Clinical and biochemical aspects of acetonemia (Ketosis) of dairy cows

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Abstract. The research goal was to study the dependence of ketosis syndrome severity of cows on the ketone body level in their blood. Ketotic cows were subjected to clinical and biochemical tests. Biochemical blood tests determined the following: total ketone bodies (TKB), beta-hydroxybutyric acid (BHB), acetoacetic acid and acetone (AcAc), BHB/AcAc ratio, glucose and alkaline reserve. It has been found that bovine ketosis occurs as acetonemic syndrome (65% of cases), gastroenteric syndrome (21%), and hepatotoxic syndrome (14%). The comparison of the ketone body levels and ketosis syndromes has revealed that the acetonemic syndrome is accompanied by the greatest TKB and BHB/AcAc ratio values. The gastroenteric syndrome is accompanied by intermediate TKB, BHB and AcAc values, and the minimum levels of glucose and alkaline reserve. The hepatotoxic syndrome is accompanied by the minimum TKB and BHB/AcAc ratio values, and the greatest glucose and alkaline reserve levels as compared to the other syndromes.

1. Introduction
One of the main objectives of the farming industry of any country is consistent improvement of the quality and volumes of farm production which in turn leads to significant intensification of production including that of dairy production.

High burden on cow body leads to its functioning “on the edge of pathology”. Even insignificant drawbacks in cattle management, nutrition and housing often lead to the development of metabolic diseases [1,2]. One of such pathological conditions is ketosis in dairy cows.

The disease is most evident for the initial 2-8 weeks after calving in high-yielding cows [3-6]. Ketosis is characterized by a mixed symptom complex manifesting in the disorders of the cardiovascular, digestive, nervous and endocrine systems, liver and other organs, and certain changes in the indices of blood, urine, milk and rumen contents [7-11].

The following 4 main syndromes are differentiated: acetonemic, gastroenteric, hepatotoxic and neurotic syndromes. In terms of disease progression, acute, subacute and chronic forms of ketosis are differentiated. Acute progression is typical of neuroticketotic syndrome; subacute and chronic progressions are typical of the acetonemic, gastroenteric and hepatotoxic syndromes.

The development of ketosis clinical pattern depends on the severity of metabolic disorders in the body and consequential increase of ketone body concentration in blood [12]. In this regard, the study of the relationship of the clinical pattern and the ketone body level of cow blood as a factor showing the degree of ketosis-induced metabolic disorders is a topical issue.
The research goal was to study the dependence of ketosis syndrome severity of cows on the ketone body level in their blood.

2. Materials and methods
The study was conducted on the Training and Experimental Farm “Prigorodnoye” of Altai State Agricultural University, Barnaul, Russia, at the end of winter stall-feeding period (March); the study group of cows included comparable ketotic Black-Pied cows aged 5-6 years and weighing 480 ± 30 kg. The group of cows was formed according to the results of Lestradet’s test (reaction with sodium nitroprusside), which detects ketone bodies in urine, and a high level of ketone bodies was later confirmed by laboratory blood tests. Ketosis was diagnosed when the level of total ketoacids (TKB) in the blood was greater than 1.033 mmol/L, and the ketone body ratio beta-hydroxybutyric acid (BHB)/acetoacetic acid and acetone (AcAc) less than 6:1. These animals were subjected to clinical and biochemical tests. Biochemical blood tests determined the following: TKB, BHB, AcAc, BHB/AcAc ratio, glucose and alkaline reserve.

The laboratory blood tests were performed at the Altai Regional Veterinary Laboratory, Clinical and Veterinary Laboratories (Altai State Agricultural University); and Clinical Physiology and Biochemistry Laboratory (Altai State University) according to conventional methods.

3. Results and Discussion
3.1. Results
The clinical study of the cows revealed the following syndromes of ketosis: acetonemic, gastroenteric, and hepatotoxic syndromes. The distribution of the main clinical syndromes in the ketotic cows is shown in Figures 1. Bovine ketosis on the Training and Experimental Farm “Prigorodnoye” occurred mostly as acetonemic syndrome (65% of cases), followed by gastroenteric syndrome (21%), and hepatotoxic syndrome (14%).

