ISSN : 2321-9602

Indo-American Journal of Agricultural and Veterinary Sciences




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ISSN 2321–9602 www.iajavs.com
Indo-American Journal of Agricultural and Veterinary Sciences

Vitamin D insufficiency in calves biochemical and clinical manifestations

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Abstract

The maintenance of a metabolically stable, highly productive herd is a current focus in the fields of animal husbandry and veterinary medicine. High milk production is indicative of a heavy strain on the animal's body; in this context, slowed metabolic processes immediately reduce milk production and call for a well-balanced diet and high-quality feed. Intense physiological and biochemical metabolic processes are required to convert a large quantity of energy and nutrients from feed into milk, and these illnesses and diseases commonly develop with a rise in milk output. Hereditary problems in the metabolism of nucleic acids, insufficiency of enzymes involved in the synthesis and breakdown of amino acids, diseases of organic acid metabolism, fatty acid shortage, and so on may all lead to metabolic illnesses in animals. Rickets is much simpler to cure if it is caught and treated in its early stages, thus early detection and prompt treatment are crucial. As a result, the degenerative process will stop, bone deformations will occur, and internal organs will undergo modifications. This article takes a contemporary look at the problem of vitamin D insufficiency in young cattle. The cause, diagnosis, and treatment of vitamin D deficiency in calves are discussed. Vitamin D's significance to animal health and well-being is outlined, along with its involvement in the prevention of rickets. The concealed phases of this disease's progression have been identified as a defining aspect of the condition. D-hypovitaminosis only manifests clinically when it is too late to save the animal's health. Mineralization of the organic matrix of bone tissues is disrupted (D-hypovitaminosis) or preexisting skeletal structures undergo osteolysis (degradation). The purpose of this study was to investigate D-hypovitaminosis in calves at one farm located in the northern districts of the Zhytomyr area (part of the Zhytomyr Polissia natural-geographical zone).

Keywords: biochemical indicators; domestic animals; rickets; vitamin D deficiency; homeostasis; physiological and biochemical status; etiological factors of the disease.

1. Introduction

One of the key areas that ensure Ukraine's food security is the intensive development of cattle breeding. Implement- ing this direction is a multifactorial task, which includes a high intensification of meat and dairy production (Grymak,2018; Borshchenko et al., 2020). In turn, the intensification of production contributes to the functioning of animal ex- change (Levchenko et al., 2010; Koreneva et al., 2018). In such conditions, any technological failure can lead to a se- vere disturbance of metabolism in domestic animals, there- fore, to the development of metabolic pathologies (Suslova& Gryban, 2010; Zhao et al., 2019; Mylostyvyi et al., 2021; Slivinska et al., 2021).

Preservation of the normal functional state of the animal organism in conditions of constant adaptation to various factors is carried out at the expense of integrating organs (Horalskyi et al., 2022), homeostasis, or the body's ability to maintain a stable state of health (Surai & Earle-Payne, 2022). According to O. Danchuk et al. (2021), homeostasisis the process of self-regulation of the body as a whole sys- tem. Peleki C. et al. (2023) indicate the metabolic basis of adaptation or the quantitative change of cell metabolic pro- cesses (Peleki et al., 2023). At the same time, the synthesis of proteins and enzymes is of great importance. Vitamins and minerals, which are part of enzymes, also take an active part in the process of homeostasis. Homeostasis is carried out by regulatory mechanisms at all organism levels, startingwith molecular and ending with the highest systemic rela- tions (Melendez & Poock, 2017).

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ISSN 2321–9602 www.iajavs.com
Indo-American Journal of Agricultural and Veterinary Sciences

Analyzing literature data, it should be noted that the pe- riods of early postnatal ontogenesis are characterized byhigh plasticity of the calves' body, intensive metabolism, and increased need for nutrients and biologically active substances (Chase et al., 2008; Osorio, 2020; Todosiuk et al., 2022).

