

Introduction

Colorectal carcinoma is the most common malignant tumor of the gastrointestinal tract (**Calle ,et al 2003**).

Colorectal carcinoma has a worldwide distribution, with the highest death rate in the United States and Eastern European countries, up to tenfold lower rates in Mexico, South America, and Africa (**James , et al 1999**).

In Egypt its incidence is increasing representing 6.55% of total Egyptian cancers, male to female ratio 2:1, with increase risk after age of 50 years (**El Bolkainy ,et al 2005**) and is the third cause of cancer deaths. Also the incidence was found to be high in young adults (**Soliman, et al 2001**).

In the United States the incidence of cancer colon and rectum in males was found to be (10.2%) of all cancers making colorectal cancer the third after cancer prostate (29.3%) and lung (14.5%). While in females it was found to be (11.1%) and also the third after cancer breast (29.7%) and lung (13.3%). Death rate of cancer colon and rectum in males was found to be (9.5%) making colorectal cancer the third after cancer lung (31.6 %) and prostate (13.3%). While in females it was found to be (9.5%) making colorectal cancer the third after cancer lung (24.7%) and cancer breast (16%). (**Landis ,et al 1998**).

More than 145000 new cases are diagnosed annually in the United States and more than 55000 patient died of this disease each year. So early detection along with improvement in medical and surgical care will be responsible for decreasing mortality of colorectal cancer observed in recent years (**Calle ,et al 2003**).

Identification of risk factor for the development of colorectal carcinoma is essential to establish screening and surveillance programs (**Kelli ,et al 2005**).

The high risk factor for colorectal carcinomas include age older than 50 years, personal or family history of colorectal cancer or adenoma, history of longstanding ulcerative colitis and genetic predisposition due to a hereditary

polyposis or non-polyposis syndrome (**Sussman , et al 2000**).

The dietary factors receiving the most common attention as predisposing to a higher incidence of cancer colon which are: (1) excess energy intake relative to requirement, (2) a low content of unabsorbable vegetable fiber, (3) a corresponding high content of refined carbohydrates , (4) intake of red meat, and (5) decreased intake of protective micronutrients .

Cigarette smoking is associated with an increased risk of colonic adenomas, especially after more than 35 years of use. Patient with uretrosigmoidostomy are also at increased risk for both adenoma and carcinoma formation (**Woodhouse 2002**).

Regional lymph node involvement is the most common form of spread of colorectal carcinoma and usually precedes distant metastasis. The likelihood of nodal metastasis increase with the tumor size, poorly differentiated histology, lymphovascular invasion and depth of invasion (**Jenkins, et al 2002**).

Metastasis genes are oncogenes or tumor-suppressor genes that elicit metastasis at their principal or sole contribution to tumorigenesis. So altered forms of certain genes promote or suppress the metastatic phenotype and then their detection in a primary tumor may have prognostic as well as therapeutic implication (**Filder, et al 1996**).

A Variety of approaches are being used to identify candidate metastases suppressor genes. One such method involve subtractive hybridization of cyclic DNA obtained from metastatic tumor cell lines and their non-metastatic counterpart .This led to discovery of nm23 (**Filder, et al 1996**).

The murine nm23 gene suppresses the metastatic behavior of malignant rodent tumor lines . Reduced nm23 expression correlate with increase metastasis in human breast cancer, melanoma, hepatocellular and ovarian carcinoma (**Tokunaga, et al 2001**).

The higher expression of nm23 has been associated with worse prognosis

in hematological neoplasm and prostatic carcinomas .The role of nm23 is less conclusive in colorectal, lung, gastric and renal cell carcinoma (**Wakimoto, et al 1998**).

The expression of nm23 in differentiated thyroid carcinoma is inversely associated with metastatic potential for follicular but not for papillary thyroid carcinoma (**Carles, et al 2001**).