Article

ROLE OF BIOMARKERS IN THE DIAGNOSIS, MANAGEMENT IN GASTROINTESTINAL DISORDERS AND GI CANCERS

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Abstract:

Background: Assessment of gastrointestinal (GI) biomarkers involved in diagnosis of GI diseases and cancers is difficult. Measurement of biomarkers is a valuable tool for the assessment of inflammatory bowel diseases and malignancies.

Objectives: To review the role of various biomarkers in diagnosis of GI disease.

Methods: The primary studies have been screened from different databases , PMC , NLM , Scopus , Google scholar etc. all the information have been reviewed and considered after consulting with medical subject headings.

Result: Many research efforts in the GI field have been placed on finding non-invasive and reliable biomarkers of GI disease that can be easily tested in body fluids without impacting the quality of life of patients. Unfortunately, the ideal biomarker is yet to be discovered and recent studies have investigated the possibility to increase the accuracy of such measurements by combining different markers.

Conclusions: we provide an update about the current knowledge on GI biomarkers, focusing on disease diagnosis, correlation with endoscopic findings, and prediction of relapse. We also summarize composite scores of clinical and laboratory markers that have been recently proposed in various scenarios of GI diseases.

Introduction:

A biomarker is characterized as any substances design, or deal with that can be estimated in body or its items and affected of result or disease. Numerous blood and stool biomarkers are at present accessible which can be utilized for the conclusion, visualization, the board, and follow-up for reaction to treatment in the gastrointestinal (GI) messes. Investigation of lab biomarkers in the GI illnesses is a captivating point for top to bottom examination and audit. In this way, the quest for novel, more exact, quicker reasonable biomarkers in the GI illnesses actually proceeds in view of various clinical proposals and clashing data in the writing today. Gastrointestinal (GI) jumble described by stomach torment or

uneasiness, changes in entrail propensities and elements of cluttered poop without a trace of recognizable natural sickness to clarify the indications. Crabby gut condition is a multifactorial problem related with various changed physiological cycles, remembering anomalies for stomach motility and instinctive awareness that are logical because of dysregulation of pathways in the mind stomach hub and the presence of invulnerable dysregulation in the GI parcel. IBS may likewise include an intricate association of neuronal and hormonal variables, like serotonin and corticotropinreleasing factor, influencing different physiological cycles. The physiological changes going with GI diorder have been demonstrated to be reflected in changes in articulation of serum biomarkers, bringing about another comprehension of the physiology of GI. The point of the current review was to create and approve a blood-based symptomatic test for GI by distinguishing serum biomarkers differentially found in GI patients contrasted and GI patients. This article audits the more normal clinically accessible atomic biomarkers for neoplasms of the stomach, pancreas, and colon. For diseases of the throat no biomarkers presently are being fused into routine clinical practice, accordingly the biomarkers that have shown the most guarantee in clinical approval studies are examined.

