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Original Article

Pathology Section

# Conventional Adenomatous Polyps: Study of Histomorphological Features using a Novel Scoring System

ANVITA NILEKANI[1], BR VANI[2], ASMA SAMREEN[3], V SRINIVASA MURTHY[4]




## ABSTRACT

**Introduction:** Conventional adenomatous polyps are dysplastic proliferations that arise from the surface of the mucosa and grow in a top-down fashion. Dysplasia is graded as low-grade and high-grade using a two-tiered grading system.

**Aim:** To grade the dysplasia in conventional adenomatous polyps by applying a novel scoring system.

**Materials and Methods:** This cross-sectional study was conducted in the Department of Pathology, ESIC Medical College and Post Graduate Institute of Medical Science and Research (PGIMSR), Rajajinagar, Bengaluru, Karnataka, India. A total of 46 cases reported as conventional adenomatous polyps were reviewed from January 2020 to June 2022. A cytological grading system was applied, evaluating eight parameters consisting of architectural and cytological features. Each parameter was scored, resulting in a total score ranging from 8 to 24. The final diagnosis was determined based on the histological pattern and the total cytological score. The results were tabulated in an excel sheet and analysed using mean, standard deviation, percentage, and frequency tables. The relationship between the independent variables was evaluated using the Chi-square test. A p-value of less than 0.05 was considered significant.

**Results:** Out of the 46 cases, most presented in the 4th decade of life 12 (32.61%) cases. The mean age of presentation was 54.56±11.91 years (mean±SD) with a male to female ratio of 1.4:1. The most common site was the sigmoid colon 17 (36.96%) cases. There were 26 cases of low-grade dysplasia with a mean score of 9.1 and 20 cases of high-grade dysplasia with a mean score of 15.2. The most common type was tubular adenoma with low-grade dysplasia 24 (52.17%) cases and a mean cytological score of 9. The high-grade dysplasia in tubular adenomas 7 (15.22%) cases, tubulovillous adenomas 11 (23.19%) cases, and villous adenomas 2 (4.35%) cases had mean scores of 13.3, 15.2, and 18, respectively.

**Conclusion:** Dysplasia in adenomatous polyps is an independent risk factor for malignancy. The cytological scoring system helps in accurately diagnosing the grade of dysplasia and simplifies the process. The present study emphasises the need for objective criteria, paving the way for implementing relevant surveillance and clinical protocols.


**Keywords:** Adenomas, Dysplasia, Intestinal polyps, Villous adenoma

## INTRODUCTION

Colorectal Cancer (CRC) is one of the most common gastrointestinal malignancies worldwide. It ranks as the fourth most common cancer among men in India, according to data from the Global Cancer Observatory (GLOBOCAN) in 2020 [1]. The incidence of colon cancer has been consistently increasing across all Indian cancer registries, with annual increases ranging from 20% to 124% [2]. The International Agency for Research on Cancer (IARC) predicts that the global burden of CRC will rise by 56% between 2020 and 2040, resulting in over three million new cases per year [3]. Hereditary CRCs, such as Lynch syndrome, familial adenomatous polyposis coli, MYUTH (Mut Y glycosylase homologue)-associated polyps, and Li-Fraumeni syndrome, are characterised by adenomas occurring at a younger age. Most uncomplicated adenomas are asymptomatic, while symptomatic patients may present with occult bleeding, which can serve as a basis for screening tests [4]. Colonoscopy is the definitive screening method for detecting these adenomas and occult CRC. Polypectomy, followed by histopathological examination of the polyps, is crucial for reducing mortality and assessing the risk of cancer progression, as nearly all CRCs arise from adenomas [5]. Conventional adenomatous polyps are neoplastic in nature, representing dysplastic clonal proliferations of the epithelium [6]. Microscopically, they are classified into tubular adenomas (formerly known as adenomatous polyps), villous adenomas, and villotubular adenomas (formerly known as mixed or tuboglandular polyps) based on their architectural patterns [7]. Dysplasia within these polyps is further graded using the revised Vienna classification of gastrointestinal epithelial neoplasia, which employs a two-tiered system of low-grade and high-grade dysplasia [8]. These lesions hold diagnostic significance as they are established as premalignant lesions for CRC, primarily based on histopathological diagnosis. However, concerns have been raised regarding interobserver agreement among pathologists regarding histologic type and degree of dysplasia [9,10]. The kappa values were lowest for features such as nuclear shape, mitotic activity, and nucleolus [10]. The grading of dysplasia involves assessing various cytological and architectural parameters. Currently, there is no existing scoring system to grade the degree of dysplasia. The present study aimed to develop a simple yet effective scoring system that incorporates the assessment of all cytological and architectural features of conventional adenomatous polyps. Such a system is clinically significant as it can predict the severity and morbidity in patients.

