

Effectiveness of Foam Sclerotherapy in Treatment of Symptomatic Haemorrhoidal Diseases at a Tertiary Care Hospital, Agra, Uttar Pradesh, India: A Prospective Interventional Study

PUNEET AGRAWAL¹, AVANISH KUMAR SAXENA², PRAKHAR VERMA³, ABHISHEK YADAV⁴, RADHIKA SAHNI⁵, ZAINUDDIN LIYAKAT PARKAR⁶, NITISH JAIN⁷, ANAM FATIMA⁸



ABSTRACT

Introduction: Haemorrhoids is a very common condition in patients presenting to surgery Outpatient Department (OPD) with complaints of bleeding per rectum. Injection Foam Sclerotherapy has been established as a safe, simple and effective non surgical modality in treatment of symptomatic grade 1 and 2 haemorrhoids.

Aim: To evaluate the effectiveness of foam sclerotherapy as a treatment modality in patients suffering with symptomatic Grade I and II haemorrhoidal diseases.

Materials and Methods: This prospective interventional study was conducted in General Surgery Department of FH Medical College and Hospital, Agra, Uttar Pradesh, India between April 2021 to September 2021. A total of 42 patients with complaints of bleeding per rectum, and who were diagnosed as a case of Grade I or II internal haemorrhoids were included. 3% Polidocanol was used as the sclerosing agent for sclerotherapy. Effectiveness of sclerotherapy was evaluated, parameters

assessed were bleeding per rectum, pain and pruritis with regular follow-ups of the patients at specific intervals.

Results: Among 42 patients 29 (69.05%) patients had grade I haemorrhoids while 13 (30.95%) presented as a case of grade II haemorrhoidal disease. Among the patients with grade I haemorrhoids, 82.76% (24/29) were treated successfully after a single session of foam sclerotherapy while 53.85% (7/13) of the patients with grade II haemorrhoids were symptomatically relieved after a single session. The success rate after 2nd session of sclerotherapy was 100% (29/29) in patients diagnosed as a case of grade I haemorrhoids comparing it to 69.23% (9/13) in those with grade II haemorrhoids. The overall cure rate for either grade of haemorrhoid after three sessions of therapy was 95.24% (40/42).

Conclusion: This study reflects that 3% polidocanol when used as a sclerosant agent was found to be cheap, safe and effective, and first line treatment modality in grade I and II haemorrhoids that can be done on outpatient basis with minimal complication.

Keywords: Bleeding per rectum, Haemorrhoids, Polidocanol

INTRODUCTION

Haemorrhoidal disease can be described as the symptomatic enlargement and/or distal displacement of anal cushions [1], and is one of the most common anorectal disease [2-4]. It is more often seen in 45-60 years age group in both the genders [5]. Literature shows that more males are affected from haemorrhoidal diseases [6]. Patients often present to the hospital late, due to the feelings of embarrassment and social stigma, and opt for self-medication and local therapies at home. There are various treatment modalities which can be used for management of haemorrhoidal diseases which include dietary and lifestyle modifications, medical treatment, sclerotherapy, rubber band ligation, laser and various surgical procedures depending upon the severity of disease [7-9].

The disease is divided into four grades depending on the extent of the prolapse into the anal canal or outside the anus, known as Goligher's classification: (1) First-degree haemorrhoids (grade I): The anal cushions bleed but do not prolapse; (2) Second-degree haemorrhoids (grade II): The anal cushions prolapse through the anus on straining but reduce spontaneously; (3) Third-degree haemorrhoids (grade III): The anal cushions prolapse through the anus on straining or exertion and require manual replacement into the anal canal; and (4) Fourth-degree haemorrhoids (grade IV): The prolapse stays out at all times and is irreducible [10]. The most common symptom and presenting complaint in patients suffering from 1 and 2 degree haemorrhoidal disease is per rectal bleeding

which often leads to severe anaemia. Most patients suffering from Grade 1 and 2 internal haemorrhoids are relieved with conservative management [11]. The recent results of phlebology in the management of haemorrhoidal diseases have been promising, and has rendered sclerotherapy the initial treatment of choice for grade 1 and 2 haemorrhoidal diseases [12,13]. The use of sclerotherapy with 3% Polidocanol foam has increased many folds for the management of haemorrhoidal disease, it has the main advantages of being cost-effective, repeatable and negligible pain over other treatment modalities [14]. Polidocanol induces an inflammatory reaction with sclerosis of the submucosal tissue and consequential suspension of the haemorrhoidal tissue [15].

