ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Study on spectrum of nephrotic syndrome in adults in a tertiary care hospital of eastern India

Pradeep Chakraborty[1], Sujata Mazumdar[2], Sayan Choudhury[3], Shyamosree Mondal[4]

[1]Professor and Head, [2]Professor, [3,4]Senior Resident, Department of General Medicine, Ramakrishna Mission Seva Pratishthan, Vivekananda Institute of Medical Sciences, Kolkata, West Bengal, India

Submission: 15-08-2022 Revision: 02-10-2022 Publication: 01-11-2022

ABSTRACT

Background: Nephrotic syndrome is a very common yet perplexing kidney disease whose spectrum has undergone a gradual change globally over time. Within various Asian countries, the spectrum of adult nephrotic syndrome varies according to the place of origin. **Aims and Objectives:** The purpose of this study is to know the clinical presentation, laboratory abnormalities, histopathological spectrum of adult nephrotic syndrome, and its changing trends compared to previous studies. **Materials and Methods:** This observational cross-sectional study includes 50 cases of biopsy proven nephrotic syndrome admitted under general medicine department of a tertiary care hospital of Kolkata from March 2020 to February 2021. Proper history taking, clinical examination, and relevant laboratory investigations were done. **Results:** The mean age of presentation was 34.56 ± 12.033 years with 27 males and 23 females. Oliguria was the most common presentation. Facial puffiness was the most predominant clinical finding closely followed by generalized swelling, pedal edema and ascites. 44 (88%) patients had serum albumin level ≤3 g/dl and all 50 (100%) patients had serum cholesterol values >200 mg/dl. 46 (92%) patients had a 24 h urinary protein level >3.5 g whereas 33 (66%) patients had 3+grade and 8 (16%) patients had 4+grade albuminuria. The most predominant renal biopsy variety was found to be focal segmental glomerulosclerosis (FSGS), seen in 27 (54%) patients followed by minimal change disease in 14 (28%) patients. 44 (88%) patients had primary glomerular disease (PGD) and 6 (12%) patients had secondary glomerular disease (SGD). The most common type of PGD and SGD was FSGS (59.09%) and lupus nephritis (4%), respectively. **Conclusion:** Widely varying etiology and clinical presentation makes early diagnosis by renal biopsy critical to properly categorize the disease and direct subsequent clinical approach in adults.

Key words: Nephrotic syndrome; Oliguria; Edema; Albuminuria

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v13i11.47525

E-ISSN: 2091-0576

P-ISSN: 2467-9100

Copyright (c) 2022 Asian Journal of Medical Sciences

This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

INTRODUCTION

Nephrotic syndrome is defined as a pentad of proteinuria >3.5 g/1.73 m^2 of body surface area/day or >50 mg/kg/day, hypoalbuminemia (<2.5 g/dl), edema, hyperlipidemia (serum cholesterol >200 mg/dl), and lipiduria. The annual incidence of nephrotic syndrome in adults is three per 100,000 persons. Approximately 80–90% of nephrotic syndrome cases in adults are idiopathic. Membranous nephropathy is the most common cause in whites, and focal segmental glomerulosclerosis (FSGS) is most common in blacks; each of these disorder accounts for approximately 30–35% of nephrotic syndrome in adults. Minimal change disease (MCD) and immunoglobulin A nephropathy each account for approximately 15% of cases. The remaining 10% of cases are secondary to an underlying medical condition.[1] The etiology of MCD and of FSGS is unknown although there have been hints over the years that an immune mechanism may be involved, at least in MCD. Clinical observations suggesting an immune mechanism are an association of the disease onset and of relapses with upper respiratory illnesses, bee stings,

Address for Correspondence:
Dr. Sayan Choudhury, Senior Resident, Department of General Medicine, Ramakrishna Mission Seva Pratishthan, Vivekananda Institute of Medical Sciences, Kolkata, West Bengal, India. **Mobile:** +91-8016681415. **E-mail:** sayanchoudhry78@gmail.com