## MATERIALS AND METHODS

The present is a cross-sectional study. The Department of Pathology at ESIC Medical College in Rajajinagar, Bengaluru, Karnataka, India, received a total of 46 cases of adenomatous polyps from January 2020 to June 2022. The study obtained approval from the Institutional Ethical Committee (No: 532/L/11/12/Ethics/ESICMC&PGIMSR/Estt. Vol-IV) and adheres to the Declaration of Helsinki.

**Inclusion and Exclusion criteria:** Inclusion criteria comprised all cases diagnosed as adenomatous polyps, while biopsies with insufficient tissue were excluded.

## Study Procedure

Demographic data, including age, sex, and polyp location, were retrieved from the patient request forms and files. Haematoxylin and Eosin (H&E) stained slides were reviewed, and the architectural pattern was classified according to the World Health Organisation (WHO) criteria, based on the percentage of villous architecture. Tubular adenoma was categorised as having less than 25% villous architecture, tubulovillous adenoma as having 25-75%, and villous adenoma as having ≥75% [11]. Cytological features were scored based on eight parameters, including cellular, architectural, and nuclear features, to determine the grade of dysplasia, as outlined in the WHO classification of digestive tract tumours [11]. These scores were further described in [Table/Fig-1].

| Parameters | Pattern | Score |
|---|---|---|
| Architectural pattern | Parallel | 01 |
| | Back to back | 02 |
| | Complex/budding | 03 |
| Nuclear pseudostratification | Lower half | 01 |
| | Luminal half | 02 |
| Mitotic activity | Mild (</=5 per 10 hpf) | 01 |
| | Moderate (6-10 per 10 hpf) | 02 |
| | Brisk/atypical (>10 per 10 hpf) | 03 |
| Nuclear polarity | Mild | 01 |
| | Moderate | 02 |
| | Severe | 03 |
| Pleomorphism | Mild | 01 |
| | Moderate | 02 |
| | Severe | 03 |
| Nuclear shape | Elongated | 01 |
| | Mixed | 02 |
| | Round | 03 |
| Nuclear chromatin | Hyperchromatic | 01 |
| | Mixed | 02 |
| | Open | 03 |
| Nucleoli | Not seen | 01 |
| | Small | 02 |
| | Large | 03 |

**[Table/Fig-1]:** The Cytological Scoring System.
HPF: High power field

All the cytomorphological features were scored for the topmost glands of a polyp as the dysplasia progresses in a top-down fashion.

1. **Architectural pattern:** Parallel glands arranged in a spaced manner were given a score of 1. Closely packed glands arranged in a back-to-back manner were given a score of 2. Complex architectural patterns with budding of glands were given a score of 3.
2. **Nuclear pseudostratification:** When the pseudostartification of the nucleus was limited to the lower half of the gland, it was scored 1. When it was seen in the luminal half, it was scored 2.
3. **Mitotic activity:** A cut-off of ≤5/10 hpf, 6-10/10 hpf, and >10/10 hpf was used to grade the mitotic activity as mild, moderate, and brisk.
4. **Nuclear polarity:** If 20% of glands showed loss of nuclear polarity, it was scored 1. If 20-40% showed loss of nuclear polarity, it was scored 2. If >40% of glands exhibited loss of nuclear polarity, it was scored 3.
5. **Pleomorphism:** Glands with nuclei of uniform size and regular nuclear border were given a score of 1. Glands with marked variation in size and irregular nuclear membrane were given a score of 3. Moderate variation was given a score of 2.
6. **Nuclear shape:** Predominantly elongated, penicillate-shaped nuclei were given a score of 1. Round-shaped nuclei were scored 3. If both shapes were seen, a score of 2 was given.
7. **Nuclear chromatin:** Unlike other neoplasia, hyperchromasia is not a sign of anaplasia in these polyps. The degree of anaplasia is determined by the openness of the chromatin. Nuclei with open chromatin were scored 3, while hyperchromatic nuclei were scored 1. Anything in between was given a score of 2.
8. **Nucleoli:** Absence of nucleoli was scored 1. Nucleoli of pinpoint size were given a score of 2. Nucleoli larger than this were scored 3.

