ORIGINAL RESEARCH PAPER

Pathology

# A STUDY ON HISTOPATHOLOGICAL GRADING OF COLORECTAL CARCINOMA IN A TERTIARY CENTRE

**KEY WORDS:** Colorectal carcinoma, Tumour stage, Nodal Metastasis, TNM Stage

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**ABSTRACT**

**Introduction:** Colorectal carcinoma is third most common cancer with incidence rate of 10.25 and mortality rate of 9.2%.It is an old age Malignancy, The changing trends with increasing incidence in young age due to life style modification.TNM stage and Nodal metastasis are important prognostic factors. Several studies indicate Grade as a stage independent prognostic factor. So our study aims to study its prognostic significance.

**Aims:** To study prognostic significance of the histopathological grade of tumour in correlation with Tumour stage, nodal metastasis and TNM stage.

**Materials and Methods:** Retrospective study of surgical resection 26 colorectal carcinoma cases with completed data was included. Data were collected from the Archive. They were studied for Grade, Tumour stage, Nodal metastasis and TNM stage .Statistical significance of the Grade is analyzed in correlation with Tumour, Nodal Metastasis and TNM stage using Chi square test.

**Results:** No Statistical significant correlation noted between Tumour stage and histopathological grade. But correlation between grade with Nodal metastasis and overall TNM Stage showed statistical significance with P valve of 0.035946 and 0.017751 respectively.

**Conclusion:** Nodal metastasis is a well known Independent prognostic factor in deciding adjuvant chemotherapy and clinical outcome. Our study showed significant correlation between the Histopathological grades with Nodal metastasis, it may also serve as additional prognostic factor.

## INTRODUCTION

Colorectal cancer is third most common cancer in the world. Its worldwide incidence is 10.2 % and the mortality rate is 9.2%.In India, it ranks fourth and fifth respectively in male and female. In male, incidence rate is 6.4% and mortality rate is 4.4%, in female it is 3.4% each[1].Highest incidence is reported in North America, followed by Australia, New Zealand and European countries. Among Asian countries, Japan has highest incidence due to change in their life style. Other countries like India, Africa, South America and South Central Asia has lower rate. Marked variation in incidence is due to various factors like dietary modification [2].

Majority of cases occur sporadically with few cases associated with familial syndrome and inflammatory bowel disease. Colorectal cancer is old age malignancy occurring after 5 th decade of life. Changing trends with increasing incidence in young age may be due to the changes in dietary habits and life style. Commonest site of occurrence is rectosigmoid region with encircling and annular type of growth in distal segments. Polypoidal and exophytic type of growth in the proximal colon [2].There are various prognostic factors such as tumour grade, lymphovascular invasion, perineural invasion, depth of invasion, tumour budding, nodal metastasis and TNM staging influence outcome [3-5], however nodal involvement remains one of the key deciding factor for adjuvant therapy [3]. Survival rate of nodal positive cases is 30 to 60% in comparison with 70 to 80 % survival in negative cases. Recurrence of 20 to 30 % is thought to be from occult nodal metastasis [4].

Both stage and nodal involvement has been well established as prognostic factors. Several multivariate analysis indicate the histopathological grade of tumour as stage independent prognostic factor [3].So our study aims to study the prognostic significance of histological grade in correlation with node metastasis and stage of the tumour.

## AIM

To study histopathological grade of colorectal cancer and its prognostic significant by correlate with nodal involvement, T stage and overall TNM stage.

## MATERIALS AND METHODS

26 cases of colorectal cancer patients who were operated between 2016 to 2018 at our institution were taken for this retrospective study. Surgical resected specimens with complete clinical data were included. Coloscopic biopsy, local resection and cases with preoperative neoadjuvant chemo or radiotherapy were excluded from this study.Datas were collected from Department of Pathology and Medical record department for past 3 years and were analyzed. Wax block collected from pathology laboratory. Sections were cut and slides were prepared using routine Hematoxylin and eosin stain. They were studied for histopathological type, grade, nodal metastasis and staged as per 8 th edition American Joint committee on Cancer guidelines [6]. Grade of tumour correlation with nodal metastasis, Tumour stage and TNM stage separately. Prognostic significant of histopathological Grade is analyzed by measuring P value using Chi square test by using Social Science Statistics calculator.

## RESULTS

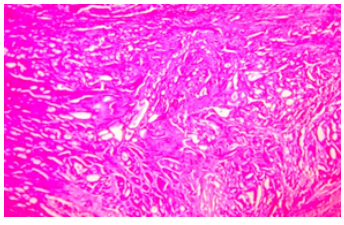
Out of 26 cases studied, 20 (76.9%) were male patients and 6 (23.1%) were female patients. 53.8%,11.5%,11.5% were well differentiated Adenocarcinoma (WDAC), moderately differentiated adenocarcinoma (MDAC), poorly differentiated adenocarcinoma (PDAC) in Male. In Female 7.7%, 3.8%, 11.5% were well, moderately and poorly differentiated adenocarcinoma respectively. Median age of occurrence of Colorectal carcinoma (CRC) is 52.3 overall, with 53.1 and 49.9 in male and female respectively [Table/ Figure 1].