No study has been done in the recent times in tertiary care rural set-up that too in western Uttar Pradesh on foam sclerotherapy in haemorrhoidal disease. Thus, this study was conducted to study the effectiveness of foam sclerotherapy in treatment of patients suffering with symptomatic grade I and II haemorrhoidal diseases in rural population of western Uttar Pradesh, India.

MATERIALS AND METHODS

A prospective interventional study was conducted in General Surgery department of FH Medical College and Hospital, Agra, Uttar Pradesh, India from 1st April 2021 to 30th September 2021. Approval was taken from Ethical committee for conducting this study, IEC/IRB NO. 04/21. 3% Polidocanol was used as the sclerosing agent for sclerotherapy.

Inclusion criteria: The study includes all the patients in the age group of 18-60 years, presenting with complaints of bleeding per rectum, diagnosed as a case of grade 1 and 2 haemorrhoids and willing to give consent for foam sclerotherapy.

Exclusion criteria: This study excludes patients presenting without any complaints of bleeding per rectum. The patients suffering from any acute inflammation in the perianal region, thrombosed haemorrhoids, proctoceles, fissures, fistulas, abscesses, proctitis, colorectal neoplasia, faecal incontinence, active liver disease, uncontrolled hypertension, uncontrolled diabetes mellitus and acute non reducible haemorrhoids were excluded from the study. Pregnant or Nursing mothers, patients on anticoagulant therapy and those with previous history of sclerotherapy session were excluded from the present study.

A total of 42 patients, who met the inclusion criteria during the study duration were enrolled from the General Surgery OPD of the hospital.

Study Procedure

The Polidocanol foam for sclerotherapy was prepared with 2 mL liquid Polidocanol 3% and 8 mL air using two 10 mL syringes and a 3 way connector. The Polidocanol foam was prepared just before each treatment [16]. Patients were investigated preoperatively for any other systemic diseases by investigations such as Complete blood counts (CBC), platelets, blood sugar, viral markers for HIV, HCV and HBsAG, and coagulation profile.

All procedures were performed in the Outpatients Department with patient in the Sims position with no local anaesthesia. All the injections were given above the dentate line to avoid discomfort or pain [15], using an open ended proctoscope, which provided a better overview during foam sclerotherapy at base of each haemorrhoidal node into the surrounding tissue of the feeding vessels at the 3, 7, and 11'0 clock, and also in piles at other positions [17,18]. The doses per sclerotherapy session were 9 mL of polidocanol foam. The 9 mL foam sclerotherapy session was equivalent to a volume of 0.9 mL polidocanol 3%, corresponding to 27 mg polidocanol [16]. The patients were discharged 30 minutes after the treatment, if the postsclerotherapy period was uneventful. The patients were also given treatment to control constipation in the form of bulk laxatives such as Ispaghula (3.5-5g/day), or osmotic agents like liquid paraffin (910-20 mL/day), sodium picosulfate (5-10 mg/day) or polyethylene glycol (1.5 g/kg/day) [19].

Sclerotherapy sessions were done at an interval of two weeks, or till the patient was symptomatically relieved. If the symptoms persisted even after the fourth sclerotherapy session, alternative treatment modalities were recommended to the patient. Patients were followed-up by the same surgeon on a monthly basis for four months after final session of sclerotherapy. During the follow-up period patients were asked to keep record of episodes of bleeding if any during or directly after passage of stools, pain, submucous abscess and pruritis ani. Bleeding was considered persistent if bleeding was present for three consecutive days even after two days post sclerotherapy session. Patients free of perianal bleeding were categorised as successfully treated. Pain was documented directly after sclerotherapy using a three-point scale ("no pain", "little pain", and "permanent pain") and during the visits using a three-point scale ("no pain", "pain during defaecation", and "permanent pain"). Pruritis was assessed by a three-point scale ("no pruritis", "occasional pruritis", and "permanent pruritis") [6]. All the parameters were recorded on bi-weekly basis when the patient reported to us for follow-up and absence of per rectal bleed for three consecutive days was rendered as treatment being effective. Adverse events, during the treatment and in the four month follow-up period, if any were recorded.

