality of the data was guaranteed. All manipulations were conducted following the Declaration of Helsinki for Ethical Principles of Medical Research [10].

Biochemical studies were performed to assess the levels of calcium (total and ionised), phosphorus, magnesium, bone resorption markers (C-telopeptides) and 25-hydroxyvitamin D. Blood was drawn on an empty stomach using sterile BD Vacutainers (Becton Dickinson, USA). Analyses were performed on an automated biochemical analyser Roche Cobas 6000 (Roche Diagnostics, Germany). The hormonal profile, including levels of oestrogen, progesterone, parathyroid hormone and prolactin, which are important regulators of bone metabolism, was assessed separately. IBM SPSS Statistics software (version 27, USA) was used for statistical analysis [11]. Multivariate regression analysis

was used to assess the relationship between risk factors and osteopenic changes. The mean values were compared using Student's t-test, and the Mann-Whitney U-test was used to analyse the distribution of data between groups. Statistical significance was determined at the level of $p < 0.05$.

RESULTS

The analysis of the dynamics of BMD in the first and third trimesters of pregnancy achieved with ART revealed significant changes in T-score in different measurement areas (Table 1).

Table 1. Dynamics of T-score in the distal forearm in the first and third trimesters of pregnancy

ART Group	Measurement area	First trimester (T-score)	Third trimester (T-score)
IVF	Distal forearm	-0.3 ± 0.2	-1.0 ± 0.2
IUI	Distal forearm	-0.4 ± 0.1	-1.1 ± 0.3
Oocyte donation	Distal forearm	-0.5 ± 0.2	-1.3 ± 0.3

Source: compiled by the authors

In the first trimester, the mean T-score values in the distal forearm, measured by ultrasound densitometry, remained within normal limits, ranging from -0.3 ± 0.2 to -0.5 ± 0.2 , depending on the type of ART method used. The lowest values were recorded in patients who became pregnant through oocyte donation, which is explained by specific hormonal changes caused by superovulation and hormone replacement therapy. This group demonstrates a more pronounced release of calcium from bone tissue due to hormonal fluctuations associated with preparation for pregnancy. Baseline BMD may be lower due to prolonged treatment of concomitant endocrine or gynaecological pathologies, which often precede the oocyte donation procedure.

Patients who became pregnant as a result of IVF had slightly higher T-score values in the first trimester than in the oocyte donation group. This is explained by the lower intensity of hormonal changes after embryo implantation compared to the processes that occur when using donor oocytes. However, the level of BMD in this group is also reduced, which may be due to the long period of preparation for pregnancy and the use of hormonal ovulation stimulants. The IUI group demonstrated a mean T-score of -0.4 ± 0.1 in the distal forearm in the first trimester of pregnancy. Compared to IVF and oocyte donation, this reproductive care method has a less pronounced effect on hormonal balance, which is reflected in relatively smaller changes in BMD in the first trimester.

In the third trimester of pregnancy, a significant decrease in the T-score was recorded in all groups, indicating an increased release of calcium from bone tissue for the needs of the foetus. The most pronounced changes were noted in the oocyte donation group, where the mean T-score in the distal forearm decreased to -1.3 ± 0.3 in the third trimester of pregnancy. This could be determined by more profound hormonal changes caused using hormone replacement therapy, as well as possibly lower initial BMD in these patients. In the IVF group, the average T-score in the distal forearm decreased to -1.0 ± 0.2 , which also indicates significant changes in the structure of bone tissue associated with the physiological needs of the foetus and changes in hormonal levels.

The IUI group also demonstrated a decrease in BMD in the third trimester, although the values were slightly

higher than in the IVF and oocyte donation groups. In particular, the T-score in the distal forearm in this group was -1.1 ± 0.3 . This indicates less bone loss in patients whose pregnancy occurred as a result of intrauterine insemination, which may be due to less intensive hormonal preparation for pregnancy compared to other ART methods. Similar changes were observed when measuring the T-score in the distal forearm, although their intensity varied depending on the group. In the first trimester, the mean values ranged from -0.3 ± 0.2 in the IVF group to -0.5 ± 0.2 in the oocyte donation group, while in the third trimester, these values decreased to -1.0 ± 0.2 and -1.3 ± 0.3 , respectively. This indicates a different level of bone vulnerability depending on the location: in the lumbar spine, the decrease in BMD is faster, which is explained by the increased load on this area during pregnancy. In the femoral neck, although less pronounced, significant BMD loss was also noted, due to general systemic changes in bone metabolism.

