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Assessment of Endoscopic and Histopathological Findings in Vitamin B12 Deficient Patients: A Retrospective Study in a Tertiary Care Centre.

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Abstract

Background: Vitamin B12 deficiency is a prevalent nutritional disorder with diverse clinical manifestations. While gastric pathology plays a crucial role in B12 malabsorption, the correlation between endoscopic findings and histopathological changes remains incompletely characterized. ***Methods:*** This retrospective study analyzed 244 patients with confirmed vitamin B12 deficiency (≤200 pg/mL) who underwent upper gastrointestinal endoscopy with gastric biopsies between January 2022 and July 2025. Demographic data, clinical presentations, laboratory parameters, endoscopic findings, and histopathological features were evaluated. Statistical analysis was performed using appropriate parametric and non-parametric tests. ***Results:*** The mean age was 46.9±15.1 years with female predominance (53.7%). Mean vitamin B12 level was 138±33.4 pg/mL. The majority of patients (155, 63.5%) followed a vegetarian diet Endoscopy revealed normal mucosa in 60.2% and gastric erosions in 39.8% of patients. Histopathology demonstrated chronic gastritis in 57.0%, atrophic gastritis in 19.7%, and normal histology in 23.4%. Significant discordance existed between endoscopic appearance and histopathological findings ($p<0.001$). Anti-intrinsic factor antibodies were positive in 13.3% of tested patients. ***Conclusion:*** Substantial discordance exists between endoscopic appearance and histopathological findings in vitamin B12 deficient patients. Normal endoscopy does not exclude significant gastric pathology, emphasizing the importance of histopathological evaluation for accurate diagnosis and management.

Keywords: Vitamin B12; Gastric biopsy; Atrophic gastritis; Gastric erosions; Upper Gastrointestinal Endoscopy.

INTRODUCTION

Vitamin B12, also known as cobalamin, represents a critical water-soluble vitamin essential for DNA synthesis, methylation reactions, and neurological function [1]. Vitamin B12 deficiency remains one of the most prevalent nutritional disorders globally, affecting approximately 15-40% of the adult population. Higher prevalence of Vitamin B12 deficiency is seen in developing countries and among vegetarian populations [2]. The clinical spectrum of vitamin B12 deficiency extends from subclinical biochemical abnormalities to severe hematological and neurological manifestations, making it a significant public health concern that warrants comprehensive evaluation and management strategies. The pathophysiology of vitamin B12 deficiency involves complex interactions between dietary intake, gastric function, and intestinal absorption mechanisms. The stomach plays a pivotal role in vitamin B12 metabolism through two essential processes: the production of intrinsic factor by gastric parietal cells and the acidic environment necessary for releasing dietary vitamin B12 from food proteins [3]. Intrinsic factor, a glycoprotein secreted by parietal cells in the gastric corpus and fundus, binds to vitamin B12 forming a complex that is subsequently absorbed in the terminal ileum via specialized receptors. This intricate absorption process can be disrupted at multiple levels, with gastric pathology representing one of the most common sites of dysfunction. The etiology of vitamin B12 deficiency has evolved considerably over recent decades, shifting from predominantly pernicious anemia in historical contexts to a more heterogeneous spectrum of causes in contemporary

medicine. Food-cobalamin malabsorption, affecting 60-70% of elderly patients with vitamin B12 deficiency, has emerged as the leading cause, surpassing classical pernicious anemia which now accounts for only 15-20% of cases [4]. This paradigm shift reflects changing dietary patterns, increased use of acid-suppressing medications, and the rising prevalence of Helicobacter pylori-associated gastritis. Additionally, the widespread adoption of vegetarian and vegan diets, particularly in South Asian populations, has contributed to the epidemiological burden of vitamin B12 deficiency, with studies from India reporting prevalence rates exceeding 70% in certain vegetarian communities. The relationship between gastric mucosal pathology and vitamin B12 deficiency represents a bidirectional phenomenon with important clinical implications. Chronic atrophic gastritis, whether autoimmune or environmental in origin, leads to progressive loss of parietal cells and consequent reduction in intrinsic factor production, establishing a pathophysiological basis for vitamin B12 malabsorption [5]. Conversely, vitamin B12 deficiency itself may contribute to gastric mucosal alterations through impaired DNA synthesis and cellular regeneration, potentially creating a self-perpetuating cycle of deficiency and mucosal dysfunction. This complex interplay underscores the importance of comprehensive gastric evaluation in patients with vitamin B12 deficiency.