**Table/Figure: 1 Histopathological Grade and clinicopathological factors correlation.**

| S. No | Clinico pathological parameters | WDAC | MDAC | PDAC | Total (n=26) |
|---|---|---|---|---|---|
| 1 | **Age** | | | | |
| | <50 | 8(30.8%) | 0 | 2(7.7%) | 10(38.5%) |
| | > 50 | | 4(15.4%) | 4(.415%) | 16(61.5%) |
| 2 | **Gender** | | | | |
| | Male | 14(53.8%) | 3(11.5%) | 3(11.5%) | 20(76.9%) |
| | Female | 2(7.7%) | 1(3.8%) | 3(11.5%) | 6(23.1%) |

| | | | | | |
|---|---|---|---|---|---|
| 3 | **Location** | | | | |
| | Ascending colon | 3(11.5%) | 0 | 1(3.8%) | 4(15.4%) |
| | Descending colon | 0 | 0 | 1(3.8%) | 1(3.8%) |
| | Sigmoid | 2(7.7%) | 2(7.7%) | 2(7.7%) | 6(23.1%) |
| | Recto-Sigmoid | 1(3.8%) | 0 | 1(3.8%) | 2(7.7%) |
| | Rectum | 10(38.5%) | 2(7.7%) | 1(3.8%) | 13(50%) |
| 4 | **Tumour stage** | | | | |
| | Tis & T1 | 2(7.7%) | 0 | 0 | 2(7.7%) |
| | T2 | 3(11.5%) | 2(7.7%) | 3(11.5%) | 8(30.8%) |
| | T3 | 11(42.3%) | 2(7.7%) | 3(11.5%) | 16(61.5%) |
| | T4 | 0 | 0 | 0 | 0 |
| 5 | **Nodal Stage** | | | | |
| | N0 | 12(46.1%) | 3(11.5%) | 1(3.8%) | 16(61.5%) |
| | N1a | 4(15.4%) | 1(3.8%) | 0 | 5(19.2%) |
| | N2a | 0 | 0 | 4(15.4%) | 4(15.4%) |
| | N2b | 0 | 0 | 1(3.8%) | 1(3.8%) |
| 6 | **Overall Stage** | | | | |
| | 0 | 1(3.8%) | 0 | 0 | 1(3.8%) |
| | I | 1(3.8%) | 0 | 1(3.8%) | 2(7.7%) |
| | IIA | 11(42.3%) | 3(11.5%) | O | 14(53.8%) |
| | IIIA | 2(7.7%) | 1(3.8%) | 1(3.8%) | 4(15.4%) |
| | IIIB | 0 | 0 | 3(11.5%) | 3(11.5%) |
| | IVA | 1(3.8%) | 0 | 1(3.8%) | 2(7.7%) |

Majority of cases (61.5%) occurred after 50 years with WDAC was 30.8%, MDAC and PDAC were 15.7% each.38.5% occur < 50 years with WDAC was 30.8% and 7.7% were MDAC & PDAC respectively. Commonest location in this study was rectum, it accounted for 50% of cases.WDAC occurred commonly in Rectum (38.5%),MDAC [ table/figure 2&3] occur equally in rectum and Sigmoid colon with 11.5% each.PDAC occurred commonly in sigmoid colon (7.7%).



**Table/Figure 2: 100x views of Moderately Differentiated adenocarcinoma**

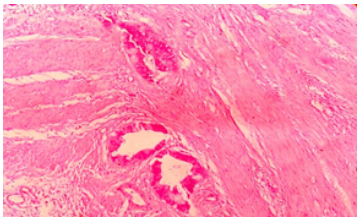


**Table /Figure 3:100x views of malignant glands infiltration into Muscular layer**

T stage (Tumour stage) showed 61.5 % of cases occurred in T3 stage out of which WDAC was 42.3 %, followed by 11.5% PDAC and 7.7% MDAC. T2 stage showed WDAC and PDAC were 11.5% each. MDAC account for 7.7% of cases. No statistically significant correlation occurred between Histopathological grade and T stage [Table/Figure 4].

**Table/Figure : 4 Histological Grade with T (tumour )stage statistical correlation.**

| Grade | Tumour stage -T3 & T4 | Tumour stage - Tis, 1 &T2 | Total |
|---|---|---|---|
| Low(WDAC&MDAC) | 13 | 7 | 20 |
| High( PDAC) | 3 | 3 | 6 |
| | 16 | 10 | 26 |
| P valve is 0.617075 with Yates correction. | | | |

Correlation between N stage and Grade, shows 46.1%, 11.5%, 3.8% of WDAC, MDAC, PDAC were negative for nodal metastasis. 5.4% WDAC and 3.8% MDAC shows N1a stage. 15.4% and 3.8% of PDAC shows N2a stage and N2b stage respectively. Poorly differentiated grade and nodal metastasis shows statistically significant correlation with P valve is 0.03595 with Yates correction [Table /Figure 5].