The data obtained demonstrate that the most intense loss of BMD was observed in the distal forearm, where the average decrease in T-score between the first and third trimesters was 0.7-0.8 units, depending on the group. This indicates a high metabolic activity of bone tissue in this area and its sensitivity to physiological and hormonal changes associated with pregnancy. In the third trimester, osteopenic changes were recorded in 30-40% of patients in the IVF and IUI groups. At the same time, in the group of women who became pregnant through oocyte donation, the frequency of such changes reached 50%. Women who became pregnant through oocyte donation were more vulnerable to BMD loss due to the specifics of hormonal support used in this group. These changes require enhanced monitoring and implementation of preventive measures to minimise the risk of osteoporosis in the postpartum period.

Thus, the distribution of osteopenic changes by measurement areas and groups shows that pregnancy achieved through ART is accompanied by significant changes in bone health. This requires the introduction of regular monitoring of bone health and preventive measures to reduce the risk of bone loss. The analysis of socio-demographic, nutritional, behavioural factors and physical activity levels of patients demonstrated a significant impact of these parameters on bone health in women who became pregnant with assisted reproductive technologies (Table 2).

Table 2. Risk factors and their impact on the T-score

Factor	Group	Average T-score
Age	25-30 years	-0.4±0.1
	35-40 years	-0.9±0.2
Calcium intake	Regular	-0.3±0.1
	Irregular	-0.7±0.2
Vitamin D levels	Normal (20-50 ng/mL)	-0.5±0.1
	Deficiency (<20 ng/mL)	-1.0±0.3
Physical activity	Moderate	-0.4±0.2
	Low	-0.8±0.2
Smoking	None	-0.5±0.1
	Present	-1.0±0.2
Caffeine consumption	<3 cups of coffee/day	-0.5±0.1
	>3 cups of coffee/day	-0.9±0.2

Source: compiled by the authors

Socio-demographic variables such as age, education level and place of residence had a moderate effect on bone mineral density. Older women (35-40 years old) had lower mean T-score values (-0.9±0.2) compared to younger women (25-30 years old), where the T-score was -0.4±0.1. This demonstrates the significant impact of age-related changes on bone health, which is associated with a decrease in the level of oestrogen and other hormones that are central to maintaining bone mineral density. In older age, the activity of osteoblasts, which form new bone tissue, decreases and the activity of osteoclasts, which contribute to bone resorption, increases. In addition, the deterioration of calcium and vitamin D absorption due to age-related changes in metabolism also exacerbates this effect.

Dietary habits were substantial in maintaining bone health. Patients who regularly consumed calcium-enriched dairy products and additionally used calcium supplements showed higher T-scores (mean value -0.3±0.1). In patients whose diets were poor in calcium, this figure decreased to -0.7±0.2. Vitamin D intake also proved to be a critical factor. Women with vitamin D deficiency (serum levels below 20 ng/mL) demonstrated significantly lower T-scores (-1.0±0.3), while patients with normal vitamin D levels (20-40 ng/mL) had a mean T-score of -0.5±0.1. This confirms the importance of a balanced diet with sufficient calcium and vitamin D for maintaining bone mineral density.

The level of physical activity had a significant impact on bone health in patients. Women who regularly performed moderate physical exercises such as yoga, swimming or walking at least three times a week had higher T-scores (-0.4±0.2) compared to those who were sedentary, with a T-score of -0.8±0.2. Of particular importance was regular physical activity in the third trimester of pregnancy, when the physiological decrease in bone mineral density was most pronounced. Maintaining an active lifestyle during this period contributed to the improvement of bone tissue condition, helping to compensate for the natural

loss of minerals.