A score ranging from 08-12 was considered as low-grade dysplasia, and 13-24 was considered as high-grade dysplasia, according to the revised Vienna classification [8]. The final diagnosis for each case was determined by considering the total cytological score and architectural pattern of tubular, tubulovillous, and villous polyps.

## STATISTICAL ANALYSIS

The results were analysed using mean, standard deviation, percentage, and frequency tables. The Chi-square test was used to evaluate the relationship between the independent variables. A p-value of less than 0.05 was considered significant.

## RESULTS

Among the 46 cases, 27 were male (58.67%) and 19 were female (41.33%), resulting in a male-to-female ratio of 1.4:1. The p-value of 0.08 suggests no statistical significance. The age range of patients was between 38 to 85 years, with a mean age of 54 years and a standard deviation of 11.9. The majority of patients (32.6%) fell into the 41-50 years age group. The most common location of the polyps was the sigmoid colon, accounting for 17 cases (27%). The transverse and descending colon each had 5 cases (11%). The demographic variables are described in [Table/Fig-2].

| Variables | n (%) |
|---|---|
| **Gender** | |
| Male | 27 (58.67%) |
| Female | 19 (41.33%) |
| Age (in years) | |
| <40 | 05 (10.87%) |
| 41-50 | 15 (32.61%) |
| 51-60 | 12 (26.08%) |
| 61-70 | 07 (15.22%) |
| >70 | 07 (15.22%) |
| **Location** | |
| Sigmoid colon | 17 (36.96%) |
| Transverse colon | 05 (10.87%) |
| Descending colon | 05 (10.87%) |
| Ascending colon | 02 (04.35%) |
| Unclassified colon | 09 (19.57%) |
| Rectum | 05 (10.87%) |
| Small intestine | 03 (06.51%) |

**[Table/Fig-2]:** Demographic variables.

The final diagnosis showed that 24 cases (52.17%) had tubular adenoma with low-grade dysplasia, with a mean score of 9. Seven cases (15.22%) had tubular adenoma with high-grade dysplasia, with a mean score of 13.3. Two cases (4.35%) had tubulovillous adenoma with low-grade dysplasia, with a mean score of 10, while 11 cases (23.91%) had tubulovillous adenoma with high-grade dysplasia, with a mean score of 15.2. Both cases of villous adenoma had high-grade dysplasia, with a mean score of 18 [Table/Fig-3].

| Final diagnosis | n (%) | Mean cytological score |
|---|---|---|
| Tubular adenoma, low-grade | 24 (52.17%) | 9.0 |
| Tubular adenoma, high-grade | 07 (15.22%) | 13.3 |
| Tubulovillous adenoma, low-grade | 02 (4.35%) | 10 |
| Tubulovillous adenoma, high-grade | 11 (23.91%) | 15.2 |
| Villous adenoma, high-grade | 02 (4.35%) | 18 |

**[Table/Fig-3]:** Final diagnosis based on cytological score for grade of dysplasia and architectural pattern.

Tubular adenoma with low-grade dysplasia was predominantly seen in the 51-60 years age group (29.17%) and most commonly located in the sigmoid colon (29.17%). Tubular adenoma with high-grade dysplasia was commonly observed in the 41-50 years age group (71.44%) and frequently located in the sigmoid colon (57.16%). The two cases of tubulovillous adenoma with low-grade dysplasia were seen in the 5th and 7th decades of life. One of these cases was located in the sigmoid colon, while the other was in the small intestine. Cases of tubulovillous adenoma with high-grade dysplasia were observed in the 4th and 5th decades of life (36.36%), most of which were located in the sigmoid colon (45.46%). Villous adenoma with high-grade dysplasia was seen in the 4th and 7th decades of life, as shown in [Table/Fig-4,5].

