

# Bovine Ketosis: A Comprehensive Biochemical and Clinical Perspective

**Dr. Bogapathi Sampath Kumar**

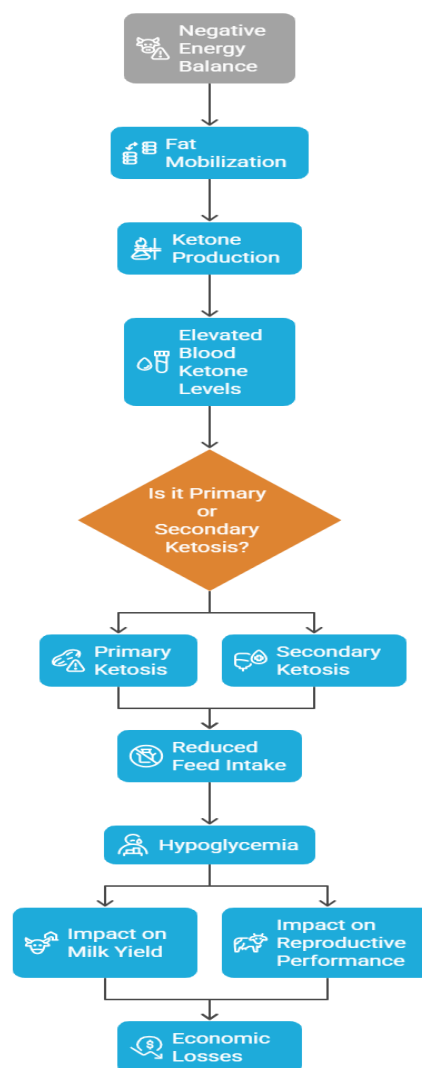
\*Assistant Professor, Department of Veterinary Biochemistry, College of Veterinary Science, Mamnoon, Warangal, PVNRTVU

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## Introduction

Bovine ketosis is a metabolic disorder that primarily affects high-producing dairy cows during early lactation. It results from negative energy balance (NEB), leading to excessive fat mobilization and subsequent ketone body production. Bovine ketosis is characterized by elevated blood ketone levels, hypoglycemia, and reduced feed intake. It is divided into primary ketosis (nutritional) and secondary ketosis (due to underlying diseases). The disorder significantly impacts milk yield, reproductive performance, and overall herd profitability. This metabolic disorder can lead to severe economic losses in dairy farming due to decreased milk yield, impaired reproductive performance, increased susceptibility to other metabolic diseases, and higher culling rates. Additionally, subclinical ketosis, which is more prevalent than clinical ketosis, often goes undetected and can have long-term effects on the productivity of the herd. The prevalence of ketosis varies among dairy herds but is estimated to affect approximately 10-30% of high-producing cows within the first few weeks of lactation. Risk factors include excessive body condition at calving, inadequate transition diets, and poor metabolic adaptation to lactation demands. Early detection and appropriate management strategies are crucial for minimizing the economic impact and improving herd health.

Bovine Ketosis Flowchart



### Ketosis in cattle is often categorized into two forms:

1. **Primary (Nutritional) Ketosis:**  
Occurs due to inadequate energy intake relative to the cow's needs, particularly in high-yielding dairy breeds.
2. **Secondary Ketosis:** Develops as a result of other illnesses such as displaced abomasum, metritis, or mastitis, which cause reduced feed intake and subsequent energy deficiency.

### Biochemical Aspects of Ketosis

During early lactation, dairy cows experience a high energy demand for milk production. When energy intake from feed is insufficient, the body mobilizes fat reserves to compensate for the deficit. This process begins with lipolysis, where hormone-sensitive lipase breaks down stored triglycerides into non-esterified fatty acids (NEFAs) and glycerol. NEFAs enter the bloodstream and are transported to the liver, where they undergo  $\beta$ -oxidation to generate acetyl-CoA, a key molecule in energy metabolism. Under normal conditions, acetyl-CoA enters the tricarboxylic acid (TCA) cycle for complete oxidation to produce ATP. However, in a state of negative energy balance, glucose availability is limited, and the capacity of the TCA cycle is overwhelmed. As a result, excess acetyl-CoA is diverted into ketogenesis, leading to the formation of ketone bodies: acetoacetate,  $\beta$ -hydroxybutyrate (BHB), and acetone.

