KNOWLEDGE AND AWARENESS OF TREATMENT PROTOCOL WITH VON WILLEBRAND'S DISEASE PATIENTS

Lasya. G[a], Dhanraj Ganapathy[b]*, Keerthi Sasanka. L[c]

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Abstract: Introduction: Von Willebrand disease (VWD) is the most common hereditary blood clotting disease in humans.The three forms of VWD are hereditary, acquired, and pseudo or platelet type. VWD type 1 is the most common type of the disorder, with mild bleeding symptoms such as nosebleeds, though occasionally more severe symptoms can occur.The various types of VWD present with varying degrees of bleeding tendency, usually in the form of easy bruising, nosebleeds, and bleeding gums.[medical citation needed] Women may experience heavy menstrual periods and blood loss during childbirth.
Aim: The aim of the study was to assess knowledge and awareness of treatment protocol with von willebrand's disease patients.
Materials and methods: This is a cross sectional descriptive survey conducted among 126 dental undergraduates in chennai.This survey consists of 15 self administered questions. The survey was conducted through an online platform.the aim of the study is to assess the knowledge and awareness of treatment protocol of von willebrand's disease patients.
Results: from the study,82.81 % are aware of treatment protocols of von willebrand disease and 17.19% are not aware of treatment protocols on von willebrand disease.70.31 % felt that desmopressin drug of treatment for von willebrand disease and 29.69% felt that desmopressin drug cannot be used for the treatment for von willebrand disease.
Conclusions : awareness of treatment protocols for von willebrand's disease among dental undergraduates in chennai was evaluated. Extensive research and awareness programs can be conducted to bring awareness and practise for the new generation of medical professionals.

Keywords: Awareness, Bleeding disorders, Blood coagulation disorders, management of bleeding disorder, innovative technique.

[a]. Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Chennai, Tamil Nadu, India
[b]. Professor and head, Department of Prosthodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Chennai, Tamil Nadu, India
[c]. Department of Prosthodontics, Saveetha Dental College and Hospital, Saveetha Institute of Medical & Technical Sciences, Saveetha University, Chennai- 600077, India.

***Corresponding Authors**

E-mail: 151901016.sdc@saveetha.com, dhanaraj@saveetha.com, keerthis.sdc@saveetha.com

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INTRODUCTION

Von Willebrand disease (VWD) is a disorder in which the blood does not clot properly. Blood contains many proteins that help the body stop bleeding. One of these proteins is von Willebrand factor (VWF).(1)Von Willebrand disease is typically an inherited disease caused by variations (mutations) in the VWF gene . The VWF gene provides instructions for making a blood clotting protein called von Willebrand factor, which is important for forming blood clots and preventing further blood loss after an injury.Like hemophilia, VWD is passed on through the genes from parent to child(2). But in hemophilia, men and women have an equal chance of getting VWD. It is possible for a person to have both von Willebrand Disease and hemophilia. Unlike hemophilia, people with VWD rarely bleed into their joints.76% of men with VWD had been diagnosed by age 10, but 50% of women with VWD were not diagnosed until after age 12.(3)Von Willebrand factor helps platelets stick together and adhere to the walls of blood vessels at the site of a wound. These groups of platelets form temporary clots, plugging holes in blood vessel walls to help stop bleeding.Once VWF is immobilised in subendothelial connective tissue, its main function is to mediate adhesive interactions of platelets exposed to rapid blood flow.von Willebrand factor (vWF) circulates in the blood in two distinct compartments(4). One, plasma vWF, is synthesized and released from endothelial cells; the second, synthesized by megakaryocytes, circulates in platelets primarily stored in the alpha granules.To find out if a person has von Willebrand disease (VWD), the doctor will ask questions about personal and family histories of bleeding. The doctor also will check for unusual bruising or other signs of recent bleeding and order some blood tests that will measure how the blood clots.Specific tests are required to diagnose which bleeding disorder is there.(5) Often these tests need to be repeated several times before an accurate diagnosis can be made. This is because the levels of clotting factors in the blood vary over time as a result of changes the body might be reacting to—such as stress, pregnancy, and infections—that can affect the test results.
The blood tests that a doctor can order to diagnose VWD (or another platelet disorder) include: Factor VIII clotting

