Introduction

The low bone mass (LBM) includes osteopenia (Op) and osteoporosis (OP), is characterized by the skeletal fragility and susceptibility to fractures, resulting from the reduced bone mass and impaired bone microarchitecture [1]. This metabolic bone disease is a topical healthcare issue across the world due to a high morbidity, mortality and significant healthcare spending [2]. There are 2000 million people afflicted by the OP all over the world [3]; it also causes 1.5 million spinal, hip and wrist fractures, resulting in 10 billion dollars being annually spent in the US only [4].

The LBM-associated gender dimorphism is well-documented [5]: its frequency significantly prevails in women after the menopause onset, when the bone fragility is more pronounced [6], while the osteoporotic spinal fractures are 3 times as frequent. However, the LBM pathogenesis in the non-menstruating women is not researched as thoroughly [7].

The aim of the study is to evaluate the LBM course in postmenopausal women, to examine the role of bone metabolism changes and their contribution into the bone mineral density (BMD) disorders.

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Materials and methods
The study was cross-sectional, recruiting 261 non-menstruating women aged 34–72 years (mean age − 48.4±0.54 years). For 90.8 % women, the menopause was physiological, for 3.1 %, it was an early-onset menopause; while for 3.5 %, it was a late-onset menopause and amenorhea, for 2.7 %, ovariectomy was performed at the earlier stages, and 4.6 % were infertile. The exclusion criteria were rheumatic bone and articular disorders, thyroid and blood circulation disorders, malignant tumors, chronic renal diseases of stage 2–4, glucocorticoid and anticonvulsant treatment, i.e. all those factors affecting the bone metabolism and associated with LBM.

The examined women were divided into two groups: 133 (51.0 %) women with LBM (main group) and 128 (49%) women with normal bone density (comparison group). The control group was made by 30 actually healthy, menstruating women aged 23–48 years (mean age - 35.5±2.31 years). 79.0% women with LBM were healthy, menstruating women aged 23–48 years (mean age – 34.7±0.91 years). 79.0% women with LBM were diagnosed with Op, the remaining 21.1 % (or 10.7 % out of the total number) – with OP. Обязательно добавить одобрение ЛЭК и согласие пациентов на участие в исследовании. This study was approved by Local Ethic Committee, all women signed the inform consent for participation in the study.

To diagnose LBM, we used X-ray “Multix-Compact-Siemens” (Germany) machine, dual-energy X-ray absorptiometry for proximal hip bone “QDR-4500-Delphi-Hologic” (USA), “Envisor-Philips” sonograph (Netherlands) in order to study the speed of ultrasound spread, its broadband attenuation. Some of the women underwent MRI “Signa-Excite-HD” (Germany) examinations. The BMD was evaluated by T-score dual X-Ray absorptiometry, X-ray Barnett-Nordin (BN), Rokhlín (R) and wedge (W) index. The blood serum was used to assess the alkaline phosphatase (AP) activity by means of “Olympus-AU-640” biochemical analyzer (Japan), to detect parathyrin, osteocalcin and osteopontin concentrations by means of enzyme immunoassay (“PR2100-Sanofi diagnostic pasteur” reader, France). Among the chemical elements, the following were measured: Ca, Co, Cr, Cu, Mg, Mn, P, Pb, Se, Sr and Zn. For that purpose, Inductively Coupled Plasma-Atomic Emission Spectroscopy (ICP-AES) (“IRIS-Intepid-II-XDL”) and atomic absorption spectrometer (“SolAAr-Mk2-MOZe”) with a graphite-furnace atomizer were used (UK).

The statistic processing of the obtained findings is performed by means of computer variational, non-parametric, correlation, one-way (ANOVA) and multivariate (ANOVA/MANOVA) dispersive analysis (Microsoft Excel and Statistica). The mean indices (M), standard errors (SE) and standard deviations (SD), the parametric Pearson correlation (r) and non-parametric Kendall correlation (t)

The LBM women have the BMD correlating with PT, CT, OC, OP, AP, Ca, Mg and Pb blood levels (T-score and W index are differently directed towards BN and R indices). Moreover, the BN index is inversely correlated to Cu (r = -0.343, p=0.008) blood levels, and the R index is reversely correlated to Co (r=-0.437, p=0.001), while the W index is directly correlated with Sr (r=+0.28, p=0.047). While comparing women with Op and OP, we revealed that OP is associated with the significantly higher (by 47.4%) blood levels of PT (t=6.41, p<0.001), by 19.0% of AP (t=4.27, p<0.001), by 9.4% of P (t=4.97, p<0.001) and by 26.9% of Pb (t=2.58, p=0.011), but with a lower Ca concentration by 4.3% (t=5.16, p<0.001).

