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Malnutrition and inflammatory parameters in patients with chronic kidney disease stages 3–5 from northern India

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Abstract

Background: Malnutrition is highly prevalent in chronic kidney disease (CKD). This study is conducted to find out the prevalence of malnutrition and its association with inflammation in patients with CKD stages 3–5.

Method: This is a hospital-based cross-sectional study conducted at the Sri Ram Murti Smarak Institute of Medical Science, Uttar Pradesh, India. CKD stages 3–5 patients were included. The nutritional status was assessed by subjective global assessment (SGA). Anthropometric and biochemical measurements were also checked at the time of enrollment.

Results: A total of 213/354 (60.2%) of patients were malnourished. The triceps skinfold thickness (TSFT) was 8.2 ± 1.2 mm and 10.9 ± 1.2 mm in the malnourished and well-nourished groups, respectively; $p < 0.001$. TSFT was ≤ 10 mm in 91.1% of patients with malnutrition. Mid-arm muscle circumference (MAMC) was 21.3 ± 2.2 cm and 24 ± 2.9 cm, and the body mass index (BMI) was 19.8 ± 1.5 and 22.5 ± 1.4 kg/m² in the malnourished and well-nourished group, respectively; $p < 0.001$. A significant direct correlation between BMI, TSFT, MAMC, and eGFR was noted. Median eGFR was 11.9 ml/min/1.73 m² in the malnourished compared to 24.2 ml/min/1.73 m² in the well-nourished group; $p < 0.001$. Serum ferritin level was 246.77 ± 18.24 mg/L in the malnourished group, higher than the well-nourished group at 237.23 ± 16.13 mg/L; $p < 0.001$. CRP was elevated (> 0.6 mg/dl) in 53.5% patients with malnutrition; $p 0.003$.

Conclusions: Malnutrition is highly prevalent in the CKD population. The incidence increases as the eGFR decrease. $TSFT \leq 10$ mm compares favorably with SGA in detecting malnutrition (sensitivity $> 90\%$), and $BMI > 20$ kg/m² compares favorably with SGA in ruling out malnutrition (specificity 97%). Malnutrition and inflammation often coexist. Early detection and appropriate management are crucial.

Keywords: Chronic kidney disease, Malnourished, Estimated glomerular filtration rate, Mid-arm muscle mass circumference, Triceps skinfold thickness

Introduction

Malnutrition is frequent in patients with chronic kidney disease, with prevalence varying from 28 to 65% [1–5]. It affects the quality of life and is associated with increased mortality and morbidity [6–9]. Causes of malnutrition in

chronic kidney disease (CKD) patients include reduced food intake due to the effect of uremia, reduced absorption of nutrients from the oedematous gut, metabolic acidosis, increased protein loss during dialysis especially peritoneal dialysis, inflammation, oxidative stress, carbonyl stress, and hormonal disorders [10–13]. There is no single ideal or well-established laboratory method for the diagnosis of malnutrition in patients with CKD. In 1987, Detzky AS et al. [14] described a special methodology, named subjective global assessment (SGA) for

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the assessment of nutritional status. It is an easy and simple method of assessing nutritional status and does not require any additional laboratory testing [15, 16]. It has been found to strongly correlate with other subjective and objective measures of nutrition in patients with pre-dialysis CKD [17] and patients on hemodialysis [18] or peritoneal dialysis [19]. Malnutrition was found in 46% of CKD patients studied using the SGA criteria by Oladele CO et al. [20] A higher prevalence of 54.8% was observed in a similar study by Liman et al. [21], using the SGA. There is a paucity of data on the nutritional status of chronic kidney disease stages 3–5 in patients from northern India, necessitating this study.