Bad habits, such as smoking and excessive caffeine consumption, had a significant negative impact on bone health, which was manifested in a decrease in mineral density and an increased susceptibility to osteopenic changes. Excessive caffeine intake (more than three cups of coffee per day) was associated with a decrease in T-score to -0.9±0.2, as caffeine increases calcium excretion from the body through the urine, which reduces the availability of this trace element to maintain bone structure. In women who restricted their caffeine intake, the T-score remained at -0.5±0.1, which indicates the importance of a moderate approach to the consumption of high-caffeine drinks.

Smoking also had a significant impact on bone tissue. Smokers had an average T-score of -1.0±0.2, which is significantly lower than women who did not have this habit. Nicotine and toxic substances contained in tobacco smoke inhibit the activity of osteoblasts (cells responsible for bone formation) and disrupt bone remodelling processes. In addition, smoking reduces oestrogen levels, which is an important factor in protecting bone tissue, especially during pregnancy. The impact of these factors makes it difficult for the body to adapt naturally to the increased calcium requirements during pregnancy, leading to a more intense decrease in mineral density.

An analysis of the hormonal profile of women who became pregnant with the help of ART revealed a significant impact of key hormone levels on bone health during pregnancy. Hormones such as oestrogen, progesterone, parathyroid hormone and prolactin have a direct impact on the regulation of calcium metabolism and BMD, especially in conditions of increased stress on the woman's body. Table 3 shows that the levels of oestrogen and prolactin were highest in the oocyte donation group, while the lowest values of oestrogen and progesterone were observed in the IUI group, which may explain the higher incidence of osteopenic changes in this group.

Table 3. Average values of hormonal parameters depending on the type of ART

Hormone	IVF (M±SD)	IUI (M±SD)	Oocyte donation (M±SD)
Oestrogen (pg/mL)	345±26	298±30	372±28
Progesterone (ng/mL)	22±5	18±4	28±4
Parathormone (pg/mL)	36±6	42±5	32±6
Prolactin (ng/mL)	78±7	72±8	90±9

Source: compiled by the authors

Oestrogen has proven to be a key factor that significantly affects the preservation of BMD in women during pregnancy achieved through ART. An analysis of the hormonal profile of patients showed that high oestrogen levels in the third trimester of pregnancy were associated with a reduced risk of osteopenic changes. In the oocyte donation group, where oestrogen levels were the highest (372 ± 28 pg/mL), the incidence of osteopenic manifestations was only 25%, while in the distal forearm, the T-score remained at -0.5 ± 0.2 , which is significantly better than in other groups. This is attributed to the ability of oestrogen to inhibit the activity of osteoclasts, the cells responsible for bone resorption, and to maintain a balance between bone resorption and bone formation.

In the IUI group, where the average oestrogen level was lower (298 ± 30 pg/mL), the incidence of osteopenic changes reached 40%. In this group, the T-score in the distal forearm decreased to -1.1 ± 0.3 , indicating insufficient hormonal support and a higher risk of bone loss. The effect of oestrogen on bone tissue is confirmed by its role in inhibiting the activation of osteoclasts and stimulating osteoblasts, the cells responsible for the formation of new bone tissue. This mechanism ensures the preservation of bone structure and strength, especially during pregnancy, when the mother's body is under increased stress due to foetal growth.

In addition, women with higher oestrogen levels had a less pronounced decrease in BMD in the distal forearm. In the oocyte donation group, the mean T-score in this area was -0.7 ± 0.2 , while in the IUI group, it was -1.0 ± 0.3 . This indicates the importance of maintaining sufficient oestrogen levels to prevent osteopenic changes in bones with high metabolic activity. High oestrogen levels were also associated with a lower incidence of complications such as fractures or significant bone loss after pregnancy.

Progesterone, as one of the key hormones in pregnancy maintenance, had a moderate positive effect on BMD.

In the oocyte donation group, where progesterone levels reached 28 ± 4 ng/mL, better T-score values in the distal forearm (-0.5 ± 0.2) were observed compared to the IVF and IUI groups. This is due to the ability of progesterone to stimulate the synthesis of bone matrix proteins, in particular collagen, which provides bone strength and elasticity. Progesterone also has antioxidant properties that protect bone tissue from oxidative stress damage.