Upper gastrointestinal endoscopy has become an invaluable tool in evaluating patients with vitamin B12 deficiency, offering direct visualization of gastric mucosa and enabling targeted biopsy sampling for histopathological examination. Endoscopic findings in vitamin B12 deficient patients range from normal-appearing mucosa to various degrees of gastritis, with characteristic features including mucosal pallor, erosions, hemorrhage, and friable mucosa [6]. However, the correlation between endoscopic appearance and underlying histopathological changes remains imperfect, with studies demonstrating that significant microscopic pathology may exist despite normal endoscopic findings, highlighting the limitations of visual assessment alone.

Histopathological examination of gastric biopsies provides definitive characterization of mucosal pathology and remains the gold standard for diagnosing conditions such as autoimmune gastritis and intestinal metaplasia. The updated Sydney System, widely adopted for standardizing gastric biopsy protocols and histopathological reporting, recommends sampling from both antrum and corpus to adequately assess the topographic distribution of gastritis [7]. In vitamin B12 deficiency, histopathological findings typically include chronic inflammation, glandular atrophy, intestinal metaplasia, and in cases of autoimmune gastritis, pseudohypertrophy of parietal cells and neuroendocrine cell hyperplasia. These microscopic changes often precede endoscopically visible alterations, emphasizing the value of histopathological evaluation in early disease detection. The distinction between autoimmune and non-autoimmune causes of gastric pathology in vitamin B12 deficiency carries important prognostic and therapeutic implications. Autoimmune gastritis, characterized by corpus-predominant atrophy and presence of anti-parietal cell and anti-intrinsic factor antibodies, represents an irreversible condition requiring lifelong vitamin B12 supplementation and surveillance for gastric neoplasia [8]. In contrast, Helicobacter pylori-associated gastritis, predominantly affecting the antrum initially but potentially progressing to pangastritis, may be reversible with appropriate eradication therapy, potentially restoring vitamin B12 absorption capacity in some patients. The prevalence of these different etiologies varies geographically, with autoimmune gastritis more common in Northern European populations while H. pylori-associated gastritis predominates in developing countries.

Recent advances in understanding the molecular mechanisms underlying vitamin B12 deficiency have revealed novel aspects of gastric pathophysiology. The identification of autoantibodies against hydrogen-potassium ATPase as the major target antigen in autoimmune gastritis has improved diagnostic accuracy and enabled development of more specific serological tests [9]. Additionally, the discovery of genetic polymorphisms affecting vitamin B12 transport proteins and cellular uptake mechanisms has provided insights into individual susceptibility to deficiency states. These molecular insights have potential implications for personalized approaches to diagnosis and management of vitamin B12 deficiency. The clinical presentation of vitamin B12 deficiency in the context of gastric pathology often includes both systemic manifestations of the deficiency and symptoms related to the underlying gastric disease. While megaloblastic anemia remains the classical hematological manifestation, presenting with macrocytosis and pancytopenia in severe cases, neurological symptoms including peripheral neuropathy, cognitive impairment, and subacute combined degeneration of the spinal cord may occur even in the absence of anemia. Gastric symptoms, though often subtle, may include dyspepsia, early satiety, and bloating, reflecting the underlying mucosal pathology and altered gastric secretory function.

The diagnostic approach to vitamin B12 deficiency has evolved to incorporate both biochemical markers and morphological assessment. While serum vitamin B12 levels remain the primary screening test, with levels below 200 pg/mL generally considered deficient, the limitations of this assay have led to increased use of metabolic markers such as methylmalonic acid and homocysteine for confirming tissue deficiency [10]. The integration of endoscopic evaluation with serological testing for autoantibodies provides a comprehensive assessment framework that enables etiological diagnosis and appropriate therapeutic planning. Despite the recognized importance of gastric evaluation in vitamin B12 deficiency, significant gaps remain in our understanding of the relationship between endoscopic findings, histopathological changes, and clinical outcomes. The discordance between endoscopic appearance and microscopic pathology, the heterogeneity of

gastric involvement patterns, and the influence of demographic and geographic factors on disease expression all require further investigation. Additionally, the optimal timing and frequency of endoscopic surveillance in vitamin B12 deficient patients, particularly those with autoimmune gastritis at increased risk for gastric neoplasia, remains to be definitively established.