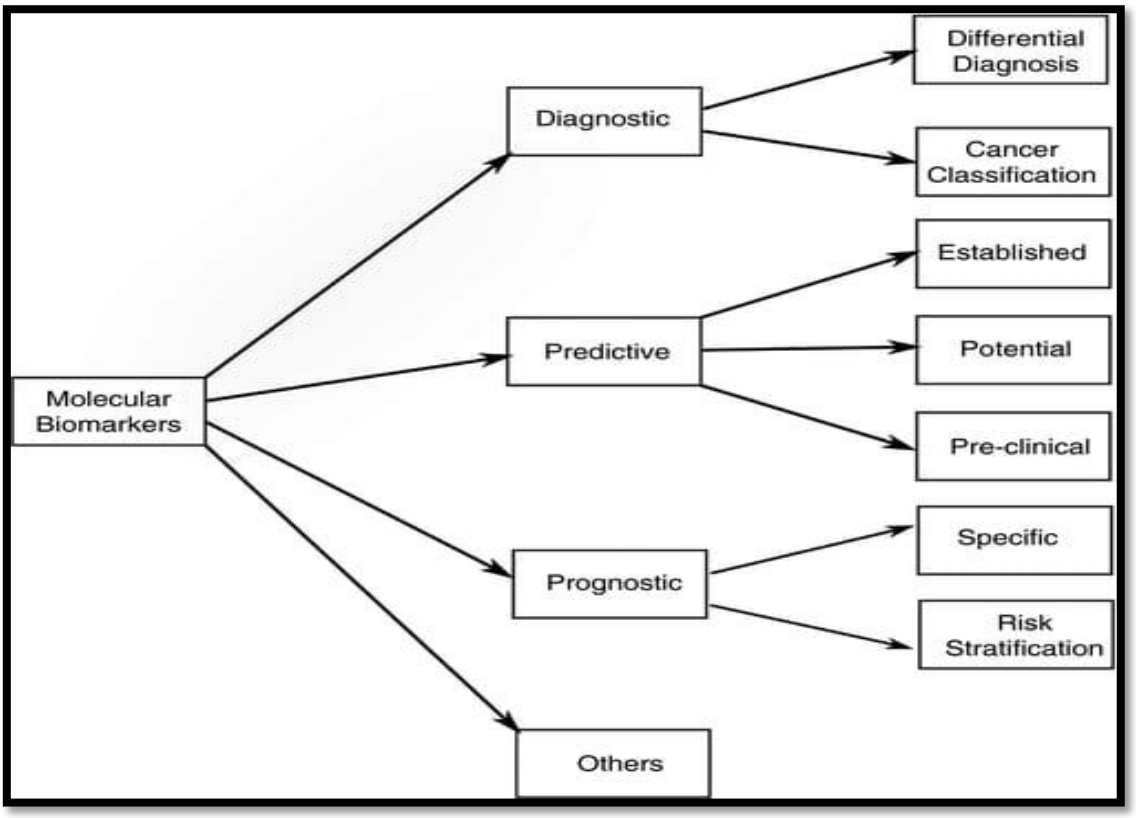

Fig. 1:Diagnostic Biomarkers Of Gi Problems

ESOPHAGUS

Tumors of the throat are among the most dangerous of gastrointestinal malignancies. Squamous cell carcinoma and adenocarcinoma are the two significant histologic kinds of esophageal malignant growth. Around the world, over 90% of esophageal malignant growths are squamous cell carcinoma; nonetheless, Survival for both cancer types can be improved assuming they are distinguished in beginning phases. Right now, there are no biomarkers in far and wide clinical use for either histologic sort of esophageal disease, but the biomarkers that have shown the most guarantee in early clinical approval studies. Seriously encouraging sub-atomic biomarkers for

esophageal neoplasia. These potential biomarkers are as of now being scrutinized.

Table 1: Biomarkers for Esophageal Neoplasia

Tumor	Biomarker	Category
Squamous cell carcinoma	**None**	
Adenocarcinoma	**aneuploidy/increased tetraploidy**	**Progression**
	17pLOH (p53)	**Progression**
	panel of aneuploidy/increased tetraploidy, 17pLOH, & 9pLOH	**Progression**
	Methylation-based gene	**Progression**

STOMACH

Gastric Adenocarcinoma The two significant histological variations of adenocarcinoma of the stomach are diffuse-type and gastrointestinal sort gastric tumors. By and large, people with diffuse-type cancers regularly have a more awful guess than those with digestive kind growths. ERBB2 is an individual from the epidermal development factor receptor (EGFR) group of receptor tyrosine kinases. Intensification of the ERBB2 quality as well as overexpression of HER2, the protein result of ERBB2, have been recognized in bosom, ovarian, esophageal adenocarcinoma, and gastric malignant growths, among others. HER2 is all the more usually overexpressed in digestive sort (21.5%) than in the diffuse kind (2%) gastric adenocarcinoma. HER2 articulation in gastric malignant growths has been proposed as a potential biomarker to anticipate guess and helpful reaction. Prior investigations proposed that HER2-positive gastric malignant growth had an unfortunate visualization, but later information recommend that HER2 articulation might have no prognostic pertinence. Trastuzumab is a monoclonal immunizer which ties to and restrains HER2 flagging. Trastuzumab notwithstanding standard chemotherapeutic specialists has shown an advantage in patients with HER-2 positive gastric diseases, proposing that HER2 can be utilized as a biomarker prescient of helpful reaction.