Material and methods

This is a hospital-based cross-sectional study conducted in the Department of Nephrology, Sri Ram Murti Smarak Institute of Medical Science, Uttar Pradesh, India, from 1st October 2018 to 30th May 2020. Patients with chronic kidney disease stages 3–5 were included. Patients on dialysis, patients with nephrotic range proteinuria, and patients on steroids were excluded. CKD was defined as an estimated glomerular filtration rate < 60 ml/min/m² for more than 3 months. The estimated glomerular filtration rate (eGFR) was calculated using creatinine-based CKD-EPI (chronic kidney disease epidemiology collaboration formula) 2009. The nutrition status was assessed by subjective global assessment (SGA). SGA was performed by one observer for all the patients, and this was based on medical history and clinical examination. Medical history included an assessment of weight and weight change, dietary intake, gastrointestinal symptoms, and the patient's functional capacity related to nutritional status. Physical examination focussed on loss of subcutaneous fat and muscle wasting, the presence of edema, and ascites. Patients were classified into class A (well-nourished), B (mildly to moderately malnourished), and C (severely malnourished) depending on the results of medical history and physical examination. Anthropometric and biochemical measurements were also taken at the time of enrollment. These anthropometric variables can be measured by different methods including dual-energy X-ray absorptiometry or bioelectrical impedance analysis; however, conventional anthropometric measures in the form of body mass index (BMI), triceps skinfold thickness (TSFT), and mid-arm muscle circumference (MAMC) were used owing to financial constraints and nonavailability of these modalities at the study center. TSFT was measured in the midline of the posterior aspect of the arm, over the triceps muscle at the level, 1 cm proximal to the halfway between the acromion process and the olecranon process with the elbow flexed at 90°. A vertical fold of skin and subcutaneous

tissue were picked gently with the left thumb, and the tips of Harpenden caliper were applied perpendicular to the skinfold at the marked level. MAMC was measured using a measuring tape, midway between the olecranon process and the acromion. The left upper limb was used for the calculation of TSFT and MAMC in all the patients. Height was measured using a stadiometer, and weight was measured using a standard weighing scale to the nearest 0.1 kg. The study was approved by the hospital ethics committee.

Statistical analysis

Continuous variables are presented as mean \pm SD. Non-parametric data are expressed as median and range. The chi-square test is used to compare nonparametric categorical variables. Mann-Whitney *U*-test is used to compare nonparametric continuous variables. Statistics are done using IBM SPSS statistics for Windows version 25.

Results

Out of 354 patients included, 243 (68.6%), 47 (13.3%), and 64 (18.1%) belonged to CKD stage 5, stage 4, and stage 3, respectively. Two-hundred thirteen (60.2%) were malnourished as per SGA. A total of 168/213 (78.9%) belonged to stage 5 CKD. Stage 3 and stage 4 CKD accounted for 23/213 (10.8%) and 22/213 (10.3%) of all malnourished cases, respectively. Out of 213 malnourished patients, 118 (55.4%) were mild to moderately malnourished (class B), and 95 (44.6%) were severely malnourished (class C). Men and women accounted for 242/354 (68.4%) and 112/354 (31.6%), respectively. The mean age was 51.68 ± 5.21 years. Diabetes mellitus was the most common cause of CKD followed by hypertension and chronic glomerulonephritis accounting for 36.2%, 22%, and 19.5%, respectively. The male-to-female ratio in the malnourished group was approximately 2:1 (141:72); *p*-value 0.28. The mean age in the malnourished and well-nourished group was 51.5 ± 5.2 years and 51.9 ± 5.3 years, respectively; *p*-value 0.95. The triceps skinfold thickness (TSFT) was 8.2 ± 1.2 mm and 10.9 ± 1.2 mm in the malnourished and well-nourished groups, respectively; *p*-value < 0.001. TSFT was ≤ 10 mm in 194/213 malnourished patients corresponding to sensitivity of 91.1% in detecting malnutrition. There was a significant positive correlation between TSFT and eGFR; *p*-value < 0.001. Mid-arm muscle circumference (MAMC) was 21.3 ± 2.2 cm in the malnourished group versus 24 ± 2.9 cm in the well-nourished group; *p*-value < 0.001. Out of 161 patients with MAMC ≤ 22 cm, 126 (78.3%) were malnourished, and 35 (21.7%) were well-nourished; *p*-value < 0.001. There was a significant positive correlation between MAMC and eGFR; *p*-value = 0.005. The body mass index (BMI) in the