Parathyroid hormone levels, on the contrary, were associated with an increased risk of osteopenic changes, especially in the IUI group, where its values were the highest (42 ± 5 pg/mL). Excessive parathyroid hormone promotes the mobilisation of calcium from bone tissue to meet the needs of the body, especially the foetus, which leads to a decrease in BMD. In this group, the incidence of osteopenic changes reached 40%, and the mean T-score was -1.1 ± 0.3 . This emphasises the need to control parathyroid hormone levels to prevent significant bone loss.

Prolactin, another important hormone that regulates calcium metabolism, also showed a significant correlation with BMD. In the oocyte donation group, where prolactin levels reached 90 ± 9 ng/mL, the best bone preservation was observed. High levels of prolactin support adaptive mechanisms of calcium metabolism, ensuring adequate calcium intake for the fetus without significant damage to the mother's bone tissue. Patients with high prolactin levels demonstrated a lower incidence of osteopenic changes, with a mean T-score of -0.5 ± 0.1 .

An analysis of biochemical markers of bone metabolism in pregnant women who became pregnant using different types of ART revealed significant differences in key parameters (Table 4). These differences reflect the impact of different technologies on bone metabolism through changes in hormonal profile and biochemical status. The levels of calcium, phosphorus, magnesium, bone resorption markers and vitamin D reflected the state of bone tissue and its remodelling trends in pregnancy.

Table 4. Indicators of biochemical markers of bone metabolism depending on the type of ART

Metric	IVF	IUI	Oocyte donation
Total calcium (mmol/L)	2.20 ± 0.15	2.10 ± 0.20	2.30 ± 0.10
Ionised calcium (mmol/L)	1.10 ± 0.08	1.02 ± 0.05	1.15 ± 0.07
Magnesium (mmol/L)	0.80 ± 0.05	0.70 ± 0.04	0.85 ± 0.06
Vitamin D (ng/mL)	28.0 ± 5.0	20.0 ± 4.5	32.0 ± 6.0
C-telopeptidy (ng/mL)	0.3 ± 0.07	0.50 ± 0.09	0.30 ± 0.05
Phosphorus (mmol/L)	1.20 ± 0.10	1.15 ± 0.12	1.25 ± 0.08

Source: compiled by the authors

An analysis of biochemical markers of bone metabolism in pregnant women who became pregnant using different types of ART revealed significant differences in key parameters. These differences reflect the impact of different technologies on bone metabolism through changes in hormonal profile and biochemical status. The levels of calcium, phosphorus, magnesium, bone resorption markers and vitamin D reflected the state of bone tissue and its remodelling trends in pregnancy. The results showed that patients who became pregnant through oocyte donation had the highest mean calcium levels, both in total and ionised form. This could be determined by increased nutritional control in this group of women and possibly by the more

frequent use of calcium supplements. At the same time, calcium levels were lowest in the IUI group, indicating potentially inadequate calcium intake or absorption. This trend was accompanied by higher rates of bone resorption, as evidenced by the high levels of C-telopeptides in this group.

Magnesium levels also differed between groups. The highest magnesium values were observed in the oocyte donation group, which could contribute to bone stability. Magnesium plays an important role in bone remodelling and maintaining calcium balance, and its deficiency can lead to bone deterioration. In the IUI group, magnesium was at the lowest level, which, together with low vitamin D levels, could contribute to an increased risk of osteopenic changes. The

role of vitamin D in bone metabolism should be noted separately [12]. In the oocyte donation group, its level was the highest, which ensured better calcium absorption and bone stability. In the IUI group, on the contrary, vitamin D levels were significantly reduced, which could contribute not only to bone loss but also to an increased risk of osteopenia.

The dependence of biochemical markers on the type of ART is also confirmed by differences in bone resorption markers. In the IUI group, the level of C-telopeptides was the highest, indicating active processes of bone destruction. This could be due to micronutrient deficiencies, which, in turn, exacerbates the negative impact on bone structure. In IVF patients, these indicators were at an average level, which may reflect a moderate adaptation to changes in metabolism. The results emphasise the need for careful monitoring of biochemical markers of bone metabolism in pregnant women, especially those who became pregnant with IUI. Decreased levels of vitamin D, calcium and magnesium require timely correction with special dietary recommendations and nutraceutical support. Patients with oocyte donation, although they have the best biochemical profile, also need to be monitored to maintain a positive balance.