STATISTICAL ANALYSIS

Epi Info™ software was used for data analysis.

RESULTS

The age and sex distribution of the patients is shown in [Table/Fig-1] in which 14/42 (33.33%) of patients were in the age group of 31-40 years. Among these 29 (69.04%) patients had grade 1 haemorrhoids while 13 (30.95%) presented as a case of grade 2 haemorrhoidal disease. No intraoperative complications were seen in any of the patients. There were no complications postoperatively except the complaint of mild to moderate pain at injection site, which were managed by conservative treatment.

Age (years)	Males	Females	Total, n (%)
18-30	3	7	10 (23.81)
31-40	6	8	14 (33.33)
41-50	4	6	10 (23.81)
51-60	3	5	8 (19.05)
Total	16 (38.10%)	26 (61.90%)	42 (100)

[Table/Fig-1]: Age and sex distribution of sample population.

The chief complaint of the patients' seeking treatment was bleeding per rectal and was satisfactorily relieved in 73.81% (31/42) of cases after a single course of the therapy. Among 1st degree haemorrhoids, 82.76% of patients (24/29) were treated successfully after 1st session while the cure rate was 100% (29/29) after the 2nd session of foam sclerotherapy, while in patients with 2nd degree haemorrhoids 53.85% (7/13) were cured after 1st session and 69.23% (9/13) after the 2nd session of foam sclerotherapy. The overall cure rate for either grade of haemorrhoid after three sessions of therapy was 95.24% (40/42) as demonstrated in [Table/Fig-2]. No sessions beyond 3rd session was attempted due to non compliance of the patient. It was also observed that increased amount of active sclerosant could be injected at each session in foam sclerotherapy as compared to other forms of liquid sclerosants.

Category of haemorrhoids	1 st session	2 nd session	3 rd session
1 st degree	24/29 (82.76%)	29/29 (100%)	-
2 nd degree	7/13 (53.85%)	9/13 (69.23%)	11/13 (84.62%)
Total	31/42 (73.81%)	38/42 (90.48%)	40/42 (95.24%)

[Table/Fig-2]: Effectiveness after 1st, 2nd and 3rd session of foam sclerotherapy.

The only complications in patients seen post session of foam sclerotherapy was transient injection site pain and pruritis ani, which were managed by a 50 mg diclofenac tablet and 180 mg fexofenadine hydrochloride tablet, respectively given post-therapy. The pain was mild to moderate, lasting for few minutes to hours. As illustrated in [Table/Fig-3], during the first session of foam sclerotherapy 34 (80.95%) out of 42 patients had no complaints of pain post-therapy, while 8 (19.05%) patients complained of having a mild to moderate pain. No patient in present study described their pain as severe or lasting for hours. The patients were followed-up on their two visit for any potential complications in between the first session of therapy and their two visit, but majority 40 (95.24%) of patients described the period in between without any complaints of pain, pruritis. 2 (4.76%) patients presented with complaints of pain during defaecation which was relieved eventually by a dose of analgesic.

S. No.	Variables	n (%)
1.	Pain during first sclerotherapy	
	No pain	34 (80.95)
	Mild to moderate pain	8 (19.05)
	Severe pain	0

2.	Pain in interval between visits 1 and 2	
	No pain	40 (95.23)
	During defaecation	2 (4.76)
	Continuous pain	0
3.	Pain in interval between visits 2 and 3	
	No pain	40 (95.24)
	During defaecation	2 (4.76)
	Continuous pain	0
4.	Pruritis before sclerotherapy	
	No pruritis	29 (69.05)
	Occasional pruritis	11 (26.19)
	Permanent pruritis	2 (4.76)
5.	Pruritis in interval between visits 1 and 2	
	No pruritis	36 (85.71)
	Occasional pruritis	4 (9.52)
	Permanent pruritis	2 (4.76)
6.	Pruritis in interval between visits 2 and 3	
	No pruritis	40 (95.24)
	Occasional pruritis	2 (4.76)
	Permanent pruritis	0

[Table/Fig-3]: Pain and pruritis during and after session of foam sclerotherapy.

