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VON WILLEBRAND DISEASE IN DOGS: A GENETIC APPROACH

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Abstract: Von Willebrand disease (VWD) is a common hereditary or acquired bleeding disorder in dogs, and is characterized by an abnormality in Von Willebrand factor (VWF), which is a glycoprotein that plays an essential role in platelet adhesion and aggregation during primary hemostasis. Most dog breeds, including the Dobermann, have DvW type I, with autosomal dominant inheritance with incomplete penetrance in some breeds and autosomal recessive in others, caused by a decrease in the total concentration of vWf, with all multimers present, but in reduced amounts. Given the importance of this disease, taking into account the clinical signs, such as prolonged bleeding, the objective literature review, through a survey of the literature, develop and detail scientific, genetic and clinical knowledge in relation to Von Willebrand disease in dogs, in addition to understanding the genetic influence on the severity and transmission of the disease.
Keywords: Genetic aspects; Cynophilia; Bleeding disorder; Heredity; Veterinary Medicine.

INTRODUCTION

Von Willebrand disease (VWD) is a common hereditary bleeding disorder in dogs. Canine DvW was first reported in 1970 in a family of German Shepherd Dogs. Subsequently, the disease was diagnosed in more than 54 dog breeds in the United States and is found in high prevalence in several of these breeds, including the Dobermann, Airedale Terrier and Scottish Terrier.

DvW is characterized by an abnormality in Von Willebrand factor (VWF), which is a glycoprotein that plays an essential role in platelet adhesion and aggregation during primary hemostasis. DvW is a hereditary hemorrhagic disease and has its transmission as an autosomal characteristic, being, according to laboratory tests, reported in

more than 54 canine breeds (most of these breeds carry defective genetic information about Von Willebrand factor).

The present work is justified since there are few findings in Brazilian literature that address Von Willebrand Disease (VWD) in dogs from a genetic perspective. This way, we seek to contemplate and unite, in a single study, reliable information from articles found, in order to serve as a research alternative for the academic community.

GOALS

In view of the above, the current literature review aims to develop and detail scientific, genetic and clinical knowledge regarding Von Willebrand disease (VWD) in dogs, in addition to understanding the genetic influence on its severity and transmission. In addition, the work also proposes to discuss the main cause of DvW, as well as the most used diagnostic methods in the field of Veterinary Medicine.

METHODOLOGY

This is an exploratory and descriptive literature review based on articles searched in the databases: *Scientific Electronic Library Online* (SciELO), *Web of Science* and Google Scholar, between September and December 2021. For the ideation of this study, the choice of topic was included and 90 complete articles were selected for analysis. Of these, 20 were selected from *Web of Science,* 15 from SciELO and 55 from Google Scholar. After careful analysis, in order to fulfill the intended objectives, 50 articles were excluded, 15 from *Web of Science,* 10 from SciELO and 25 from Google Scholar, which did not meet the inclusion criteria (relationship of the article to the selected theme, scientificity, year of publication, articles published between 1980 and 2021, analysis, interpretation of data, presentation of results and those in Portuguese and English being accepted.).

The following keywords were used: "Von willebrand disease", "genetic aspects", "veterinary medicine" and "dogs", in addition to their correlates in English. Aiming at a better visualization of the studies found, a reference flowchart was created, showing the number of articles found per database and selected for the study (Figure 1).

