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Prognostic significances of Cox-2, Cyclin D1 and P21 expression in colorectal cancer patients

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Introduction

* **Colorectal cancer (CRC) is the 3rd commonest cancer and the 4th most frequent cause of cancer related death worldwide.**
* **It is important to detect novel prognostic markers for CRC patients to detect recent targeted therapy and to improve patients' survival.**

* **Cyclooxygenase-2 (COX-2) is an enzyme that is upregulated in response to inflammation and carcinogenesis.**
* **Cyclin D1 is an oncogene which regulates cell cycle progression.**
* **Cyclin D1 is blocked by cyclin D1-dependent kinase (CDK) inhibitors, such as p27 and p21.**

* **Many studies have evaluated Cox-2, cyclin D1& p21 expression as prognostic factors for survival of patients with CRC.**
* **However, the results of the studies are conflicting.**

AIM of the work

* **To evaluate immunohistochemical expression of COX-2 in colon cancer patients correlating its expression with the cell cycle markers cyclin D1, and p21.**
* **To analyze the relationship between their expression, clinicopathological criteria and the prognosis of patients.**

MATERIAL& METHOD

* **Expressions of Cox-2,Cyclin D1 and P21 were evaluated using immunohistochemistry in 60 patients of colon cancer, that were followed up for 3 years.**
* **The relationship between their level of expressions and prognosis of patients was analyzed.**

RESULTS

❑Cox-2& Cyclin-D expression in the studied cases:

* **The expression of Cox-2& Cyclin-D in CRC was positively associated with higher grade and advanced stage of the tumor, presence of L.N spread, peritoneal dissemination ($p<0.001$), and distant metastases ($p=0.012$)& ($p=0.009$)respectively.**

❑P-21 expression in the studied cases

* **The expression of P21 in CC was significantly correlated with lower grade& early stage of the tumor, absence of L.N, distant metastases (p<0.001), bilaterality and ascites.**

Follow up and clinical results

* **Low Cox-2 &Cyclin D1and high P21expression were associated with;**
* **Optimal surgical eradication of the tumor.**
* **Increased 3-year overall survival (OS) rate.**
* **Low incidence of recurrence after therapy (P <0.001).**