DISCUSSION

The results of this study demonstrated that 95.24% (40/42) of the patients were successfully treated after multiple sessions (3 sessions) of injection foam sclerotherapy establishing it a safe, simple and effective non surgical modality for the management of internal haemorrhoids. Polidocanol is a sclerosant and has an anaesthetic effect as well. Thus it offers painless sclerotherapy which can be easily administered on outpatient basis. Thus foam sclerotherapy was preferred in this study as it had clear advantages over other conventional modalities such as being cheap, effective, almost painless, administrable on an outpatient basis with very few complication and an acceptable recurrence rate [16].

Polidocanol developed as a detergent first in 1931 [20], and later in 1936 was used as an anaesthetic agent in Germany [21]. Currently, polidocanol is the most frequently used sclerotherapy agent, and it is also a non ionic surfactant that mainly targets endothelial cells [15]. Internal haemorrhoids are one of the most common cause of painless bleeding per rectum in adult population. They are often uncommon in extremes of age. The treatment of clinical haemorrhoids depends on the grade of haemorrhoids. Grade 1 and 2 haemorrhoids are usually treated using non operative methods [22]. Polidocanol 3% foam when injected at the base of the haemorrhoid causes marked vasospasm, damage to the haemorrhoidal endothelium and subsequent inflammatory reaction within two minutes and induces a fibrotic reaction by 30 minutes of giving the injection [23]. The foam formulation has the advantage that it increases the proportion of active drug on the endothelium and leads to homogeneous distribution of drug microbubbles [16].

The frequency of treatment sessions was reduced significantly with the use of foam sclerotherapy. Results after even a single session of foam sclerotherapy encourages the patient and surgeon to opt for a non operative therapy in haemorrhoidal disease. An important observation in present study was the reduction of active sclerosant agent needed for therapeutic success by as much as 50% as compared to liquid sclerotherapy. Thus, a higher volume of foamy polidocanol can be injected which in turn provides better endothelial adhesion increasing the sclerosing capacity and efficacy [24]. The chief complaint of the patients' seeking treatment was bleeding per rectal and was satisfactorily relieved in majority (73.81%) of cases after a single course of the therapy. Local pain during injection was the only side-effect observed after sclerotherapy. This was well

tolerated by patients in all age group by using low dose of analgesics (50 mg Diclofenac tablet). Thus, foam sclerotherapy showed a good safety profile.

Safety of sclerotherapy with Polidocanol could be demonstrated in this study. Comparing with a study conducted by Bhuiya MF et al., in 2010, the efficacy and safety of sclerotherapy with polidocanol 3% in present study was compared with 5% phenol in oil in the treatment of first- and second-grade haemorrhoidal disease [2]. After one sclerotherapy session, success rates of 60.4% with phenol in oil and 73.80% with 3% Polidocanol foam were evaluated. After two treatment sessions, a total of 76.18% of the patients were treated successfully in phenol group as compared to 90.47% in the present study, thus proving superior efficacy of 3% Polidocanol between the two groups [Table/Fig-4] [15,25,26]. Post-therapy injection site pain was more profound in the phenol group as compared to the 3% Polidocanol group that had no serious adverse events.

S. No.	Study	Place and publication year	Efficacy of 1 st session of sclerotherapy	Efficacy of 2 nd session of sclerotherapy	Efficacy of 3 rd session of sclerotherapy
1.	Bhuiya MF et al., (5% Phenol) [25]	Bangladesh 2010	60.4%	76.18%	-
2.	Moser KH et al., (3% Polidocanol foam) [26]	Germany 2013	88%	-	-
3.	Lobascio P et al., (3% Polidocanol foam) [15]	Italy 2021	78.8%	86%	-
4.	Present study (3% Polidocanol foam)	Western UP, India 2023	73.81%	90.48%	95.24%

[Table/Fig-4]: Comparison with previous studies [15,25,26].

Comparing present study with that conducted by Lobascio P et al., and Moser KH et al., the cure rate after 1st session was 78.8% and 88% in their respective study while 73.81% in present study, while the success rate after 2nd session was 90.48% in present study as compared to 86% in the former study. Success rate after the 3rd session came out to be 95.24% in present study.

In our experience, no life-threatening or major complications occurred in the perianal and prostatic area with our approach. Furthermore, the low rate of postoperative pain was due to injection above the dentate line.

Limitation(s)

The non availability of long-term results poses as an important limitation in present study due to the already mentioned recurrences after therapy of haemorrhoids with non surgical techniques. It may be presumed that stronger preference for foam therapy may lead to long term results. To evaluate the long-term efficacy of foam sclerotherapy further research studies are needed in this regard. Present study has the limitations of lack of a control group and data on long-term effectiveness of the treatment, which may reduce the impact of results.