Ketone bodies serve as alternative energy sources for peripheral tissues, including the brain, muscles, and mammary glands. However, excessive accumulation of ketone bodies leads to metabolic acidosis, reduced appetite, and impaired liver function. Elevated BHB and NEFA concentrations in the blood are hallmark indicators of ketosis. Additionally, the liver's inability to process excessive NEFAs efficiently results in fat

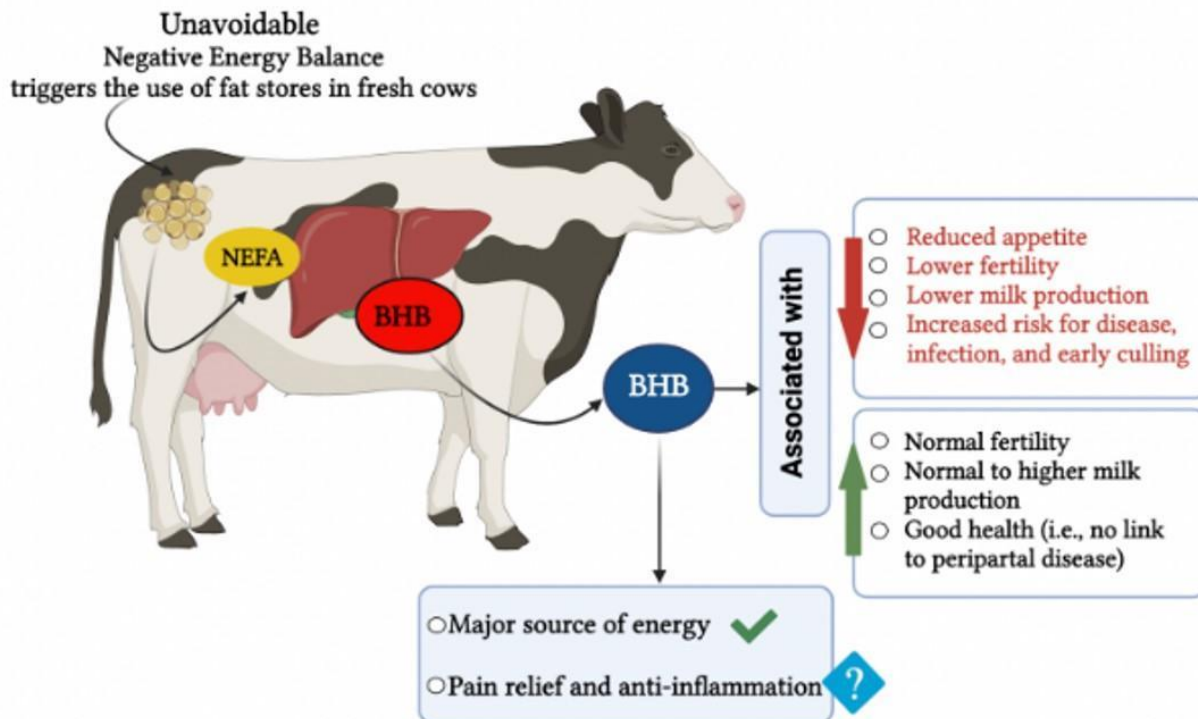
accumulation, contributing to fatty liver syndrome, which further exacerbates metabolic dysfunction. The severity of ketosis depends on factors such as the cow's genetic predisposition, body condition score at calving, and dietary management during the transition period.

### Energy Metabolism in Cattle

- Dairy cows experience high energy demands during early lactation.
- NEB occurs when dietary intake does not meet the energy requirements, leading to fat mobilization.
- Lipolysis releases non-esterified fatty acids (NEFAs) into circulation, transported to the liver for oxidation.
- The liver metabolizes NEFAs via  $\beta$ -oxidation.
- Incomplete oxidation leads to the production of ketone bodies: Acetoacetate (AcAc),  $\beta$ -hydroxybutyrate (BHB), Acetone
- Excessive ketone body accumulation results in metabolic acidosis and clinical ketosis.