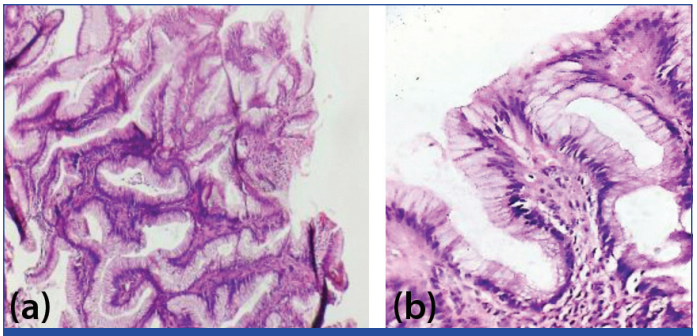
| Age group (in years) | Tubular adenoma, low-grade | Tubular adenoma, high-grade | Tubulovillous adenoma, low-grade | Tubulovillous adenoma, high-grade | Villous adenoma, high-grade |
|---|---|---|---|---|---|
| <40 | 04 (16.67%) | 01 (14.28%) | - | - | - |
| 41-50 | 05 (20.83%) | 05 (71.44%) | - | 04 (36.36%) | 01 (50%) |
| 51-60 | 07 (29.17%) | - | 01 (50%) | 04 (36.36%) | - |
| 61-70 | 05 (20.83%) | 01 (14.28%) | - | 02 (18.18%) | - |
| >70 | 03 (12.50%) | - | 01 (50%) | 01 (09.10%) | 01 (50%) |
| Total | 24 (100%) | 07 (100%) | 02 (100%) | 11 (100%) | 02 (100%) |

**[Table/Fig-4]:** Age distribution among the different types and grades of conventional adenomatous polyps.

| Site | Tubular adenoma, low-grade | Tubular adenoma, high-grade | Tubulovillous adenoma, low-grade | Tubulovillous adenoma, high-grade | Villous adenoma, high-grade |
|---|---|---|---|---|---|
| Sigmoid colon | 07 (29.17%) | 04 (57.16%) | 01 (50%) | 05 (45.46%) | - |
| Transverse colon | 02 (08.33%) | 01 (14.28%) | - | 02 (18.18%) | - |
| Descending colon | 03 (12.50%) | - | - | 02 (18.18%) | - |
| Ascending colon | 01 (04.17%) | 01 (14.28%) | - | - | - |
| Unclassified colon | 07 (29.17%) | - | - | 01 (09.09%) | 01 (50%) |
| Rectum | 02 (08.33%) | 01 (14.28%) | - | 01 (09.09%) | 01 (50%) |
| Small intestine | 02 (08.33%) | - | 01 (50%) | - | - |
| Total | 24 (100%) | 07 (100%) | 02 (100%) | 11 (100%) | 02 (100%) |

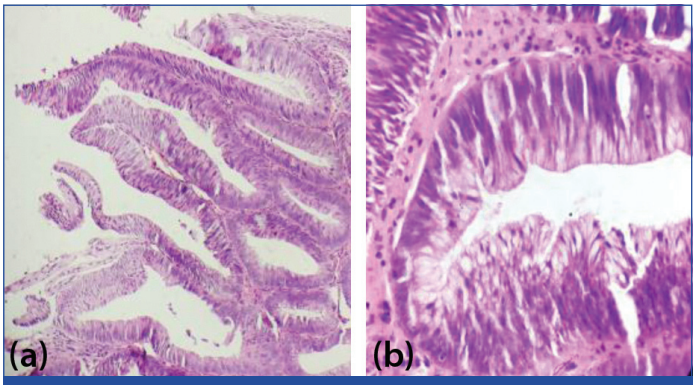
**[Table/Fig-5]:** Site distribution among the different types and grades of conventional adenomatous polyps.

A case of a polyp with a predominantly tubular pattern, back-to-back closely packed glands (02), nuclear pseudostratification limited to the lower half (01), without loss of nuclear polarity (01), <5 mitoses per 10 hpf (01), uniformly sized nuclei (01), elongated nuclei (01), hyperchromatic nuclei (01), and absence of nucleoli (01) was given a total score of 09. It was diagnosed as tubular adenoma with low-grade dysplasia [Table/Fig-6a,b].