It is known that the physiological maturity of newborn animals depends on the physiological and biochemical statusof the cows-mothers during the dry period, the change of which initiates the appearance of disturbances in the func- tional system “mother-fetus”, which affect the harmonious development of the fetus in the last trimester of pregnancy (Polupan & Klimkovetskyi, 2020).

An organism cannot live without an environment, the in- fluence of which affects homeostasis in one way or another, to one degree or another; therefore, its indicators are not stable values; they change to the necessary extent under various influences of the habitat and the body's reaction to these influences (Danchuk & Karpovskiy, 2016). When homeostasis is disturbed, the body loses the ability to effec- tively control physiological and biochemical processes that directly determine the maintenance of vital functions, in- cluding the restoration of homeostasis itself.

It is known that the biochemical indicators of blood fullyreflect the metabolism of proteins, fats, carbohydrates, vita- mins, macro-micro elements, hormones, as well as water- mineral characteristics of the body (Yefimov, 2004; Yuskiv, 2014; Kissera & Storchak, 2017). In addition, the quantita- tive characteristics of these indicators of cattle blood depend on various factors, one of which is the provision of nutrients and vitamin-mineral substances to the needs of the animal's body (Slivinska et al., 2017).

Metabolic disorders, which may arise as a result of insuf- ficiency or imbalance of rations with nutrients and biologi- cally active substances, non-compliance with the feedingregime and structure of the ration taking into account the physiological state and the period of lactation, feeding of low-quality silage and haylage containing an excess of oil, leading to a decrease in the milk productivity of cows, as well as cause the development of diseases caused by meta- bolic disorders: osteodystrophy, hypovitaminosis A and D, ketosis, postpartum hypocalcemia, and hypophosphatemia); heart pathologies (myocardiodystrophy); liver (cirrhosis, hepatodystrophy), digestive system (dystonia of the antrum, acidosis of the scar, shift of the rennet) development of polymorbid (multiple) internal pathology (Levchenko et al., 2010; Sakhniuk et al., 2015; Honcharenko et al., 2019).

The works of many scientists are devoted to the study of metabolic pathology, in particular, D-hypovitaminosis (rick- ets) in young cattle (Hollis, 2005; Tyshkivska et al., 2007). This disease is caused by a disorder of D-vitamin and phos- phorus-calcium metabolism in the body of calves. Rickets is characterized by a violation of the structure of bone tissue and its calcification, with subsequent functional changes in the nervous, cardiovascular, digestive, and respiratory sys- tems (Apukhovska, 2000; Ross et al., 2011).

Vitamin D is an active anti-rickets factor (Sahay & Sa- hay, 2012). Today it is known that vitamin D, together with active metabolites, belong to the components of the hormo- nal system of the body, which regulate calcium-phosphorus exchange and participate in the mineralization of bone tissueand the maintenance of calcium homeostasis (Garkavy et al.,2001). In recent decades, discoveries have been made in studying vitamin D metabolism, its enzymatic conversion into active metabolites, and its effects on tissues. Of great interest are the data indicating that the regulation of this exchange occurs by a feedback mechanism and that the action of vitamin D on cells is similar to the action of steroid hormones (Yuskiv et al., 2007).

The pathogenesis of rickets is quite complex and consistsof the fact that the lack of vitamin D in the body of young animals and children leads to a decrease in the level of ion- ized calcium in the blood, a decrease in the synthesis of calcium-binding protein, which ensures the transport of calcium ions through the intestinal wall and the occurrence of hypocalcemia (Chanchlani et al., 2020). There is a gener- ally accepted point of view that hypocalcemia contributes to the activation of the activity of the parathyroid glands and the hyperproduction of parathyroid hormone, which pro- motes the removal of inorganic calcium from the bones, impaired absorption of phosphorus and calcium salts in the small intestine (Do et al., 2012; Sahay & Sahay, 2012; Turimov et al., 2023).

Vitamin D plays a significant role in the metabolism of calcium and phosphorus in the body of animals. It is neces- sary for the assimilation of minerals from milk and feed, regulation of osteosynthesis, osteogenesis, embryonic de- velopment, and other vital processes (Vlizlo et al., 2007; Tyshkivska, 2008; Nelson et al., 2016). Lack of Vitamin D is one of the reasons for the increase in the death of young cattle and a decrease in productivity (Goff, 2008; Dittmer & Thompson, 2011).