**Table 1: Biochemical Pathways Involved in Ketone Body Formation**

Step	Pathway	Key Enzymes	Products
1	Lipolysis	Hormone-sensitive lipase	NEFAs, glycerol
2	$\beta$ -oxidation	Acyl-CoA dehydrogenase	Acetyl-CoA
3	Ketogenesis	HMG-CoA synthase	Acetoacetate, BHB, Acetone
4	Ketone Utilization	Succinyl-CoA transferase	Energy production



## Overview of periparturient ketosis and its relation to lactation performance, fertility, and health, during the first weeks after calving

### Clinical Manifestations of Ketosis

#### 1. Subclinical Ketosis:

- Mild elevation of ketone bodies without noticeable clinical signs.
- Can predispose cows to clinical ketosis or other metabolic disorders.

#### 2. Clinical Ketosis:

- Marked reduction in appetite and milk yield.
- Neurological signs (nervous ketosis) such as head pressing and ataxia.
- Acetone-like odor in breath and milk.

**Table 2: Clinical Signs and their Implications**

Clinical Sign	Biochemical Basis	Diagnostic Value
Reduced feed intake	Hypoglycemia, high BHB	Blood glucose < 2.2 mmol/L
Acetone odor	Elevated ketone bodies	Urine ketone test positive
Weight loss	Increased lipolysis	NEFA > 0.7 mmol/L
Nervous signs	Hypoglycemia, CNS involvement	BHB > 3.0 mmol/L

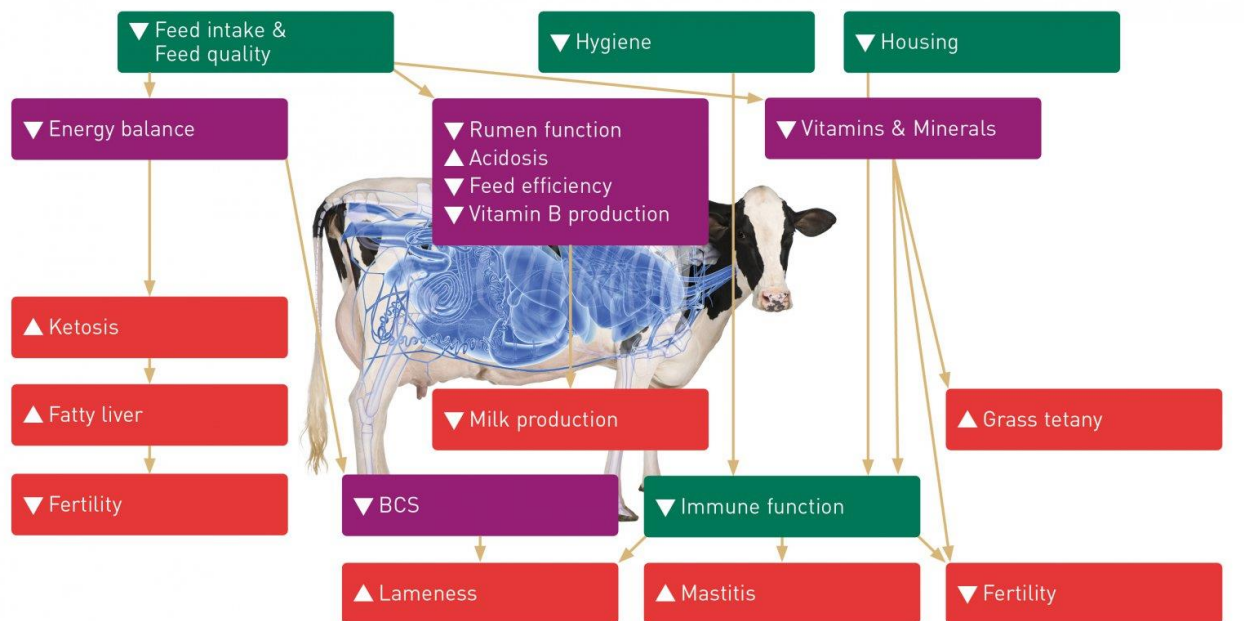
Effects on a dairy cow where feed intake, feed quality, hygiene and housing are “not optimal”

▼ = decrease/negative effect

### Diagnosis of Bovine Ketosis

#### Blood Tests

- **BHB levels:** Gold-standard test.



