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Reference Values for Coagulation Parameters in Canine and Feline Species Assessed by the Horiba Yumizen G200: A Tool for Clinical Interpretation in Veterinary Medicine

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Abstract

Bleeding is a common clinical finding in animals and is often associated with one or more alterations in the hemostatic system. In dogs, the most frequent causes include thrombocytopenia, disseminated intravascular coagulation (DIC), and rodenticide toxicity. In contrast, these conditions are less common in cats, where hemorrhagic manifestations are more frequently linked to hepatic disorders, feline infectious peritonitis (FIP), and neoplasms. Congenital coagulopathies are considered rare in both species. Unlike in human medicine, coagulation profiles are infrequently utilized in veterinary practice, and the existing literature primarily comprises isolated case reports. In this context, the present study aimed to evaluate the performance of a semi-automated coagulation analyzer (Yumizen G200—Horiba) using canine and feline samples, with the objective of proposing a laboratory protocol suitable for implementation in routine veterinary clinical practice. For this purpose, blood samples were collected from clinically healthy animals, comprising 140 dogs and 44 cats of both sexes and adult age, after applying the exclusion criteria. The parameters analyzed included prothrombin time (PT), activated partial thromboplastin time (aPTT), and fibrinogen concentration (FIB). One of the main challenges encountered during the study was the recruitment of truly healthy animals, as patients referred for clinical evaluation are typically those presenting with underlying health conditions. The results obtained are consistent with the limited literature available on hemostatic parameters in animals, and they demonstrate the

efficacy of the analyzer for conducting such evaluations. Therefore, the establishment of reference intervals, alongside the integration of this equipment into veterinary practice, represents a significant advancement in both the quality and efficiency of diagnosing various coagulopathies.

Keywords

Coagulopathies, Thrombocytopenias, Coagulation Profile, Fibrinogen, D-Dimer, Hemostasis Analyzer, Dogs, Cats

1. Introduction

Hemorrhage is a common clinical finding in animals and may have either congenital or acquired origins, typically associated with one or more hemostatic abnormalities. The underlying etiology aids in distinguishing between primary hemostatic disorders—affecting platelets or vascular integrity—and secondary disorders involving the coagulation cascade [1] [2]. In addition to hemorrhagic manifestations, hemostatic dysfunctions may also lead to thrombosis, thromboembolism, and subsequent organ failure. In dogs, the most frequently reported causes of coagulopathies include thrombocytopenia, disseminated intravascular coagulation (DIC), and rodenticide toxicity. These conditions are comparatively rare in cats, which more commonly exhibit clotting abnormalities secondary to hepatic diseases, feline infectious peritonitis (FIP), and neoplasm conditions that predispose them to spontaneous bleeding. In felines, thrombocytopenia is more often associated with bone marrow suppression due to retroviral infections [3]. Among congenital coagulopathies—although rare—the most frequently observed is Hemophilia A [4], which presents a clinical profile remarkably similar to that seen in humans [1]. Accordingly, the evaluation of hemostasis, alongside the use of complementary diagnostic tests, is essential for the accurate diagnosis and prognostic assessment of hemostatic disorders in veterinary patients.

Hemostasis is the physiological mechanism responsible for preventing blood loss while maintaining blood fluidity [2]. It represents a dynamic balance between hemorrhage and thrombosis, ensuring that blood neither extravasates from the vasculature nor clots inappropriately within it. To achieve this, the body possesses regulatory mechanisms that inhibit both excessive bleeding and inappropriate thrombus formation. Additionally, the structural integrity and elasticity of blood vessels are essential for maintaining hemostatic function. When these regulatory systems are in balance, overall hemostasis is preserved. However, any disruption to this equilibrium may result in either thrombosis or hemorrhage [5].

Didactically, hemostasis is divided into two phases: primary and secondary. Primary hemostasis involves the interaction between platelets and damaged vascular endothelium, leading to the formation of a platelet plug at the site of injury. This process, in conjunction with vasoconstriction, is generally sufficient to achieve

effective hemostasis in capillaries and venules. However, in larger vessels with higher blood flow and pressure, the formation of a stable fibrin network is essential. This occurs through the activation of secondary hemostasis, which involves a complex cascade of enzymatic reactions that ultimately stabilize the initial platelet plug [6] [7].

