M.C.E. Society's

M.A. RANGOONWALA COLLEGE OF DENTAL SCIENCES & RESEARCH CENTRE, PUNE

Recognized by Dental Council of India & Affiliated to M.U.H.S. Nashik

2390-B, K.B. Hidayatullah Road, Azam Campus, Camp, Pune-411001 (Maharashtra)
Tel: 91-20-26430959, 26430960, 26430961 Fax No. 91-20-26430962
E-mail: info@mardentalcollege.org Website: www.mardentalcollege.org

Name of the Partnering Agency/Institution: Dr D. Y Patil Dental college and Hospital

Number of Participants : 4 faculty

Duration :3 years (17th Feb 2023 – 16th Feb 2026)

A collaborative research is being carried out at Dr D.Y Patil Dental college and Hospital titled " **The possible association of Salivary pH, flow rate, viscosity, buffering capacity and MMP20 in the etiology of Molar Incisor Hypomineralization: A Clinical Study** " The synopsis of the aforementioned study has been drafted and has been approved by the IEC. Two researchers from the Department of Pedodontics and Preventive Dentistry, and one from the Department of Biochemistry are involved, the names of whom are as follows.

1. Dr. Rooposhi Saha
2. Dr Nilesh Rathi
3. Dr Vanishree B.K
4. Dr Namrata Khanna
5. Dr Yusuf Chunawala

M.A.R.D. COLLEGE M.C.E.S. PUNE

PRINCIPAL
M. A. RANGOONWALA COLLEGE OF DENTAL SCIENCES & RESEARCH CENTRE, PUNE

M.A. RANGOONWALA COLLEGE OF DENTAL SCIENCES AND RESEARCH CENTER, PUNE

DEPARTMENT OF PEDODONTICS & PREVENTIVE DENTISTRY

In association with

Dr. D. Y. PATIL DENTAL COLLEGE & HOSPITAL, PUNE

SYNOPSIS

The possible association of salivary pH, flow rate, viscosity buffering capacity and MMP20 in the etiology of Molar Incisor Hypomineratization: A Clinical study

Topic of Synopsis

DR. ROOPOSHI SAHA

The possible association of salivary pH, flow rate, viscosity, buffering capacity and MMP20 in the etiology of Molar Incisor Hypomineratization: A Clinical study

Topic of synopsis

Submitted to

The

MAHARASHTRA UNIVERSITY OF HEALTH SCIENCE

The possible association of salivary pH, flow rate, viscosity, buffering capacity and MMP20 in the etiology of Molar Incisor Hypomineratization: A Clinical study

1.	**TITLE**	The possible association of salivary pH, flow rate, viscosity, buffering capacity an MMP20 in the etiology of Molar Incisor Hypomineratization: A Clinical study
2.	**INTRODUCTION**	Molar Incisor Hypomineralization (MIH) is a novel disease that has come up in thi century in the field of pediatric dentistry[1]. MIH mostly affects the enamel of the firs permanent molars, which help us to grind food[2], it might or might not involve th permanent incisors, responsible for biting and cutting of dietary substrates and also pla a crucial role in phonetics[3]. 13.5-14.2% overall average has been reported by recen systematic reviews, which is constantly increasing[4]. In MIH, teeth have morphologically normal enamel however it is deficient in it structure[5]. Affected enamel is more porous, softened, and shows white, yellow, o brownish opacities; this might be due to the decrease in the quantity and quality o minerals[6]. Therefore, the defective tooth becomes more fragile with increase susceptibility to caries aggravated sensitivity issues[6]; leading to challenging dent procedures[5]. There is no definitive treatment for this condition[7], but only palliativ treatment can be provided to prolong the vitality of the tooth, and to improve the ora health-related quality of life of the children. According to the enamel hypomineralization rate, MIH was classified into differen degrees of severity. White, yellow, or brown demarcated opacities, were assigned as mild degree of MIH; and post-eruptive enamel breakdown jointly with opacities, cariou lesions, or complex restorations disconnected to caries pattern, was defined as severe[8]. Systemic health disturbances that occur during the permanent teeth mineralizatio period have been suggested as to play a possible role in the etiology of MIH[9]. Amon these disorders, early childhood diseases, i.e. asthma[10], frequent use of antibiotics[11], a well as genetic influences[12] (considering that enamel-forming cells are geneticall controlled) should be highlighted. In summary, over the last decade, more than 3 systemic etiological hypotheses have been identified; some are well established, an others are more contemporary[13].