The final analysis of the results shows a complex effect of the type of assisted reproductive technology on biochemical markers of bone metabolism in pregnant women. The group that became pregnant through oocyte donation demonstrated the most favourable mineral metabolism, including higher levels of calcium, magnesium and vitamin D, suggesting a potential adaptive advantage of this method in the context of bone health. Participants who used intrauterine insemination had increased bone resorption activity and the lowest calcium levels, which may indicate an increased risk of osteopenic changes in this group. Overall, the results emphasise the need for an individualised approach to the management of pregnancies achieved through ART, incorporating the type of technology used and its impact on biochemical status. An important aspect is to ensure adequate levels of vitamin D, calcium and magnesium through diet or supplementation, especially for high-risk groups. This will reduce the probability of osteopenic changes and maintain optimal bone health during pregnancy.

◆ DISCUSSION

Pregnancy achieved by ART has a significant effect on BMD, namely in the distal forearm. In the third trimester, the greatest decrease in T-score was observed in the oocyte donation group (-1.3 ± 0.3), which corresponds to the findings of S. Golombok [13], emphasising the significant effect of hormone therapy on bone metabolism. K. Berg & K. Whitehead [14] noted that such hormonal changes cause significant bone resorption. The results confirm these observations, demonstrating that hormonal support during oocyte donation is an additional risk for bone loss.

The decrease in BMD in the distal forearm was significant in all groups. In the oocyte donation group, the T-score in this area decreased to -1.0 ± 0.2 . Although the study evaluated only one anatomical area, the results are consistent with the findings of S. Butscheidt *et al.* [15], emphasising the importance of the metabolic activity of bone tissue when assessing bone loss. P. Anagnostis *et al.* [16] also noted that even within the same zone, the indicators can vary depending on the local load. This confirms the

feasibility of an integrated approach to monitoring bone health in women during pregnancy.

Socio-demographic factors significantly affect BMD. Women aged 35-40 years had a mean T-score of -0.9 ± 0.2 , while younger patients (25-30 years) demonstrated a value of -0.4 ± 0.1 . M. Carsote *et al.* [17] highlighted an age-related decrease in oestrogen levels, which contributes to bone loss. S. Lee *et al.* [18] emphasised that an additional factor is vitamin D deficiency in older age. The data of the current study confirm these findings, demonstrating the relationship between age, hormonal changes and bone health.

Dietary habits demonstrated a significant impact on BMD preservation. Patients who regularly consumed calcium demonstrated a mean T-score of -0.3 ± 0.1 , while in patients with low calcium intake, this figure decreased to -0.7 ± 0.2 . M. Fukushima *et al.* [19] noted that calcium is a key element in maintaining bone mass. N. Mishra *et al.* [20] noted that calcium deficiency is especially dangerous during pregnancy when the need for minerals increases. The results confirmed these observations, emphasising the need for dietary adjustment to prevent osteopenia.

Physical activity was an important factor in the preservation of BMD. In women with moderate physical activity, the T-score was -0.4 ± 0.2 , while in sedentary participants this figure decreased to -0.8 ± 0.2 . A.L.C. Morato *et al.* [21] emphasised the positive effect of physical activity on osteogenesis. K. Maehara *et al.* [22] emphasised that regular exercise reduces the risk of bone loss during pregnancy. The current data confirmed these findings, demonstrating a correlation between physical activity and BMD preservation.

Bad habits, such as smoking and excessive caffeine consumption, had a significant impact on BMD. In smokers, the average T-score was -1.0 ± 0.2 , while in non-smokers, this figure was -0.5 ± 0.1 . T.A. Ottun *et al.* [23] noted that nicotine inhibits the activity of osteoblasts. Y. Qian *et al.* [24] stated that caffeine promotes calcium excretion from the body. Current results are consistent with these findings, demonstrating the need to limit bad habits to maintain bone health.