- Normal: < 1.2 mmol/L
- Subclinical ketosis: 1.2–2.9 mmol/L
- Clinical ketosis: > 3.0 mmol/L

- **NEFA levels:** Indicates fat mobilization.
  - Prepartum: > 0.4 mmol/L (risk factor)
  - Postpartum: > 0.7 mmol/L (ketosis likely)

#### Urine and Milk Tests

- Ketone strips (Acetoacetate detection)
- Milk BHB concentration > 0.15 mmol/L indicates subclinical ketosis

#### Liver Function Tests

- **Aspartate aminotransferase (AST):** Elevated in fatty liver.
- **Glutamate dehydrogenase (GDH):** Hepatic stress indicator.

**Table 3: Diagnostic Biomarkers for Bovine Ketosis**

Biomarker	Normal Range	Ketosis Indicator
BHB	< 1.2 mmol/L	> 3.0 mmol/L

NEFA	< 0.4 mmol/L (prepartum)	> 0.7 mmol/L (postpartum)
Glucose	2.2–4.5 mmol/L	< 2.2 mmol/L

#### Prevention and Management Strategies

##### Nutritional Management

- **Energy-dense diets:** Increase propionate precursors (grain-based diets).
- **Adequate fiber:** Prevents ruminal acidosis and optimizes fermentation.
- **Niacin supplementation:** Reduces NEFA mobilization.

##### Monitoring and Early Detection

- Regular BHB testing in postpartum cows.
- Proper transition diet management.

##### Treatment Approaches

- **IV Dextrose (50% solution):** Immediate energy source.
- **Propylene Glycol (300 mL/day):** Enhances gluconeogenesis.
- **Glucocorticoids** (e.g., **Dexamethasone**): Stimulates hepatic glucose production.

**Table 4: Treatment Strategies for Bovine Ketosis**

Treatment	Mechanism	Dosage
IV Dextrose	Rapid glucose supply	500 mL (50%)
Propylene Glycol	Enhances glucose synthesis	300 mL/day
Niacin	Reduces lipolysis	6–12 g/day
Insulin	Reduces NEFA release	0.2 IU/kg

**Recent findings:** These recent findings underscore the multifaceted nature of ketosis in dairy cows and emphasize the importance of integrated approaches encompassing early detection, individualized treatment, and comprehensive metabolic understanding to enhance herd health and productivity.

**Advancements in Early Detection:** Early and accurate detection of subclinical ketosis is crucial for effective management. Researchers have developed a graphene-based biosensor capable of detecting  $\beta$ -hydroxybutyrate ( $\beta$ HB) levels in dairy cows. This sensor demonstrated high selectivity and sensitivity, effectively distinguishing  $\beta$ HB even in the presence of other compounds like glucose and urea. When tested with real milk samples, the biosensor consistently measured  $\beta$ HB concentrations, indicating its potential as a reliable tool for early ketosis detection in dairy herds.

**Metabolomic Profiling Insights:** A study utilizing gas chromatography/mass spectrometry (GC/MS) analyzed the plasma metabolomic profiles of cows with clinical and subclinical ketosis. The research identified distinct metabolic alterations associated with ketosis, including disruptions in glucose regulation and lipid metabolism. These findings contribute to a deeper understanding of the metabolic pathways involved in ketosis, potentially guiding the

development of targeted interventions and preventive strategies.

**Association Between Ketosis and Reproductive Performance:** Research from the University of Minnesota examined the relationship between ketosis, milk yield, and reproductive outcomes. The study found that cows experiencing ketosis coupled with low milk yield during the first week of lactation had reduced pregnancy rates and longer intervals to conception. Conversely, cows with ketosis but moderate to high milk yield did not exhibit significant reproductive issues. This suggests that early lactation milk production levels may influence the reproductive impact of ketosis, highlighting the need for nuanced management strategies based on individual cow performance.

### Conclusion

Bovine ketosis is a multifactorial disorder requiring an integrated approach for prevention and management. Understanding the biochemical basis, early diagnosis, and targeted nutritional strategies can minimize economic losses and improve herd health.

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