activity—To measure the amount of factor VIII in the blood. Von Willebrand factor antigen—To measure the amount of VWF in the blood Ristocetin cofactor or other VWF activity—To measure how well the VWF works. Von Willebrand factor multimers—To measure the makeup or structure of the VWF.Platelet aggregation tests—To measure how well the platelets are working.Bleeding disorders can result from inherited genetic defects or be acquired due to use of anticoagulant medications or medical conditions such as liver dysfunction, chronic kidney disease, and autoimmune disease.A patient's bleeding disorder may be unrecognized, and bleeding episodes can appear spontaneously or after dental extraction. 6 Management includes coordination with the hematologist, minimally invasive dentistry, local hemostatic measures, and avoiding analgesics such as aspirin and other nonsteroidal anti-inflammatory drugs.(6)After consultation with the hematologist prior to dental extraction, patients with the mild forms of hemophilia A and vWD are normally treated preoperatively by desmopressin acetate, which stimulates the release of vWF from the Weibel-Palade bodies of endothelial cells(7). This in turn increases the levels of vWF (as well as coagulant factor VIII) threefold to fivefold.6 One hour prior to the dental procedures, desmopressin acetate can be administered intravenously (0.3 µg/kg in 50 mL of normal saline), subcutaneously (0.3 µg/kg using the 15-µg/mL concentration), or intranasally (150 µg).18 However, intravenous administration of desmopressin acetate may have cardiovascular side effects, such as a slightly elevated heart rate, hypotension, and headache.18,45 Desmopressin acetate is not recommended for young children and patients with ischemic heart disease.(8)Our team has extensive knowledge and research experience that has translated into high quality publications(9–17),(18–23),(24–30).

MATERIALS AND METHODS

This is a cross sectional descriptive survey conducted among 126 dental undergraduates in chennai. This survey consists of 15 self administered questions. The survey was conducted through an online platform. The survey was easy to create and the data was gathered among heterogeneous populations. The questionnaire was approved by the review board of saveetha dental college chennai. To eliminate the response bias we did simple random sampling .The collection was done using google forms. Followed by tabulation of data using excel sheets.

Data were analyzed with the SPSS version (22.0). Descriptive statistics as number and percent were calculated to summarise qualitative data. Chi-square test was used to analyze and compare the education level of undergraduates and their knowledge on treatment protocols of von Willebrand's disease patients. The result was presented by using bar charts and frequency tables.

RESULTS

From the results ,4.69% belonged to 18- 19 years**,** 13.28% belong to 20-21 years, 34.36% belong to 24-25 years and 47.66% belong to 22-23 years.90.63% belongs to females and 9.38% belongs to male.18.75 % belong to 1st year,25% belong to 2nd year ,34.38% belong to 3rd year and 21.88% belong to 4th year and intern .89.84 % are aware of von willebrand disease and 10.16% are not aware of von willebrand disease.82.81 % are aware of treatment protocols of von willebrand disease and 17.19% are not aware of treatment protocols on von willebrand disease.70.31 % felt that desmopressin drug of treatment for von willebrand disease and 29.69% felt that desmopressin drug cannot be used for the treatment for von willebrand disease.57.03 % felt that platelet concentrates can be used as treatment of choice for VWD patients and 42.97% felt that platelet concentrates can be used as treatment of choice for VWD patients 53.13 % felt that factor 8 concentrates can be used as treatment of choice for VWD patients and 46.88 % felt that factor 8 concentrates can not be used as treatment of choice for VWD patients .51.56 % felt that recombinant factor 7 can not be used as treatment of choice for VWD patients and 48.44% felt that recombinant factor 7 can be used as treatment of choice for VWD patients..57.81 % felt that replacement therapy can not be used as treatment of choice for VWD patients and 42.19 % felt that replacement therapy can be used as treatment of choice for VWD patients.67.97 % felt that commonly seen in females and 32.03% felt that commonly seen in males.37.5% felt that blood in urine and stool,22.66% felt that increased menstrual flow, 14.84% felt nosebleed and 25% felt all the options are right. **:**Bar graph showing the association of responses based on year of study with the awareness of the treatment protocols of VWD disease. Chi square test was done,p value :0.028 (p <0.05) and was statistically significant.This shows 4th years and interns have more self awareness about VWD disease than the other years.

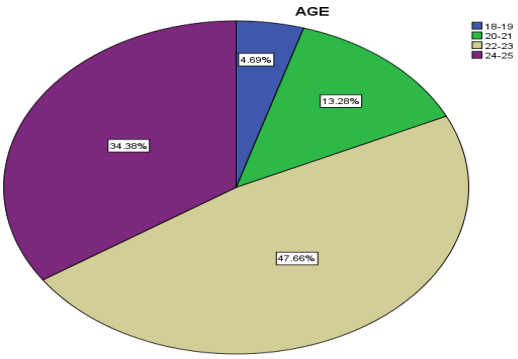

Figure 1: Pie Chart showing the percentage distribution of the age of participants . 4.69% belonged to 18- 19 years (blue) , 13.28% belong to 20-21 years (green), 34.36% belong to 24-25 years (purple) and 47.66% belong to 22-23 years (beige)

