



## Acute Phase Proteins as Predictive Biomarkers of Survival and Mortality in Dromedary Camels: A Review

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### ABSTRACT

Dromedary camels (*Camelus dromedarius*) are vital for the socioeconomic and ecological sustainability of arid and semi-arid regions. However, their health management remains challenging due to subtle clinical signs and limited diagnostic tools. Acute phase proteins (APPs), such as haptoglobin (Hp), serum amyloid A (SAA), fibrinogen (Fb), and C-reactive protein (CRP), have emerged as promising biomarkers for early disease detection and prognosis in veterinary medicine. While previous reviews have broadly addressed APPs in camels, this paper offers a focused and updated synthesis on their prognostic value, particularly as predictors of survival and mortality in both infectious and non-infectious conditions. The review highlights how SAA and Hp show marked increases in diseases like pneumonia, mastitis, lameness, and dystocia, correlating with disease severity and prolonged recovery. It further discusses recent findings from retrospective and prospective studies that support the use of APPs in multi-marker prognostic panels. Unlike earlier reviews, this paper also explores the impact of environmental, physiological, and methodological variables on APP levels, which complicate clinical interpretation. In addition, it outlines emerging diagnostic approaches, including portable biosensors and machine learning-based tools, that could enhance field-based health monitoring. Current barriers to clinical application, such as assay variability and lack of standardized reference ranges, are critically assessed, and the need for multicenter trials and camel-specific diagnostic validation is emphasized. In conclusion, this review underscores the underutilized potential of APPs in camel medicine and offers a roadmap for translating these biomarkers into routine clinical practice.

**Keywords:** Acute Phase Proteins, Biomarkers, Dromedary Camels, Inflammatory Response, Prognosis.

### INTRODUCTION

Dromedary camels (*Camelus dromedarius*) play a pivotal role in the livelihoods of communities inhabiting arid and semi-arid regions, where other livestock species often fail to thrive due to harsh environmental conditions (Abdimahad et al. 2025). Their physiological adaptations—such as efficient water retention, thermoregulation and the ability to utilize poor-quality forage—make them uniquely suited to desert ecosystems (Faye 2013). Beyond their resilience, camels contribute significantly to food security, providing meat, milk, and hides, and also serve as beasts of burden in many parts of North Africa, the Middle East, and South Asia (Padalino and Menchetti 2024). Moreover, their role in maintaining ecological balance by grazing in areas unsuitable for agriculture underlines their environmental importance (Kurtu 2004; Ibrahim et al. 2025).

Despite their adaptability, camels are not immune to disease, and health challenges—particularly infectious and inflammatory conditions—can lead to significant economic losses (Abdallah and Faye 2013). One of the critical limitations in camel veterinary medicine is the difficulty of early diagnosis and accurate prognosis (Niehaus 2022). Clinical signs in camels often remain subtle or nonspecific until advanced stages of disease, reducing the effectiveness of therapeutic interventions (Wernery et al. 2014). Hence, there is a growing need for reliable biomarkers in dromedary camels that can signal the onset and severity of disease at early stages (Tharwat 2023).

The acute phase response (APR) is a conserved systemic reaction to tissue injury, infection, or inflammation, characterized by profound changes in the concentrations of plasma proteins known as acute phase proteins (APPs) (Gruys et al. 2005). These proteins, produced predominantly by the liver under the influence of

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pro-inflammatory cytokines, play crucial roles in restoring homeostasis and modulating the immune response (Sander et al. 2010). In veterinary diagnostics, APPs have been extensively studied in various species, including cattle and horses, as indicators of disease progression, severity, and treatment efficacy (Murata et al. 2004; Petersen et al. 2004). However, research into their diagnostic and prognostic utility in dromedary camels is relatively limited but expanding (Tharwat 2020).

Given the potential of APPs to reflect the intensity and course of inflammatory responses, there is increasing interest in their application as prognostic tools in camels (Tharwat 2023). Certain APPs, such as haptoglobin, serum amyloid A, and fibrinogen, have shown promise in assessing disease severity and predicting clinical outcomes (El-Deeb et al. 2022). Nonetheless, comprehensive evaluation of their predictive value in determining survival or mortality remains underexplored.

This review aims to critically examine current knowledge regarding the role of acute phase proteins as predictive biomarkers of survival and mortality in dromedary camels. By consolidating recent findings and identifying research gaps, the review seeks to inform the development of effective diagnostic strategies and improve clinical outcomes in camel health management.