**Table /Figure: 5 Histopathological Grade with N stage statistical correlation.**

| Grade | Nodal positive | Nodal negative | Total |
|---|---|---|---|
| Low(WDAC&MDAC) | 5 | 15 | 20 |
| High( PDAC) | 5 | 1 | 6 |
| | 10 | 16 | 26 |
| P valve is 0.035946 with Yates correction. | | | |

Comparing Grade with TNM stage, it shows 42.3 % of WDAC in IIA, followed by 7.7% III A and 3.8% each in IV A, I, O respectively. MDAC showed 11.5 % and 3.8% cases in IIA & IIIA respectively. PDAC shows 11.5% in III B with 3.8% each in I, III A and IV A stage. Higher stages- III and IV show statistically significant correlation with higher grade .P valve is 0.017751 with Yates correction [Table/Figure 6].

**Table/Figure : 6 Histopathological Grade with overall TNM stage statistical correlation.**

| Grade | TNM Stage III &IV | TNM Stage I &II | Total |
|---|---|---|---|
| Low(WDAC&MDAC) | 4 | 16 | 20 |
| High( PDAC) | 5 | 1 | 6 |
| | 9 | 17 | 26 |
| P valve is 0.017751 with Yates correction. | | | |

## DISCUSSION

Median age of presentation in our study was 52.3 while in other studies, it was 71 in study by K.Derwinger et al[3] and 54.5 in Hashmi et al[7].

In gender, CRC occur slightly more in male (50%) than in female (49.5%) in K.Derwinger et al[3] study and similarly 51% and 49% in study by Hashmi et al[7]. Our study shows CRC occurred more commonly in male (76.9%) than in female (23.1%), but the difference being high.

In Hashmi et al [7] study, CRC commonly occur in colon (65.2%) followed by rectum (34.8%).The Present study, it occurred commonly in rectum (50%) and followed by sigmoid colon (23.07%) .Histopathological grade I is common in present study, it account for 61.5%. In K.Derwinger et al [3] and Hashmi et al [7], grade II and grade III were common and it accounted for 73.8% & 74% and 17.4 % & 23% respectively.

Majority of histopathological type were adenocarcinoma in our study similar to that of other studies done by Poornakal.S.et al [8] and Hashmi et al [7], In Tumor stage (T stage) majority cases were in T 3 (61.5%), followed by 30.8% in T 2, 7.2% in T1 which similar to Hashmi et al [7] study where 81% in T3 followed by 11% T4, 7% T2, 1% T1 stage.

Studies conducted by K.Derwinger et al [3] shows significant correlation between T stage and Grade of tumour. High grade of tumour occurred in higher T stage with P valve <0.0001. But our study showed no such significant statistical correlation between T stage and grade of tumour.

In present study majority cases were in N 0 stage (61.4%) followed by N1 19.2%, N2a 15.4%, N2b 3.8% .In Hashmi et al [7], N 0 was 32%, N1 was 30%, N2a and N2b were 19% each.

Hashmi et al [7]and K.Derwinger et al [3] studies showed significant correlation between N stage and Grade of tumour with P valve are <0.001 and 0.0001 respectively. Similarly our

study showed statistical significant correlation between high grade and nodal positivity with p valve is 0.035946 with Yates correction.

Comparing overall TNM stage, 41.4% cases in Stage III, followed by 36.1% in Stage II, 12.1% in stage IV and 10.4% in stage I in study by K.Derwinger et al [3]. Present study showed 53.8% in stage II, 26.8% in Stage III and 7.6% cases in Stage IV and I each. Significant correlation occurred between higher stage and higher grade with P valve of 0.017751 (Yates correction), similar to K.Derwinger et al study with P valve of <0.0001.

Nodal Metastasis is an important factor in deciding overall stage of tumour and is critical in deciding adjuvant chemotherapy. The Radiological Assessment of Nodal and T stage is done by CT scan and MRI. CT scan is only moderately sensitivity and highly specificity in identify the nodal metastasis [9 ]. Advanced radiological equipment like PET CT has improved sensitivity and specificity of nodal Metastasis diagnosis. But the availability and feasibility of those equipments in peripheral hospital in our countries is limited. So by using histological grading, sensitivity may be improved, thus preventing excess treatment with chemotherapy in selected cases. However histopathological grade of tumour may subject to observer variation. Similarly each component of TNM stage is also subjected to variation (K.Derwinger et al)[3].therefore cannot be dismissed on this ground, but it may require further refinement, based on consensus with pathologist and similar studies with large sample sizes may be required.

## CONCLUSION

Majority of colorectal cancer occur over age of 50 years with male predominance. The commonest location in our study was Rectum. The commonest histopathological type is Adenocarcinoma, well differentiated type (grade I).Statistical significant correlation (P valve-0.035946 was noted between histological grade and nodal metastasis. It has already been known that the Lymph node status is an Independent prognostic factor in staging, deciding adjuvant chemotherapy and outcome.

Significant correlation (P valve-0.017751) between overall TNM staging and histopathological grading was also noted. But when T staging (tumour) alone was considered, it showed no significant correlation. So, histopathological grading which is showing significant correlation with nodal metastasis may also serve as an additional prognostic factor. The independent prognostic significance of histological grading has to be validated by more similar studies with large sample size.

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