insect bites, and poison ivy, dermatitis, the increased occurrence of atopic symptoms in patients with MCD, and the response to immunosuppressive agents such as steroids, cyclophosphamide, chlorambucil, and nitrogen mustard. The presenting features are edema which is either generalized or localized, gastrointestinal disturbances such as diarrhea and abdominal pain, respiratory difficulty either from abdominal distension with or without pleural effusion. Physical findings include hepatomegaly, ascites, pleural effusion, and hypertension (less common). Diagnosis is confirmed in the background of the clinical features by blood examination showing serum hypoalbuminemia (<2.5 g/dl),[2] hypercholesterolemia (>200 mg/dl)[3], and urine examination showing heavy (3+ or 4+) proteinuria, 24 h urinary protein >3.5 g/1.73 m^2 of body surface area. In adults, nephrotic syndrome comprises a diverse group of diseases, with considerable demographic, socioeconomic, geographic area, and race variation, including both primary and secondary conditions. For this reason, early kidney biopsy is critical to properly categorize the disease and direct subsequent clinical approach in adults. In a study from Nepal by Subedi et al.,[4] the most common etiology of nephrotic syndrome was FSGS (26.62%) followed by MN (24.5%), mean age of study population was 35.37 (standard deviation:13.52) years with female: male ratio of 1.5:1. The study of Najam-ud-Din et al.,[5] in Peshawar reported that all (100%) patients had edema, 43.20% had oliguria, 17.28% presented with abdominal tenderness, 15.22% patients had fever, 13.16% showed hematuria, 10.28% patients had uremia, and 2.5% of the patients had thrombosis.

With this background in mind, this study was initiated with the aim to know the clinical presentation, laboratory abnormalities, histopathological spectrum of adult nephrotic syndrome, and its changing trends compared to previous studies.

Aims and objectives

The aim of the study was to know the clinical presentation, laboratory abnormalities, histopathological spectrum of adult nephrotic syndrome, and its changing trends.

MATERIALS AND METHODS

This observational cross-sectional study included 50 cases of biopsy proven nephrotic syndrome admitted in the Department of General Medicine of Vivekananda Institute of Medical Sciences, Ramakrishna Mission Seva Pratishthan, Kolkata, from March 2020 to February 2021. The study was conducted after obtaining permission from the Institutional Ethics Committee. Patients who were above 12 years, having suggestive features of nephrotic syndrome on the basis of history, clinical assessment, and confirmatory laboratory work up (urine routine examination, liver function test, lipid profile, viral serology, 24 h urinary protein, renal biopsy followed by histopathological examination and immunofluorescence [IF]) were included while cases with infective condition such as UTI, bleeding diathesis and pregnant patients were excluded from the study. After taking informed consent, data collection was done by proper history taking (interview questionnaire) and by relevant laboratory reports later on. The ethical clearance was obtained from the Institutional Ethics Committee. Kidney biopsy was performed in the prone position. Lower pole of the left kidney was preferred to reduce the risk of inadvertent injury to a major vessel. Automatic 18-gauge spring loaded biopsy guns were used to perform renal biopsy and biopsies were usually performed after ultrasound marking or under real-time, ultrasound guidance under local anesthesia with light sedation with ketamine and midazolam. Biopsy samples were called adequate if two cylinders with a minimal length of 1 cm and a diameter of at least 1.2 mm were obtained and it contained at least 5 glomeruli. The biopsy material was subjected to histopathology with hematoxylin and eosin stain and IF. IF examination was done by direct method using fluorescein isothiocyanate conjugated antibodies against immunoglobulin G, A, and M, complement C3, C1q, kappa, and lambda light chains.

Statistical analysis

Categorical variables were expressed as number of patients and percentage of patients and compared, if required, using Pearson's Chi-Square test for Independence of Attributes/Fisher's Exact Test as appropriate. Continuous variables were expressed as Mean±Standard Deviation and compared using unpaired t test/One-Way ANOVA if the data followed normal distribution or Median and Interquartile Range and compared using Mann–Whitney U test/Kruskal–Wallis Test if the data did not follow normal distribution. Association between continuous variables was captured by Pearson's Correlation Coefficient, if the data followed normal distribution or Spearman's Rank Correlation Coefficient if the data did not follow normal distribution. The statistical software SPSS version 22 has been used for the analysis. An alpha level of 5% has been taken, that is, if any $P<0.05$ it has been considered as significant.

RESULTS

In our study, maximum (15) patients including five males and ten females belonged to the age group of 21–30 years, 12 patients (five males and seven females) were within 31–40 years, nine patients (seven males and

two females) were within 41–50 years with 8 patients (five males and three females), and six patients (five males and one female) within the age group of ≤20 years and 51–60 years, respectively (Table 1). As a whole, the mean age of patients was 34.56±12.033 years with 27 (54%) male participants and 23 (46%) females. The male to female ratio was 1.17:1.