		It makes sense that the protein makeup of saliva is connected to illness, given that sal regulates enamel remineralization and that MIH is linked to increased saliva flow ra It has been observed that the flow rates, viscosity, pH, and acid buffering ability of M patients' saliva and the protein composition of MIH saliva may display recognisa alterations that either induce or exacerbate the clinical signs of this illness[14]. Outstandingly, saliva is a body fluid with complex composition, capable of playing l of roles connected with oral and systemic health[15]. It contains bicarbonate ic responsible for the buffering capacity, neutralizing organic acids produced by bacte food substrates fermentation[16]. Hence, teeth demineralization could be minimiz Several saliva components or proteins can interact with pathogenic bacteria and may involved in the protection of dental tissues, such as statins, mucins, lactofer defensins, and peroxidases[17]. Although saliva contains numerous peptides, many of them have not yet b characterized[17]. With scientific advances, state-of-the-art techniques, such as m spectrometry analysis, for example, have provided a better understanding of the cou of pathologies, identifying biomarkers at a molecular level[18]. Since inconclusive literature with contrasting results exists, this study will be carr out to compare and establish an association between MIH, MMP20, salivary pH, fl rate, viscosity and buffering capacity in children.
3.1	**PRIMARY RESEARCH QUESTION**	Is there any correlation between occurrence of MIH and salivary MMP20 of a child?
3.2	**OTHER RESEARCH QUESTION 1**	Is there any correlation between occurrence of MIH and salivary pH, flow rate, viscosity and buffering capacity in a child?
3.3	**OTHER RESEARCH QUESTION 2**	Not applicable
4.1	**Null HYPOTHESIS**	There is no difference in the occurrence of MIH and salivary MMP20 of a child.
4.2	**Alternative HYPOTHESIS 1**	There is difference in the occurrence of MIH and salivary pH, flow rate, viscosity & buffering capacity of a child.

4.3	**OTHER HYPOTHESIS 2**	Not applicable
5.	**REVIEW OF LITERATURE**	1. Jalevik B. 2001 A sample of 516 Swedish 8-year-old kids had a lot o hypomineralization in their permanent first teeth. Among 95 kids (18.4%), ther was at least one molar with distinct opacity. The incisors usually showe concurrent opacities. The afflicted children had 3.2 (SD 1.8) hypomineralize teeth on average, 2.4 of which were first molars. A total of 6% of the kids ha severe problems, 5% had moderate deficiencies, and 7% had teeth that were jus minimally hypomineralized. More than one tooth was impacted in 15% of case which suggests systemic cause. Throughout the first year of life, the afflicte children, particularly the males, were said to have experienced increased healt issues, including asthma (albeit there were only 4 cases). Children with an without enamel abnormalities had comparable breastfeeding histories.[19] 2. Weerheijm K 2003. Molar Incisor Hypomineralisation (MIH) is defined as hypomineralisation of systemic origin of one to four permanent first molar frequently associated with affected incisors. MIH molars are fragile and carie can develop very easily in those molars. Although MIH molars are well know by paediatric dentists and their occurrence is related in severe cases to majo clinical problems, only limited data of the size of the problem are available. Th prevalence of MIH ranges in the literature from about 3.6 to 25% and seems t differ in certain regions and birth cohorts. Unfortunately more complet comparable valid data are lacking at the moment. It seems that severa aetiological factors can cause the enamel defects and that their occurrence i child related.For children with repeated illnesses in the first years after birth an children with opacities on erupted molars or incisors it seems useful to increas the frequency of dental check-ups during the period of erupting first permanen molars[6]. 3. Hussein A.S.2015 Molar-Incisor First permanent molars and commonl permanent incisors are affected by the condition of hypomineralized enamel o systemic origin known as hypomineralization (MIH). It is seen as a worldwid

issue, and information from Malaysia and other South-East Asian nati limited. As a result, the purpose of this study was to examine the prevalenc severity of MIH in a group of kids aged 7 to 12 who were enrolled in a paec dentistry clinic at the Faculty of Dentistry, Universiti Teknologi MARA (U Malaysia.[20]

4. Almuallem, 2018 Recent data indicates that molar-incisor hypominerali: (MIH) is a frequently – encountered dental condition worldwide. The con could be associated with dental complications that might affect patients' q of life as well as create treatment challenges to dentists. The affected tee more prone to caries and post-eruptive enamel breakdown, therefore, believed that this condition might be responsible for a substantial proporti childhood caries since the condition has high prevalence. MIH is common as such it should be diagnosed and managed in primary care wherever pos: Early diagnosis can lead to more effective and conservative management[21]