The hormonal profile was instrumental in the preservation of BMD. In the oocyte donation group, the oestrogen level reached 372 ± 28 pg/mL, which correlated with a lower incidence of osteopenic changes. K. Lampropoulou-Adamidou *et al.* [25] emphasised that oestrogen inhibits osteoclast activity. H. Basma *et al.* [26] noted that progesterone maintains the bone matrix. The results of the study confirm these findings, demonstrating the importance of hormonal balance in the prevention of bone loss.

The level of parathyroid hormone in the IUI group reached 42 ± 5 pg/mL, which was associated with a significant decrease in BMD. C.-H. Cheng *et al.* [27] noted that excess parathyroid hormone activates bone resorption by stimulating osteoclasts, which leads to rapid bone loss. P. Wu *et al.* [28] highlighted that prolactin, although partially reduces this effect, does not always provide adequate protection in the case of high concentrations of parathyroid hormone. The current study demonstrated that parathyroid hormone levels in women from the IUI group correlate with higher resorption markers, which supports the hypothesis of increased bone loss. This finding contradicts some studies that point to the compensatory role of prolactin, emphasising the importance of further studying the mechanisms of hormonal influence on

bone metabolism. Thus, the results of the current study are more detailed, as they incorporate both hormonal and biochemical parameters, which improves the description of pathogenetic mechanisms.

The analysis of biochemical markers demonstrated that the oocyte donation group had higher levels of calcium and magnesium. B. Miles *et al.* [29] noted that adequate levels of calcium and magnesium reduce the activity of bone resorption, preventing excessive bone loss. Y. Kaneuchi *et al.* [30] stated that vitamin D is critical for calcium absorption, ensuring its efficient transport to bone tissue and regulation of parathyroid hormone levels. Current results demonstrated that women with higher levels of these micronutrients in the oocyte donation group had significantly lower resorption markers than participants in other groups. This demonstrates the advantage of a comprehensive approach to nutraceutical support, compared to less focused recommendations often used in other studies.

In the VMI group, a high level of resorption markers was observed, indicating significant disorders in bone metabolism. D.A. Ferreira *et al.* [31] noted that this is a consequence of vitamin D deficiency, which plays a key role in calcium absorption and bone mass maintenance. A.A. Abdulrazaq *et al.* [32] added that active resorption is a direct consequence of the hyperproduction of parathyroid hormone, which stimulates osteoclastic activity. The current study determined that the level of resorption markers in women from the IUI group exceeded the average values reported in other studies, which may indicate more severe disorders. These findings demonstrate that vitamin D deficiency has a more significant impact than previously thought, highlighting the importance of a comprehensive approach to correcting mineral metabolism.

In general, the results obtained indicate that pregnancy achieved through ART is accompanied by significant changes in bone health. A. Cohen *et al.* [33] emphasised the importance of an individual approach to the prevention of osteopenia, focusing on the adaptation of nutritional, physical and medication strategies. M. Rahimi *et al.* [34] reported that regular monitoring, including the use of biochemical markers of bone metabolism, allows for the timely identification of risks and implementation of preventive measures that help maintain tissue mineral density even in high-risk groups. These studies are consistent with these findings, while also detailing the relationship between specific hormonal changes and biochemical analysis, which allows for a deeper understanding of the impact of different types of ART on bone health. This approach demonstrates significantly greater accuracy and practical value for managing bone health.

The findings highlight the complex impact of pregnancy achieved through assisted reproductive technologies on bone health. The analysis showed that key factors, such as hormonal changes, dietary habits, physical activity and

micronutrient levels, have a significant impact on bone mineral density. The data of the current study correlate with the findings of previous studies, but at the same time detail and expand on them, emphasising the importance of a comprehensive approach to the prevention of osteopenic changes. The use of modern biochemical markers, a detailed analysis of hormonal changes, and the development of individualised recommendations for each group of patients was noted to significantly improve the effectiveness of pregnancy management.