The coagulogram evaluates the quantitative profile of components involved in the coagulation cascade. When combined with platelet quantification, this analysis provides a comprehensive assessment of all elements involved in the hemostatic process [8]. Unlike in human medicine, the complete coagulogram is rarely employed in veterinary practice, with existing literature primarily limited to isolated case reports involving conditions such as thrombocytopenia, snake envenomation, hepatic diseases, and Hemophilia A [4]. In contrast, fibrinogen measurement is more commonly reported, given its role as an acute phase protein. Additionally, D-dimer—a fibrinolytic byproduct that increases in states of hypercoagulability and hyperfibrinolysis [9] [10]—has also been identified in various clinical scenarios, including portal vein thrombosis [11]. Its measurement represents a highly valuable tool for the early diagnosis of thrombotic events in dogs [12]-[14].

Yumizen hemostasis analyzers utilize configurable testing protocols, enabling their application across a variety of animal species. The compact Yumizen G200 model is particularly well-suited for use in Veterinary Medicine, offering three reference methodologies: coagulometric, immunoturbidimetric, and chromogenic. This analyzer can perform a comprehensive coagulation profile in a rapid and semi-automated manner. Additionally, it features pre-calibrated assays for fibrinogen and D-dimer detection, thereby reducing the risk of errors associated with manual procedures.

The scientific validation of any new technology intended for routine laboratory use is essential to establish its credibility. Specifically, regarding automated devices, many professionals remain cautious about the accuracy and reliability of the data generated by such equipment. Therefore, validating the performance of the device is critical to enhance confidence in its results and to provide a solid foundation for broader adoption of the evaluated methodology.

In this context, the aim of the present study is to evaluate the performance of the semi-automated Horiba Yumizen G200 hemostasis analyzer in assessing hemostatic parameters in canine and feline species and to propose a laboratory protocol that can be implemented in veterinary clinical routine that represents an improvement in the quality and speed of diagnosing different coagulopathies.

2. Material and Methods

2.1. Study Design

For this purpose, 345 samples were collected from dogs and cats, all adults (from

six months of age onward) of both sexes and different breeds, clinically healthy at the Veterinary Hospital for Dogs and Cats (Sorocaba, SP, Brazil) and at Transfucão—Veterinary Blood Bank and Hemotherapy Center (São Paulo, SP, Brazil) following the tutor signing the term of consent. The exclusion criteria included: 1) elevated or decreased fibrinogen and D-dimer values; 2) pre-analytical issues, such as coagulated samples or the presence of fibrin; and 3) measurement errors in any parameter detected by the equipment, even after repeat testing. Following the application of these criteria, a total of 188 clinically healthy animals were selected for the establishment of reference values, comprising 140 dogs and 44 cats, all adult and of both sexes. All samples were collected via venipuncture into citrate-containing tubes and subsequently centrifuged to obtain plasma. The parameters analyzed included prothrombin time (PT), activated partial thromboplastin time (aPTT), D-dimer (DDi) and fibrinogen concentration (FIB) based on manufacture instructions for the semi-automated Horiba Yumizen G200 (Montpellier, France). The equipment was calibrated using the commercial Yumizen G Control (Horiba, Montpellier, France) according to the manufacturer's instructions. Analytical reliability was ensured through routine internal quality controls with low and high control materials, and inter-run precision was verified by repeated measurements across multiple sessions, demonstrating consistent, accurate, and reproducible results.

The study was conducted in accordance with current ethical guidelines and did not involve the experimental use of animals, as defined by the criteria established by CONCEA. Blood samples were collected via the same venous access routinely used for clinical purposes, without causing additional discomfort to the animals. Additionally, all tutors were fully informed and provided written consent through a Free and Informed Consent Form (FICF), authorizing the use of the samples for research purposes. Therefore, given the absence of experimental manipulation, the study is not subject to submission for evaluation by the CEUA, in accordance with the guidelines [15].