5. Bekes k. 2020 Uncertain pathophysiology characterises the endemic paed condition known as molar incisor hypomineralization (MIH). We proposec the protein content of saliva is related to illness because saliva regulates en remineralization and MIH is connected to increased saliva flow rates. enrolled 5 kids between the ages of 6 and 14 with MIH demonstrating at one hypersensitive molar and 5 kids without hypomineralization to test According to this study, MIH patients' salivary proteaneous compositic altered, revealing a catabolic environment associated to inflammation.[22]

6. Zilberman 2020. Enamel formation is a highly coordinated process. The ena protein matrix, secreted by the ameloblasts, contains three main prote amelogenin, enamelin and ameloblastin. These proteins are specific to ena and are degrade by specific proteases, MMP20 and KLK4. Human mutation genes coding for the enamel proteinases cause variable degrees hypomineralization. In MIH permanent molars the mineral content is very and the protein content may reach 30-40% in volume. We should look at function of MMP20 and KLK4 during the first two years of life in orde understand the findings in MIH[23].

7. Aline leite de Farias 2022 to evaluate the existence and severity of th relationship between MIH and enamel hypomineralization in the secon permanent molars. When first permanent molars badly impacted by molar incisor hypomineralization are being considered for extraction, the secon permanent molar is crucial (MIH). The first and second permanent molars ar most affected by enamel hypomineralization. Patients with severe MIH in th first permanent molars are more likely to have mild second permanent mola abnormalities. Dental caries experience was increased when ename hypomineralization was present.[24]

8. Toledo S et al, 2022 Saliva is a rich-bodily fluid with recognized clinica diagnosis roles and this research aimed at investigating if there is any change i the salivary proteome signatures of MIH children with distinct degrees o severity. Fifty schoolers (6–10 years) were equally assigned into the followin groups: G1 (Control group - Healthy teeth), G2 (Mild MIH with white/cream opacity and free of caries), G3 (Mild MIH with yellow/brown opacity and fre of caries), G4 (Severe MIH with white/creamy, yellow/brown opacitie including post-eruptive fracture and free of caries), G5 (Severe MIH witl white/creamy, yellow/brown opacities, post-eruptive fracture, and caries) Unstimulated saliva samples were collected and later explored using mas spectrometry analysis. In total, 6,471 proteins were found, 5,073 exclusivel from MIH children, and 778 overlapping among the different degrees of th disturb. The Biological Pathways displayed distinct patterns among the groups being different according to the degrees of MIH. Gene- Odontology difference might not be verified regarding the biological processes and cellula components. Conversely, with respect to molecular function, alterations amon groups were evident, with the presence of proteins that would contribute to MI in children with the severe condition (i.e, calcium ion binding, microtubul binding, platelet-derived growth factor binding). In conclusion, the results of thi study support important salivary proteomic changes in MIH children, accordin to distinct degrees of severity, reinforcing the interplay between the clinica characteristics and changes in the salivary proteome.

OPERATIONAL DEFINITIONS:

Molar incisor hypo mineralisation (MIH) is a common developmental dental cor that presents in childhood. Areas of poorly formed enamel affect one or mor permanent molars and can cause opacities on the anterior teeth. MIH presents a v of challenges for the dental team as well as functional and social impacts for af children.

MMP20 (Enamelysin) has been shown to be expressed by secretory stage amelol It is the only proteinase present in the enamel matrix during the secretory stage main function of MMP20 is to cleave the most abundant enamel matrix pr amelogenin. It is also likely responsible for generating an enamelin cleavage pr MMP20 will also cleave the KLK4 propeptide to produce catalytically active K Human MMP20 is expressed from a gene on chromosome 11q22-q23. Seven dif human MMP20 mutations are known to cause autosomal recessive hypomaturati hypoplastic-hypomaturation Amelogenesis Imperfecta (AI). The teeth are normal i but the enamel layer does not contrast well with dentin on radiographs and the er tends to chip away. The lack of functional MMP20 in mammalian species wi enamel (baleen whales), demonstrate that MMP20 is essential for enamel formatic is not essential for any other biological function.