Discussion
With LBM, the BMM develop a single homeostatic mechanism of Ca and P metabolism regulation in post-menopausal women [8]. The PT has a negative impact on bone structure [9], while the reduced Ca concentrations may lead to an increased PT secretion in the LBM women. The osteoclasts accelerate the bone-contained mineral compounds’ dissolution. In case of hypocalcaemia, CT secretion usually drops down, affecting osteoblasts and leading to the elevated calcitriol production; as a result, Ca and P’s mobilization from bone intensifies. OC, being the Y-carboxylated protein, is synthesized by osteoblasts, while the bone mineralization is regulated by Vitamin D [10]. In the non-menstruating LBM women, the importance of OC association with osteoblasts via osteoclastogenesis and intensified synthesis of anti-inflammatory interleukin-6 [11], insulin-like growth factor (IGF), osteoprotegerin, nuclear factor NF-kB [12, 13], C-telopeptide of collagen [14] is confirmed for the LBM pathogenesis.

The changes in Sr concentrations observed in the menopausal women’s blood serum belong to the LBM-

Fig 1. Difference in osteoassociated chemical indices in the blood of non-menstruating women from the main group by contrast to the menstruating women from the comparison group, taken as 100 %.
inducing factors. Strontium produces an anti-resorptive effect on bone, reduces osteoclast differentiation, and stimulates bone formation via pre-osteoclast proliferation. It is worthy of note that, according to our data, LBM in the non-menstruating women is attended by the increased strontiemia, prevailing in the OP cases. In this light, it should be observed that the increased Sr ion concentration may cause bone fragility by replacing Ca ions present in the bone. For the matrix metalloproteinases (MMPs) to be able to perform their destructive functions in the LBM subjects, Zn ions should also be present. Empowered by Zn, aggrecanase, gelatinase, collagenase, elastase intervene into the bone pathology and disrupt aggrecan, biglycan, verzikan, decorin, fibronectin, fibromodulin ratio. It should also be mentioned that women with LBM demonstrate the reduced Zn concentrations, probably due to the protein binding.

By contrast, Co, Mn and Pb have no effect on BMD formation, while Cr and Se are associated with W index exclusively (D=2.00, p=0.003 and D=1.46, p=0.049 respectively). By means of variation, dispersion and correlation analyses, we’ve managed to make a practical conclusion: AP activity index >158 U/l (>M+SD for the OP women) reflects severe LBM presence (PPV=76.0%).

Conclusions

LBM (the Op and OP ratio is 4:1) develops in every one in two non-menstruating women; its development being associated with high OC concentrations, half of them – OP concentrations. It depends on a history of primary arterial hypertension, diabetes mellitus and leukocytoclastic vasculitis comorbidities. The OP development is significantly different from the OP development due to the higher PT, P, Pb and AP concentrations (negative predictive value), though lower Ca concentrations. The LBM pathogenesis also involves CT, Mg, Sr and Zn.

Conflicts of interests. Authors declare the absence of any conflicts of interests and their own financial interest that might be construed to influence the results or interpretation of their manuscript.

Information on the individual contributions:
Syniachenko O.V. — Research concept and paper composition; Klymovytsky F.V. — Collection and statistical processing of findings; Moroziuk D.M. — Instrumental and laboratory examination of women; Iermolaieva M.V. — Analysis of reference data, study design and findings’ analysis; Liventsova K.V. — Findings’ analysis and illustrations