**The acute phase response in camelids**

The acute phase response (APR) is a highly conserved, systemic reaction triggered by infection, inflammation, trauma, or stress, aiming to restore homeostasis and limit tissue damage (Speelman et al. 2022). In mammals, the APR represents a central component of the innate immune response and is characterized by physiological, metabolic, and behavioral changes, most notably the hepatic synthesis of acute phase proteins (APPs) (Murata et al. 2004). These proteins serve diverse immunomodulatory, antimicrobial, and regulatory functions, making them valuable biomarkers of health and disease (Jain et al. 2011).

**Overview of the APR in mammals**

In general, the APR is initiated within hours of an inflammatory stimulus and is orchestrated by pro-inflammatory cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) (Cray et al. 2009). These cytokines act on hepatocytes to modulate the synthesis of APPs, which can be broadly categorized into positive APPs (whose serum concentrations increase) and negative APPs (whose concentrations decrease during inflammation) (Murata et

al. 2004). Positive APPs include C-reactive protein (CRP), haptoglobin (Hp), serum amyloid A (SAA), fibrinogen, and ceruloplasmin, among others (Petersen et al. 2004). These proteins participate in pathogen neutralization, opsonization, clotting, and regulation of the immune response (Robinson et al. 2023).

**Mechanisms of APP production**

The liver plays a pivotal role in APP production, acting as the primary site of synthesis in response to cytokine signaling (Sander et al. 2010). IL-6 is considered the main inducer of hepatic APP synthesis, while IL-1 and TNF-α contribute to early-phase signaling and the amplification of the inflammatory cascade (Rose-John 2018). The transcriptional regulation of APP genes involves signaling pathways such as JAK/STAT and NF-κB, which are activated by cytokine-receptor interactions on hepatocytes (Hu et al. 2021). The kinetics and magnitude of APP production vary depending on the type and severity of the stimulus, and also by species, age, and physiological status of the animal (Tharwat 2023).

**Species-Specific characteristics of APR in camels**

Table 1 provides a comparative overview of the APR characteristics in camels relative to cattle, sheep, and horses. This table highlights key differences in the dynamics of APPs, fever response, and environmental adaptations. Notably, camels exhibit a robust but occasionally delayed or prolonged APP response, particularly involving Hp and SAA, and a comparatively muted febrile reaction, likely reflecting their physiological adaptation to arid environments. These features contrast with the typically rapid and pronounced APR seen in cattle and horses. Such species-specific differences underscore the importance of tailored diagnostic thresholds and interpretations when using APPs as inflammatory biomarkers in camelid medicine.

Studies indicate that haptoglobin and serum amyloid A are among the most responsive APPs in camels, with their serum concentrations rising significantly during bacterial infections, parasitic infestations and systemic inflammatory conditions (El-Bahr and El-Deeb 2016). Moreover, camels appear to have a relatively subdued fever response compared to other domestic species, possibly due to their adaptation to arid environments, which also influences their inflammatory and metabolic responses (Faye and Bengoumi 2018). Additionally, the APR in camels may be prolonged or delayed depending on the nature of the inflammatory stimulus, suggesting a unique

**Table 1:** Comparative overview of acute phase reaction (APR) characteristics in camels, cattle, sheep and horses

Feature / Species	Camels (Tharwat 2023)	Cattle (Bagga et al. 2016)	Sheep (Eckersall et al. 2007)	Horses (Smith et al. 2023)
Major Acute Phase Proteins (APPs)	Haptoglobin, Serum Amyloid A (SAA)	Haptoglobin, SAA, Fibrinogen	Haptoglobin, SAA, α1-acid glycoprotein	SAA, Fibrinogen
APP Response Intensity	Moderate to high	High	Moderate	High
Onset of APR	May be delayed depending on stimulus	Rapid (within 24–48h)	Rapid	Rapid
Duration of APR	Sometimes prolonged	Short (returns to baseline quickly)	Variable	Short to moderate
Fever Response	Often blunted or mild	Marked fever typical	Marked fever typical	Moderate to high fever
Environmental Influence	Adapted to arid climates; may modulate APR	Less environmental modulation	Moderate influence	Environmental stress can affect response
Clinical Implication	Requires species-specific interpretation of APPs	Well-characterized APP ranges	Moderate characterization	SAA widely used clinically as biomarker

regulatory mechanism of immune modulation in this species (El-Deeb and Buczinski 2015). Such peculiarities highlight the importance of species-specific reference ranges and diagnostic interpretations when utilizing APPs as biomarkers in camelid medicine (Tharwat 2023).