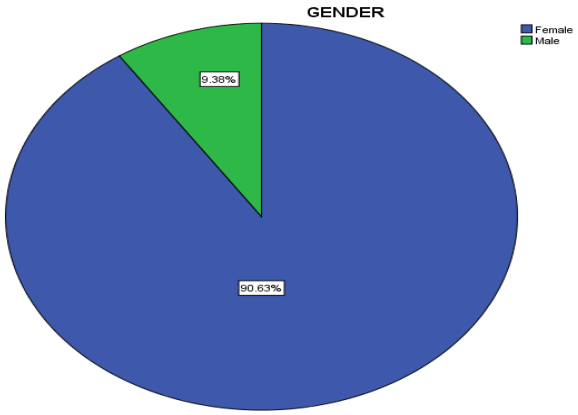

Figure 2: pie chart showing the percentage distribution of gender of participants .90.63% female (blue) and 9.38% male (green)

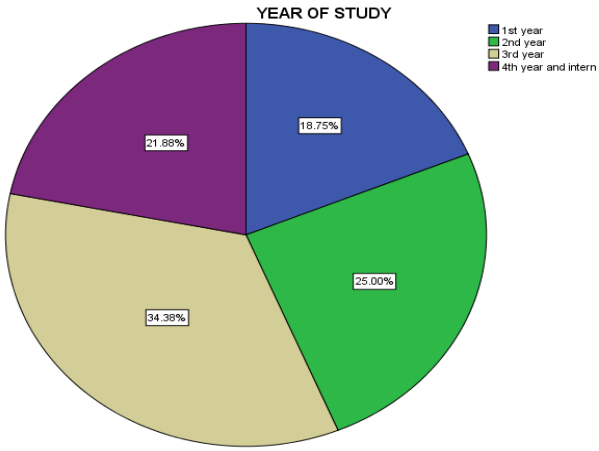

Figure 3: Pie Chart showing the percentage distribution of the year of study .18.75 % belong to 1st year (blue),25% belong to 2nd year (green),34.38% belong to 3rd year (beige) and 21.88% belong to 4th year and intern (purple)

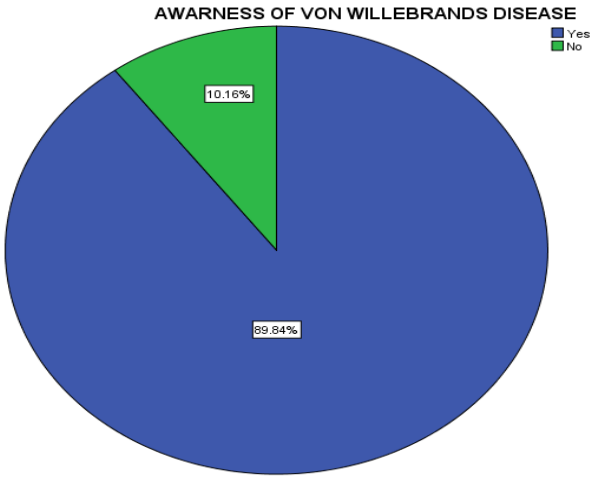

Figure 4: Pie Chart showing percentage distribution of the awareness of von willebrand disease.89.84 % are aware of von willebrand disease (blue)and 10.16% are not aware of von willebrand disease (green)

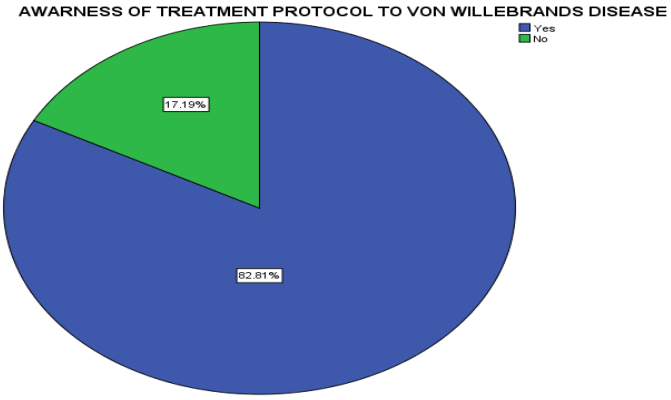

Figure 5: Pie Chart showing percentage distribution of the awareness of the treatment protocols von willebrand disease.82.81 % are aware of treatment protocols of von willebrand disease (blue)and 17.19% are not aware of treatment protocols on von willebrand disease (green)

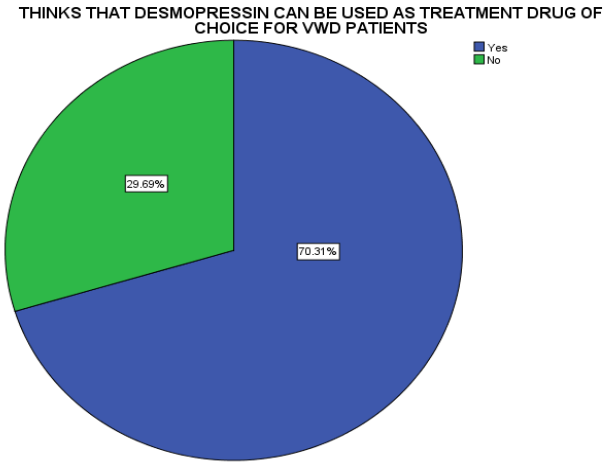

Figure 6: Pie Chart showing percentage distribution of using desmopressin drug of treatment for von willebrand disease.70.31 % felt that desmopressin drug of treatment for von willebrand disease (blue)and 29.69% felt that desmopressin drug cannot be used for the treatment for von willebrand disease(green)