Rickets in calves is associated with vitamin D deficiency(Krueger et al., 2014; Vlizlo et al., 2015). In addition, the development of this pathology is facilitated by hypovita- minosis – A, B1, C, as well as a lack and disturbance of the metabolism of calcium, phosphorus, magnesium, cobalt, copper, and zinc in the body.

In particular, a complex neurohormonal mechanism car- ries out the exchange and homeostasis of calcium, phospho- rus, and magnesium. This complex's center is 1,25-dihydroxycholecalciferol, parathyroid hormone, and calci- tonin. Their target organs are bone and connective tissue, kidneys, and intestines. In

these organs, their biotransfor- mation takes place, as well as the processes of mobilization, deposition, allocation, and reabsorption of ions Ca2+, P5+ Mg2+ (DeLucia et al., 2003; Yuskiv et al., 2007).

D-hypovitaminosis in calves occurs more often in the winter-stall period and if the animals are kept without walk-ing – at any time of the year. The disease proceeds in hid- den, subclinical, and clinically expressed forms (Hymøller & Jensen, 2011; Casas et al., 2015).

Diagnosis of rickets at the stage of bone tissue defor- mation is not difficult since the disease symptoms are pretty characteristic. Detection of the subclinical course of the disease has some difficulties. Diagnosing rickets in calves should be done comprehensively, considering the conditionsof keeping animals, feeding, and the results of a biochemicalblood test.

This work aimed to study the distribution, etiology, clini-cal, and biochemical status of calves with D- hypovitaminosis in one of the farms of Zhytomyr Polissia.

2. Materials and methods

The materials for the study were clinically healthy and rickets-sick calves, aged 1–3 months, belonging to LLC “Mozhary” of the Zhytomyr region. The work was per- formed at the Department of Normal and Pathological Mor- phology of Hygiene and Expertise. The research was carriedout according to the State initiative topic: "Biochemical and morphological changes in domestic animals due to metabol- ic and invasive pathologies – State registration number 0122U200482).

During the study, three groups of animals formed: clini- cally healthy calves with a subclinical course and a clinical- ly pronounced course. A total of 83 animals were studied.

It is worth noting that research (manipulation) on ani- mals was carried out following the existing regulatory doc- uments that regulate the organization of work using experi- mental animals and compliance with the principles of the “European Convention for the Protection of Vertebrate An- imals Used for Experimental and Other Scientific Purposes” (Strasbourg, 1986), “General ethical principles of experi- ments on animals”, approved by the First National Congress on Bioethics (Kyiv, 2001) (European Convention, 1986).

General clinical and laboratory research methods were used in the research. To analyze the general condition of calves in production conditions, a clinical examination was performed, body temperature was measured, and respiration and pulse rates were determined. To analyze hematological indicators in calves under production conditions, we took blood from the jugular vein before morning feeding using vacuum systems “V- TUBETM” (manufactured by AB Med-ical, South Korea). The obtained, biometrically processed biochemical indicators, analyzed, agree with other research- ers' data and are further accepted by us as the norm (Levchenko et al., 2002).

The state of mineral metabolism in calves was deter- mined by the content of 25OHD3 in the blood serum (by theimmunoenzymatic ELISA method), total calcium (arsenase- III reagent), inorganic phosphorus (by the method of UV detection of the phosphomolybdate complex), the activity ofalkaline phosphatase and its isoenzymes (by the method of Wagner, Putilin) (Levchenko et al., 2010).

Statistical processing of the received digital data wasperformed using the Microsoft Excel program. Arithmetic mean values (M), mean squared error (m), and correlation coefficient (r) were determined. The probability of differ- ences was assessed with Student's t-test (Horalskyi et al.,2019). The results of the obtained digital data of the studiedindicators were considered reliable at $P < 0.05–0.001$.