malnourished and well-nourished group was 19.8 ± 1.5 and 22.5 ± 1.4 kg/m², respectively; p -value < 0.001. Out of 141 well-nourished patients, 137 (97.2%) had BMI > 20 kg/m² corresponding to specificity of 97.2% in ruling out malnutrition. There was a significant direct correlation between BMI and eGFR; p -value 0.013. Serum triglyceride levels in the malnourished and well-nourished groups were 149.6 ± 15.3 and 138.01 ± 17.2 , respectively; p -value < 0.001. Median eGFR in the malnourished group was 11.9 ml/min/1.73 m² versus 24.2 ml/min/1.73 m² in the well-nourished group; p -value < 0.001. Serum ferritin level was 246.77 ± 18.24 mg/L and 237.23 ± 16.13 mg/L, respectively, in the malnourished and well-nourished group; p -value < 0.001. Serum albumin in the malnourished and well-nourished groups was 3.03 ± 0.64 mg/dl and 3.50 ± 0.56 mg/dl, respectively; p -value < 0.001. Hypoalbuminemia (serum albumin < 3.5 g/dl) was present in 153/213 (71.8%) of patients with malnutrition; p -value < 0.001. High sensitivity CRP was elevated (> 0.6 mg/dl) in 114/213 (53.5%) patients with malnutrition and 53/141 (37.6%) of well-nourished patients; p -value 0.003. Hemoglobin in the malnourished group and the well-nourished group was 7.74 ± 0.95 mg/dl and 8.84 ± 0.95 mg/dl, respectively; p -value < 0.001. Total protein in the malnourished group versus the well-nourished group was 4.8 ± 0.7 mg/dl and 5.0 ± 0.7 mg/dl, respectively; p -value = 0.005. In patients with eGFR ≤ 30 ml/min/1.73 m², 190/290 (65.5%) were malnourished, whereas in patients with eGFR > 30 ml/min/1.73 m², only 23/41 (36%) patients were malnourished. In patients with eGFR > 30 ml/min/1.73m², the difference in serum ferritin between the malnourished and well-nourished groups did not reach statistical significance. Baseline characteristics and the results are summarized in Tables 1, 2, 3, 4, and 5

Discussion

Malnutrition in CKD is not entirely explained by reduced nutritional intake. A delicate interplay of multiple factors, including hormonal imbalances, decreased appetite and food intake, inflammation, increased catabolism, nutrient losses in dialysate, and metabolic derangements, predispose chronic kidney disease patients to malnutrition. There is a paucity of data regarding the prevalence of malnutrition in patients with chronic kidney disease in India. This study highlights the prevalence of malnutrition in CKD stages 3–5 patients from a single center in North India. In our study, out of 354 patients, 213 (60.2%) were malnourished as per SGA criteria. Out of 213 malnourished patients, 118 (55.4%) were mild to moderately malnourished (class B), and 95 (44.6%) were severely malnourished (class C). This is similar to the previously reported prevalence of 28 to 65% [1–5]. A prevalence of

Table 1 Baseline characteristics

Characteristic	Mean ± SD
Age (years)	51.68 ± 5.21
BMI (kg/m ²)	20.9 ± 1.9
eGFR (ml/min/1.73 m ²)	18.45 ± 14.34
TSFT (mm)	9.3 ± 1.8
MAMC (cm)	22.3 ± 2.8
Hemoglobin (g/dl)	8.2 ± 1.1
Total protein (g/dl)	4.8 ± 0.7
Serum albumin (g/dl)	3.2 ± 0.65
Serum iron ((mcg/dl))	61.2 ± 6.4
Serum ferritin ((ng/ml))	242.97 ± 18.03
TIBC (mcg/dl)	244.9 ± 82.4
Total cholesterol (mg/dl)	187 ± 10
LDL (mg/dl)	131.3 ± 8.6
HDL (mg/dl)	36.3 ± 2.3
TG (mg/dl)	251 ± 116.7

SD standard deviation, BMI body mass index, eGFR estimated glomerular filtration rate, TSFT triceps skinfold thickness, MAMC mid-arm muscle circumference, TIBC total iron-binding capacity, LDL low-density lipoprotein, HDL high-density lipoprotein, TG triglycerides

Table 2 Distribution of anthropometric and laboratory parameters between malnourished and well-nourished patients with chronic kidney disease