We found that oliguria was the most common presentation while none had hematuria. 16 (32%) patients had similar swelling in the past and 1 (2%) patient had a past skin infection with no patient having a history of sore throat (Table 2).

On clinical examination, all 50 (100%) patients had facial puffiness while 45 (90%) patients had both generalized swelling and pedal edema and 32 (64%) patients had ascites. Hypertension was present in 11 (22%) patients including 2 newly diagnosed hypertensive patients. Scrotal/vulval/sacral edema was found in 8 (16%) patients (Table 3).

The most predominant renal biopsy variety was found to be FSGS, seen in 27 (54%) patients followed by MCD in 14 (28%) patients, 1 (2%) patient had focal proliferative and diffuse sclerosing Immunoglobulin (IgA) Nephropathy, 2 (4%) patients had MGN, and 2 (4%) patients had Membranoproliferative glomerulonephritis (MPGN). Lupus nephritis (LN) was seen in 4 (8%) patients among which 1 (2%) each belonged to classes I, II, III, and V. (Table 4).

Table 1: Age and sex distribution of the study population (n=50)

Sex	Age range (years)					
	≤20	21–30	31–40	41–50	51–60	Total
Male	5	5	5	7	5	27
Female	3	10	7	2	1	23
Total	8	15	12	9	6	50

Table 2: Frequency of different presenting illnesses in the study population

Presenting illness	Frequency	Percentage
Decreased urine output	37	54.0
Fever	5	10.0
Diarrhea	0	0.0
Breathlessness	2	4.0
Upper respiratory tract infection	0	0.0
Pneumonia	1	2.0
Cellulitis	2	4.0
Other infection	2	4.0
Features of cancer	0	0.0
Autoimmune disease	4	8.0

44 (88%) patients had Primary glomerular disease (PGD) and 6 (12%) patients had secondary glomerular disease (SGD) (Table 5).

The most common type of PGD and SGD was FSGS (59.09%) and LN (4%), respectively (Figure 1).

FSGS was the most common biopsy type in both males and females while LN was exclusively found in the female population (Figure 2).

While considering 24 h urinary protein, LN patients had the maximum proteinuria (mean 4.53 g/d) closely followed by FSGS (mean 4.51 g/d) and MCD had the minimum (mean 3.64 g/d) proteinuria (Figure 3).

Table 3: Frequency of clinical examination findings in the study population

Examination finding	Frequency	Percentage
Generalized swelling	45	90.0
Facial puffiness	50	100.0
Ascites	32	64.0
Pedal edema	45	90.0
JVP engorgement	2	4.0
Pleural effusion	20	40.0
Pericardial effusion	2	4.0
Organomegaly	7	14.0
Pallor	15	30.0
Hypertension	11	22.0
Skin rash/Pustule	4	8.0
Scrotal/vulval/sacral edema	8	16.0

Table 4: Frequency of different renal biopsy variety in the study population

Renal Biopsy	Frequency	Percentage
Focal Proliferative and diffuse sclerosing IgA Nephropathy	1	2.0
FSGS	27	54.0
LN, class III	1	2.0
LN, class I	1	2.0
LN, class II	1	2.0
LN, class V	1	2.0
MCD	14	28.0
MGN	2	4.0
MPGN	2	4.0
Total	50	100.0

IgA: Immunoglobulin A, FSGS: Focal segmental glomerulosclerosis, LN: Lupus nephritis, MCD: Minimal change disease, MGN- Membranous glomerulonephritis, MPGN: Membranoproliferative glomerulonephritis