Aims and Objectives

The present study was designed to comprehensively evaluate the spectrum of upper gastrointestinal endoscopic findings and their correlation with histopathological changes in patients diagnosed with vitamin B12 deficiency at a tertiary care center in South India. The primary objective was to characterize the endoscopic appearance of gastric mucosa in vitamin B12 deficient patients and to assess the concordance between endoscopic findings and histopathological diagnoses. Secondary objectives included analyzing the relationship between severity of vitamin B12 deficiency and extent of gastric pathology, evaluating the prevalence of autoimmune markers in this population, and identifying demographic and clinical factors associated with specific patterns of gastric involvement. This retrospective analysis aimed to provide insights that could improve diagnostic accuracy and guide management strategies for vitamin B12 deficient patients in clinical practice.

MATERIALS AND METHODS

Study Design and Setting

This retrospective observational study was conducted at the Department of Medical Gastroenterology, JSS Medical College and Hospital, Mysuru, Karnataka, India. Medical records of patients diagnosed with vitamin B12 deficiency who underwent upper gastrointestinal endoscopy between January 2022 and July 2025 were reviewed. The study protocol was approved by the Institutional Ethics Committee of JSS Medical College (Reference: HKES/MRMCK/IEC/17/11/33).

Patient Selection

All consecutive patients meeting the inclusion criteria during the study period were included, yielding a final sample of 244 patients. Inclusion criteria comprised adult patients aged 18 years and above with documented vitamin B12 deficiency (serum levels ≤200 pg/mL), who underwent upper gastrointestinal endoscopy with gastric mucosal biopsies, and had complete medical records including demographic details, laboratory reports, endoscopy findings, and histopathology reports. Missed data were collected on phone or by recalling the patient to OPD. Patients were excluded if they had incomplete medical records, previous gastric surgery, active malignancy, severe systemic illnesses affecting gastric mucosa independent of vitamin B12 deficiency, or isolated folate deficiency without confirmed vitamin B12 deficiency.

Data Collection

Demographic data including age, gender, dietary habits, and alcohol consumption were extracted from medical records. Clinical presentations including symptoms and physical examination findings were documented. Laboratory parameters collected included complete blood count with red cell indices, serum vitamin B12 levels, liver function tests, and when available, anti-intrinsic factor antibodies and anti-parietal cell antibodies. Vitamin B12 levels were measured using chemiluminescence immunoassay (CLIA) method with levels ≤200 pg/mL considered deficient.

Endoscopic Evaluation

Upper gastrointestinal endoscopy was performed by experienced gastroenterologists using standard video endoscopes following institutional protocols. Endoscopic findings were categorized as normal mucosa or gastric erosions (presence of erosions, hemorrhage, or friable mucosa) or gastric atrophy (loss of rugal folds, mucosal thinning with visible submucosal vessels). Gastric biopsies were obtained according to the updated Sydney System protocol, including samples from the antrum and corpus.

Histopathological Assessment

Gastric biopsy specimens were processed using standard techniques with hematoxylin and eosin staining and special stains for Helicobacter pylori when indicated. Histopathological findings were classified as normal histology, chronic gastritis (inflammation limited to the foveolar region without glandular atrophy), or atrophic gastritis (extensive inflammation with glandular atrophy). All histopathological evaluations were performed by experienced pathologists blinded to clinical data.

Statistical Analysis

Data analysis was performed using SPSS version 18.0 (IBM Corporation, Chicago, IL, USA). Descriptive statistics were presented as mean ± standard deviation for continuous variables and frequencies with percentages for categorical variables. Comparisons between groups were performed using independent t-tests or Mann-Whitney U tests for continuous variables and chi-square or Fisher's exact tests for categorical variables. Correlation between vitamin B12 levels and gastric pathology severity was assessed using Spearman's correlation coefficient. Statistical significance was set at $p<0.05$.