3. Results and discussion

One of the urgent problems of age-related physiology of dairy breeds of cattle; the formation of the physiological andbiochemical status of the calf organism during the periods ofearly postnatal ontogenesis (newborn, milk feeding, and intensive growth), which are in the process of individual development of animals, are essential in research and serve as one of the most critical factors, as they are associated with profound morphological, biochemical and physiologi- cal changes in organs, tissues, and systems of the body as a whole. Protein exchange is the basis of all vital processes in the animal body. All the changes in the body are reflected in the protein composition of the blood since it is connected with the processes of protein formation in other organs and tissues and is responsible for the entire complex of metabol- ic processes.

The diagnosis of Vitamin D deficiency is based on sev- eral factors, which include the conditions of animal housing:walking or stable housing can affect the exposure of animals to sunlight, which is an essential source of Vitamin D for the body. An analysis of rations is carried out to assess the vit- amin-mineral status of animals, including the content of vitamin D, calcium, and phosphorus (the ratio between cal- cium, phosphorus, and vitamin

D). An average balance between these three components is essential to ensure the normal metabolism of calcium and phosphorus (Pyatnychko et al., 2014). During the work at the farm, the

conditions of keeping and feeding animals were studied, and clinical and experimental studies were conducted. Diagnosis and preva- lence of D-hypovitaminosis among calves 1–3 months old were studied using clinical and laboratory methods. It was established that the disease occurred in two forms: subclini- cal (45.8 %) and clinically expressed (24.1 %), the latter occurring much less often. A total of 83 animals were exam-ined (Fig. 1).

It is known from practical experience that rickets is one of the common diseases. A hidden form of D-Vitamin defi- ciency is detected in 60–100 % and clinically expressed in 30–5% of growing young cattle (Levchenko et al., 2016; Flores-Villalva et al., 2021). Therefore, according to the authors (Tyshkivska & Sakhjuk 2008), a hidden form of D-hypovitaminosis is detected in 60–90 % of calves, which leads to profound disturbances of metabolic processes in the animal's body, endochondral bone formation, which is caused by a disorder of D-vitamin and phosphorus-calcium metabolism.

The conducted analysis of keeping and feeding of young cattle and the obtained results of blood tests allow us to statethat the main etiological factors of D-hypovitaminosis in calves are lack of exercise, insufficient insolation when kept without walking, low supply of their primary nutrients and biologically active substances. Animals in the experimental farm are fed diets with an insufficient content of vitamin D2 in feed (hay, hay, silage, straw), with an excess of calcium, adeficiency (63.2 %), or an excess (120.05 %) of phosphorus and digestible protein, sugar which causes the occurrence of this disease.