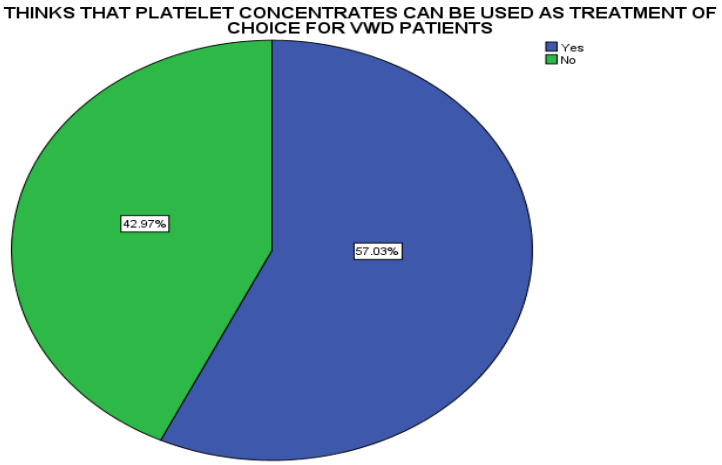

Figure 7: Pie Chart showing percentage distribution that platelet concentrates can be used as treatment of choice for VWD patients .57.03 % felt that platelet concentrates can be used as treatment of choice for VWD patients (blue) and 42.97% felt that platelet concentrates can be used as treatment of choice for VWD patients (green).

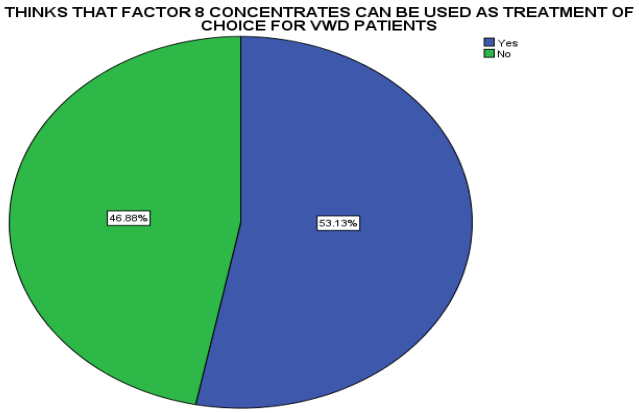

Figure 8: Pie Chart showing percentage distribution that factor 8 concentrates can be used as treatment of choice for VWD patients .53.13 % felt that factor 8 concentrates can be used as treatment of choice for VWD patients (blue) and 46.88 % felt that factor 8 concentrates can not be used as treatment of choice for VWD patients (green)

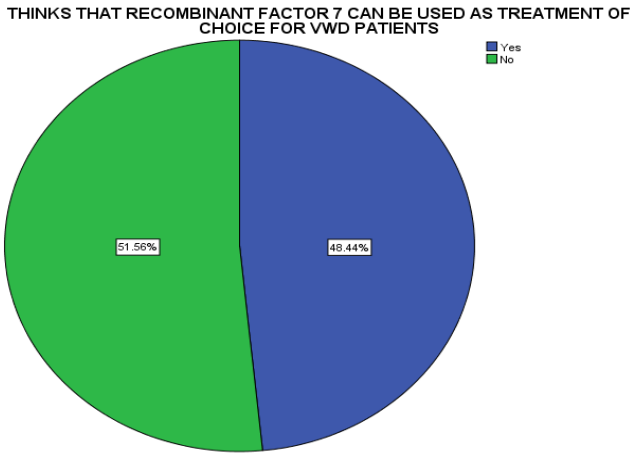

Figure 9: Pie Chart showing percentage distribution that recombinant factor 7 can be used as treatment of choice for VWD patients .51.56 % felt that recombinant factor 7 can not be used as treatment of choice for VWD patients (green) and 48.44% felt that recombinant factor 7 can be used as treatment of choice for VWD patients (blue)