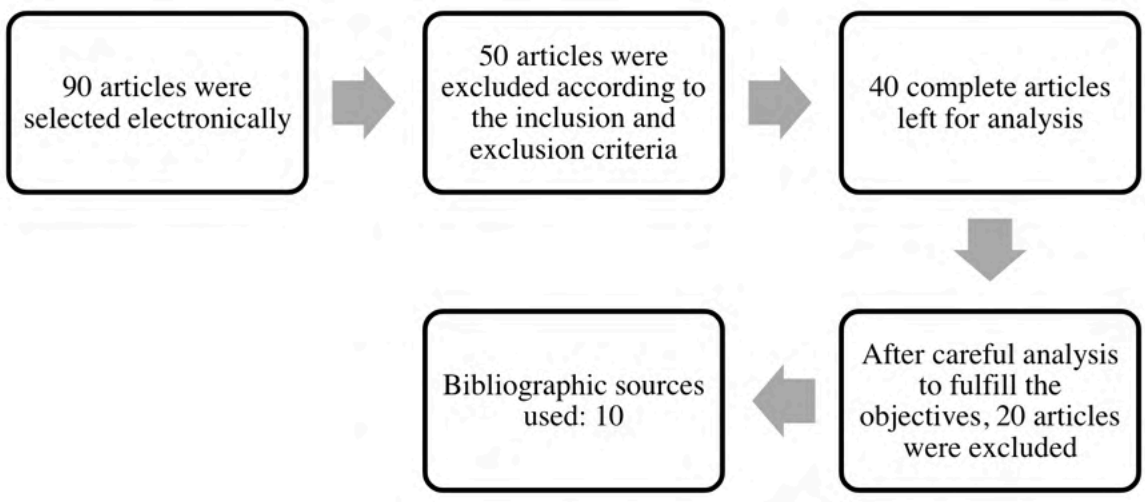

Figure 1: Reference search flowchart.

Source: Prepared by the authors.

RESULTS AND DISCUSSION

Since the discovery of von Willebrand disease, 3 types have been identified: 2 are quantitative deficiencies (types 1 and 3), with decreased circulating factor, and the other is qualitative (type 2), where the factor structure is abnormal, inherited from recessive form. Von Willebrand disease can be hereditary or acquired, the former being more common in dogs. Legacy DvW has 3 basic subtypes, based on vWf multimeric pattern and inheritance mode.

Most dog breeds, including the Dobermann, have DvW type I, with autosomal dominant inheritance with incomplete penetrance in some breeds and autosomal recessive in others and is caused by a decrease in total vWf concentration, with all multimers present, but in reduced amounts. DvW type III is the most severe form of the disease, which is inherited in a recessive manner.

Some breeds have only type III as is the case with the Scottish terrier breed, in which recessive homozygotes have a severe bleeding disorder. In general, affected dogs show similar clinical signs, such as: prolonged bleeding in surgical wounds, changes of deciduous teeth and hematuria (appearance of erythrocytes in the urine).

Among the diagnostic methods, the enzyme immunoassay (ELISA) in dogs is the most used to quantify the total plasma concentration of vWF, being it the priority in the diagnosis of DvW in canine species. Oral mucosal bleeding time (OST) can be used for detection of clinical expression of DvW and as a pre-surgical test. Ristocetin-induced platelet aggregation (RIPA) may be decreased, as many types of DvW are characterized by hyporesponsiveness to ristocetin.

Other tests, such as botrocetin cofactor assays and multimeric analysis, are performed only by a few institutions. Currently, the real-time PCR test is also used, which can be done in two ways. The first way is by divergent PCR assay and the second using fluorescence-labeled probes and during the evaluation by agarose gel electrophoresis, in DvW type 1 all multimers are present, whereas in type 2 the high and intermediate molecular weight are lost.

Studies involving DvW in Veterinary Medicine are important to demonstrate that this disease exists, and that probably, in Brazil, many diagnoses are no longer identified by not performing routine diagnostic tests.

CONCLUSION

It is noticed that the studies referring to diseases of genetic and hereditary character have a great importance in the prophylaxis of diseases in animals in general. It is worth mentioning that the more scientific research on these pathologies, the greater the chance of early treatment, improving the quality of life of affected animals. In Brazil, there are several cases reported and there is a need to highlight Von Willebrand's disease in the small animal medical clinic, with the aim of increasing the frequency of routine examinations, even in asymptomatic animals.

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