APPROPRIATE METHODS OF MEASUREMENT:

Assessment of MIH

The diagnosis of MIH will be made by visual inspection, using headset light, gauze cleaning and drying teeth) and clinical mirror. MIH detection will be perfo according to the European Academy of Paediatric Dentistry (EAPD)[1] criteria.

Saliva samples collection and preparation

Unstimulated saliva samples will be obtained from all participants. The s participants will be told to skip all oral hygiene treatments, chewing gum, and relievers for 8 hours, as well as to skip eating, drinking, and brushing for 1 hour be examination. Salivette will be used to collect saliva (Sarstedt, Germany). Subjects

asked to spit and samples were stored in Oragen DNA self-collection kits at roor temperature until been processed. No centrifugation was performed in the saliv samples. After centrifuging the samples at 4 °C for 10 min. at 10,000 rpm, they will b kept at 20 °C until they are used. Saliva will be examined for pH and buffering capacity

APPROPRIATE STUDY INSTRUMENTS:

a) Mouth mirror

b) Salivette

c) Centrifuge machine.

d) Measuring cup

e) pH meter

f) Viscometer

g) Elisa reader.

STEPS IN THE CONDUCT OF STUDY

Subjects will be divided into two groups, Group I and Group II. Group I will consist c subjects with MIH. Group II will consist of subjects without MIH.

The subjects will then be scrutinized for MIH, salivary MMP20, pH, flow rate, viscosit & buffering capacity using appropriate methods.

Methods of Data collection: The data will be collected by subject examination fulfillin the inclusion criteria, in subject information sheet.

Appropriate data management and analysis procedure:

Statistical analysis will be performed using Statistical Product and Service Solutio (SPSS)version 21 for Windows (SPSSInc, Chicago, IL).

Descriptive quantitative data will be expressed in mean and standard deviatio respectively.

Descriptive qualitative data will be expressed in percentage.

Data normality will be checked by using Shapiro – Wilk test.

		Confidence interval is set at 95% and probability of alpha error (level of significa set at 5%. Power of the study set at 80%. Intergroup comparison between both groups in respect to quantitative study parame will be done using unpaired t test(parametric)/Mann Whitney U test (non -parametr Intergroup comparison between both groups in respect to qualitative study parame will be done using Chi square test. Appropriate data analysis plan and methods: As mentioned above. Additional points for Research in AYUSH: Not applicable Additional points for RCT: Not applicable Additional points for all Experimental Studies: Not applicable
8.	**REFERENCE STYLE (Vancouver)**	1. Weerheijm KL, Duggal M, Mejàre I, Papagiannoulis L, Koch G, Martens I Hallonsten AL. Judgement criteria for molar incisor hypomineralisation (M in epidemiologic studies: a summary of the European meeting on MIH helc Athens, 2003. Eur J Paediatr Dent. 2003b Sep;4(3):110-3. PMID: 14529329. 2. Gaiser S, Deyhle H, Bunk O, White SN, Müller B. Understanding nano-anato of healthy and carious human teeth: a prerequisite for nanodentist Biointerphases. 2012 Dec;7(1-4):4. doi: 10.1007/s13758-011-0004-8. Ep 2012 Feb 9. PMID: 22589047. 3. Abdalla R. Teaching dental anatomy & morphology: An updated clinical-digital-based learning module. Eur J Dent Educ. 2020 Nov;24(4):650-659. d 10.1111/eje.12552. Epub 2020 Jul 1. PMID: 32531077. 4. Lopes LB, Machado V, Mascarenhas P, Mendes JJ, Botelho J. The prev of molar-incisor hypomineralization: a systematic review and meta-analysis. Rep. 2021 Nov 17;11(1):22405. doi: 10.1038/s41598-021-01541-7. PM 34789780; PMCID: MC8599453. 5. Taylor GD. Molar incisor hypomineralisation. Evid Based Dent. Mar;18(1):15-16. doi: 10.1038/sj.ebd.6401219. PMID: 28338027.

M.A.R.D. COLLEGE M.C.E.S. PUNE

6. Weerheijm KL. Molar incisor hypomineralisation (MIH). Eur J Paediatr Den 2003 Sep;4(3):114-20. PMID: 14529330

7. Mast P, Rodrigueztapia MT, Daeniker L, Krejci I. Understanding MIH definition, epidemiology, differential diagnosis and new treatment guidelines Eur J Paediatr Dent. 2013 Sep;14(3):204-8. PMID: 24295005.