Table 5: Type of glomerular disease in the study population

Glomerular disease	Frequency	Percent
PGD	44	88.0
SGD	6	12.0
Total	50	100.0

PGD: Primary glomerular disease, SGD: Secondary glomerular disease

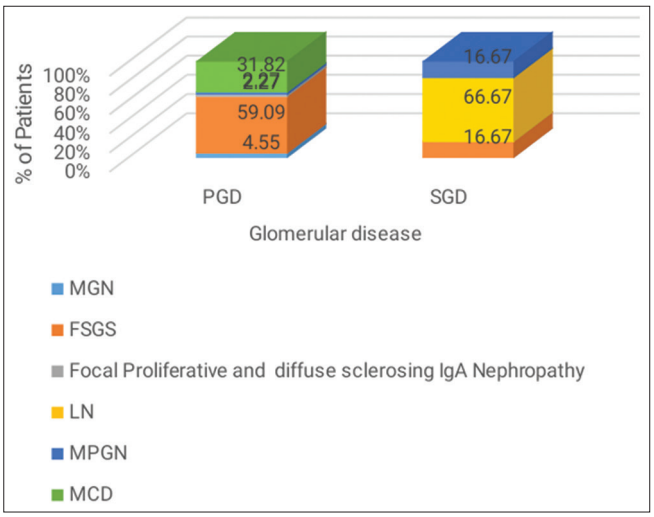

Figure 1: Correlation between type of glomerular disease and renal biopsy variety

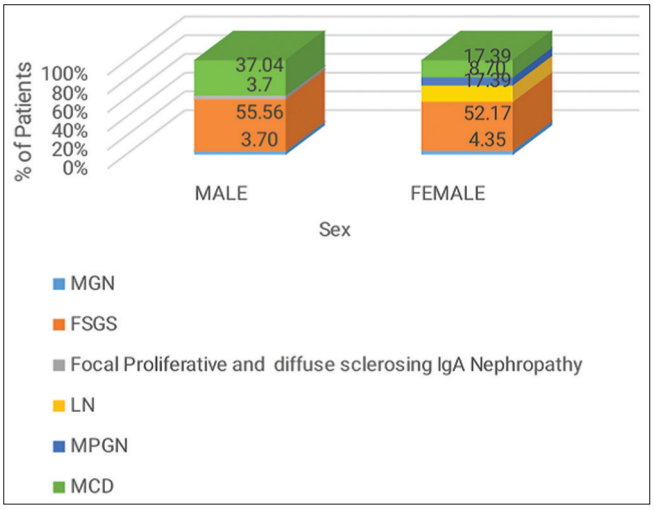

Figure 2: Correlation between sex of the patient and renal biopsy

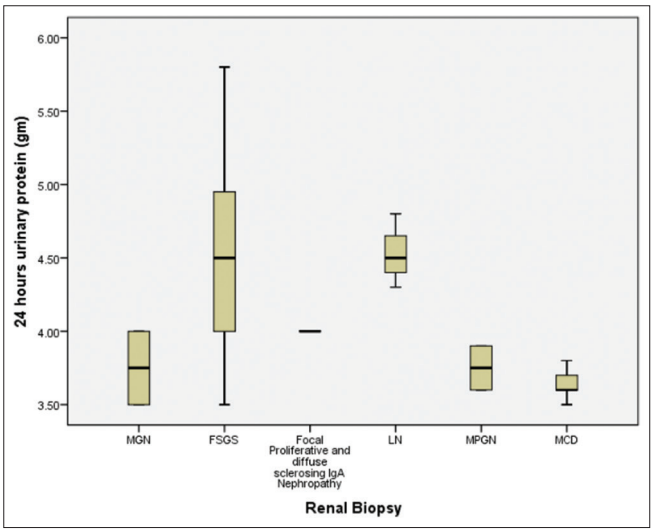

Figure 3: Distribution of maximum and minimum protein associated with each renal biopsy type