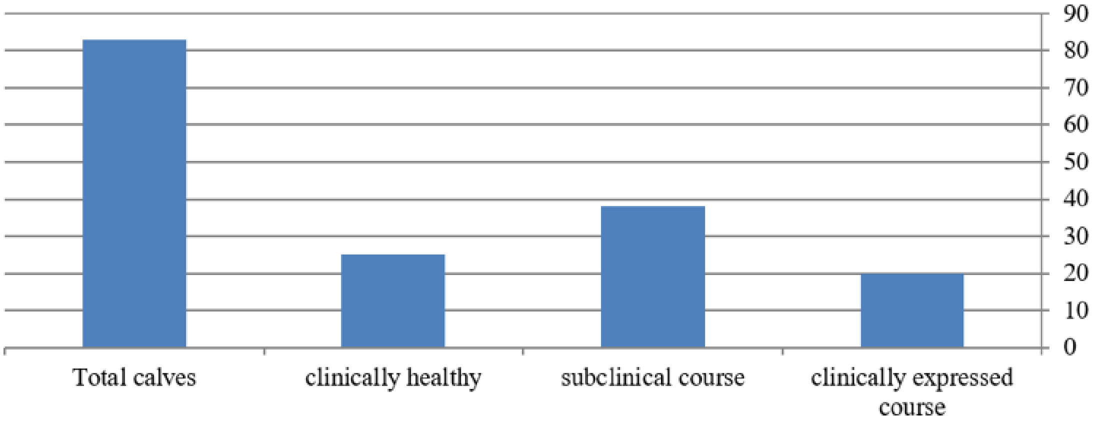

Fig. 1. Spread of D-hypovitaminosis in calves

Analyzing the obtained data, it should be noted that mostoften, the relevant indicators are used for the diagnosis of rickets in animals in veterinary medicine: the diet in termsof its content of vitamin D, calcium, phosphorus (phos- phorocalcium exchange); the results of the analysis of ani- mal housing conditions, biochemical research of blood se- rum for the content of macroelements and the level of activi- ty of alkaline phosphatase and synovial fluid (Levchenko et al., 2016). However, it is recognized that a highly informa- tive method for the diagnosis of rickets is the determination of the level of 2,3-diphosphoglyceric acid. However, due to the complex procedure, this technique has yet to become widespread in practice concerning veterinary laboratory research.

Our studies have shown that a violation of phosphorus- calcium nutrition is complicated by a pronounced deficiency of Vitamin D (25.8 %), a deficiency of trace elements – cobalt, copper, and zinc, the supply of which was, respec- tively, 57.6 %, 96.2 and 85.6 % out of necessity Such an imbalance of mineral substances in feed is the reason for the development of specific diseases in animals, including D- hypovitaminosis (Garkavy et al., 2001; Levchenko &Petrenko, 2010).

The subclinical course of D-hypovitaminosis in calves was not pronounced. It was characterized by non-specific symptoms: decreased appetite, taste distortion (allotriopha- gia), dryness, and skin laxity. Calves were noted to have tense movements, frequent crossing of limbs, and an in- crease in the volume of the abdomen. Calves were depend- ent and difficult to lift; complicated movements and short- term clonic tonic convulsions were noted. Animals were often diagnosed with atony of the stomachs. Similar results have been obtained in research (Pyatnychko et al., 2014) that were manifested by characteristic symptoms, i.e., a decrease in appetite, and messy hair, followed by the devel- opment of short stature. As a result of the research of Stadnyk A. M. (2008) with co-authors, in calves, there is a decrease in appetite and licking, and they lag in growth and development. The intensity of movements is disturbed, and the tone of skeletal muscles decreases. Animals

often cross their limbs, limp, lie down more, and rise poorly; some calves develop bone distortions, swelling of joints, and de- formation of the spine and chest. The analysis of blood and urine indicators of calves showed that the hemoglobin con- tent, the number of erythrocytes, leukocytes, and the con- centration of calcium, inorganic phosphorus, and protein are significantly lower in patients with rickets compared to clinically healthy ones (Stadnyk & Kravtsiv, 2008).

In the existing conditions, the most characteristic symp- toms of the clinically pronounced course of rickets in calves were a delay in growth and development, a decrease in fat- ness, a tendency to licking and allotriophagia, softening and partial resorption of the last ribs. Thickening of the carpal joints, the curvature of the limbs (X-shaped posture of the thoracic limbs), osteolysis of the last tail vertebrae, and shakiness of the teeth were noted in the sick animals.

Many researchers note that calcium accounts for most mineral substances in animals' bodies. It is the main compo- nent of teeth and skeleton. Calcium is involved in the nerv- ous excitability of the system, in the normal functioning of the heart and skeletal muscles, regulates the permeability of cell membranes and blood coagulation, and also affects the availability of phosphorus from feed (Li & Saha, 2021). Phosphorus is part of bone tissue, is contained in nucleic acids, is closely related to calcium, and plays an essential role in carbohydrate metabolism (St-Jules et al., 2017).

The diagnosis of rickets in calves was carried out com- prehensively, considering the conditions of keeping and feeding, the presence of exercise, and insolation for animals;for this, clinical and unique research methods were used. Thus, our studies have shown that during the subclinical course of rickets, hypocalcemia was diagnosed in 45.8 % of test calves, and the total calcium content was in the range from 1.65 to 2.65 (2.21 ± 0.06 mmol/l), which is likely less ($P < 0.01$) than in clinically healthy animals, and more ($P < 0.05$) compared to animals with clearly expressed symptoms of the disease (Table 1).