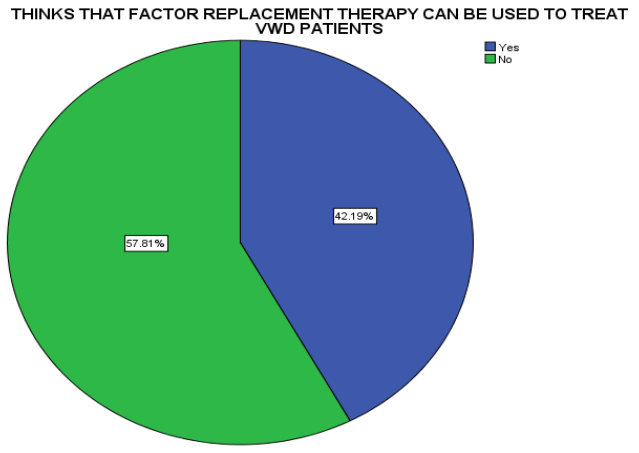

Figure 10: Pie Chart showing percentage distribution that replacement therapy can be used as treatment of choice for VWD patients .57.81 % felt that replacement therapy can not be used as treatment of choice for VWD patients (green) and 42.19 % felt that replacement therapy can be used as treatment of choice for VWD patients (blue)

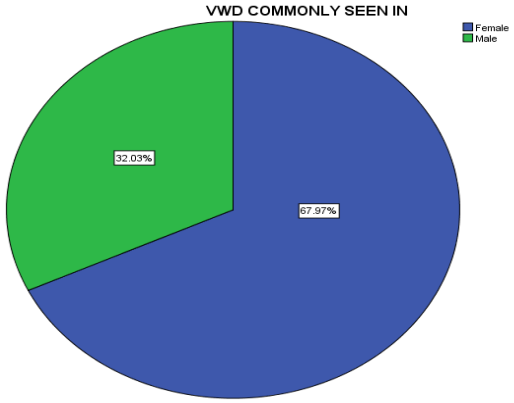

Figure 11: Pie Chart showing percentage distribution that VWD is commonly seen in.67.97 % felt that commonly seen in females (blue) and 32.03% felt that commonly seen in males (green)

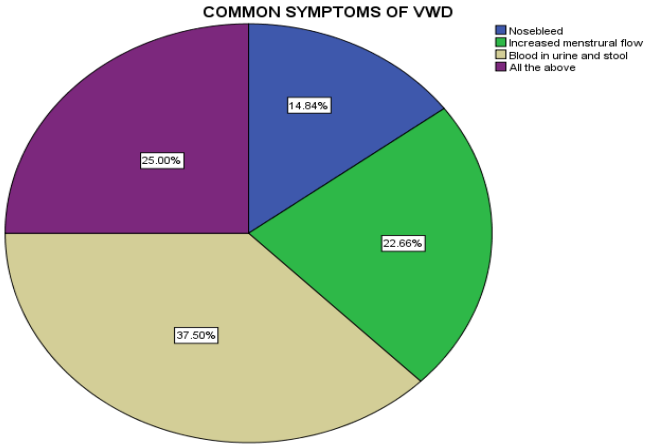

Figure 12: Pie Chart showing percentage distribution that the common symptoms of VWD .37.5% felt that blood in urine and stool (beige) ,22.66% felt that increased menstrual flow (green),14.84% felt nosebleed (blue) and 25% felt all the above options are right.

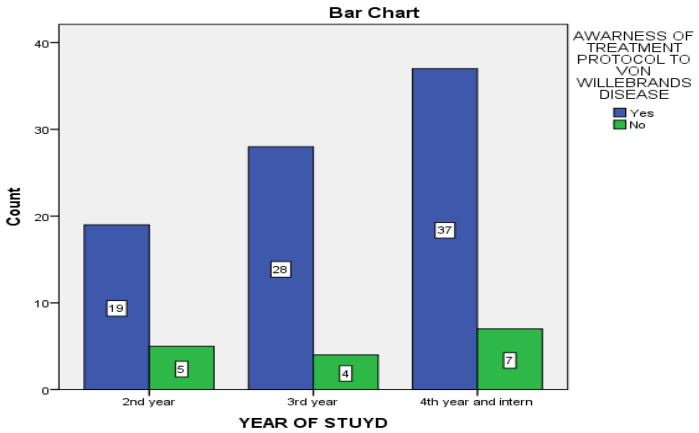

Figure 13: Bar graph showing the association of responses based on year of study with the awareness of the treatment protocols of VWD disease.Green stands for no and blue stands for yes .X axis represents year of study and Y axis represents awareness of the treatment protocols of VWD disease . Chi square test was done,p value :0.028 (p <0.05) and was statistically significant.This shows 4th years and interns have more self awareness about VWD disease than the other years.