**Acute phase proteins in dromedary camels**

**Classification of acute phase proteins**

Acute phase proteins (APPs) are blood-borne proteins whose serum concentrations significantly fluctuate in response to inflammation, infection, trauma, or stress (Ansar and Ghosh 2016). These proteins are generally classified into three categories based on the magnitude of their response: major, moderate and minor (Murata et al. 2004; Ceciliani et al. 2012). Major APPs can increase by 10- to 100-fold within 24 to 48 hours, moderate APPs usually exhibit a two- to tenfold rise, and minor APPs show a slight or delayed increase in response to an acute-phase stimulus (Schrödl et al. 2016).

**Common APPs identified in dromedary camels**

**Serum Amyloid A**

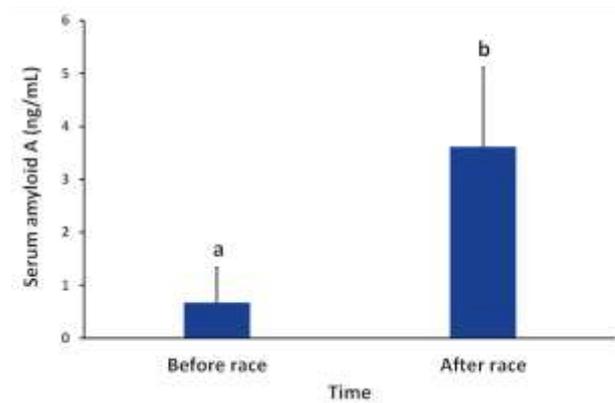
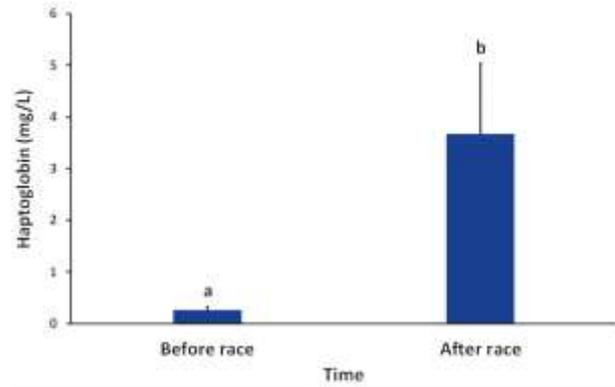
SAA is a highly responsive APP associated with high-density lipoprotein and involved in immune cell recruitment and cytokine regulation (Mohanty et al. 2025). In camels, SAA has demonstrated rapid and substantial increases in conditions such as racing-induced stress and bacterial infections (Tharwat and Al-Sobayil 2015a) (Fig. 1). The SAA was also increased significantly in male dromedaries just after the procedure of electroejaculation (Tharwat and Al-Sobayil 2018) (Fig. 2). In camel calves with tick infestation, SAA was tested significantly high in diseased versus healthy control animals (Tharwat et al. 2024) (Fig. 3). According to El-Deeb and Buczinski (2015), SAA levels were significantly elevated in camels with urinary tract infections and decreased following successful treatment, reinforcing its utility as a major APP and a potential monitoring tool for clinical progression.

**Haptoglobin (Hp)**

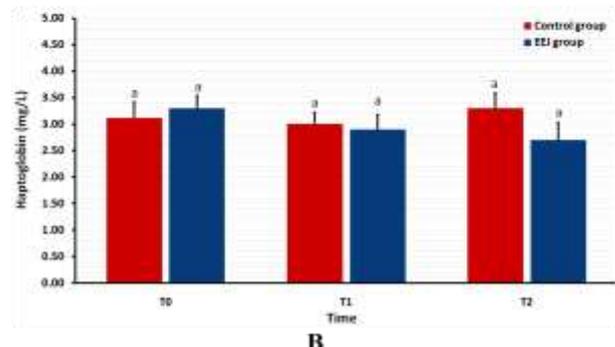
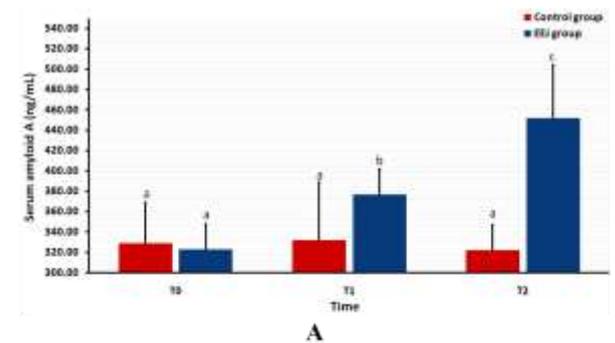
Haptoglobin (Hp) is a hemoglobin-binding protein that limits oxidative damage and deprives pathogens of iron (Goldenstein et al. 2012). In healthy dromedary camels, Hp levels are relatively low, but studies have shown significant elevations during various inflammatory conditions such as pneumonia, urinary tract infections, and during the periparturient period (Tharwat and Al-Sobayil 2015b) (Fig. 4). In camel neonatal animals with tick infestation, Hp was tested significantly high in diseased versus controls (Tharwat et al. 2024). Despite these increases, Greunz et al. (2018) observed that the fold change in Hp concentrations in camels was relatively modest, suggesting that Hp functions as a minor to moderate positive APP in this species.