Hypocalcemia with a clinically pronounced course of D- hypovitaminosis was diagnosed in 24.1 % of calves, with an average value for the group of 2.05 ± 0.05 mmol/l, which is probably less ($P < 0.001$) than in healthy animals, and also less ($P < 0.05$) according to the indicator in young animals with a subclinical course of the disease.

The content of inorganic phosphorus in the blood serum of calves with a subclinical course of the disease was 2.05 ±
0.03 mmol/l, which does not differ significantly from the values of clinically healthy animals.

During the chronic course of the disease, hypophos- phatemia was diagnosed in 24.1 % of calves. Thus, the con- tent of inorganic phosphorus was probably lower ($P < 0.001$) than in clinically healthy animals and young animals with subclinical D-hypovitaminosis ($P < 0.01$).

Table 1
The content of total calcium and inorganic phosphorus in the blood serum of calves with D-hypovitaminosis

A group of researched animals	Biometric indicator	Total calcium, mmol/l	Inorganic phosphorus, mmol/l
Clinically healthy (n = 25)	Lim M ± m	2.10–2.49 2.31 ± 0.07	1.81–2.56 2.15 ± 0.05
Subclinical course (n = 38)	Lim M ± m	1.65–2.56 2.21 ± 0.06	1.77–2.51 2.05 ± 0.03
P <		0,01	0.2
Clinically expressed course (n = 20)	Lim M ± m	1.63–2.54 2.05 ± 0.05	1.43–2.42 1.85 ± 0.04
P_1<		0.001	0.01
P_2 <		0.05	0.01

Note: P< – animals with a subclinical course of the disease compared to clinically healthy ones; P_1< – animals with a clinical course of the disease compared to clinically healthy ones; P_2< – animals with a clinically pronounced course compared to a subclinical one

The conclusion from the analysis of literary data (Stadnyk & Fedorovych, 2008; Battault et al., 2013; Zafalonet al., 2020) allows us to state that the role of vitamin D3 is not limited to regulating calcium and phosphorus metabo- lism. At the current stage of research, it was established that vitamin D3 has a regulatory effect on the proliferation of all organs and tissues, as well as on the synthesis of lipids, enzymes, and hormones, not limited to calcium-

reactive ones, but also thyrotropin, glucocorticoids, prolactin, gas- trin, and others. Recent studies also indicate the effect of vitamin D3 on carbohydrate metabolism, which was exper- imentally confirmed in an experiment with rats. It was found that insulin synthesis depends on the presence of vitamin D3in the body and less on the calcium level. Thus, to ensure the body's vital activity, it is necessary to receive vitamin D3 throughout life.Alkaline phosphatase is one of the most essential en- zymes in the animal body. It is found in many tissues and plays a significant role in phosphorus-calcium and othertypes of metabolism (Nadtochy et al., 2013; Nischemenko etal., 2016). Intestinal enterocytes synthesize alkaline phos- phatase and participate in the transport through the entero- cyte membrane of glucose and other monomers, as well as phosphorylation reactions (Sharma et al., 2014). This en- zyme can regulate the differentiation of osteoblasts and serves as a unique marker for them. A sharp change in the activity of this enzyme is observed in pathological condi- tions of the animal's body, associated with impaired blood supply to organs, pathologies of bone growth, etc. With the low activity of this enzyme in the body, there is a lack of magnesium and zinc, and protein deficiency is observed.Alkaline phosphatase is involved in maintaining homeosta- sis, regulating growth, and adapting the organism to theconditions of the external environment (Millán, 2006;Fernandez & Kidney, 2007). Increased alkaline phosphataseactivity in the serum is most often registered in liver andbone tissue pathology. Damage to the liver parenchyma causes a slight increase in serum enzyme activity since alka-line phosphatase is tightly bound to cell membranes. In thepathology of bone tissue, when osteoblasts are increased(during the development of rickets, osteodystrophy), thebone isoenzyme of alkaline phosphatase increases in theblood. In these cases, the activity of total alkaline phospha- tase in blood serum and synovial fluid increases 3–10 times. As a result of our research, it was established that a sig- nificant increase in the activity of alkaline phosphatase incalves during the subclinical course of the disease (112.3 ± 7.6 vs. 83.7 ± 5.8 units/l) in clinically healthy young animals($P < 0.05$) occurs due to increased activity of bone isozyme.