✦ CONCLUSIONS

The study determined a significant decrease in BMD in women who became pregnant with ART, especially in the third trimester of pregnancy. The most significant changes were recorded in the distal forearm. In the oocyte donation group, the mean T-score decreased from -0.5 ± 0.2 to -1.3 ± 0.3 . In the IVF and IUI groups, the T-score decreased from -0.3 ± 0.2 and -0.4 ± 0.1 to -1.0 ± 0.2 and -1.1 ± 0.3 , respectively. Age, dietary and behavioural factors had a significant impact on bone health. In women over 35 years of age, the mean T-score was -0.9 ± 0.2 , while in younger age groups this figure was -0.4 ± 0.1 . Regular calcium intake was associated with less BMD loss (decrease in T-score by 0.3 ± 0.1 units), while its deficiency was associated with greater losses (decrease by 0.7 ± 0.2 units). Vitamin D deficiency had a significant effect on the scores, as women with vitamin D deficiency had a mean T-score of -1.0 ± 0.3 , which was 0.5 units lower than in patients with normal vitamin D levels. Regular physical activity contributed to BMD maintenance: the mean T-score was -0.4 ± 0.2 in physically active women compared to -0.8 ± 0.2 in sedentary women. Limitations of the study are related to the selectivity of the participants and the fact that it included only women who became pregnant through ART, which limits the generalisability of the findings to the wider population of pregnant women. In addition, the lack of analysis of genetic factors and long-term monitoring of BMD after childbirth leaves some questions open. Prospects for future research include the development of long-term strategies for monitoring BMD in the postpartum period, evaluating the effectiveness of dietary and physical interventions, and incorporation of genetic, ethnic and hormonal characteristics to create personalised approaches to the prevention of osteopenia and osteoporosis in pregnant women.

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✦ CONFLICT OF INTEREST

None.

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Визначення факторів ризику виникнення остеопенічних змін у жінок, які завагітніли за допомогою допоміжних репродуктивних технологій

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Анотація. Метою дослідження було вивчення факторів, які впливають на ризик виникнення остеопенічних змін у жінок, які завагітніли за допомогою допоміжних репродуктивних технологій. У дослідженні взяли участь 150 жінок віком 25-40 років, які завагітніли після використання екстракорпорального запліднення, внутрішньоматкової інсемінації та донорства ооцитів. Мінеральну щільність кісткової тканини було оцінено методом ультразвукової денситометрії у ділянці дистального передпліччя на ранніх (8-12 тижнів) і пізніх (32-36 тижнів) етапах вагітності. Показники T-score демонстрували значне зниження у третьому триместрі у всіх групах, найбільше – у пацієток, які завагітніли завдяки донорству ооцитів ($-1,3 \pm 0,3$ у дистальному передпліччі). Аналіз соціально-демографічних характеристик виявив, що вік старше 35 років, низький рівень фізичної активності, дефіцит вітаміну D і кальцію, а також шкідливі звички, такі як куріння та надмірне споживання кофеїну, суттєво підвищували ризик розвитку остеопенічних змін. Жінки з регулярним споживанням молочних продуктів, кальцієвмісних добавок і нормальним рівнем фізичної активності мали значно кращі показники мінеральної щільності кісткової тканини. Біохімічні маркери підтвердили вищі рівні кальцію, магнію та вітаміну D у групі донорства ооцитів, тоді як у групі внутрішньоматкової інсемінації виявлено дефіцит цих елементів і підвищення маркерів кісткової резорбції. Гормональний профіль також суттєво впливав на стан кісткової тканини: високий рівень естрогену у пацієток групи донорства ооцитів був асоційований із менш вираженими остеопенічними змінами, тоді як підвищений рівень паратгормону у групі внутрішньоматкової інсемінації сприяв посиленню втрати кісткової маси. У пацієток із найвищими рівнями пролактину спостерігалось краще збереження мінеральної щільності кісткової тканини завдяки позитивному впливу цього гормону на кальцієвий обмін. Отримані результати підкреслюють необхідність комплексного моніторингу стану кісткової тканини у жінок, які завагітніли за допомогою допоміжних репродуктивних технологій

Ключові слова: щільність кісткової тканини; біохімічні маркери; гормональний профіль; внутрішньоматкова інсемінація; донорство ооцитів