Newer Tumor Markers in Detection of Colorectal Carcinoma

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ABSTRACT

Colorectal cancer (CRC) is one of the most common malignant neoplasms in Egypt. Adenomatous polyps and inflammatory bowel diseases (IBD) are considered the commonest pre-malignant lesions for CRC. Adipocytokines (Adiponectin, Resistin and Visfatin) are promising markers that may play a role in early detection of CRC.

Aim of work: to assess levels of Adiponectin, Resistin and Visfatin in pre-malignant & malignant colorectal lesions.

Patients and methods: 114 patients were studied and divided into 4groups; CRC group (34 patients), IBD group (24 patients), colonic polyps group (27 patients) and control group (29 patients) (patients with different indications for colonoscopy and showed negative full colonoscopic examination) by measuring levels of Adiponectin, Resistin and Visfatin in each patient of each group using ELISA technique.

Results: Adiponectin is increased in CRC group rather than other 3 studied groups and its level decreased in IBD than polyp, Visfatin is significantly higher in control group than the other 2 groups (benign and CRC) and it increased in IBD than Polyp with inverse relation with stage of CRC. Resistin level has no significance in CRC group but it increased in IBD than polyp groups and it has direct relation with CRC staging.

Conclusion: Adiponectin and Visfatin are good biomarker in early detection of CRC while Resistin is good biomarker in premalignant lesion and progression of CRC.

Key words: Adiponectin- Resistin – Visfatin – Colorectal cancer – Premalignant lesion.

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LIST OF ABBREVIATIONS

- **ACF**: Aberrant crypt foci
- **ACG**: American collage of gastroenterology
- **AF**: activation functions
- **AFAP**: attenuated familial adenomatous polyposis
- **AJCC**: American joint committee on cancer
- **APC**: attenuated adenomatous polyposis coli
- **5-ASA**: 5-aminosalicylic acid
- **CBC**: Complete blood count
- **CD**: Crohn's disease
- **CE**: contrast enhancement
- **CEA**: carcinoembryonic antigen
- **CIN**: chromosomal instability
- **CRC**: colorectal cancer
- **CT**: computerized tomography
- **DALM**: dysplasia-associated lesions or masses
- **DCBE**: double contrast barium enema
- **DBD**: DNA binding domains
- **DCC gene**: deleted in colon cancer
- **ESR**: erythrocyte sedimentation rate
- **FAP**: familial adenomatous polyposis
- **FCC**: familial colorectal cancer
- **FGF**:F Growth Factor
- **FIT**: fetal immunohistochemical staining
- **FOBT**: fecal occult blood testing

- **GBP28**: gelatin-binding protein-28
- **GIT**: gastrointestinal tract
- **HNPCC**: hereditary non polyposis colorectal cancer
- **IBS**: irritable bowel syndrome
- **IL**: interleukin
- **IGFBP**: insulin-like growth factor binding protein
- **MSI**: microsatellite instability
- **NBI:** Narrow Band Imaging
- **NCI**: national cancer institute
- **NHL**: non Hodgkin lymphoma
- **NO**: nitrous oxide
- **NSAIDs**: non steroidal anti-inflammatory drugs
- **PBEF**: pre-B cell colony-enhancing factor
- **PJS**: Peutz–Jeghers syndrome
- **SE**: surface enhancement
- **STAT**: signal transducer and activator of transcription
- **SOCS**: suppressors of cytokine signaling
- **UC**: ulcerative colitis
- **T2D**: Type 2 Diabetes
- **TE**: tone enhancement
- **TNF:** tumour necrotic factor
- **TSG**: tumour suppressor gene
- **WHI**: Women's Health Initiative
- **WHO**: World heath organization

INTRODUCTION

Colorectal cancer (CRC) is considered the fourth most commonly diagnosed cancer and the second leading cause of cancer- related deaths in the United States. More than 50,000 die from CRC annually accounting for approximately 10% of all cancer deaths. Each year, approximately 140,000 individuals are diagnosed with CRC ***(Jemal et al., 2005)***.

In Egypt, colorectal carcinoma is one of the most common malignant neoplasms ***(Zalata et al., 2000)***. According to National Cancer Institute (NCI) statistics, in males CRC ranks the sixth most common cancer after bladder, liver, Non Hodgkin Lymphoma (NHL), lung and leukemia, while in females it ranks the fifth common cancer after breast, Non Hodgkin Lymphoma (NHL), leukemia and liver cancer. The median age of CRC cases in Egypt is 48 years for both males and females ***(Elattar, 2005)***.

Unlike western countries - where CRC is prevalent among elderly people, 35% of the Egyptian patients with CRC are under 40 years of age. Also, the histopathological criteria and the mutational profile of the tumors diagnosed in Egypt are different from those of the western countries. In general, they are of high histological grade and stage and they carry more mutations ***(Bahnassy et al., 2002)***.

Many risk factors for CRC development have been incriminated, including environmental and genetic factors. Although inherited susceptibility results in the most striking increases in risk, the majority of CRCs are sporadic rather than familial ***(Wei et al., 2004)***.

Colon cancer screening used to identify individuals at an early stage, has improved outcome. Recent decreases in rates of death from colorectal cancer indicate that screening methods such as Colonoscopy techniques, technologies, and quality control measures have advanced to improve detection, classification, and removal of early neoplasias ***(Wallace and Kiesslich , 2010)***.

Image enhancement methods such as chromoendoscopy and its modalities, such as "digital" chromoendoscopy also Ultra-high magnification systems, including optical magnification and confocal endomicroscopy and I-scan technology that consisted of three types of algorithms: surface enhancement (SE), contrast enhancement (CE), and tone enhancement (TE) all are designed to enhance minute mucosal structures ***(Kodashima et al., 2010 and Wallace et al.,2010)***

Discovery of novel markers that is highly specific and sensitive will also improve strategies for the management of cancer by facilitating a rapid determination of tumor responses to novel therapies. A variety of noninvasive molecular approaches to colorectal cancer screening are emerging with potential to improve screening effectiveness. These approaches are based on the sensitive assay of molecular markers in stool, blood. New methods have been shown to detect both colorectal cancers and precancerous lesions with high accuracy ***(Ahlquist , 2010).***

Detection of DNA molecular markers in serum is an exciting new technology that shows increasing promise as a way to screen colorectal cancer. Detecting premalignant adenoma is the key target of any approach of screenings which aim at preventing colorectal cancer. In this point, serum DNA testing with molecular markers has shown to be superior to fecal occult blood testing for adenoma detection ***(An SW et al., 2009).***

There are many new approaches in the development of high-performance molecular markers that are ideal screening tools being sensitive, specific, and cost-effective. Individuals with a positive serum DNA test are referred for colonoscopy. Ultimately, introduction of new serum-based DNA test with a panel of molecular markers is expected to encourage participation in screening program of colorectal cancer ***(An SW et al., 2009).***

Adipocytokines are serum markers which are adipocyte-secreted hormones associated with some malignancies such as colorectal, breast, and prostate cancer. Adipocytokines measured by blood levels of adiponectin, leptin, resistin, visfatin, and C-peptide. Resistin and visfatin may be good biomarkers of colorectal malignant potential and stage progression. Adiponectin level may be a good biomarker of colorectal adenoma ***(Nakajima et al., 2010).***