References

1. Sugimoto T, Sato M, Dehle FC, Brnabic AJ, Weston A, Burge R. Lifestyle-Related Metabolic Disorders, Osteoporosis, and Fracture Risk in Asia: A Systematic Review. Value Health Reg Issues. 2016;9:49-56. https://doi.org/10.1016/j.vhri.2015.09.005.
2. Wong SK, Chin KY, Suhaimi FH, Ahmad F, Ima-Niwana S. The Relationship between Metabolic Syndrome and Osteoporosis: A Review. Nutrients. 2016;8(6):347. https://doi.org/10.3390/nu8060347.
3. Reginster JY, Burlet N. Osteoporosis: a still increasing prevalence. Bone. 2006;38(2 Suppl 1):S4-S9. https://doi.org/10.1016/j.bone.2005.11.024.
4. Nayak NK, Khedkar CC, Khedkar GD, Khedkar CD, autors; Caballero B, Finglas PM, Toldrá F, editors. Osteoporosis: encyclopedia of food and health. Oxford: Academic Press; 2016. 181-185 pp.
5. Ochsmann E, Rüger H, Kraus T, Drexler H, Letzel S, Münster E. Gender-specific risk factors for acute low back pain: starting points for target-group-specific prevention. Schmerz. 2009;23(4):377-384. https://doi.org/10.1007/s00482-009-0779-4.
6. D’Amelio P, Rossi P, Isiaa G, et al. Bone mineral density and singh index predict bone mechanical properties of human femur. Connect Tissue Res. 2008;49(2):99-104. https://doi.org/10.1080/03008200801913940.
7. Horikawa K, Kasai Y, Yamakawa T, Sudo A, Uchida A. Prevalence of osteoarthritis, osteoporotic vertebral fractures, and spondylothesis among the elderly in a Japanese village. J Orthop Surg (Hong Kong). 2006;14(1):9-12. https://doi.org/10.1177/230949900601400103.
8. Rousseau JC, Delmas PD. Biological markers in osteoporosis. Nat Clin Pract Rheumatol. 2007;3(6):346-356. https://doi.org/10.1038/ncprheum0508.
9. Hintz peter B, Scheidt-Nave C, Müller MJ, Schenk L, Mensig GB. Higher prevalence of vitamin D deficiency is associated with background among children and adolescents in Germany. J Nutr. 2008;138(8):1482-1490. https://doi.org/10.1093/jn/138.8.1482.
10. Hari Kumar KV, Muthukrishnan J, Verma A, Modi KD. Correlation between bone markers and bone mineral density in postmenopausal women with osteoporosis. Endocr Pract. 2008;14(9):1102-1107. https://doi.org/10.4158/ep.14.9.1102.
11. Nermow Y, Granberg B, Säilä M, Weidenhielm L. Osteoblast dysfunction in male idiopathic osteoporosis. Calcif Tissue Int. 2006;78(2):90-97. https://doi.org/10.1007/s00223-005-0158-9.
12. Nakamura M, Nakamichi Y, Nakamura H, Udagawa N. Nihon Rinsho. 2009;67(5):889-896.
13. Xu R. Effect of whey protein on the proliferation and differentiation of osteoblasts. J Dairy Sci. 2009;92(7):3014-3018. https://doi.org/10.3168/jds.2008-1702.
14. Trento LK, Pietropoli A, Ticconi C, et al. Role of type I collagen C telopeptide, bone-specific alkaline phosphatase and osteocalcin in the assessment of bone status in postmenopausal women. J Obstet Gynaecol Res. 2009;35(1):152-159. https://doi.org/10.1111/j.1447-0756.2008.00868.x.
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Клинико-патогенетические особенности сниженной костной массы у постменопаузальных женщин

Резюме. Актуальность. Сниженная костная масса (СКМ) в виде остеопении (Оп) и остеопороза (ОП) является одной из наиболее актуальных проблем здравоохранения. Постменопаузальный период у женщин считается основным фактором риска развития патологического процесса. Цель исследования: оценить клинико-патогенетические особенности СКМ у женщин в постменопаузальном периоде.

Материалы и методы. Под наблюдением находилась 261 неменструирующая женщина, средний возраст 48 лет, у которых в 91 % случаев имела место физиологическая менопауза, а у остальных — патологическая. Критериями исключения были женщины с воспалительными ревматическими болезнями суставов, онкологической патологией, болезнями системы крови и щитовидной железы, получавшие глюкокортикоидные гормоны и антиконвульсанты. У 133 (51 %) женщин установлена СКМ (основная группа) в соотношении Оп и ОП 4 : 1, для диагностики которой применяли методы рентгеновской абсорбциометрии и ультразвуковой денситометрии. Среди маркеров костного метаболизма изучали уровни в крови паратиреоидного гормона, кальцитонина, остеокальцина, остеопонтина, щелочной фосфатазы и остеоассоциированных химических элементов. При обследовании использовали биохимический, иммуноферментный, атомно-эмиссионный и атомно-абсорбционный методы.

Результаты. Возраст женщин коррелирует с параконтурами минеральной плотности костей, а развитие СКМ во всех случаях связано с высокими показателями в крови остеокальцина, у 1/2 из них — остеопонтина, зависит от наличия коморбидных артериальной первичной гипертензии, сахарного диабета типа 2 и лейкоцитокластического васкулита. От Оп формирование ОП достоверно отличается более высокими уровнями в крови паратиреоидного гормона (на 47 %), щелочной фосфатазы (на 19 %), фосфора (на 9 %) и свинца (на 27 %), но меньшими значениями кальция (на 4 %), причем активность щелочной фосфатазы имеет прогностическую значимость в отношении выраженности СКМ. В патогенезе последнего участвуют также кальцитонин, магний, стронций и цинк.

Выводы. СКМ развивается у каждой второй женщины в постменопаузальном периоде, а дальнейшая разработка патогенетической терапии должна быть направлена на коррекцию концентраций в организме остеокальцина и остеопонтина, причем критерием эффективности лечебных мероприятий может быть угнетение активности щелочной фосфатазы.

Ключевые слова: сниженная костная масса; постменопауза; женщины; костный метаболизм