![Figure 1](image_url)

**Figure 1.** The distribution of major clinical syndromes in ketotic cows (n=59).

The following was found under hepatotoxic syndrome: enlargement and shift of the area of liver percussion and lover tenderness. The mucous membranes were characterized by pallor with icteric tint. Hepatotoxic syndrome was also characterized by tachycardia and weakening of cardiac impulse and heart tones. The pulse was regular, soft in terms of vascular wall tension, and small in terms of pulse wave velocity.

Gastroenteric syndrome was characterized by slower rumination, reduced feed intake, and forestomach hypotony. Most cows with this syndrome had intestinal hypotony. At the same time, in 30% of animals with gastroenteric syndrome, increased intestinal peristalsis, mucus and foul-smell in fecal matter was found. Intestinal auscultation revealed crepitation and flowing sounds in small intestine, and significant flatulence in large intestine.

Acetonemic syndrome manifested in reduced feed intake, increased respiratory and heart rates, and pale mucous membranes. However, these clinical symptoms are not constant and are not present in all
cows with this syndrome. Acetonemic syndrome is most illustrative of subclinical ketosis. The key point of acetonemic syndrome is a high level of ketone bodies in blood. The levels of ketone bodies and their fractions under this syndrome were much higher than those under other syndromes.

To reveal the dependence of the levels of ketone bodies and the fractions on the clinical manifestations of one or another ketosis syndrome, biochemical blood tests of ketotic cows were performed. The biochemical test results are presented in Table 1. Ketosis of cows regardless of the syndrome is accompanied by high levels of TKB, AcAc, and BHB; low glucose and alkaline reserve, and low BHB/AcAc ratio values relative to the physiological ranges.

| Indices            | Acetonemic, n=24 | Gastroenteric, n=18 | Hepatotoxic, n=17 |
|--------------------|------------------|---------------------|-------------------|
| TKB, mmol/L        | 3.22±0.28        | 2.85±0.24           | 2.27±0.22         |
| AcAc, mmol/L       | 0.85±0.06        | 1.16±0.09           | 1.06±0.09         |
| BHB, mmol/L        | 2.36±0.19        | 1.69±0.14           | 1.21±0.09         |
| BHB/AcAc           | 2.78±0.25        | 1.46±0.21           | 1.14±0.09         |
| Glucose, mmol/L    | 1.8±0.16         | 1.42±0.12           | 1.94±0.17         |
| Alkaline reserve, mmol/L | 18.71±1.62 | 13.18±1.19           | 19.82±1.6         |

Under acetonemic syndrome, the greatest TKB values were observed; these values exceeded those under gastroenteric and hepatotoxic syndromes by 13% (P <0.05) and 42% (P <0.05), respectively. The BHB/AcAc ratio value under acetonemic syndrome was 2 times (P < 0.05) greater than the corresponding value under hepatotoxic syndrome, and 1.9 times (P<0.05) greater than that under gastroenteric syndrome. The BHB level in the blood of the cows with acetonemic syndrome was the greatest one, while the AcAc level, on the contrary, was the smallest as compared to the other ketosis syndromes under study.

Under acetonemic syndrome, the glucose level was lower than that under hepatotoxic syndrome by 7% and, on the contrary, greater than that under gastroenteric syndrome by 27%.

The alkaline reserve level in the blood of cows with acetonemic syndrome was lower by 5% (P > 0.05) than that with hepatotoxic syndrome and, on the contrary, greater by42% (P < 0.05) than that in the cows with gastroenteric syndrome.