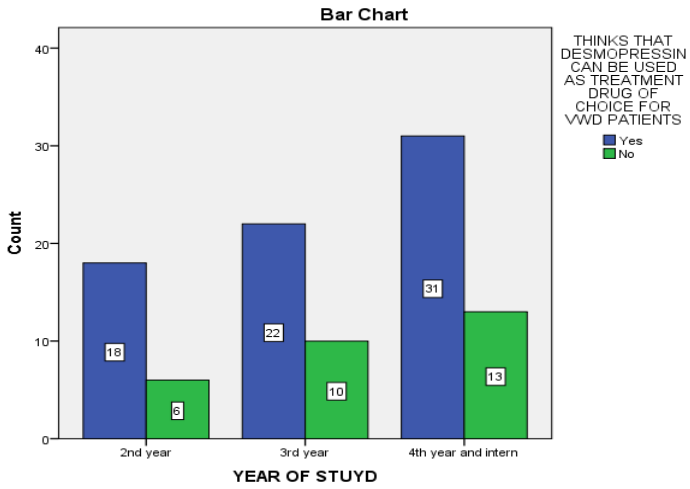

Figure 14: Bar graph showing the association of responses based on year of study with the perception that desmopressin can be used as a drug for treatment .Green stands for no and blue stands for yes .X axis represents year of study and Y axis represents perception that desmopressin can be used as a drug for treatment . Chi square test was done,p value :0.028 (p <0.05) and was statistically significant. This shows 4th years and interns have more self awareness about VWD disease than the other years.

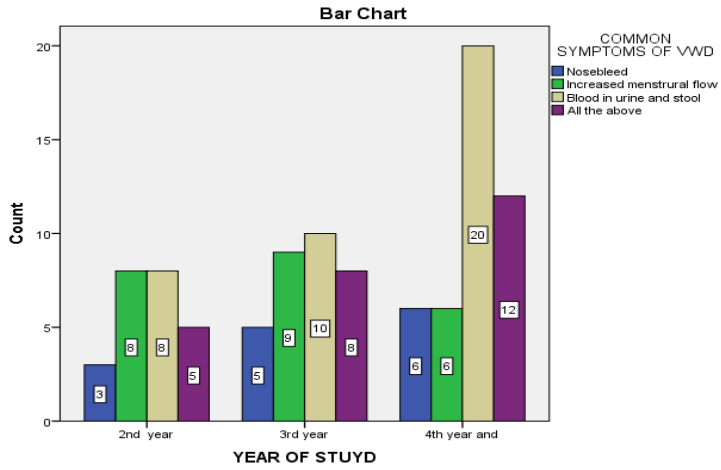

Figure 15: Bar graph showing the association of responses based on year of study with that awareness on the symptoms of VWD disease .Green stands for increased menstrual flow,beige stands for blood in urine and stool , blue stands for nosebleed and purple stands for all of the above .X axis represents year of study and Y axis represents awareness of the symptoms of VWD disease . Chi square test was done,p value :0.028(p <0.05) and was statistically significant.This shows 4th years and interns have more awareness about VWD disease than the other years.

DISCUSSION

The disease prevalence is about only 1%. More often, it can be detected in women based on the bleeding tendency during menstruation. The disease may be severe in people with 'O' blood group(31). Type 1 includes 60%-80% of the cases. Type 2 includes(3)20-30%. Type 3 accounts(32)for less than 5% of all the cases. Acquired VWD occurs most often in individuals over 40 years with no prior bleeding history.It is an inherited disease where the parent carrying the gene may or may not be symptomatic. Type 1 and type 2 are inherited if the gene is passed on to the offspring from either of the parents. Type 3 is inherited only if the gene is passed from both the parents(33). Acquired VWD is seen in patients with autoantibodies(1).when compared to the previous articles knowledge and awareness of treatment protocol of von willebrand's disease patients is more seen in final years and interns.It is an inherited disease where the parent carrying the gene may or may not be symptomatic.(34,35) Type 1 and type 2 are inherited if the gene is passed on to the offspring from either of the parents. Type 3 is inherited only if the gene is passed from both the parents. Acquired VWD is seen in patients with auto antibodies.(36). In our study 82.81 % are aware of treatment protocols of von willebrand disease , compared to the previous study the

awareness scales were raised.(37). In our study 57.03 % felt that platelet concentrates can be used as treatment of choice for VWD patients, whereas only 49% felt that platelet concentrates can be used as treatment of choice for VWD patients. (38). The future scope in the present study states that we expect further more awareness studies on von willebrand's disease, so that new technologies and advancements in medical sciences can be useful for the treatment protocol. The limitations of the study will be there is limited sample size and the study is homogenous as it is only related to only dental students in saveetha dental college, chennai.

CONCLUSION

From our study we can conclude that there is a significant increase in awareness of treatment protocols for von willebrand's disease among dental undergraduates in chennai. Many awareness programmes should be done among the younger population to evaluate the importance of treatment protocol for von Willebrand's disease. Within the limits of the study, awareness of treatment protocols for von willebrand's disease among dental undergraduates in chennai was evaluated. Extensive research and awareness programs can be conducted to bring awareness.

Conflict of interest: There was no conflict of interest in the present study.