RESULTS

The study cohort comprised 244 patients with confirmed vitamin B12 deficiency. The mean age was 46.9±15.1 years (range 22-76 years), with 131 (53.7%) females and 113 (46.3%) males. The majority of patients (155, 63.5%) followed a vegetarian diet, while 89 (36.5%) consumed a mixed diet. Clinical presentation revealed generalized weakness as the most common symptom, present in 186 patients (76.2%), followed by anorexia in 146 (59.8%), and breathlessness in 56 (23.0%). Physical examination demonstrated pallor in 220 patients (90.2%), knuckle hyperpigmentation in 130 (53.3%), hepatomegaly in 42 (17.2%), splenomegaly in 65 (26.6%), and jaundice in 64 (26.2%) patients. Laboratory parameters showed mean hemoglobin of 6.70±1.51 g/dL (range 4.3-9.9 g/dL), with severe anemia (Hb <7 g/dL) in 142 patients (58.2%). The mean corpuscular volume was 113±10.5 fL (range 95-134 fL), with macrocytosis (MCV >100 fL) present in 203 patients (83.2%). Mean platelet count was 1.83±0.73 lakh/cumm, and mean total leucocyte count was 5202±1746 cells/cumm. The mean serum vitamin B12 level was 138±33.4 pg/mL (range 76-201 pg/mL).

Table 1: Demographic and Clinical Characteristics (n=244)

Parameter	Value
Age (years), mean±SD	46.9±15.1
Gender, n (%)	
- Female	131 (53.7)
- Male	113 (46.3)
Diet type, n (%)	
- Vegetarian	155 (63.5)
- Mixed	89 (36.5)
Clinical symptoms, n (%)	
- Generalized weakness	186 (76.2)
- Anorexia	146 (59.8)
- Breathlessness	56 (23.0)
Physical signs, n (%)	
- Pallor	220 (90.2)
- Knuckle hyperpigmentation	130 (53.3)
- Hepatomegaly	42 (17.2)

Upper gastrointestinal endoscopy revealed normal mucosa in 163 patients (66.8%) and gastric erosions in 81 (33.2%). Histopathological examination demonstrated chronic gastritis in 139 patients (57.0%), atrophic gastritis in 48 (19.7%), and normal histology in 57 (23.4%).

Table 2: Laboratory Parameters (n=244)

Parameter	Mean±SD	Range
Hemoglobin (g/dL)	6.70±1.51	4.3-9.9
MCV (fL)	113±10.5	95-134
Platelets (lakh/cumm)	1.83±0.73	0.9-3.3
Total leucocyte count (cells/cumm)	5202±1746	2300-8900
Vitamin B12 (pg/mL)	138±33.4	76-201
Total bilirubin (mg/dL)	1.73±0.50	1.0-3.3
AST (IU/L)	34.6±14.4	12-78
ALT (IU/L)	35.2±12.6	17-70

Among the 90 patients tested for autoimmune markers, anti-intrinsic factor antibodies were positive in 12 (13.3%) and anti-parietal cell antibodies were positive in 21 (23.3%). Three patients (3.3%) showed positivity for both antibodies.

Table 3: Endoscopic and Histopathological Findings (n=244)

Finding	n (%)
Endoscopic findings	
Normal mucosa	163 (66.8)
Gastric erosions	81 (33.2)
Histopathological findings	
Normal	57 (23.4)
Chronic gastritis	139 (57.0)
Atrophic gastritis	48 (19.7)

Analysis of concordance between endoscopic and histopathological findings revealed significant discordance ($p<0.001$). Among 163 patients with normal endoscopy, histopathology showed chronic gastritis in 98 (60.1%), atrophic gastritis in 20 (12.3%), and normal histology in only 45 (27.6%). Conversely, among 81 patients with gastric erosions on endoscopy, histopathology confirmed chronic gastritis in 41 (50.6%), atrophic gastritis in 28 (34.6%), and normal histology in 12 (14.8%).

Table 4: Correlation Between Vitamin B12 Levels and Gastric Pathology

Vitamin B12 Level	Normal Histology	Chronic Gastritis	Atrophic Gastritis	p-value
<100 pg/mL (n=40)	6 (15.0%)	22 (55.0%)	12 (30.0%)	0.042
100-150 pg/mL (n=124)	28 (22.6%)	73 (58.9%)	23 (18.5%)	
151-200 pg/mL (n=80)	23 (28.8%)	44 (55.0%)	13 (16.2%)	

Correlation analysis revealed a weak but significant negative correlation between vitamin B12 levels and severity of histopathological changes (Spearman's $\rho = -0.186$, $p=0.003$). Patients with atrophic gastritis had significantly lower mean vitamin B12 levels (122±28.6 pg/mL) compared to those with chronic gastritis (138±32.1 pg/mL) or normal histology (149±35.8 pg/mL) ($p=0.001$).