8. Negre-Barber A, Montiel-Company JM, Catalá-Pizarro M, Almerich-Silla JM Degree of severity of molar incisor hypomineralization and its relation to dental caries. Sci Rep. 2018 Jan 19;8(1):1248. doi: 10.1038/s41598-018-19821-0 PMID: 29352193; PMCID: PMC5775201.

9. Salem K, Aziz D, Asadi M. Prevalence and Predictors of Molar Incisor Hypomineralization (MIH) among Rural Children in Northern Iran. Iran J Publi Health. 2016 Nov;45(11):1528-1530. PMID: 28032070; PMCID: PMC518226

10. Rizzardi KF, da Silva Toledo E, Ferraz LFC, Darrieux M, Girardello R, de Lim Marson FA, Parisotto TM. Association between asthma and enamel defects i primary and young permanent teeth – A systematic review. Pediatr Pulmono 2022 Jan;57(1):26-37. doi: 10.1002/ppul.25737. Epub 2021 Nov 8. PMID 34698451.

11. Ghanim A, Manton D, Mariño R, Morgan M, Bailey D. Prevalence o demarcated hypomineralisation defects in second primary molars in Iraq children. Int J Paediatr Dent. 2013 Jan;23(1):48-55. doi: 10.1111/j.1365 263X.2012.01223.x. Epub 2012 Jan 25. PMID: 22276809.

12. Vieira AR, Kup E. On the Etiology of Molar-Incisor Hypomineralization. Caries Res. 2016; 50(2):166-9. doi: 10.1159/000445128. Epub 2016 Apr 26. PMID 27111773.

13. Garot E, Rouas P, Somani C, Taylor GD, Wong F, Lygidakis NA. An updat the aetiological factors involved in molar incisor hypomineralisation (MIH systematic review and meta-analysis. Eur Arch Paediatr Dent. 2 Feb;23(1):23-38. doi: 10.1007/s40368-021-00646-x. Epub 2021 Jun 24. PM 34164793.

14. Bekes K, Mitulović G, Meißner N, Resch U, Gruber R. Saliva proteomic patte in patients with molar incisor hypomineralization. Scientific reports. 2020 M 5;10(1):1-1.

15. Khurshid Z, Zohaib S, Najeeb S, Zafar MS, Rehman R, Rehman IU. Advan of Proteomic Sciences in Dentistry. Int J Mol Sci. 2016 May 13;17(5):728. 10.3390/ijms17050728. PMID: 27187379; PMCID: PMC4881550.

16. de Sousa ET, Lima-Holanda AT, Nobre-Dos-Santos M. Changes in the saliv electrolytic dynamic after sucrose exposure in children with Early Childh Caries. Sci Rep. 2020 Mar 5;10(1):4146. doi: 10.1038/s41598-020-61128 PMID: 32139791; PMCID: PMC7057989.

17. Pappa E, Vougas K, Zoidakis J, Vastardis H. Proteomic advances in saliv diagnostics. Biochim Biophys Acta Proteins Proteom. 2(Nov;1868(11):140494. doi: 10.1016/j.bbapap.2020.140494. Epub 2020 Jul PMID: 32663525.

18. Vitorino R, Lobo MJ, Ferrer-Correira AJ, Dubin JR, Tomer KB, Domingues P Amado FM. Identification of human whole saliva protein components us proteomics. Proteomics. 2004 Apr;4(4):1109-15. doi: 0.1002/pmic.2003006 PMID: 15048992.

19. Jälevik B, Klingberg G, Barregård L, Norén JG. The prevalence of demarca opacities in permanent first molars in a group of Swedish children. A Odontologica Scandinavica. 2001 Jan 1;59(5):255-60.

20. Hussein AS, Ghanim AM, Abu-Hassan MI, Manton DJ. Knowle management and perceived barriers to treatment of molar-inc hypomineralisation in general dental practitioners and dental nurses in Malay European archives of paediatric dentistry. 2014 Oct;15:301-7

21. Almuallem Z, Naudi-Busuttil A. Molar–incisor hypomineralization(MIH)- overview .British Dental Journal. 2018 Oct 12; 225(7):601-609.

22. Bekes K, Mitulović G, Meißner N, Resch U, Gruber R. Saliva proteomic patte in patients with molar incisor hypomineralization. Scientific reports. 2020 M 5;10(1):1-1.