2.2. Complementary Exams

To confirm the clinical health of enrolled animals, a comprehensive evaluation comprising hematologic and infectious disease screenings was conducted. Complete blood count (CBC) analysis assessed erythrocyte and leukocyte counts, hemoglobin concentration, and platelet numbers to identify anemia, inflammatory processes, or other hematologic abnormalities. Serological assays were performed to detect prior exposure to prevalent infectious agents, including *Leishmania*, *Ehrlichia*, *Anaplasma, Borrelia* and *Dirofilaria* for dogs, as well as feline immunodeficiency virus (FIV) and feline leukemia virus (FeLV). for cats, while polymerase chain reaction (PCR) assays were employed to identify pathogen-specific DNA, providing sensitive detection of active infections. This integrated approach ensured inclusion of only animals free from subclinical or active infectious conditions.

2.3. Method Recommended by CLSI-C28-A3 (2010) for Constructing Reference Values

Reference intervals were established in accordance with the CLSI C28-A3 guidelines [16]. Clinically healthy individuals' representatives of the target population were selected following the application of predefined exclusion criteria. Potential outliers were identified using Dixon's test and Tukey's method and were evaluated for possible exclusion. Data distribution was assessed statistically using the Shapiro-Wilk test, and only parameters demonstrating normal distribution were analyzed using parametric methods. Reference intervals were calculated as the mean ± 2 standard deviations, encompassing the central 95% of the reference population.

3. Result

The primary challenge of the study was obtaining homogeneous samples free from pre-analytical interference. Veterinarians were instructed to avoid hemodilution and to ensure that samples were free of clots. All analyses were conducted by the same pathologist, following the implementation of quality control procedures to verify the performance of the equipment, thereby minimizing methodological variability and ensuring consistency in the results. The average and standard deviation (SD) were described in Table 1 (Canine) and Table 2 (Feline) according to sexes and species.

Table 3 describes the reference values based on the results according to species assessed by the Horiba Yumizen G200.

Table 1. Coagulation parameters in canine specie assessed by the Horiba Yumizen G200 (average ± SD).

Parameter	Female (n = 71)	Male (n = 69)
PT (s)	9.9 ± 1.350	10.1 ± 1.663
aPTT (s)	13.4 ± 1.842	13.2 ± 1.502
FIB (g/L)	2.74 ± 0.975	3.10 ± 0.985
DDi (ng/mL FEU)	190 ± 1.93	180 ± 1.79

Table 2. Coagulation parameters in feline specie according to sex assessed by the Horiba Yumizen G200 (average ± SD).

Parameter	Female (n = 22)	Male (n = 22)
PT (s)	13.2 ± 1.443	12.5 ± 1.219
aPTT (s)	15.6 ± 6.667	15.2 ± 3.605
FIB (g/L)	2.15 ± 0.749	1.99 ± 0.619
DDi (ng/mL FEU)	90 ± 1.55	120 ± 1.64

Table 3. Reference values for coagulation parameters in canine and feline specie assessed by the Horiba Yumizen G200 calculated from a normally distributed population (Gaussian distribution).

Reference Values	Canine (n = 140)	Feline (n = 44)
PT (s)	6.98 - 13.02	10.17 - 15.63
aPTT (s)	9.24 - 16.66	4.80 - 20.70
FIB (g/L)	0.93 - 4.91	0.70 - 3.44
DDi (ng/mL FEU)	176.28 - 183.72	96.96 - 103.04

4. Discussion

The evaluation of hemostatic parameters in dogs and cats represents a critical diagnostic approach in veterinary medicine, particularly in cases presenting with hemorrhagic, thrombotic, or systemic inflammatory conditions. Hemostasis is a complex and integrated physiological process encompassing primary hemostasis, secondary hemostasis (the coagulation cascade), and fibrinolysis, and depends on the coordinated interaction of vascular structures, platelets, and coagulation factors. Disruptions at any stage of this process can result in clinically significant consequences, thereby necessitating precise and reliable laboratory assessment.