In calves during the clinical course of D-hypovitaminosis, the activity of alkaline phosphatase was, on average, 129.1 ± 6.5 U/l, which is probably higher than the value in clinically healthy young animals ($P < 0.001$) and in animals with a subclinical course of the disease ($P < 0.01$; Table 2).

Total alkaline phosphatase and its bone isoenzyme activ-ity during D-hypovitaminosis increases by 1.8 times, indi- cating a violation of bone tissue's mineralization process (Table 2).

Table 2
The activity of alkaline phosphatase and its isozymes in calves

A group of researched animals	Biometric indicator	Alkaline phosphatase, units/l	
		general	bone
Clinically healthy (n= 25)	Lim M ± m	61,3–177,5 83,7 ± 5,8	54,3–169,3 67,4 ± 4,9
Subclinical course (n=38)	Lim M ± m	81,4–207,6 112,3 ± 7,6	71,5–192,7 102,5 ± 5,6
P <		0,05	0,05
Clinically expressed course (n=20)	Lim M ± m	98,7–361,2 129,1 ± 6,5	91,3–391,4 120,9 ± 4,4
P_1 <		0,001	0,001
P_2 <		0,01	0,01

Note: P< – animals with a subclinical course of the disease compared to clinically healthy ones; P_1 < – animals with a clinical course of t[he] disease compared to clinically healthy ones; P_2 < – animals with clinically pronounced D-hypovitaminosis compared to subclinical

Significant violations of the functional state of the calf's body during the subclinical and clinically expressed course of D-hypovitaminosis are confirmed by the results of a bio- chemical study of blood serum: a decrease in the content of 25-hydroxycholecalciferol to 2.56 ng/ml (typically – 32.0–90.0 ng/ml), hypocalcemia, respectively, in 55 and 81 % (2.2 ± 0.07 and 2.0 ± 0.04 mmol/l), a probable increase in the activity of alkaline phosphatase and its bone isoenzyme ($P < 0.001$).

4. Conclusions

1. It has been established that D-hypovitaminosis in calves is widespread on the farm. Therefore, the subclinical course was recorded in 45.8 % of animals, and the clinical course in 24.1 %. Pathology was more often registered in the winter-spring period.
2. The main etiological factors of the disease in calves are hypodynamia and insufficient insolation of animals, low availability of cholecalciferol (25.8 %), violation of the calcium-phosphorus ratio (2.7–4.2 : 1 versus 1.5–2.0 : 1), with a deficiency of trace elements - cobalt, zinc, copper, thesupply of which was 57.6, 85.6 and 96.2 % of the need, respectively.
3. Characteristic symptoms of the disease in calves are licking, allotriophagia, thickening of carpal joints, partial resorption of the last ribs and tail vertebrae, and loose teeth.
4. The most informative laboratory tests for diagnosing pathology are determining the content of

cholecalciferol,total calcium, inorganic phosphorus, alkaline phosphatase activity, and its bone isoenzyme in blood serum. Violationof mineral homeostasis in the body of calves, especially during the winter-stall period, requires further study of a more versatile and in-depth approach to the pathogenesis of D-hypovitaminosis and

the implementation of targeted treatment and prevention measures - primarily the use of complex mineral preparations of prolonged action.

Prospects for further research. Further research consists in elucidating the mechanisms of pathogenetic interrelation- ships of D-vitamin metabolism, which will allow for deep- ening the pathogenesis and development of reasonable treatment and prevention of the disease.

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