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REFERENCES

i. Mullah-Ali AM, Chan AK, Lillicrap D, Decker K, Seroski W, Moffat K, et al. Undetected factor VIII in a patient with type 3 von Willebrands disease mistaken as severe haemophilia A. Haemophilia. 2009 Nov;15(6):1258–61.

ii. Saif MA, Thachil J, Brown R, Bigger BW, Wynn RF, Nash M, et al. Is it congenital or acquired von Willebrands disease? Haemophilia. 2015 Jan;21(1):e113–5.

iii. Gallego L, Junquera L. Association von Willebrands disease and nevoid basal cell carcinoma syndrome (Gorlin syndrome) [Internet]. Vol. 14, Haemophilia. 2008. p. 835–7. Available from: http://dx.doi.org/10.1111/j.1365-2516.2008.01681.x

iv. Von Willebrand Factor. In: Drugs and Lactation Database (LactMed). Bethesda (MD): National Library of Medicine (US); 2018.

v. Abed H, Ainousa A. Dental management of patients with inherited bleeding disorders: a multidisciplinary approach. Gen Dent. 2017 Nov;65(6):56–60.

vi. Mahlangu SP, Mahlangu J, Shangase SL. Dental management of patients with inherited bleeding disorders: a retrospective study [Internet]. Vol. 73, South African Dental Journal. 2018. Available from: http://dx.doi.org/10.17159/2519-0105/2018/v73no8a3

vii. Rasaratnam L, Chowdary P, Pollard D, Subel B, Harrington C, Darbar UR. Risk-based management of dental procedures in patients with inherited bleeding disorders: Development of a Dental Bleeding Risk Assessment and Treatment Tool (DeBRATT). Haemophilia. 2017 Mar;23(2):247–54.

viii. Moosajee S, Rafique S. Dental Management of Patients With Acquired and Congenital Bleeding Disorders. Prim Dent J. 2020 Jun;9(2):47–55.

ix. Duraisamy R, Krishnan CS, Ramasubramanian H, Sampathkumar J, Mariappan S, Navarasampatti Sivaprakasam A. Compatibility of Nonoriginal Abutments With Implants: Evaluation of Microgap at the Implant-Abutment Interface, With Original and Nonoriginal Abutments. Implant Dent. 2019 Jun;28(3):289–95.

x. Anbu RT, Suresh V, Gounder R, Kannan A. Comparison of the Efficacy of Three Different Bone Regeneration Materials: An Animal Study. Eur J Dent. 2019 Feb;13(1):22–8.

xi. Sekar D, Mani P, Biruntha M, Sivagurunathan P, Karthigeyan M. Dissecting the functional role of microRNA 21 in osteosarcoma. Cancer Gene Ther. 2019 Jul;26(7-8):179–82.

xii. Sekar D. Circular RNA: a new biomarker for different types of hypertension. Hypertens Res. 2019 Nov;42(11):1824–5.

xiii. Bai L, Li J, Panagal M, M B, Sekar D. Methylation dependent microRNA 1285-5p and sterol carrier proteins 2 in type 2 diabetes mellitus. Artif Cells Nanomed Biotechnol. 2019 Dec;47(1):3417–22.

xiv. Sivasamy R, Venugopal P, Mosquera E. Synthesis of Gd2O3/CdO composite by sol-gel method: Structural, morphological, optical, electrochemical and magnetic studies. Vacuum. 2020 May 1;175:109255.

xv. Sekar D, Nallaswamy D, Lakshmanan G. Decoding the functional role of long noncoding RNAs (lncRNAs) in hypertension progression. Hypertens Res. 2020 Jul;43(7):724–5.

xvi. Preethi KA, Lakshmanan G, Sekar D. Antagomir technology in the treatment of different types of cancer. Epigenomics. 2021 Apr;13(7):481–4.

xvii. Preethi KA, Sekar D. Dietary microRNAs: Current status and perspective in food science. J Food Biochem. 2021 Jul;45(7):e13827.

xviii. Bakshi HA, Mishra V, Satija S, Mehta M, Hakkim FL, Kesharwani P, et al. Dynamics of Prolyl Hydroxylases Levels During Disease Progression in Experimental Colitis. Inflammation. 2019 Dec;42(6):2032–6.

xix. Ezhilarasan D. Dapsone-induced hepatic complications: it's time to think beyond methemoglobinemia. Drug Chem Toxicol. 2021 May;44(3):330–3.

xx. Thakur RS, Devaraj E. Lagerstroemia speciosa(L.)