**Fibrinogen**

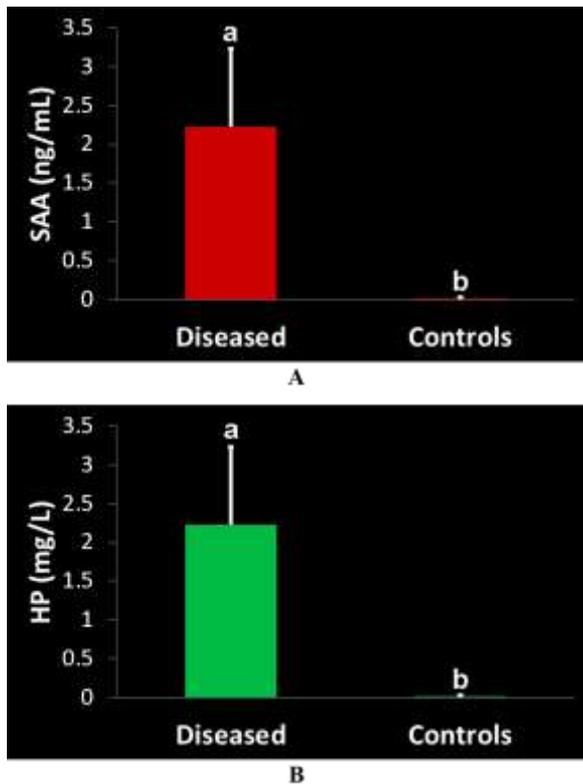
Fibrinogen is a glycoprotein involved in coagulation and tissue repair (Pieters and Wolberg 2019). It acts as a moderate APP in dromedary camels, with elevated levels reported in animals suffering from chronic inflammation, such as lymph node abscesses and respiratory diseases (Greunz et al. 2018). Fibrinogen also showed promise as a supportive diagnostic marker when combined with other APPs in differentiating between acute and chronic disease states (Hernández-González et al. 2025).



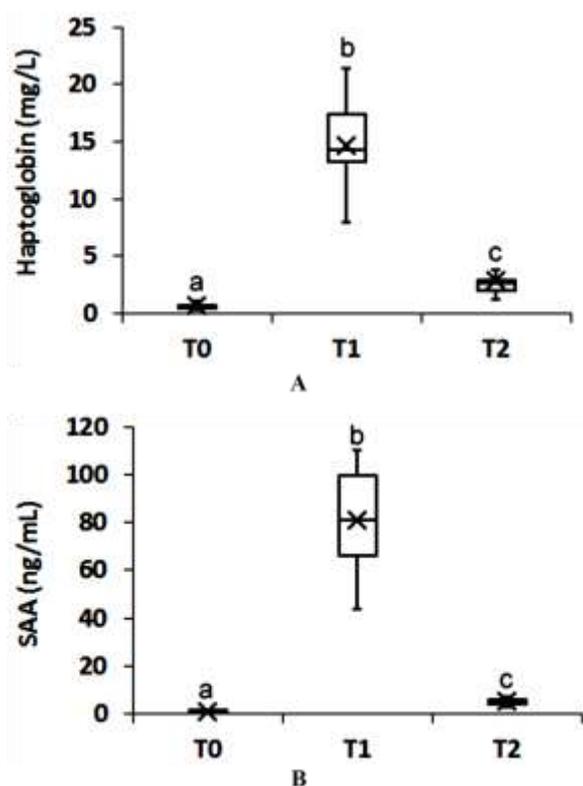
**Fig. 1:** Mean serum concentrations of haptoglobin (A) and serum amyloid A (B) in racing camels before and after a 5-km race. <sup>a, b</sup> Significant difference at P<0.05 (Adapted from Tharwat and Al-Sobayil, 2015a).



**Fig. 2:** Effect of stimulation by electroejaculation (EEJ) on concentrations of serum amyloid A (A) and haptoglobin (B) in male dromedary camels (mean±SD, n=20) compared to control group (n=10). T0: just before EEJ; T1: directly after EEJ; T2: 24h after EEJ. <sup>a,b,c</sup> Values differ significantly (Adapted from Tharwat and Al-Sobayil, 2018).