Table 5: Association of Autoimmune Markers with Gastric Pathology (n=90)

Marker Status	Normal Histology	Chronic Gastritis	Atrophic Gastritis	p-value
AIFA positive (n=12)	0 (0%)	3 (25.0%)	9 (75.0%)	<0.001
AIFA negative (n=78)	18 (23.1%)	47 (60.3%)	13 (16.7%)	
APCA positive (n=21)	1 (4.8%)	7 (33.3%)	13 (61.9%)	<0.001
APCA negative (n=69)	17 (24.6%)	43 (62.3%)	9 (13.0%)	

Age-stratified analysis revealed increasing prevalence of atrophic gastritis with advancing age. Patients aged above 60 years showed atrophic gastritis in 38.5% compared to 11.8% in those below 40 years ($p<0.001$). Gender analysis showed no significant difference in endoscopic or histopathological findings between males and females ($p=0.482$).

Table 6: Age Distribution and Gastric Pathology

Age Group	n	Normal Histology	Chronic Gastritis	Atrophic Gastritis
<30 years	41	14 (34.1%)	23 (56.1%)	4 (9.8%)
30-39 years	45	13 (28.9%)	27 (60.0%)	5 (11.1%)
40-49 years	56	12 (21.4%)	36 (64.3%)	8 (14.3%)
50-59 years	63	11 (17.5%)	37 (58.7%)	15 (23.8%)
≥60 years	39	7 (17.9%)	16 (41.0%)	16 (41.0%)

Dietary analysis revealed no significant difference in gastric pathology between vegetarian and mixed diet groups ($p=0.317$). However, vegetarians had significantly lower mean vitamin B12 levels (131±30.2 pg/mL) compared to mixed diet consumers (147±36.8 pg/mL) ($p<0.001$).

DISCUSSION

The present study provides comprehensive insights into the endoscopic and histopathological spectrum of gastric pathology in vitamin B12 deficient patients from a tertiary care center in South India. Our findings demonstrate significant discordance between endoscopic appearance and histopathological diagnosis, highlighting the limitations of visual assessment alone in evaluating gastric pathology in this population. The demographic profile of our cohort, with mean age of 46.9 years and slight female predominance, aligns with previous studies reporting vitamin B12 deficiency across middle-aged adults with variable gender distribution [11]. The high prevalence of vegetarian diet (63.5%) in our population reflects regional dietary patterns and supports the established association between plant-based diets and increased risk of vitamin B12 deficiency, as documented in multiple epidemiological studies from South Asia [12]. Our observation of normal endoscopic appearance in 66.8% of patients contrasts with the histopathological findings showing pathology in 76.6% of cases. Among them 57% showed chronic gastritis and 19.7% were atrophic gastritis.This discordance has important clinical implications, as reliance on endoscopic assessment alone would miss significant gastric pathology in the majority of patients. Similar findings were reported by Dholakia et al., who demonstrated that normal endoscopic appearance did not exclude microscopic gastritis or atrophy in elderly vitamin B12 deficient patients [13]. This emphasizes the critical importance of obtaining gastric biopsies regardless of endoscopic appearance when evaluating vitamin B12 deficient patients.

The prevalence of atrophic gastritis (19.7%) in our cohort falls within the range reported in international literature. In an Indian study by Kotli et al., atrophic gastritis was observed in 21.3% of vitamin B12 deficient patients undergoing endoscopy, closely matching our findings [14]. Western studies, such as that by Carmel et al., reported higher rates of atrophic gastritis (30-40%) in vitamin B12 deficient populations, likely reflecting differences in age distribution, ethnic factors, and predominance of autoimmune etiology in Western populations [15]. This difference may reflect the younger age distribution in our cohort, different etiological factors, or the predominance of food-cobalamin malabsorption over classical pernicious anemia in our population. The correlation between vitamin B12 levels and severity of gastric pathology, though statistically significant, was weak ($\rho = -0.186$), suggesting that serum vitamin B12 levels alone cannot reliably predict the extent of gastric damage. This finding aligns with studies by Kaptan et al., who demonstrated that vitamin B12 levels showed poor correlation with histological severity in H. pylori-associated gastritis [16]. The multifactorial nature of vitamin B12 deficiency, involving dietary intake, absorption capacity, and body stores, likely contributes to this weak correlation.