Pers. triggers oxidative stress mediated apoptosis via intrinsic mitochondrial pathway inHepG2cells [Internet]. Vol. 35, Environmental Toxicology. 2020. p. 1225–33. Available from: http://dx.doi.org/10.1002/tox.22987

xxi. Ezhilarasan D, Shebi S, Thomas J, Chandrasekaran N, Mukherjee A. Gracilaria foliifera (Forssk.) Børgesen ethanolic extract triggers apoptosis via activation of p53 expression in HepG2 cells [Internet]. Vol. 15, Pharmacognosy Magazine. 2019. p. 259. Available from: http://dx.doi.org/10.4103/pm.pm_379_18

xxii. P. K, M. P, Samuel Rajendran R, Annadurai G, Rajeshkumar S. Characterization and toxicology evaluation of zirconium oxide nanoparticles on the embryonic development of zebrafish, Danio rerio [Internet]. Vol. 42, Drug and Chemical Toxicology. 2019. p. 104–11. Available from: http://dx.doi.org/10.1080/01480545.2018.1523186

xxiii. Balusamy SR, Perumalsamy H, Veerappan K, Huq MA, Rajeshkumar S, Lakshmi T, et al. Citral Induced Apoptosis through Modulation of Key Genes Involved in Fatty Acid Biosynthesis in Human Prostate Cancer Cells: In Silico and In Vitro Study. Biomed Res Int. 2020 Mar 18;2020:6040727.

xxiv. Arvind P TR, Jain RK. Skeletally anchored forsus fatigue resistant device for correction of Class II malocclusions-A systematic review and meta-analysis. Orthod Craniofac Res. 2021 Feb;24(1):52–61.

xxv. Venugopal A, Vaid N, Bowman SJ. Outstanding, yet redundant? After all, you may be another Choluteca Bridge! Semin Orthod. 2021 Mar 1;27(1):53–6.

xxvi. Ramadurai N, Gurunathan D, Samuel AV, Subramanian E, Rodrigues SJL. Effectiveness of 2% Articaine as an anesthetic agent in children: randomized controlled trial. Clin Oral Investig. 2019 Sep;23(9):3543–50.

xxvii. Varghese SS, Ramesh A, Veeraiyan DN. Blended Module-Based Teaching in Biostatistics and Research Methodology: A Retrospective Study with Postgraduate Dental Students. J Dent Educ. 2019 Apr;83(4):445–50.

xxviii. Mathew MG, Samuel SR, Soni AJ, Roopa KB. Evaluation of adhesion of Streptococcus mutans, plaque accumulation on zirconia and stainless steel crowns, and surrounding gingival inflammation in primary molars: randomized controlled trial [Internet]. Vol. 24, Clinical Oral Investigations. 2020. p. 3275–80. Available from: http://dx.doi.org/10.1007/s00784-020-03204-9

xxix. Dhanraj G, Rajeshkumar S. Anticariogenic Effect of Selenium Nanoparticles Synthesized Using Brassica oleracea. J Nanomater [Internet]. 2021 Jul 10 [cited 2022 Feb 20];2021. Available from: https://www.hindawi.com/journals/jnm/2021/8115585/

xxx. Ganapathy D, Ramadoss R, Yuwanati M, Karthikeyan M. Rarity of mucormycosis in oral squamous cell carcinoma: A clinical paradox? Oral Oncol. 2022 Feb;125:105725.

xxxi. Treatment and management of Von Willebrand disease [Internet]. Vol. 3, Haemophilia. 1997. p. 4–8. Available from: http://dx.doi.org/10.1111/j.1365-2516.1997.tb00173.x

xxxii. Budde U, Federici AB, Rand JH. Pathophysiology, Epidemiology, Diagnosis, and Treatment of Acquired von Willebrand Syndrome [Internet]. Von Willebrand Disease. 2011. p. 214–30. Available from: http://dx.doi.org/10.1002/9781444329926.ch19

xxxiii. Maharaj D, Walker ID, Mcewan HP, Nisbet CE, Erskine JG. Co-incidental Von Willebrands disease and immune thrombocytopenia in pregnancy: treatment with high dose intravenous immunoglobulin [Internet]. Vol. 8, Clinical & Laboratory Haematology. 1986. p. 227–31. Available from: http://dx.doi.org/10.1111/j.1365-2257.1986.tb00099.x

xxxiv. Green D. Acquired Von Willebrand Syndrome [Internet]. Hemophilia and Von Willebrand Disease. 2018. p. 191–207. Available from: http://dx.doi.org/10.1016/b978-0-12-812954-8.00012-6

xxxv. Cain GF, Massin CR. Von Willebrand Disease: Diagnosis and Management. Nova Biomedical; 2012. 190 p.

xxxvi. Koutts J, Versace R, Furby F, Castaldi PA. Pseudo von willebrands disease [Internet]. Vol. 16, Pathology. 1984. p. 364. Available from: http://dx.doi.org/10.1016/s0031-3025(16)38073-4

xxxvii. Belavic JM. New treatment for von Willebrand disease [Internet]. Vol. 35, The Nurse Practitioner. 2010. p. 13–4. Available from: http://dx.doi.org/10.1097/01.npr.0000387146.77239.5e

xxxviii. Green D. The Von Willebrand Factor [Internet]. Hemophilia and Von Willebrand Disease. 2018. p. 135–48. Available from: http://dx.doi.org/10.1016/b978-0-12-812954-8.00009-6