**Fig. 3:** Serum concentrations of serum amyloid A (SAA; A) and haptoglobin (HP; B) in camel calves (n=21) with tick infestation compared to healthy controls (n=10). <sup>a,b</sup>P<0.0001. (Adapted from Tharwat et al. 2024).



**Fig. 4:** Box and whiskers plots of serum haptoglobin (A) and serum amyloid A (SAA) in camels during the periparturient period. Box represents the 75th and 25th percentiles while whiskers extend to the 95th and 5th percentiles. T0, 3 wk before expected parturition; T1, within 12h of parturition; T2, 3 wk after parturition. Values with different letters differ significantly (P<0.5) (Adapted from Tharwat and Al-Sobayil, 2015b).

### C-Reactive Protein (CRP)

C-Reactive Protein (CRP) is a classical marker of inflammation that binds to microbial phosphocholine, promoting complement activation (Sproston and Ashworth 2018). In camels, CRP concentrations have been shown to rise significantly in pneumonic conditions, suggesting a role in the innate immune response to respiratory pathogens (Ahmed et al. 2021). Tharwat and Al-Sobayil (2015a) also reported increased CRP levels in racing camels, supporting its classification as a moderate APP.

### $\alpha$ 1-Acid Glycoprotein

$\alpha$ 1-Acid Glycoprotein (AGP), also known as orosomucoid, is a moderate APP involved in immunomodulation and drug binding (Ceciliani and Lecchi 2019). Although extensively characterized in cattle and other ruminants, AGP data in camels remain limited. Nevertheless, its inclusion in camelid APP panels is supported by analogies with other species and indirect references in inflammation-related studies (Murata et al. 2004; Ceciliani and Lecchi 2019). Further research is warranted to determine its diagnostic value in camel medicine.

### Ceruloplasmin

Ceruloplasmin (Cp) is a copper-carrying enzyme with oxidase activity, contributing to iron metabolism and antioxidant defense mechanisms (Liu et al. 2022). In camels, elevated Cp levels have been documented in cases of reproductive tract infections, such as endometritis and urinary tract disorders (El-Deeb et al. 2022). Cp levels were positively correlated with the severity of disease and normalized after effective treatment, indicating its potential as a moderate APP for both diagnostic and prognostic applications (Liu et al. 2022).

### Prognostic role of APPs in disease conditions

APPs play a critical role in the innate immune response and are widely recognized as valuable biomarkers for evaluating disease severity and predicting clinical outcomes in animals (Cray 2012). In dromedary camels, APPs such as haptoglobin (Hp), serum amyloid A (SAA), fibrinogen, and C-reactive protein (CRP) have been investigated as prognostic indicators in both infectious and non-infectious conditions (El-Deeb and Buczinski 2015; Greunz et al. 2018; Ahmed et al. 2021).

### Infectious diseases

In camelid medicine, infectious diseases such as respiratory, urinary and endometrial infections, as well as mastitis, are associated with significant increases in APP concentrations. Studies by El-Deeb and Buczinski (2015), Faye and Bengoumi (2018) and El-Deeb et al. (2022) have shown that in respiratory, urinary, and endometrial infections, levels of SAA, Hp, and CRP significantly increase in proportion to the severity of clinical signs. Elevated APPs during the acute phase also correspond to longer recovery periods and higher morbidity (Faye and Bengoumi 2018). In camels with mastitis, it was reported that APPs (Fb, Cp, SAA, Hp) significantly elevated compared to the control animals (Darwish 2023).

### Non-Infectious conditions

APPs are equally responsive to non-infectious

stressors such as trauma, racing, and periparturial stress (Tharwat and Al-Sobayil 2015a; Tharwat and Al-Sobayil 2018; Tharwat 2020). In cases of subjected to electroejaculation, the level of SAA increased significantly immediately after the procedure but returned to baseline values 24h later (Tharwat and Al-Sobayil 2018). Persistently elevated APPs post-surgery has been linked to delayed wound healing or secondary infections (Tharwat 2023). During periods of extreme environmental heat, dromedary camels experience physiological stress that induces an acute phase response. Research by Meléndez et al. (2020) indicated that high ambient temperatures cause significant elevations in Hp levels, reflective of systemic inflammation. Though data specific to camels are limited, similar findings in cattle and sheep suggest that APPs may serve as early prognostic indicators of heat stress susceptibility in camels.