Hereditary disorders, such as von Willebrand disease observed in specific canine breeds, exemplify primary hemostatic abnormalities that underscore the necessity for targeted laboratory evaluation [2]. In contrast, acquired coagulopathies—such as disseminated intravascular coagulation (DIC)—are frequently associated with severe systemic conditions, including sepsis, pancreatitis, and neoplastic processes. These cases require comprehensive assessment of multiple hemostatic parameters, including PT, aPTT, FIB concentration, DDi levels, and fibrin degradation products [1]. Collectively, these assays enable a segmented analysis of the hemostatic system, and their integrated interpretation facilitates the identification of underlying etiologies related to distinct pathways of the coagulation cascade [17].

Despite advancements in laboratory methodologies, the interpretation of hemostatic assays in veterinary medicine remains challenging, primarily due to the limited availability of widely validated reference intervals for different species and clinical contexts. A major constraint in establishing such reference values is the difficulty in obtaining samples from clinically verified healthy animals. Companion animals typically present to veterinary clinics only when exhibiting clinical signs, thereby hindering the assembly of control populations free from systemic or subclinical alterations. Furthermore, the limited sample size for certain species, such as felines, and the absence of breed stratification represent additional study limitations. According to surveys by the Brazilian Institute of Geography and Statistics [18] and the Brazilian Institute for Animal Protection, over 70% of dogs and cats in Brazilian homes are of mixed or undefined breeds, reflecting both stray population management issues and adoption trends [19]. Consequently, future

work should aim to expand these cohorts, including larger numbers of animals across diverse breeds and age groups, to improve the robustness and generalizability of reference intervals in veterinary practice.

A critical consideration in the interpretation of hemostatic assays in small animals is the necessity for species-specific and validated reference intervals. Studies have demonstrated significant physiological variations not only between dogs and cats but also among different breeds and age groups, highlighting the importance of methodological standardization [20]. Furthermore, much of the equipment routinely employed in veterinary laboratories was originally designed for human diagnostics; although minor protocol adaptations may enhance analytical performance, prior validation for veterinary use remains essential to ensure reliability [21]. Accordingly, the development of robust, population-based reference data that reflect the realities of veterinary clinical practice is crucial for ensuring both diagnostic accuracy and therapeutic efficacy.

Another critical aspect concerns pre-analytical variables, which have a direct impact on the accuracy of coagulation test results. Factors such as the blood collection technique, duration of tourniquet application, type and volume of anticoagulant used, time elapsed between sample collection and processing, and conditions of sample transportation are all crucial determinants of the stability of coagulation factors and platelets [21]. Minor deviations in any of these steps can introduce laboratory artifacts and lead to misinterpretation of results, such as falsely prolonged clotting times or pseudothrombocytopenia resulting from EDTA-induced platelet aggregation, particularly when inappropriate anticoagulants are used for the intended analyses.

The availability of literature specifically addressing hemostasis in dogs and cats remains limited, posing significant challenges for veterinary research and clinical practice. While studies have contributed valuable insights into coagulation profiles in specific conditions [22] [23], these investigations often involve small sample sizes or focus on particular disease states. Such studies, while informative, corroborate the need for reference values and species-specific hemostatic profiles and, consequently, highlight the necessity for further investigation in this field.

5. Conclusion

Laboratory evaluation of hemostasis in dogs and cats is a critical component of veterinary clinical practice, enabling the early detection of coagulation disorders that may pose a significant threat to the animal's life. The availability and appropriate application of species-specific reference intervals tailored to the clinical context are essential for the accurate interpretation of results and the implementation of effective therapeutic strategies. Continued progress in the standardization of diagnostic assays, advancement of analytical technologies, and generation of robust, population-based reference data should be considered priorities in veterinary laboratory medicine. Consequently, the establishment and regular updating of reference values are indispensable in clinical scenarios where urgent and

informed therapeutic decisions are required. Moreover, future studies should aim to expand sample sizes and include diverse breeds to enhance the reliability and applicability of reference intervals across species.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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