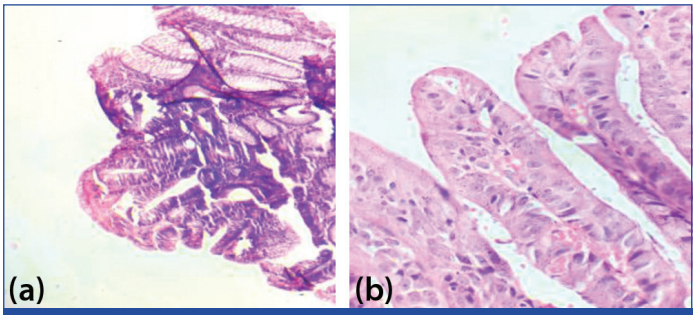

**[Table/Fig-6a,b]:** Tubular adenoma with low-grade dysplasia (H&E stained 10X and 40X) (Cytological score=9).

A case with predominantly villous architecture, back-to-back glands (02), nuclear pseudostratification extending to the upper half (02), 20-40% of glands showing loss of nuclear polarity (02), 6-8 mitoses/10 hpf (02), mild to moderate pleomorphism (02), predominantly elongated nuclei (01), hyperchromatic nuclei (01), and absence of nucleoli (01) was given a total cytological score of 13. The final diagnosis for present case was villous adenoma with high-grade dysplasia [Table/Fig-7a,b].




**[Table/Fig-7a,b]:** Villous adenoma with high-grade dysplasia (H&E stained 10X and 40X) (Cytological score=13).

A case with tubulovillous architecture, back-to-back architecture (02), nuclear pseudostratification extending to the upper half (02), 20-40% with loss of nuclear polarity (02), 8-10 mitoses/10 hpf (02), moderate pleomorphism (02), rounded nucleus (02), open chromatin (02), and prominent pinpoint nucleoli (02) was given a total score of 16 and diagnosed as tubulovillous adenoma with high-grade dysplasia [Table/Fig-8a,b].




**[Table/Fig-8a,b]:** Tubulovillous adenoma with high-grade dysplasia (H&E stained 10X and 40X) (Cytological score=16).

## DISCUSSION

Colorectal Cancer (CRC) typically arises from non cancerous protrusions of the mucosal epithelium lining, known as polyps. According to Fearon ER and Vogelstein B [12], polyps progress to cancer in a slow, multistep manner. They proposed a concept wherein genetic events, such as the inactivation of the APC gene in colonic cells, lead to mucosal proliferation and the development of early and late adenomas. The accumulation of these genetic events eventually leads to the development of colonic cancer [12]. This concept was supported by a study conducted by the Mayo Clinic group, where they followed a cohort of patients with

adenomatous polyps. The study showed an increased risk of malignant transformation over time: 2.5% risk after 5 years, 8% after 10 years, and 24% after 20 years. Hence, it is known that all sporadic adenomas harbor Adenomatous Polyposis Coli (APC) gene mutations. Additional Kristen Rat Sarcoma Viral Oncogene Homologue (KRAS) mutations are observed in some adenomas, particularly those with tubulovillous and villous architectural patterns [13].

Several literature studies have demonstrated good agreement in recognising adenomatous features, but there is less consensus regarding the assessment of histological type and grade of dysplasia. These studies found high interobserver variability, especially when it comes to moderate and high-grade dysplasia [10,14]. To address this concern, present study introduces a novel cytological scoring system to stratify and simplify the grading of dysplasia in adenomatous polyps.

In present study, there was a slight male predominance with a male-to-female ratio of 1.4:1. This finding aligns with other studies, such as Eshghi MJ et al., who reported a male-to-female ratio of 1.6:1, and Khanam T et al., who reported a ratio of 2.2:1 [5,15]. However, in present study and in the study by Eshghi MJ et al., the male predominance did not reach statistical significance [5].

Age is a major risk factor in adenomatous polyps. In present study, the mean age was 54±11.9 years, which is comparable to the study conducted by Eshghi MJ et al., who reported a mean age of 55.3 years [5]. Khanam T et al., reported a higher mean age of 60.2 [15]. The majority of cases were located in the sigmoid colon (37%), which is similar to the findings of Eshghi MJ et al., who reported a prevalence of 27.2% in that location [5]. A study by Konishi F and Morson BC noted that polyps with high-grade dysplasia were predominantly found in the left-side of the colon and rectum. These polyps exhibited an anatomic distribution pattern similar to that of colorectal cancer and frequently displayed chromosomal instability [16].