CONCLUSION(S)

Polidocanol 3% foam has been found to be a very effective sclerosing agent for the management of 1st and 2nd degree haemorrhoidal disease. It has proved to be very useful in symptomatic patients with complains of bleeding, and where surgery cannot be performed immediately, such as those with severe anaemia. The results of this study conclude that foam sclerotherapy is a safe and highly effective treatment modality for grade 1 and 2 haemorrhoidal disease with almost 100% success rate for 1st grade haemorrhoids with multiple sessions of foam sclerotherapy. More studies are required with a large

sample size and follow-up for longer duration to better understand the effectiveness of foam sclerotherapy in Indian population.

REFERENCES

- [1] Lohsiriwat V. Approach to hemorrhoids. *Curr Gastroenterol Rep.* 2013;15(7):332. Doi: 10.1007/s11894-013-0332-6.
- [2] Gallo G, Sacco R, Sammarco G. Epidemiology of hemorrhoidal disease. In: Ratto C, Parello A, Litta F (ed.), *Hemorrhoids. Coloproctology. Vol 2.* Cham: Springer; 2018:03-07.
- [3] Johanson JF. Nonsurgical treatment of hemorrhoids. *J Gastrointest Surg.* 2002;6(3):290-94. Doi: 10.1016/S1091-255X(01)00081-6.
- [4] Serra R, Gallelli L, Grande R, Amato B, De Caridi G, Sammarco G, et al. Hemorrhoids and matrix metalloproteinases: A multicenter study on the predictive role of biomarkers. *Surgery.* 2016;159(2):487-94. Available from: <http://dx.doi.org/10.1016/j.surg.2015.07.003>.
- [5] Johanson JF, Sonnenberg A. The prevalence of haemorrhoids and chronic constipation. *Gastroenterol.* 1990;98(2):380-86.
- [6] Mishra S, Sahoo AK, Elamurugan TP, Jagdish S. Polidocanol versus phenol in oil injection sclerotherapy in treatment of internal hemorrhoids: A randomized controlled trial. *Turk J Gastroenterol.* 2020;31(5):378-83. Doi: 10.5152/tjg.2020.19276. PMID: 32519957; PMCID: PMC7289163.
- [7] Corman ML. *Haemorrhoids.* In: Corman ML (ed) *Colon and rectal surgery, 5th edn.* Williams & Wilkins, Philadelphia. 2005: 177-253.
- [8] Madoff RD, Fleshman JW. American Gastroenterological Association technical review on the diagnosis and treatment of haemorrhoids. *Gastroenterol.* 2004;126(5):1463-73.
- [9] Sim AJW, Murie JA, Mackenzie I. Comparison of rubber band ligation and sclerosant injection for first and second degree haemorrhoids: A prospective clinical trial. *Acta Chir Scand.* 1981;147(8):717-20.
- [10] Madoff RD, Fleshman JW. American Gastroenterological Association medical position statement: Diagnosis and treatment of hemorrhoids. *Gastroenterology.* 2004;126(5):1461-62.
- [11] Perera N, Liolitsa D, Iype S, Croxford A, Yassin M, Lang P, et al. Phlebotonics for haemorrhoids. *Cochrane Database Syst Rev.* 2012;15(8):CD004322.
- [12] Uncu H. Sclerotherapy: A study comparing polidocanol in foam and liquid foam. *Phlebology.* 2010;25(1):44-49. Doi: 10.1258/phleb.2009.008064.
- [13] Hamel-Desnos C, Desnos P, Wollmann JC, Ouvry P, Mako S, Allaert FA. Evaluation of the efficacy of polidocanol in the form of foam compared with liquid form in sclerotherapy of the greater saphenous vein: Initial results. *Dermatol Surg.* 2003;29(12):1170-75. Doi: 10.1111/j.1524-4725.2003.29398.x.
- [14] Lobascio P, Minafra M, Laforgia R, Giove C, Trompetto M, Gallo G. The use of sclerotherapy with polidocanol foam in the treatment of second-degree hemorrhoidal disease- A video vignette. *Colorectal Dis.* 2019;21(2):244-45.
- [15] Lobascio P, Laforgia R, Novelli E, Perrone F, Di Salvo M, Pezzolla A, et al. Short-term results of sclerotherapy with 3% polidocanol foam for symptomatic second- and third-degree hemorrhoidal disease. *J Invest Surg.* 2021;34(10):1059-65. Doi: 10.1080/08941939.2020.1745964. Epub 2020 Apr 15. PMID: 32290709.
- [16] Shekhar R, Gupta VK. Efficacy of foam sclerotherapy in treatment of grade I and grade II bleeding hemorrhoids at Nalanda Medical College and Hospital, Patna. *Int Surg J.* 2020;7(9):2925-28. Available from: <http://dx.doi.org/10.18203/2349-2902.isj20203769>.
- [17] Aakerud L. Sclerotherapy of haemorrhoids. A prospective randomised trial of polidocanol and phenol in oil. *Coloproctology.* 1995;17:73.
- [18] Blanchard CE. *A Text-book of Ambulant Proctology.* Medical Success Press; 1928.
- [19] Portalatin M, Winstead N. Medical management of constipation. *Clin Colon Rectal Surg.* 2012;25(1):12-19. Doi: 10.1055/s-0032-1301754. PMID: 23449608; PMCID: PMC3348737.
- [20] van der Vleuten CJ, Kater A, Wijnen MH, Schultze Kool LJ, Rovers MM. Effectiveness of sclerotherapy, surgery, and laser therapy in patients with venous malformations: A systematic review. *Cardiovasc Intervent Radiol.* 2014;37(4):977-89.
- [21] Leopold CS, Maibach HI. Effect of cutaneously applied nonionic surfactants and local anesthetic bases on thermal sensations. *Pharmazie.* 2004;59(1):50-54.
- [22] Korkis AM, McDougall CJ. Rectal bleeding in patients less than 50 years of age. *Dig Dis Sci.* 1995;40(7):1520-23. Doi: 10.1007/BF02285201. PMID: 7628276.
- [23] Orsini C, Brotto M. Immediate pathologic effects on the vein wall of foam sclerotherapy. *Dermatol Surg.* 2007;33(10):1250-54. Doi: 10.1111/j.1524-4725.2007.33261.x.
- [24] Rosa B. Polidocanol foam: A breath of fresh air for the treatment of internal hemorrhoids. *GE Port J Gastroenterol.* 2019;26(3):153-54.
- [25] Bhuiya MF, Rahman S, Ali A. Effectivity of injection sclerotherapy on early hemorrhoids reported to surgical outpatient department. *Journal of Armed Forces Medical College Bangladesh.* 2010;6(2):25-27.
- [26] Moser KH, Mosch C, Walgenbach M, Bussen DG, Kirsch J, Joos AK, et al. Efficacy and safety of sclerotherapy with polidocanol foam in comparison with fluid sclerosant in the treatment of first-grade hemorrhoidal disease: A randomised, controlled, single-blind, multicentre trial. *Int J Colorectal Dis.* 2013;28(10):1439-47.