DISCUSSION

A similar study by Basu et al.,[6] showed that the mean age of presentation for adult nephrotic syndrome was 34±18.91 years and most (80.85%) patients were below 60 years of age. In the study by Golay et al.,[7] 57.8% patients were males and 42.19% patients were females with a male to female ratio of 1.37:1 with the average age at presentation of 33.68±13.88 years. In the study of Sarkar and Haque[8] they found hematuria in 25 (35%) patients and oliguria in 6 (8%) patients. Another study by Kshirsagar et al.,[9] had 36% patients with oliguria whereas microscopic hematuria was observed in 9.78% patients. In the study of Najam-ud-Din et al.,[5] 43.20% patients had oliguria, 15.22% patients had fever, 17.28% patients had abdominal tenderness with 13.16%, and 2.5% patients had hematuria and thrombosis, respectively. In the studies by Sarkar and Haque[8], Kshirsagar et al.,[9] and Najam-ud-Din et al.,[5] all (100%) patients had edema though the distribution of edema is not specifically mentioned in any of the studies. The studies of Sarkar and Haque[8] and Kshirsagar et al.,[9] had 36% and 26% hypertensive patients, respectively. In the study of Basu et al.,[6] MCD was the most common histological pattern constituting 38.29% with IgA nephropathy in 21.29% of cases, membranous GN in 14.89%, FSGS in 8.53%, LN in 10.63%, and diabetic nephropathy in 4.25%. Rathi et al.,[10] had studied the changing histologic spectrum of adult NS over 5 decades in north India and found that there was nearly five-fold increase in the incidence of FSGS. In the study of Golay et al.,[7] the most common histological lesions were FSGS (24.63%) followed by MCD (23.9%), MN (22.44%), IgA nephropathy (7.32%), and MPGN (6.83%). In the study by Basu et al.,[6] 85.12% patients had PGD, the most common pattern being MCD and 14.88% had SGD and most common pattern being LN. The study of Gopaliah et al.,[11] had 77.78% patients with PGD and 12.22% patients with SGD and the most common biopsy type in PGD and SGD was IgA nephropathy and diabetic nephropathy, respectively. In another study by Kshirsagar et al.,[9] the percentage of PGD and SGD was 78.3% and 21.77%, respectively, and the most common biopsy pattern in PGD and SGD was MCD and amyloidosis, respectively. In a similar study by Golay et al.,[7] 88.05% patients had PGD and 11.95% patients had SGD; the most common biopsy pattern in PGD and SGD being FSGS and LN, respectively. In the study by Konana et al.,[12] the most common histological type was MCD in both males (33.8%) and females (28.8%) whereas the study of Golay et al.,[7] showed FSGS to be the most common type in males (28.27%) and MCD being the most common type in females. In the study of Basu et al.,[6] LN showed female preponderance (M: F 4:1). The study of Kshirsagar

et al.,[9] showed that nephrotic syndrome associated with SLE was noted exclusively in females. In another study by Rathi et al.,[10] LN was found to be more common in females. In the study of Basu et al.,[6] membranous glomerulopathy had the highest proteinuria. The study results of Konana et al.,[12] showed MN patients exhibiting significantly increased daily proteinuria (gm/d) (median:9.5 IQR 6.6–12). Another study by Hertig et al.,[13] on 11 SLE patients having idiopathic nephrotic syndrome, all had mean proteinuria of 9.23±6 g/24 h. Hence, it is evident from the above discussion that oliguria was the commonest symptom and facial puffiness was the commonest finding present in all patients while most of the patient in the study population had either generalized of localized swelling. The most common type of renal biopsy was FSGS followed by MCD and small percentage of other types. PGD was more common than SGD, FSGS was the predominant lesion in both PGD and SGD as well as in both sexes, and LN was found exclusively in females. LN patients had a maximum 24 h urinary protein excretion followed by FSGS. The varied clinical, laboratory, and histopathological presentation of nephrotic syndrome could be due to considerable demographic, socioeconomic, geographic area, race, genetic, and environmental variation. The use of electron microscopy can explain the increased diagnosis of FSGS and MN, which are otherwise likely to be misdiagnosed as MCD. Early and proper histological diagnosis by renal biopsy can aid in better categorization and improved outcome in these patients.

Limitations of the study

The small sample size and inability to perform electron microscopy due to non-availability at our center and poor affordability of the patient population are the main limitations of the study. However, further large-scale studies are recommended to describe and compare the clinico-histopathological spectrum of nephrotic syndrome in different geographical areas.

CONCLUSION

1. Nephrotic syndrome in adults was more common in <40 years of age and among the male population.
2. Decreased urine output was the most common presenting illness.
3. Facial puffiness was the most predominant clinical finding closely followed by generalized swelling and pedal edema.
4. The most predominant renal biopsy variety was FSGS, followed by MCD.
5. PGD was more common than SGD.
6. FSGS was the predominant lesion in both PGD & SGD as well as in both sexes.
7. LN was found exclusively in females.
8. LN patients had a maximum 24 h urinary protein excretion followed by FSGS.

ACKNOWLEDGMENT

We wish to express our heartfelt gratitude to all who helped in completion of the study.