The present study describes eight parameters that can be used to grade dysplasia. The aim is to establish objective criteria for grading and reduce inter-observer variability in the assessment of histologic type and grade of dysplasia. Previous studies by Mollasharifi T et al., and Van Putten PG et al., on adenomatous polyps have shown only fair to moderate interobserver agreement in grading dysplasia [10,14]. Reproducibility of histopathological parameters has always been a concern. Some literature studies suggest a three-tiered system for grading dysplasia as mild, moderate, and severe. However, in present study, authors adopted the Vienna Two-tiered system of grading dysplasia, categorising the eight cytomorphological parameters to arrive at a cytological score. A score of ≤12 was considered low-grade dysplasia, while ≥13 was considered high-grade dysplasia. Applying this grading system, 27 out of the 46 cases had low-grade dysplasia with a mean cytological score of 9.1, and 19 cases had high-grade dysplasia with a mean score of 15.2.

The grading of dysplasia in adenomas, especially in the context of concurrent colorectal carcinoma, is of importance. A study by Morson B found that out of 38 cases of adenomas, four exhibited severe dysplasia and were removed during bowel resection for carcinoma. Additionally, five out of 21 adenomas with severe dysplasia developed a second or metachronous colorectal adenocarcinoma, which was present in the original operation specimens [17]. This suggests that in patients who have already undergone resection for colorectal carcinoma, the diagnosis of high-grade dysplasia in an adenomatous polyp may serve as a marker for an increased risk of developing a secondary adenocarcinoma.

The grading of dysplasia is a practical determinant of subsequent Colorectal Cancer (CRC) risk. The current guidelines by the American College of Gastroenterology (ACG) recommend a multi-step screening protocol, starting at 45 years of age for individuals with no family history. In individuals with a family history, screening should begin at 40 years or 10 years earlier than the youngest affected relative. It has been observed that the degree of cellular dysplasia is associated with the risk of a polyp harboring colorectal malignancy. The risk of a low-grade dysplasia polyp progressing to CRC is 6%, while polyps with high-grade dysplasia have a 35% risk of malignancy. Additionally, patient age is a factor in the risk of a polyp containing malignancy, with older patients being more likely to have a malignant polyp [18]. Adenomatous polyps with high-grade dysplasia require more aggressive colonic surveillance, typically once every three years [19]. Previous studies have not described a scoring system for grading dysplasia in adenomatous polyps. The present study considers various cytomorphological features and architectural patterns to arrive at the final score. It provides a reliable and efficient method for grading dysplasia with high accuracy and reproducibility. Early detection of high-grade adenomas offers an opportunity to reduce morbidity and choose an appropriate, less invasive, tailor-made surgical management.

### Limitation(s)

However, the study had limitations, including a smaller sample size and a lack of follow-up data. Conducting a study with a larger group of patients and long-term surveillance would be beneficial for further validation of the scoring system. Additional studies are needed to refine the risk stratification and establish precise diagnostic criteria. These efforts will contribute to reducing morbidity and mortality associated with adenomatous polyps.

## CONCLUSION(S)

The cytological scoring system aids in the accurate diagnosis of the grade of dysplasia and simplifies the process. It reduces the underdiagnosis of high-risk adenomas, which can result in inadequate colonic surveillance, as well as the overdiagnosis, which may lead to unnecessary surveillance, invasive procedures, and morbidity. Furthermore, early detection and management of high-grade adenomas are of utmost importance for cancer prevention.

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**PARTICULARS OF CONTRIBUTORS:**
1. Assistant Professor, Department of Pathology, ESIC Medical College and PGIMSR, Rajajinagar, Bengaluru, Karnataka, India.
2. Professor, Department of Pathology, ESIC Medical College and PGIMSR, Rajajinagar, Bengaluru, Karnataka, India.
3. Senior Resident, Department of Pathology, ESIC Medical College and PGIMSR, Rajajinagar, Bengaluru, Karnataka, India.
4. Professor and Head, Department of Pathology, ESIC Medical College and PGIMSR, Rajajinagar, Bengaluru, Karnataka, India.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**
Dr. BR Vani,
Professor, Department of Pathology, ESIC Medical College and PGIMSR, Rajajinagar, Bengaluru-560010, Karnataka, India.
E-mail: vanidr@yahoo.com

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