Characteristic	Malnourished	Well-nourished	p -value
Age (years)	51.5 ± 5.2	51.9 ± 5.3	0.95
BMI (kg/m ²)	19.8 ± 1.5	22.5 ± 1.4	< 0.001
BMI > 20 kg/m ²	74 (34.7%)	137 (97.2%)	< 0.001
eGFR (ml/min/1.73 m ²)	14.6 ± 11.4	24.2 ± 16.3	< 0.001
TSFT (mm)	8.2 ± 1.2	10.9 ± 1.2	< 0.001
TSFT ≤ 10 mm	194 (91.8%)	23 (16.3%)	< 0.001
MAMC (cm)	21.3 ± 2.2	23.9 ± 2.9	< 0.001
MAMC ≤ 22 cm	126 (68.9%)	35 (26.7%)	< 0.001
Hemoglobin (g/dl)	7.75 ± 0.95	8.8 ± 0.9	< 0.001
Total protein (mg/dl)	4.8 ± 0.72	5.0 ± 0.7	0.005
Serum albumin (g/dl)	3.03 ± 0.64	3.5 ± 0.6	< 0.001
Serum albumin ≤ 3.5 g/dl	153 (71.8%)	47 (33.3%)	< 0.001
Serum iron ((mcg/dl))	60.9 ± 6.45	61.8 ± 6.36	0.07
Serum ferritin ((ng/ml))	246.8 ± 18.2	237.2 ± 16.1	< 0.001
TIBC (mcg/dl)	243.02 ± 78.46	247.8 ± 88.2	0.91
HS-CRP ((> 0.6 mg/dl))	114/213 (53.5%)	53/141 (37.6%)	0.003
Total cholesterol (mg/dl)	187.8 ± 9.6	185.7 ± 10.5	0.09
LDL (mg/dl)	131.5 ± 8.9	131.04 ± 8.01	0.50
HDL (mg/dl)	36.2 ± 2.3	36.5 ± 2.4	0.36
TG (mg/dl)	149.6 ± 15.3	138.01 ± 17.2	< 0.001

BMI body mass index, eGFR estimated glomerular filtration rate, TSFT triceps skinfold thickness, MAMC mid-arm muscle circumference, TIBC total iron-binding capacity, HS-CRP high sensitivity C-reactive protein, LDL low-density lipoprotein, HDL high-density lipoprotein, TG triglycerides

Table 3 Distribution of anthropometric and laboratory parameters between well-nourished and malnourished CKD patients with eGFR ≤ 30 ml/min/1.73 m²

Characteristic	Malnourished (65.5%)	Well-nourished (34.5%)	p-value
Age (years)	51.6 \pm 4.9	52.3 \pm 4.9	0.63
BMI (kg/m ²)	19.9 \pm 1.5	22.5 \pm 1.4	< 0.001
TSFT (mm)	8.2 \pm 1.2	11.0 \pm 1.1	< 0.001
MAMC (cm)	21.2 \pm 2.3	23.9 \pm 2.9	< 0.001
Hemoglobin (g/dl)	7.8 \pm 1.0	9.0 \pm 0.9	< 0.001
Total protein (mg/dl)	4.8 \pm 0.7	5.0 \pm 0.7	0.03
Serum albumin (g/dl)	3.0 \pm 0.7	3.5 \pm 0.6	< 0.001
Serum ferritin ((ng/ml))	247.0 \pm 18.6	235.5 \pm 15.9	< 0.001
TG (mg/dl)	149.0 \pm 15.5	136.4 \pm 17.1	< 0.001

BMI body mass index, TSFT triceps skinfold thickness, MAMC mid-arm muscle circumference, TG triglycerides

Table 4 Distribution of anthropometric and laboratory parameters between well-nourished and malnourished CKD patients with eGFR > 30 ml/min/1.73m²

Characteristic	Malnourished (36%)	Well-nourished (64%)	p-value
Age (years)	50.5 \pm 6.8	51.0 \pm 6.0	0.67
BMI (kg/m ²)	19.8 \pm 1.5	22.5 \pm 1.4	< 0.001
TSFT (mm)	8.0 \pm 1.4	10.7 \pm 1.2	< 0.001
MAMC (cm)	21.9 \pm 1.5	24.0 \pm 2.7	< 0.004
Hemoglobin (g/dl)	7.7 \pm 0.5	8.4 \pm 0.8	< 0.001
Total protein (mg/dl)	4.5 \pm 0.5	5.0 \pm 0.8	0.008
Serum albumin (g/dl)	3.0 \pm 0.6	3.5 \pm 0.5	< 0.001
Serum Ferritin ((ng/ml))	245.2 \pm 15.5	241.5 \pm 16.1	0.71
TG (mg/dl)	154.4 \pm 12.2	142.0 \pm 17.0	< 0.001