GASTROINTESTINAL STROMAL TUMOR:

Gastrointestinal stromal cancers (GISTs) are the most widely recognized mesenchymal growths of the GI parcel. While GISTs happen most frequently in the stomach, they can be observed somewhere else the luminal stomach and extraordinarily likewise outside the stomach related framework. The cell of beginning has been recognized as the interstitial cell of Cajal, which manages peristalsis in the intestinal system. Most GISTs are irregular, emerging in light of the fact that a physical addition of-work change in the tyrosine kinase quality KIT. Imatinib, a tyrosine kinase inhibitor utilized for the therapy of Philadelphia-positive constant myelogenous leukemia, has shown benefit in the treatment of GISTs on the grounds that the KIT and PDGFRA kinases are focuses of this chemotherapeutic specialist. 44 Localized GISTs, in which careful resection is finished, don't need further clinical treatment. Nonetheless, patients with unresectable cancers, progressed metastatic, or intermittent illness might be contender for Imatinib therapy. Later examinations recommend there might be a job for adjuvant imatinib treatment after resection of the essential GIST to build paces of repeat free endurance

Table2: Biomarker for Gastric Neoplasia

Tumor	Biomarker	Category
Gastric Adenocarcinoma	HER2 (ERBB2 gene)	Therapeutic Response
	Serum pepsinogensI and II	Diagnosis
Hereditary Diffuse Gastric Cancer	CDH1 gene	Diagnosis

Gastrointestinal stromal tumor(GIST)	CD117 (KITprotein)	Diagnosis
	DOG1	Diagnosis
	KIT gene	Therapeutic Response; Prognosis
	PDGFRA gene	Therapeutic Response

COLON

SPORADIC COLORECTAL CANCER : Overall colorectal disease rate and death rates are on the ascent, conversely .as of late, stool DNA tests have been the atomic way to deal with colorectal malignant growth screening that has been most seriously studied.Several review have analyzed the paces of discovery of cutting edge adenomas and obtrusive cancers between guaiac testing and stool DNA tests. One review looked at waste mysterious blood testing utilizing Hemoccult and HemoccultSensa (Beckman Coulter, Fulterton, CA), a stool DNA test with a 23-marker measure (SDT-1) and another original stool DNA test (SDT-2) with just 3 designated markers; colonoscopy was utilized as the "highest quality level" for adenomas or malignant growth recognition. Generally speaking, there was no huge distinction in paces of recognition for colorectal neoplasia between the HemoccultSensa and the SDT-1; discovery rates for SDT-1 were fundamentally more prominent than Hemoccult. Identification rates for colorectal neoplasia by SDT-2 were fundamentally better compared to both of the waste mysterious blood location tests. In addition, SDT-2 had fundamentally higher paces of discovery for cutting edge adenomas < 1 cm contrasted with either Hemoccult or HemoccultSensa. 69 One disadvantage, in any case, was a higher misleading positive rate (16%) utilizing SDT-2 (for example colonoscopy was typical in those with a positive test result) than either Hemoccult (4%) or HemoccultSensa (5%).69 Nevertheless, stool DNA testing as a screening methodology (Table 5) has as of late been embraced by the American Cancer Society, the US Multi-Society Task Force, the American College of Radiology, and the American College of Gastroenterology, yet not yet by the US Preventive Services Task Force.

Table3: Biomarker for Gastric Neoplasia

Tumor	Biomarker	Category
Gastric Adenocarcinoma	HER2 (ERBB2 gene)	Therapeutic Response
	Serum pepsinogensI and II	Diagnosis
Hereditary Diffuse Gastric Cancer	CDH1 gene	Diagnosis
Gastrointestinal stromal tumor(GIST)	CD117 (KITprotein)	Diagnosis
	DOG1	Diagnosis
	KIT gene	Therapeutic Response; Prognosis
	PDGFRA gene	Therapeutic Response

PANCREAS

PANCREATIC ADENOCARCINOMA:

Pancreatic adenocarcinomas start from the ductal epithelium and progress from insignificant dysplasia [pancreatic intraepithelial neoplasia

(PIN) grades 1A and 1B) to serious dysplasia [PIN grades 2 and 3) preceding turning into an obtrusive growth. No biomarkers are presently prescribed for routine use to evaluate for pancreatic disease. Conversely, CA19-9 has been demonstrated to be a clinically helpful biomarker for observing restorative reaction and for the early location of repetitive infection after therapy , However, CA19-9 isn't without its impediments including the absence of explicitness for pancreatic malignant growth since different circumstances, for example, biliary cholestasis can lift the levels of this protein. While most instances of pancreatic disease are inconsistent, there is familial grouping seen in roughly 5-10% of cases and in 10-20% of such cases an innate part might be involved. There are various heritable circumstances that increment the gamble of a person to foster pancreatic malignant growth, and explicit hereditary tests are accessible to recognize causative transformations for the majority of these heritable circumstances. 58 However, no wide-spread clinical suggestions are accessible as of now for pancreatic disease separating these high gamble people.