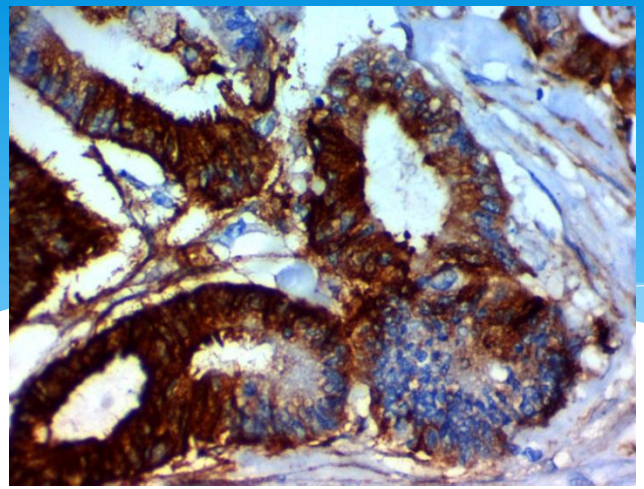


Fig 1 B

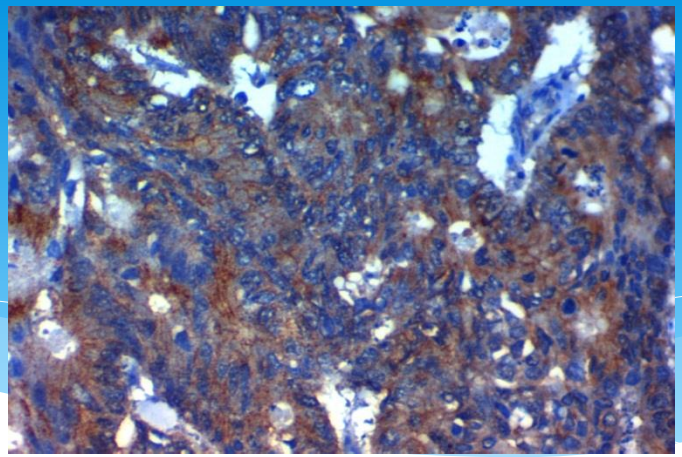


Fig 1 A

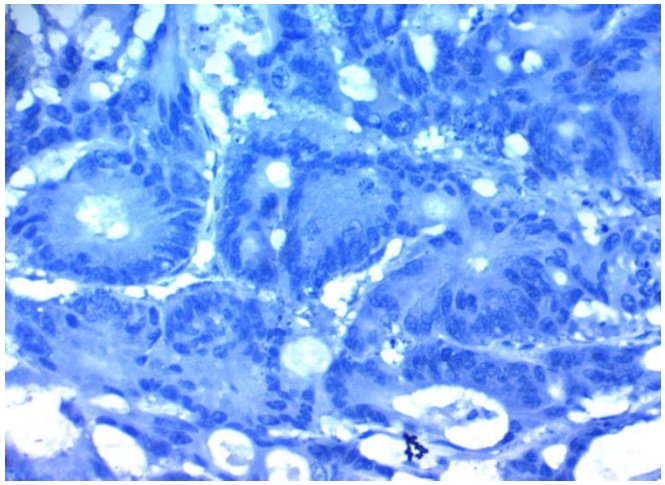


Fig 1 D

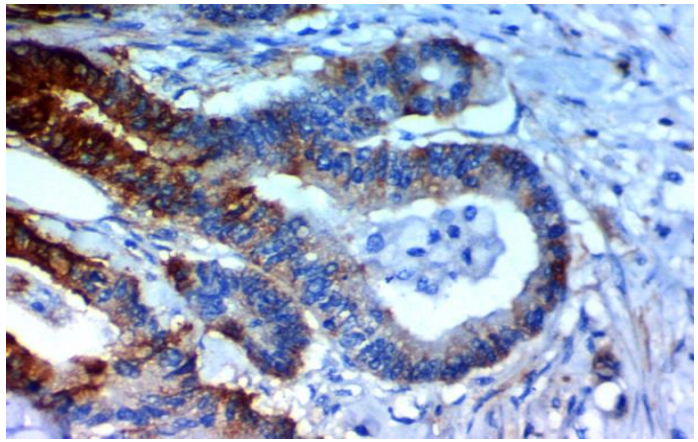


Fig 1 C

Fig 1 immunohistochemical expression of Cox-2 in colorectal carcinoma (CRC)A; High expression in the cytoplasm of poorly differentiated CRC x400, B; High expression in the cytoplasm of moderately differentiated CRCx400, C; low expression in the cytoplasm of well differentiated CRCx400 , D; negative expression in the cytoplasm of well differentiated CRCx400 .

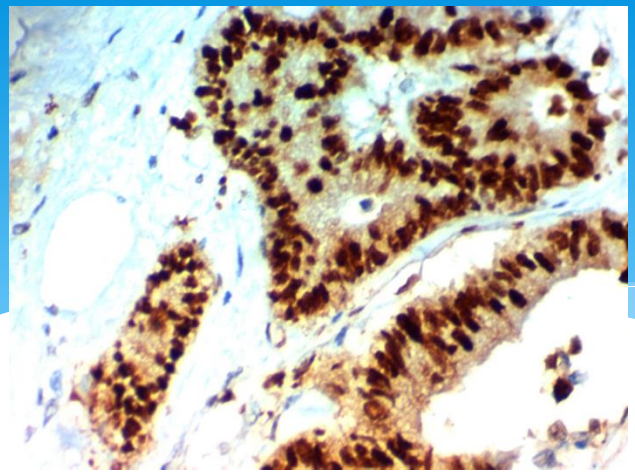


Fig 1 B

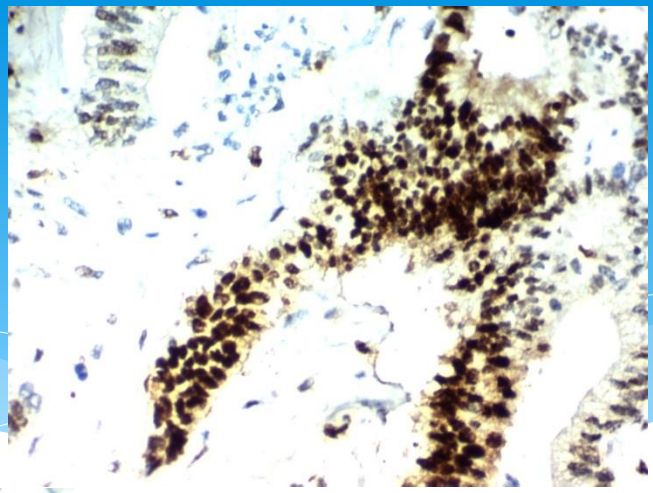


Fig 1 A

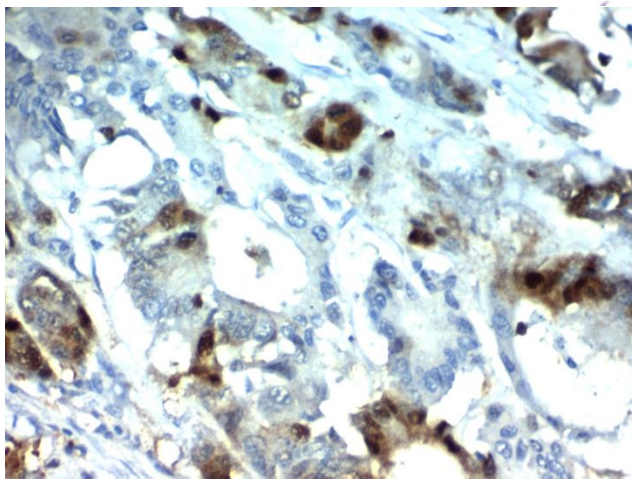


Fig 1 C

Fig 2 immunohistochemical expression of Cyclin D 1 in colorectal carcinoma (CRC)A; High expression in the nucleus of poorly differentiated CRC x400, B; High expression in the nucleus of moderately differentiated CRCx400, C; low expression in the nucleus of well differentiated CRCx400 ,