#### **Correlation between APP levels and clinical outcomes**

Numerous studies have demonstrated strong correlations between APP concentrations and clinical outcomes in diseased camels. For instance, Ahmed et al. (2021) observed that higher Hp, CRP and Fb levels in pneumonic camels were significantly associated with longer durations of illness, reduced appetite, and increased mortality rates. In lame racing camels, El-Deeb and Abdelghani (2022) found that levels of SAA were highly elevated in lame racing camels indicative of the severity of inflammation and pain, and they declined proportionally with clinical improvement following 10-day therapy. The latter study concluded that in addition to clinical examination of lame camels, SAA levels could be a useful diagnostic and predictive tool for lameness in racing dromedary camels (El-Deeb and Abdelghani 2022).

#### **Predictive value of APPs for mortality**

##### **Retrospective and prospective study findings**

Retrospective analyses in cases of dystocia suggest that elevated APPs, Hp and SAA, are closely linked to adverse outcomes such as fetal and maternal mortality. For instance, camels experiencing prolonged dystocia exhibited significantly higher Hp and SAA, with Hp correlating to fetal death and dam mortality (Ali et al. 2016). Prospective cohort studies, such as those following camels with pneumonia or other clinical conditions, further confirm that higher Hp and fibrinogen levels are observed in non-survivors. In pneumonic camels, mean Hp exceeded 1.0g/L among those that died (Ahmed et al. 2021). These data consistently support the prognostic value of APPs in predicting survival in camels.

#### **Cut-off values and threshold concentrations**

Establishing diagnostic thresholds is essential for clinical utility. In pneumonia, Hp thresholds near 1.0g/L and CRP around 13mg/L differentiated severe cases (Ahmed et al. 2021). While exact mortality-specific cut-offs remain underexplored, increasing duration of dystocia was associated with significant increases in SAA and Hp (Ali et al. 2016). In clinical practice, SAA and Hp concentrations above these values, especially in the context of systemic disease, may warrant heightened intervention (Ahmed et al. 2021).

#### **Time course of APP response relative to mortality**

The temporal dynamics of APP elevation are critical for timely prognosis. In dystocia settings, both Hp and SAA increased progressively with duration of the condition, peaking shortly before fetal and dam mortality (Ali et al. 2016). In experimental models, Hp and fibrinogen peaked between three to five days post-insult, while SAA exhibited a more rapid but variable response (Greunz et al. 2018). Thus, early elevations in fast-responding APPs (e.g., SAA) followed by sustained increases in slower indicators (Hp, fibrinogen) may signal escalating severity and imminent mortality risk (Ali et al. 2016).

#### **Multi-marker panels vs single markers**

Relying on a single APP may limit prognostic accuracy. Multi-marker panels combining Hp, SAA, CRP, and fibrinogen capture complementary response kinetics and improve stratification. El-Deeb et al. (2022) demonstrated that combining Hp, SAA, and fibrinogen underscoring combined predictive power for diagnosis of endometritis. In the context of mortality, serum panels showing simultaneous elevations in Hp and SAA were more strongly associated with non-survival than either marker alone (Ali et al. 2016). Therefore, integrated APP profiles are recommended for clinical prognosis.

#### **Factors influencing acute phase proteins levels in camels**

The concentrations of APPs in dromedary camels can be influenced by a wide array of physiological, environmental, and pathological factors. These variables must be carefully considered when interpreting APP levels as predictive biomarkers of survival and mortality (El-Deeb and Buczinski 2015).

#### **Age, sex and physiological status**

Age-related differences in APP concentrations have been observed in various species, including camels. Younger animals, especially neonates, may show elevated levels of specific APPs due to the immaturity of their immune systems or passive transfer from maternal sources (Ahmadi-Hamedani et al. 2014). In adult camels, sex and reproductive status also play a critical role (Tharwat and Al-Sobayil 2015b). For example, pregnant and lactating females typically exhibit higher levels of SAA and Hp, likely due to hormonal modulation and physiological stress associated with gestation and milk production (El-Deeb and Buczinski 2015). Such physiological elevations may not necessarily indicate pathology, thus complicating diagnostic interpretations.

#### **Environmental stressors**

Environmental stress, including extreme temperatures, poor nutritional status, and transportation, can significantly alter APP profiles in camels. Heat stress, in particular, is known to trigger systemic inflammatory responses that result in elevated APP synthesis (Faye and Bengoumi 2018). Similarly, inadequate nutrition or water deprivation may lead to metabolic imbalances that provoke acute phase responses (Amin et al. 2023). Seasonal variations in APP levels have also been noted, suggesting that environmental factors have both acute and chronic modulatory effects on APP expression (Ahmed Adel El-Sayed 2025).