23. Zilbermam U. Amelogenesis and MIH-Role of MMP20 and KLK4. Rom J D Med. 2020, Vol XXIII; No 3-4; 193-203

24. Elora Silva Toledo, Karina Ferreira Rizzardi, Fabíola Galbiatti de Carvalh Marinês Nobre-dos-Santos, Juliana Mozer Sciani, Thaís Manzano Parisot Salivary Proteomic Patterns in Children Affected by Different Severity Degre of Molar Incisor Hypomineralization. Research Square; DO https://doi.org/10.21203/rs.3.rs-2309540/v1

Appendix 'A'

Name of The P.G college	**M.A.Rangoonwala College of Dental Science & Research Centre, Pune**
Department	**Pediatric and Preventive Dentistry**
Name of the Principal investigator & college	**Dr. Rooposhi Saha, Professor, M.A. Rangoonwala College of Dental Science & Research Centre, Pune**

Through Proper Channel Only

To
The Registrar,
MUHS, Nashik-422004.

Subject: - Submission of Topic of Research project

Respected Sir,

I, Dr. Rooposhi Saha, Professor in Pediatric and Preventive dentistry, am submitting the Title of my research project as mention below along with names of my co investigators.

TITLE OF SYNOPSIS:
The possible association of salivary pH, flow rate, viscosity, buffering capacity and MMP20 in the etiology of Molar Incisor Hypomineratization: A Clinical study

Kindly accept and register my Title of research project.

Principal investigator
Dr Rooposhi Saha
Professor, Pedodontics & Preventive Dentistry

M.A.R.D. COLLEGE M.C.E.S. PUNE

Co investigator
Dr Nilesh Rathi
Prof. & Head, Pedodontics & Preventive Dentistry, DPU

Co investigator
Dr Vanishree B. K.
Reader, Pedodontics & Preventive Dentistry

Co investigator
Dr Namrata Khanna
Reader, Biochemistry

Co investigator
Dr Yusuf Chunawala
Prof. & Head, Pedodontics & Preventive Dentistry, MARDC

Dr. Yusuf Chunnawala

(Name and signature of HOD)

TRUE COPY

M.A. RAN... ...OF DENTAL SCIE... ..., PUNE

Dr. Ramandeep Duggal

(Signature and Seal of Dean of the college)

M.A.R.D. COLLEGE M.C.E.S. PUNE

ETHICS COMMITTEE OF M.C.E. SOCIETY

Azam Campus, Pune - 411 001. (INDIA)
Tel. : 91-020-26430959 Fax : 91-020-26430962
E-mail - dr.farha.mardc@gmail.com
Reg.No. - ECR/511/INST/MH/2014/RR-20

P.A. Inamdar
President

Dr. Farha Rizwan
Secretary

Dr. P. M. Bulakh
Chairman

Ref. No: MCES/EC/ 853 /2023

Date: 14 SEP 2

ANNEXURE III

To,

Dr. Rooposhi Saha

Professor

Department of Pedodontics

M. A. Rangoonwala College of Dental Sciences and Research Centre,

Pune.

Dear Madam/Sir,

The Ethics Committee of the M.C.E.Society, Pune. reviewed the project entitled **"The Possible Association of Salivary pH, Flow Rate, Viscosity, Buffering Capacity and MMP20 in the Etiology of Molar Incisor Hypomineratization: A Clinical Study"**

During its regular meeting held on 08th September 2023 attended by the E.C. members.

Kindly submit the following documents:-

1. C.V. of Principal Investigator
2. C.Vs of Co- Investigators
3. Marathi and Hindi translation of Consent form

The project has been

[√] Approved

[×] Approvable, subject to the amendments listed below

[×] Disapproved for reasons listed below

[×] Terminated for reason listed below

Subject to the PI providing the following:

- At least three months animal study report
- [√] A six-monthly detailed report of the clinical trial/study √
- [√]A written report of each serious or unexpected (as per the Investigator's Brochure) adverse event with regard to the study
- [√] Not to make any. amendments/revisions to any study-related document or patient-safety related information, without prior approval of the EC
- [√] To keep the EC informed of the study completion or discontinuation, with reasons
- [×] To submit justification for approval to restart studies discontinued earlier by the EC

Yours sincerely,

Dr. Farha Rizwan
SECRETARY
Ethical Committee
M. C. E. Society
Azam Campus, Pune-1

Ethical Committee M. C. E. Society ★ PUNE

Dr. P. M. Bulakh
CHAIRMAN
Ethical Committee
M. C. E. Society
Azam Campus, Pune-1.