REFERENCES

1. Jenette JC and Mandal AK. The Nephrotic Syndrome. Diagnosis and Management of Renal Diseases and Hypertension. Durban NC: Carolina Academic Press; 1994.
2. Vogt BA and Avner ED. In: Behrman RE, Kliegman RM and Jenson HB, editors. Nephrotic Syndrome. Nelson Textbook of Pediatrics. 17th ed. Philadelphia: WB Saunders Company; 2004. p. 1753-1757.
3. Indian Pediatric Nephrology Group and Indian Academy of Pediatrics. Consensus statement on management of steroid sensitive nephrotic syndrome. Indian Pediatr. 2001;38(9):975-986.
4. Subedi M, Bartaula B, Pant AR, Adhikari P and Sharma SK. Pattern of glomerular disease and clinicopathological correlation: A single-center study from Eastern Nepal. Saudi J Kidney Dis Transpl. 2018;29(6):1410-1416.
   https://doi.org/10.4103/1319-2442.248302
5. Najam-ud-Din, Khan AZ, Shah SJ, Anwar N and Hakeem F. Clinical presentations of nephrotic syndrome in patients of a tertiary care hospital at Peshawar. J Ayub Med Coll Abbottabad. 2013;25(3-4):31-34.
6. Basu K, De S, Sengupta M, Karmakar S, Sircar S and Roychowdhury A. Histological spectrum of adult onset nephrotic syndrome in a tertiary care referral centre. IOSR J Dent Med Sci. 2019;18(1):66-70.
   https://doi.org/10.9790/0853-1801076670
7. Golay V, Trivedi M, Kurien AA, Sarkar D, Roychowdhary A and Pandey R. Spectrum of nephrotic syndrome in adults: Clinicopathological study from a single center in India. Ren Fail. 2013;35(4):487-491.
   https://doi.org/10.3109/0886022X.2013.768939
8. Sarkar A and Haque F. A Study on clinico pathological spectrum of nephrotic syndrome in adult patients in a teaching hospital in Eastern India. 2018;5(5):E55-E58.
   https://doi.org/10.21276/ijcmr.2018.5.5.41
9. Kshirsagar GR, Gadgil N, Margam S, Chaudhari C, Kumavat PV and Pagare S. Histopathological spectrum of adult nephrotic syndrome over 16 years at a tertiary care center in Mumbai with clinicopathological electron microscopy and immunoflurescence correlation of renal biopsies. Ann Pathol Lab Med. 2017;4(6):705-713
   https://doi.org/10.21276/APALM.1326
10. Rathi M, Bhagat RL, Mukhopadhyay P, Kohli HS, Jha V, Gupta KL, et al. Changing histologic spectrum of adult nephrotic syndrome over five decades in North India: A single center experience. Indian J Nephrol. 2014;24(2):86-91.
    https://doi.org/10.4103/0971-4065.127892
11. Gopaliah LR, Sudakaran I, Nalumakkal SV, Narayanan R and Vareed BM. Spectrum of biopsy-proven renal diseases: A single center experience. Saudi J Kidney Dis Transpl.

2018;29(2):392-400.
https://doi.org/10.4103/1319-2442.229295

12. Konana G, Varma V, Eswarappa M, Puri S, Mathihally G, Madhyastha R, et al. Histologic patterns of primary adult onset nephrotic syndrome and their clinical characteristics; A single center study from South India. J Nephropathol. 2017;6(4):304-308.
https://doi.org/10.15171/jnp.2017.49
13. Hertig A, Droz D, Lesavre P, Grünfeld JP and Rieu P. SLE and idiopathic nephrotic syndrome: Coincidence or not? Am J Kidney Dis. 2002;40(6):1179-84.
https://doi.org/10.1053/ajkd.2002.36875

Authors Contribution:
PC- Concept and design of the study, preparation of the first draft of the manuscript; **SM-** Concept and design of the study, interpretation of the results, and preparation of the manuscript; **SC-** Co-ordination, statistical analysis, review of the literature, and preparation of the manuscript; **SM-** Statistical analysis and interpretation, preparation, and revision of the manuscript.

Work attributed to:
Ramakrishna Mission Seva Pratishthan, Vivekananda Institute of Medical Sciences, Kolkata - 700 026, West Bengal, India.

Orcid ID:
Dr. Pradeep Chakraborty - https://orcid.org/0000-0003-4971-0305
Dr. Sujata Mazumdar - https://orcid.org/0000-0002-0175-3480
Dr. Sayan Choudhury - https://orcid.org/0000-0002-8622-806X
Dr. Shyamosree Mondal - https://orcid.org/0000-0003-2935-7911

Source of Funding: None, **Conflicts of Interest:** None.