Gastroenteric syndrome was characterized by intermediate values of TKB, BHB and AcAc, and the minimum levels of glucose and alkaline reserve as compared to the other syndromes. The glucose level amounted to 1.42 ± 0.12 mmol/L; less by 21% than that in the cows with acetonemic syndrome, and by 27% than that with hepatotoxic syndrome. The alkaline reserve level under gastroenteric syndrome was lower than that under acetonemic and hepatotoxic syndromes by 30% and 34% respectively.

The TKB value under gastroenteric syndrome was by 26% greater than this value in the blood of cows with hepatotoxic syndrome, and by 11.5% lower than that in the cows with acetonemic syndrome. The levels of blood ketone body fractions (BHB and AcAc) relative to the other syndromes are most clearly demonstrated by the BHB/AcAc ratio. The analysis of this ratio revealed that although the AcAc value of 1.16 ± 0.09 mmol/L under gastroenteric syndrome was the greatest one as compared to the other syndromes – 0.85 ± 0.06 mmol/L (acetonemic syndrome) and 1.06 ± 0.09 mmol/L (hepatotoxic syndrome), it was the ratio of the fractions (BHB/AcAc) that indicated that the blood level of AcAc under gastroenteric syndrome was not higher than that under hepatotoxic syndrome and, on the contrary, lower than that under acetonemic syndrome.

The TKB value under hepatotoxic syndrome was minimum and lower by 20% than that under gastroenteric syndrome, and by 11.5% than that under acetonemic syndrome. The BHB/AcAc ratio was also the lowest under this syndrome; lower than that under acetonemic and gastroenteric syndromes 2.5 times and by 22% respectively.
At the same time, the levels of glucose and alkaline reserve under hepatotoxic syndrome were higher as compared to those under the other ketosis syndromes; the glucose level amounted to 1.94 ± 0.17 mmol/L, and alkaline reserve level – to 19.82 ± 1.6 mmol/L.

3.2. Discussion

The conducted research found that ketosis of cows under all studied syndromes was characterized by high levels of TKB, AcAc, BHB, and low levels of glucose, alkaline reserve and BHB/AcAc ratio relative to the physiological ranges.

Acetonemic syndrome was characterized by the highest TKB, BHB/AcAc ratio and intermediate levels of glucose and alkaline reserve; that was indicative of the initial stage of ketosis development and (or) a high degree of compensatory mechanisms in the body of the sick cows.

The reduced TKB value under gastroenteric syndrome as compared to that of acetonemic syndrome, but still higher as compared to hepatotoxic syndrome, and intermediate AcAc levels relative to acetonemic and hepatotoxic syndromes show the intensification of gluconeogenesis and lipolysis, and more intensive utilization of fatty acids as an energy substrate as compared to acetonemic syndrome. However, the shortage of glucose in the body leads to the condensation of excess acetyl-CoA formed through beta-oxidation and to resulting synthesis of large amounts of AcAc; that results in the reduction of the BHB/AcAc ratio. The low values of the BHB/AcAc ratio show the deterioration of redox processes in the liver under gastroenteric syndrome as compared to that under acetonemic syndrome.

Under hepatotoxic syndrome, the lowest TKB and BHB/AcAc ratio was found and, on the contrary, the highest levels of glucose and alkaline reserve as compared to the other syndromes. The increased glucose and alkaline reserve levels with simultaneous TKB and BHB reduction and AcAc increase, as evidenced by the low BHB/AcAc ratio value, are indicative of a significant disorder of the redox processes in liver. Increased blood levels of AcAc in ketotic cows with hepatotoxic syndrome are caused by greater, as compared to gastroenteric syndrome, disorder of fatty acid utilization in hepatocytes and resulting development of fatty liver infiltration. The higher level of alkaline reserve under hepatotoxic syndrome as compared to that of the other syndromes is determined by lower metabolic intensity in the body in general and in the liver in particular and by resulting reduced blood content of various under-oxidized metabolic products.

4. Conclusion

1. Ketosis of cows is manifested as acetonemic, gastroenteric and hepatotoxic syndromes.
2. The intensity of ketosis syndromes depends on the blood levels of ketone bodies and their fractions.

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