PARTICULARS OF CONTRIBUTORS:

1. Professor, Department of General Surgery, FH Medical College, Agra, Uttar Pradesh, India.
2. Professor and Head, Department of General Surgery, FH Medical College, Agra, Uttar Pradesh, India.
3. Resident, Department of General Surgery, FH Medical College, Agra, Uttar Pradesh, India.
4. Assistant Professor, Department of General Surgery, FH Medical College, Agra, Uttar Pradesh, India.
5. Resident, Department of General Surgery, FH Medical College, Agra, Uttar Pradesh, India.
6. Resident, Department of General Surgery, FH Medical College, Agra, Uttar Pradesh, India.
7. Resident, Department of General Surgery, FH Medical College, Agra, Uttar Pradesh, India.
8. Resident, Department of General Surgery, FH Medical College, Agra, Uttar Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Abhishek Yadav,
Assistant Professor, Department of General Surgery, FH Medical College, Etamadpur,
Agra-283204, Uttar Pradesh, India.
E-mail: aby_dude@yahoo.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Aug 06, 2022
- Manual Googling: Oct 06, 2022
- iThenticate Software: Nov 10, 2022 (21%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval Obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Aug 05, 2022**

Date of Peer Review: **Sep 03, 2022**

Date of Acceptance: **Nov 11, 2022**

Date of Publishing: **Jan 01, 2023**