BMI body mass index, TSFT triceps skinfold thickness, MAMC mid-arm muscle circumference, TG triglycerides

Table 5 Sensitivity and specificity of triceps skinfold thickness (TSFT) and body mass index (BMI) in detecting malnutrition

Characteristic	Malnutrition	Sensitivity/specificity
TSFT ≤ 10 mm	Yes 194/213	Sensitivity 91.1%
TSFT > 10 mm	No 118/141	Specificity 83.7%
BMI ≤ 20 kg/m ²	Yes 139/213	Sensitivity 65.3%
BMI > 20 kg/m ²	No 137/141	Specificity 97.2%

65% was shown by a study from eastern India by Prakash et al. [5] In our study, there was a male predominance in the malnourished group, with a male:female ratio of 141:72 (66.2% vs 33.8%). A similar finding was reported by Prakash et al. [5] who observed that 71% of malnourished CKD patients were men. A study by Peter Stenvinkel et al. [7] also showed male predominance with 61% of patients with CKD and malnutrition being men. This could be because men are more likely to seek medical attention than women. However, the role of hormonal factors could not be ruled out. In our study, there

was no statistical difference in age between the patients with malnutrition compared to those who were well-nourished. These findings were similar to the study done by Jai Prakash et al. [5] Diabetes mellitus was the most common cause of chronic kidney disease in our study followed by hypertension, chronic nondiabetic glomerulonephritis, and chronic tubulointerstitial nephritis. Similar results were shown by Kalantar-Zadeh et al. [22] The triceps skinfold thickness (TSFT) was significantly lower in the malnourished compared to the well-nourished groups (8.2 \pm 1.2 mm and 10.9 \pm 1.2 mm, respectively). TSFT was ≤ 10 mm in 91.1% patients with malnutrition and in 16.3% well-nourished patients; *p*-value < 0.001. This highlights the high sensitivity of TSAT ≤ 10 mm in detecting malnutrition. These findings were similar to Lawson J. A. et al. [1] and by Jai Prakash et al. [5] Mid-arm muscle circumference (MAMC) in the malnourished group was significantly lower compared to the well-nourished group (21.3 \pm 2.2 cm and 24 \pm 2.9 cm, respectively). Out of 161 patients with MAMC ≤ 22 cm, 126 (78.3%) were malnourished, and 35 (21.7%) were well-nourished; *p*-value < 0.001. This was similar

to the findings observed by Lawson J. A. et al. [1] and Jai Prakash et al. [5]. The body mass index (BMI) in the malnourished group was significantly lower (19.8 ± 1.5 versus 22.5 ± 1.4 kg/m²). These observations were similar to the study done by Jai Prakash et al. [5], Lawson J. A. et al. [1], and R. H. Mak et al. [23]. Out of 141 well-nourished patients, 137 (97.2%) had BMI > 20 kg/m². This suggests high specificity of BMI > 20 kg/m² in ruling out malnutrition. There was a statistically significant direct correlation between TSFT, MAMC, BMI, and eGFR. Median eGFR in the malnourished group was significantly lower than well-nourished group (11.9 ml/min/1.73 m² versus 24.2 ml/min/1.73m²; p -value < 0.001). In our study, 190/213 (89.2%) patients with malnutrition had eGFR < 30 ml/min/1.73m²; p -value < 0.001. Similar results were reported by Zimmerman J. et al. [24]. This reveals that the incidence of malnourishment increases with deteriorating renal function. Serum albumin in the malnourished and well-nourished groups was 3.03 ± 0.64 mg/dl and 3.50 ± 0.56 mg/dl, respectively; p -value < 0.001. Similar findings were reported by Emmanuel I. Agaba et al. [25] and by Jai Prakash et al. [5]. Pre-dialysis hypoalbuminemia has also been found to be a strong predictor of mortality in CKD patients undergoing maintenance dialysis [8, 26–28]. The low level of serum albumin is also reported as a marker of malnutrition [25, 29, 30]. Hemoglobin in the malnourished group was significantly low compared to the well-nourished group (7.74 ± 0.95 mg/dl and 8.84 ± 0.95 mg/dl, respectively; p -value < 0.001). Similar trends were observed by the studies of Emmanuel I. Agaba et al. [25] and Lowrie E. G. et al. [26]. In our study, serum triglyceride (TG) was the only significant parameter found to be increased in malnourished CKD patients as compared to the well-nourished group (149.59 ± 15.28 vs $138. \pm 17.23$ mg/dl, p < 0.001). Similar observations were made by Emmanuel I. et al. [25] and Jai Prakash et al. [5]. The presence of increased serum TG levels further heightens the already increased cardiovascular risk in malnourished CKD patients. In our study, serum cholesterol was not statistically different between the malnourished and the well-nourished group. In the subgroup analysis of patients with eGFR \leq 30 ml/min/1.73 m² and > 30 ml/min/1.73m², the anthropometric indices in the form of TST, MAMC, and BMI and the laboratory indices in the form of hemoglobin, total protein, and albumin were significantly lower in the malnourished group in comparison with the well-nourished group.