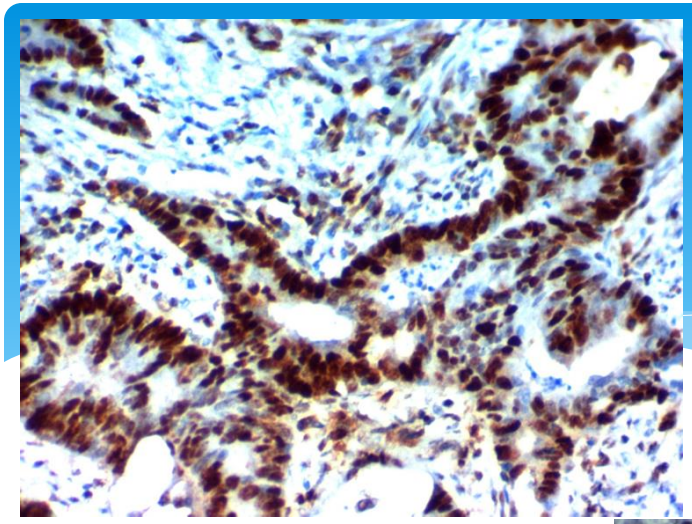
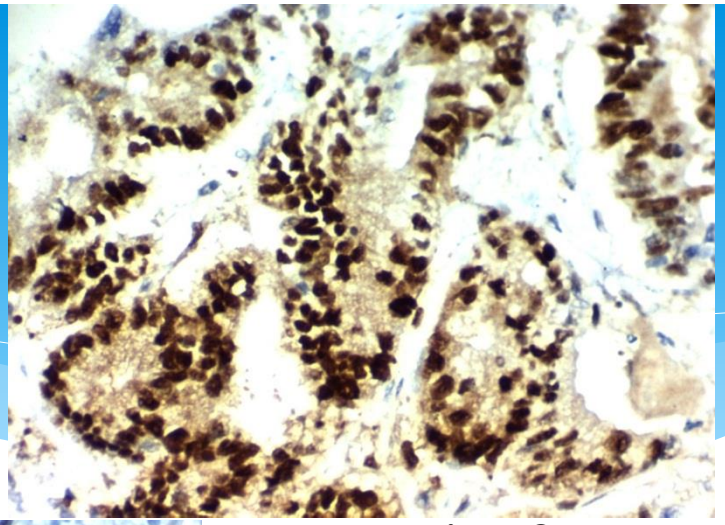


Fig 1 C



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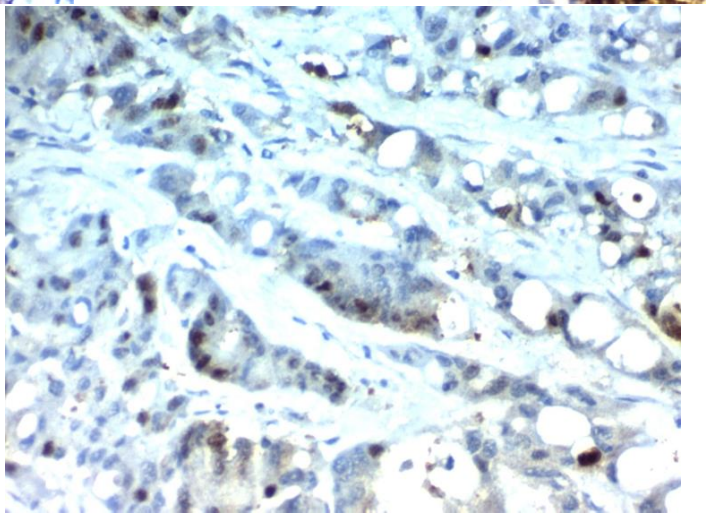

Fig 1 C

Fig 3 immunohistochemical expression of P21 in colorectal carcinoma (CRC)A; High expression in the nucleus of well differentiated CRC x400, B; High expression in the nucleus of moderately differentiated CRCx400, C; low expression in the nucleus of poorly

Summery& conclusion

* **High levels of expression of Cox-2 &Cyclin D1 in poorly differentiated and advanced stage CRC suggests that they play a role in tumor initiation& progression.**
* **Cox-2 &Cyclin D1are markers of poor prognosis in CRC patients.**
* **P21is a marker of good prognosis in CRC patients.**

* **These results clarified the roles of inflammation and disturbances in cell cycle control in progression and poor prognosis of CRC patients.**

Recommendations

* **We recommend that a large scale study on large number of patients with CRC to prove our results and detect the value of IHC in prediction of CRC patients prognosis and response to therapy.**

Thank you

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