### Concurrent diseases or coinfections

The presence of concurrent infections or comorbid conditions can lead to synergistic increases in APP levels, potentially amplifying or masking the severity of the primary disease (Azma et al. 2015). Coinfections with bacterial, viral, or parasitic agents are particularly common in camels under extensive management systems and may result in overlapping inflammatory signatures (Tharwat et al. 2024). For instance, camels co-infected with *Trypanosoma evansi* and bacterial pathogens show markedly elevated levels of Hp and SAA compared to animals with single infections. This underscores the importance of comprehensive clinical and laboratory evaluation when assessing APP values for prognostic purposes (El-Bahr and El-Deeb 2016).

### Handling and sampling techniques

Pre-analytical variables such as sample collection, handling and storage can significantly impact the accuracy of APP measurements. Hemolysis, delayed processing, and inconsistent sampling times may lead to artifactual increases or decreases in APP levels (Tharwat 2023). Moreover, physical restraint and stress during sampling can itself provoke transient acute phase responses, particularly in excitable animals such as young or unaccustomed camels. Therefore, standardization of sample collection protocols is crucial to minimize variability and enhance the diagnostic utility of APPs in camel medicine (Mohamed et al. 2021).

### Clinical applications and diagnostic integration

The growing body of evidence supporting the diagnostic and prognostic utility of APPs in dromedary camels has opened avenues for their clinical integration, particularly in field and herd management contexts (Tharwat 2020). This section explores the practical applications of APPs in camel health management, emphasizing their role in point-of-care diagnostics, herd-level surveillance, clinical assessment tools and decision-making frameworks.

### Point-of-care diagnostics using APPs

Point-of-care testing (POCT) for APPs offers a promising approach to enhance timely diagnosis and monitoring of disease conditions in camels, particularly in remote or resource-limited settings where laboratory access is restricted. Technologies such as lateral flow immunoassays and portable immunoturbidimetric analyzers are being adapted for rapid detection of key APPs such as CRP, Hp, SAA, and fibrinogen (Tecles et al. 2025). Early detection through POCT enables timely interventions that may significantly improve survival rates in critically ill or injured camels. Furthermore, APPs measured at the point of care can provide immediate insights into the presence and severity of inflammatory conditions, making them valuable for veterinary decision-making on-site (Cray et al. 2009; Cray 2012; El-Deeb et al. 2022).

### Role in herd health monitoring

At the herd level, APPs serve as sensitive indicators of subclinical inflammation and early disease outbreaks (Tharwat 2023). Regular monitoring of baseline and fluctuating levels of APPs can detect subtle changes in

health status before overt clinical signs emerge. For instance, longitudinal tracking of SAA or Hp in large camel herds has been shown to correlate with stress-related and infectious disease burdens. Thus, integration of APP measurements into herd health programs may enable proactive management strategies, including early isolation of affected animals, vaccination timing, and optimization of nutrition to support immune resilience (Faye and Bengoumi 2018).

### Integration with clinical scoring systems

Incorporating APP levels into existing clinical scoring systems has the potential to enhance diagnostic precision and prognostic accuracy in dromedaries (Tharwat 2020). For example, combining APP data with physiological parameters such as heart rate, respiratory rate, and body temperature can refine assessments of disease severity and guide triage decisions. Clinical algorithms incorporating APPs have demonstrated utility in other large animal species (Cecilian et al. 2012) and preliminary studies suggest similar applicability in camels, particularly in cases of septicemia, pneumonia, or post-surgical inflammation. Such integration supports a more nuanced evaluation of patient condition and may guide therapeutic interventions more effectively (El-Deeb and Buczinski 2015; Ahmed et al. 2021).

### Limitations and knowledge gaps

Although APPs are increasingly recognized as potential biomarkers in dromedary camels, several scientific and practical limitations must be addressed to improve their prognostic reliability and clinical utility. This section outlines the key knowledge gaps that constrain the broader adoption and standardization of APP-based diagnostics in camelid medicine.

### Limited reference ranges for acute phase proteins

A major limitation in the use of APPs in dromedaries is the absence of clearly defined, species-specific reference ranges. Existing studies provide inconsistent baseline values for APPs such as Hp, SAA, and fibrinogen in healthy and diseased camels (El-Deeb et al. 2020). These inconsistencies are likely due to differences in geographical location, age, sex, physiological status and analytical methods. Thus, without standardized reference intervals, clinicians and researchers face difficulties in distinguishing between physiological variation and disease-associated changes, thereby limiting the diagnostic value of APP measurements (Ahmadi-Hamedani et al. 2014).