Renal failure contributes to inflammation as a result of the accumulation of pro-inflammatory compounds and a decrease in the activity of superoxide dismutase, and glutathione peroxidase leading to increased oxidative stress and decreased antioxidative activity [31]. High sensitivity

CRP was elevated (> 0.6 mg/dl) in 114/213 (53.5%) patients with malnutrition and 53/141 (37.6%) of well-nourished patients; p -value 0.003. Similar observations were made in the study by Jai Prakash et al. [5] in which 83/131 (63%) malnourished patients had elevated CRP compared to 24/72 (33%) in the well-nourished group. Serum ferritin level was 246.77 ± 18.24 mg/L and 237.23 ± 16.13 mg/L, respectively, in the malnourished and well-nourished group, p -value < 0.001. Similar observations were made by Jai Prakash et al. [5]. Serum ferritin and CRP are the markers of inflammation and are significantly elevated in malnourished CKD patients. Serum albumin is also considered a negative phase reactant, and low serum albumin in CKD is thought to be a marker of inflammation than malnutrition. In patients with eGFR > 30 ml/min/1.73 m², the difference in serum ferritin between the malnourished and the well-nourished group did not reach the statistical difference. This suggests that ferritin as an inflammatory marker becomes more important with eGFR \leq 30 ml/min/1.73 m². However, this needs to be reproduced in a bigger study.

This study has certain limitations. It is a single-center hospital-based study and does not reflect the true prevalence of malnutrition in CKD patients in the community. The majority of patients belonged to CKD stage 5 which might be the reason for the very high prevalence of malnutrition in our study group. The high sensitivity of TSFT \leq 10 mm and high specificity of BMI \geq 20 kg/m² need to be reproduced in a bigger study.

Conclusions

Malnutrition is highly prevalent in the pre-dialysis CKD population. The incidence increases with the decrease in eGFR. TSFT \leq 10 mm compares favorably with SGA in detecting malnutrition (sensitivity > 90%), and BMI > 20 kg/m² compares favorably with SGA in ruling out malnutrition (specificity 97%). Malnutrition and inflammation often coexist. Early detection and appropriate management are needed.

Abbreviations

TSFT: Triceps skinfold thickness; MAMC: Mid-arm muscle circumference; BMI: Body mass index; SGA: Subjective global assessment; CRP: C-reactive protein; eGFR: Estimated glomerular filtration rate.

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Authors' contributions

RS, HS, NB, and IW contributed to the design and development of the study. RS and NB contributed to data collection. RS, HS, NB, and IW contributed to data analysis and interpretation. RS, HS, NB, and IW participated in the writing of the manuscript. RS and IW participated in the critical review. RS, HS, NB, and IW provided approval for the final manuscript. The authors read and approved the final manuscript.

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Availability of data and materials

Data and material will be available on request.

Declarations**Ethics approval and consent to participate**

The study is approved by the institutional ethics committee of the Shri Ram Murli Smarak Institute of Medical Sciences under reference no. SRMSIMS/IEC/2018-19/551 dated 26th September 2018. Since this is an observational study, the consent to participate has been waived off by the ethics committee of the Shri Ram Murli Smarak Institute of Medical Sciences.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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