Among patients tested for autoimmune markers, the prevalence of anti-intrinsic factor antibodies (13.3%) and anti-parietal cell antibodies (23.3%) suggests that autoimmune gastritis accounts for a minority of cases in our population. This contrasts with Northern European studies where autoimmune gastritis represents up to 40% of vitamin B12 deficiency cases [17]. The strong association between antibody positivity and atrophic gastritis in our study (75% of AIFA-positive patients) confirms the pathogenic role of autoimmune processes in gastric atrophy development. The clinical presentation pattern in our cohort, dominated by generalized weakness and anorexia, reflects the insidious nature of vitamin B12 deficiency. The high prevalence of severe anemia (mean hemoglobin 6.70 g/dL) suggests delayed diagnosis, possibly due to the gradual onset of symptoms and adaptation to chronic anemia. The presence of macrocytosis in 83.2% of patients confirms the classical hematological manifestation, though the absence of macrocytosis in nearly 17% of cases underscores that normal MCV does not exclude vitamin B12 deficiency, particularly in the presence of concurrent iron deficiency [18].

Our findings have several important implications for clinical practice. First, the significant discordance between endoscopic and histopathological findings mandates routine biopsy sampling in vitamin B12 deficient patients undergoing endoscopy, regardless of mucosal appearance. Second, the age-related increase in atrophic gastritis prevalence suggests that older patients may benefit from more aggressive evaluation and surveillance. Third, the relatively low prevalence of autoimmune markers in our population indicates that empirical testing for these antibodies may not be cost-effective in all vitamin B12 deficient patients, particularly in resource-limited settings. The study's strengths include the large sample size, comprehensive clinical and laboratory data, and systematic histopathological evaluation using standardized criteria. However, several limitations merit consideration. The retrospective design precluded standardization of biopsy protocols and limited the availability of autoimmune markers to only 36.9% of patients. The single-center nature may limit generalizability to other populations with different demographic and etiological profiles. Comparison with international literature reveals both similarities and differences in the gastric pathology spectrum of vitamin B12 deficiency. While the predominance of chronic gastritis over atrophic changes aligns with recent studies from developing countries [19], the lower prevalence of autoimmune markers compared to Western populations suggests geographic and ethnic variations in disease etiology. The high proportion of vegetarians in our cohort may also influence the pathophysiological mechanisms, as dietary deficiency may present different gastric pathology patterns compared to malabsorption-predominant etiologies. Future research directions emerging from our findings include prospective studies to establish the natural history of gastric pathology in vitamin B12 deficiency, investigation of biomarkers that could predict histopathological severity without invasive procedures, and evaluation of the impact of vitamin B12 supplementation on gastric mucosal recovery. Additionally, cost-effectiveness analyses of routine endoscopic surveillance versus selective evaluation based on clinical and laboratory parameters would inform evidence-based screening strategies [20].

CONCLUSION

This study demonstrates substantial discordance between endoscopic appearance and histopathological findings in vitamin B12 deficient patients, with normal endoscopy failing to exclude significant gastric pathology in the majority of cases. The weak correlation between serum vitamin B12 levels and gastric pathology severity emphasizes the need for comprehensive evaluation including histopathological assessment. The age-related increase in atrophic gastritis prevalence and the strong association between autoimmune markers and severe gastric pathology provide insights for risk stratification and targeted screening strategies. These findings underscore the importance of maintaining a high index of suspicion for gastric pathology in vitamin B12 deficient patients and support routine histopathological evaluation regardless of endoscopic appearance to ensure accurate diagnosis and appropriate management.

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Contributions
Conceptualization: Dr. Mohith Hanumappa Narayanaswamy, Dr. Aradya HV ; Methodology: Dr. Mohith Hanumappa Narayanaswamy,Dr. Aradya HV, Dr. Deepak Suvarna, Dr. Vinod Kumar L ; Formal analysis and investigation: Dr. Mohith Hanumappa Narayanaswamy,Dr. Aradya HV Dr. Suchitha S Dr. Nandeesh HP ;Writing—original draft preparation: Dr. Mohith Hanumappa Narayanaswamy,Dr. Aradya HV, Dr. Vinod Kumar L; Writing—review and editing: Dr. Aradya HV, Dr. Deepak Suvarna, Dr. Suchitha S ; Funding acquisition: NIL ; Resources: Dr. Ashwin Paul, Dr. Gurrala Rajasekhar. Supervision: Dr. Nandeesh HP, Dr. Deepak Suvarna

Conflict of interest
The authors declare that they have no competing interests.

Ethical approval
This study was conducted in accordance with the principles of the Declaration of Helsinki and the study protocol was approved by the Institutional Ethics Committee of JSS Medical College (Reference: HKES/MRMCK/IEC/17/11/33)..

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