### Lack of longitudinal and large-scale studies

Most available research on APPs in dromedary camels is cross-sectional in nature and lacks follow-up or outcome-based data. This presents a significant gap in understanding the time-course dynamics of APP expression during disease progression and recovery (Faye and Bengoumi 2018). Longitudinal studies involving larger sample sizes and repeated measurements are essential to assess the temporal relationship between APP levels and clinical outcomes, including survival and mortality. Such studies would help identify critical thresholds and trends that are predictive of prognosis rather than merely reflecting acute inflammation (Tharwat 2023).

### Need for standardization of assays

Currently, there is no universally accepted methodology for the quantification of APPs in camels. Studies have employed various analytical techniques, ranging from enzyme-linked immunosorbent assays to colorimetric and turbidimetric assays, each with different sensitivities and inter-assay variability (El-Bahr and El-Deeb 2016). This lack of standardization impairs reproducibility, hampers cross-study comparisons, and complicates the establishment of clinical cut-off values. Therefore, the development and validation of camel-specific, standardized assays are therefore urgently needed to ensure consistency in APP measurement across laboratories (Tharwat 2023).

### Future directions

In advancing the clinical relevance of APPs as prognostic biomarkers in dromedary camels, future research should prioritize technological innovation, data integration, and collaborative frameworks. The following areas represent key directions for advancing this field.

#### Development of APP biosensors for field use

The reliance on centralized laboratory diagnostics for APP quantification limits their routine use in camel health monitoring, especially in remote desert and pastoral settings. The development of portable, user-friendly biosensors capable of detecting APPs like Hp, SAA, and fibrinogen in real time could dramatically improve diagnostic speed and accessibility (Zhang et al. 2022; Mir et al. 2023). Recent advances in nanotechnology, microfluidics, and electrochemical sensing provide a foundation for creating highly sensitive and specific biosensors tailored for field conditions. These devices could enable real-time decision-making for herd management, early disease detection, and prognosis (Gedda et al. 2021; Amin et al. 2023).

#### Application of machine learning for predictive analytics

The growing availability of large-scale veterinary datasets presents an opportunity to leverage machine learning (ML) techniques to enhance predictive accuracy (Hennessey et al. 2022). ML algorithms can be trained on datasets containing APP levels, clinical signs, hematological parameters, and survival outcomes to identify patterns and forecast disease progression. In veterinary medicine, ML has shown efficacy in predicting mastitis in dairy cows and respiratory diseases in cattle. Incorporating APP data into these models could improve their prognostic power for camels, especially under conditions of infectious disease outbreaks or environmental stressors (Luo et al. 2023; Monteiro et al. 2025).

#### Collaborative research and multicenter trials

To ensure the reliability and generalizability of APP-based biomarkers, collaborative, multicenter research efforts are essential. Coordinated trials involving different regions, camel breeds, and health management systems will help establish standardized APP reference values and improve our understanding of regional variations in biomarker dynamics (Aljazzar 2025). Furthermore, such collaborations can facilitate the development of evidence-based clinical guidelines and best practices for APP usage

in camelid veterinary care. Shared data platforms and open-access repositories could further enhance scientific transparency and accelerate progress in the field (Abdallah and Faye 2023).

### Conclusion

This review highlights the novel potential of APPs as predictive biomarkers for mortality and clinical outcomes in dromedary camels—a relatively underexplored area in camelid medicine. Among the APPs studied, Hp, SAA, and C-reactive protein emerge as the most promising candidates for early identification of high-risk animals, particularly in conditions such as pneumonia, dystocia, and lameness. Their strong correlation with inflammation and disease severity underscores their utility not only for diagnosis and prognosis but also for guiding timely clinical interventions. While multi-marker panels offer superior predictive value over individual APPs, the translation of these findings into clinical practice is currently hindered by the lack of standardized reference ranges, assay inconsistency, and limited longitudinal data. To unlock the full potential of APPs in camel health management, we call for collaborative, multicenter research initiatives aimed at developing standardized, field-applicable diagnostic tools. Such coordinated efforts are essential to validate APPs for routine use, ultimately improving survival outcomes and supporting more effective herd health strategies in camel-reliant regions.

### DECLARATIONS

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**Conflict of Interest:** The authors declare that there is no conflict of interest.

**Data Availability:** All data supporting the findings of this study are available within the manuscript, and no additional data sources are required.

**Author's Contribution:** MT: conceived, designed the experiment, carried out the practical work, wrote the manuscript draft and prepared the figures and tables. AA: analyzed the hematological and biochemical parameters and carried out postmortem examination. MM: revised and edited the manuscript draft. All authors read, revised and approved the final manuscript version for publication.

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