Table 4: BIOMARKERS FOR PANCREATIC NEOPLASIA

Tumor	Biomarker	Category
Adenocarcinoma	**CA19-9**	**Therapeutic Response; Prognosis**
Pancreatic cystic neoplasms	**Cyst fluid CEA**	**Diagnosis**
	PathFinder TG	**Diagnosis**

Table 5: SEVERAL BIOMARKERS AND ITS ROLES IN HUMAN BODY

S.N	BIOMARKERS	RESULTS
1	Caspase-3 and pAkt in muscle, and urinary 3-MH	Role of caspase-3, phosphatidylinositol-3 kinase, and 3-methylhistidine in the pathophysiology of skeletal muscle loss in weight-losing pancreas cancer patients.
2	Four messenger RNA biomarkers (KRAS, MBD3L2, ACRV1, and DPM1) in salivary samples.	The logistic regression model using four biomarkers yielded an area under the curve value of 0.971 (cutoff 0.433) to detect resectable pancreatic cancer with 90.0% sensitivity and 95.0% specificity.
3	AREG, EGF, sHER2, TGF-α	Exploratory analyses suggested that high AREG might predict progression-free survival in patients with pancreatic cancer treated with erlotinib.
4	Circulating tumor cells	Alterations in circulating tumor cells predicted the progression of pancreatic ductal adenocarcinoma, treatment response, and clinical outcomes.
5	VEGF-A and VEGF-R2	Validation of circulating biomarkers using the immunological multiparameter chip technology (IMPACT) platform on plasma specimens collected on.
6	DNA	Circulating tumor DNA as a prognostic marker in patients with pancreatic cancer.
7	Chromogranin A	To validate the performance of Brahms Chromogranin A II

		Kryptor assay to monitor the course of disease in patients with well-defined gastroentero-pancreatic neuroendocrine tumors.
8	AREG	Identification of AREG for the detection of pancreatic cancer by the biosensor

	BIOMARKERS	DESCRIPTION
9.	Interleukin-1ß (IL-1ß)	A proinflammatory cytokine that plays a central role in inflammatory diseases such as IBD.16 Glucocorticoids released during stress have a significant downregulatory effect on IL-1ß.1
10.	Growth-related oncogene-a (GRO-a)	A chemokine associated with chemotactic migration and activation of neutrophils,18 which may be involved in tissue injury in IBD patients.
11.	Brain-derived neurotrophic factor (BDNF)	A nerve growth factor thought to be a regulator of neuronal transmission,19, 20 which may play an important stimulant role in long-term regulation of gastrointestinal motility.
12.	Anti-Saccharomyces cerevisiae antibody (ASCA IgA)	An antibody that may reflect a generalized loss of immunotolerance. High levels of ASCA IgA are frequently found in Crohn's disease patients.
13.	Antibody against CBir1 (Anti-CBir1)	An antibody against bacterial flagellin.22 Bacterial flagellin is recognized by cells of the gut mucosa, which may then activate innate immunity
14	Antihuman tissue	tTG is a tissue-repair enzyme23 and the major autoantigen in coeliac disease.
15.	transglutaminase (tTG)	Anti-tTG testing can aid in the diagnosis of coeliac disease.2
16.	Tumour necrosis factor (TNF)-like weak inducer of apoptosis (TWEAK)	A cytokine that controls cellular activities such as proliferation, migration, differentiation, apoptosis, and angiogenesis.25–27 TWEAK levels are downregulated in autoimmune pathologies.
17	Antineutrophil cytoplasmic antibody (ANCA)	Autoantibodies that target antigens present in neutrophils,29 which have been identified in the serum of 50% to 80% of ulcerative colitis patients
18.	Tissue inhibitor of metalloproteinase-1 (TIMP-1	An inhibitor of metalloproteinases (MMPs) that break down extracellular matrix proteins involved in wound healing, angiogenesis, and tumour-cell metastasis. In the gut, altered TIMP activity can result in tissue destruction, intestinal barrier function impairment, bacterial influx, and excessive immune response.3
19.	Neutrophil gelatinase-associated lipocalin (NGAL	Belongs to the lipocalin family of proteins.32 In the viscera, NGAL is involved in a range of functions including molecular transport and GI mucosal regeneration.

Conclusions:

We provide an update about the current knowledge on biomarkers of intestinal inflammation in IBD, focusing on disease diagnosis, correlation with endoscopic findings, and prediction of relapse. We also summarize composite scores of clinical and laboratory markers that have been recently proposed in various scenarios of disease activity.

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