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GIT Dysfunction in Parkinsons Disease

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ABSTRACT: Objective &Background of the study: This study was conducted in a tertiary center Tirunelveli medical college hospital over a period of 3 years with 100 parkinsons disease patients.Parkinsons disease which is a severe disabling condition with incapacitating motor and non-motor features affecting all systems but earliest and most common manifestation is chiefly as GIT symptoms such as drooling of saliva(hyper salivation); dysphagia ;impaired gastric emptying and constipation.Both environmental and genetic factors interact to cause sporadic PD. As a result, the search for potential environmental factors has been ongoing in PD research.(1)some elements of disease development have been identified, most importantly neuroinflammation, oxidative stress, and αSyn misfolding and aggregation(. (2)Misfolding and aggregation of αSyn is suspected to lead to LP in surviving neurons, and thus combatting αSyn aggregation has been suggested to be of potential therapeutic value.(3)review by Pan-Montojo and Reichmann suggests an important role of toxic environmental substances in the etiology of sporadic PD.(4)Braaks hypothesis states that the disease originate in the intestine and then spread to the brain via the vagus nerve ,a phenomenon that would involve other neuronal types than the dopaminergic neurons.Thatswhy the peripheral nondopaminergic impairments will precede the alteration of dopaminergic neurons in the central nervous system.(5)(dual-hit hypothesis, stating that sporadic PD starts in two places: the neurons of the nasal cavity and the neurons in the gut (6)Braak's hypothesis states that sporadic PD is caused by a pathogen that enters the body via the nasal cavity, and subsequently is swallowed and reaches the gut, initiating Lewy pathology (LP) in the nose and the digestive tract. A staging system describing the spread of LP from the peripheral to the central nervous system had been postulated.There has been criticism to Braak's hypothesis, in part because not all patients follow the proposed staging system. .GUT-BRAIN axis in PD is of growing interest.

AIM AND OBJECTIVES:

Main objective is that often the entire GIT which is affected in parkinsons disease is often

overlooked which may lead to disastrous consequence like aspiration pneumonia leading to death .

To see if the earlier GI symptoms in PD helps in identification of risk factors, and to studyif the current advances in neuroprotective and therapeutic biomarkers of PD would benefit the PD patients earlier who are presenting with GI disturbances.

MATERIALS AND METHODS:100 Patients with parkinsons disease in neurology OPD were enrolled in this study

Right from the premotor stage of Parkinsons disease , these GIT manifestations are common.Diagnosis was by H/o, clinical examination ,Leed questionnaire which is very simple was used, USG abdomen wasdone to rule out any comorbid conditions .Endoscopy and colonoscopy were done when and where needed.Barium meal series and barium enema were done in suspected cases.GastricScintiscan and colonic transit time could not be done since these facilities were not available in our tertiary care centre.

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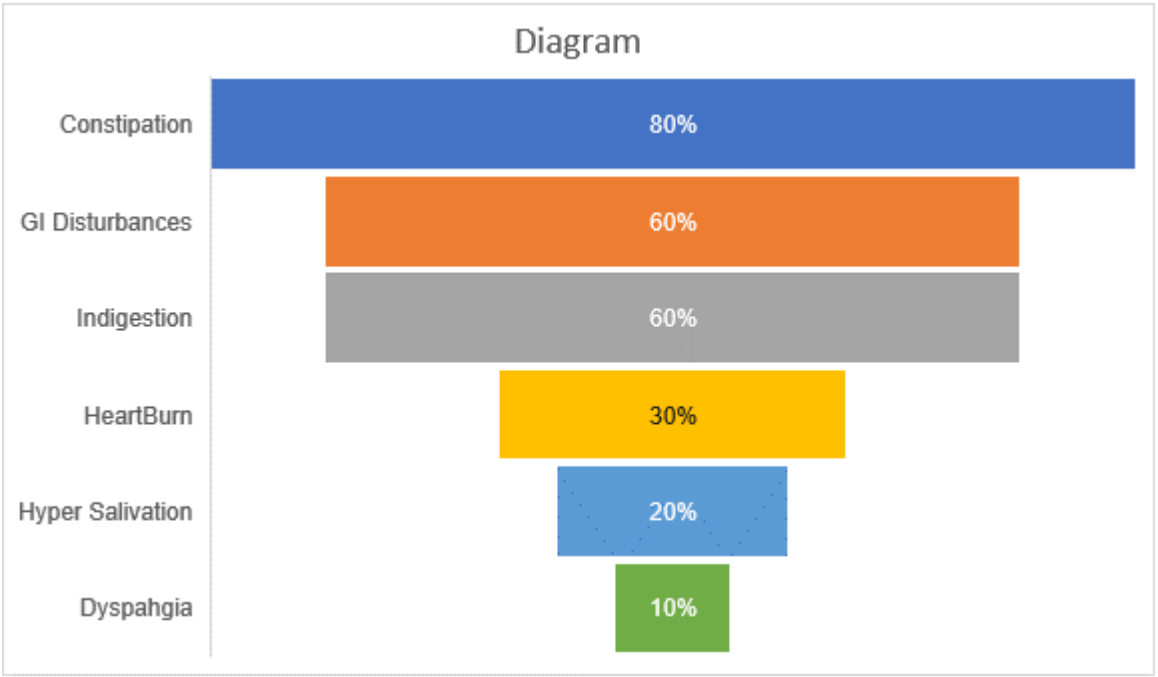
LEEED CRITERIA:

Patient ID: Date:	**How often have you *had* this symptom over the last 2 months?** Tick only one box per question.	**How often *has this symptom interfered with your normal activities (eating, sleeping, work, leisure)* over the last 2 months?** Tick only one box per question
1. Indigestion Indigestion is a pain or discomfort in the upper abdomen. 	☐ Not at all ☐ Less than once a month ☐ Between once a month and once a week ☐ Between once a week and once a day ☐ Once a day or more	☐ Not at all ☐ Less than once a month ☐ Between once a month and once a week ☐ Between once a week and once a day ☐ Once a day or more
2. Heartburn Heartburn is a burning feeling behind the breastbone. 	☐ Not at all ☐ Less than once a month ☐ Between once a month and once a week ☐ Between once a week and once a day ☐ Once a day or more	☐ Not at all ☐ Less than once a month ☐ Between once a month and once a week ☐ Between once a week and once a day ☐ Once a day or more
3. Regurgitation Regurgitation is an acid taste coming up into your mouth from your stomach.	☐ Not at all ☐ Less than once a month ☐ Between once a month and once a week ☐ Between once a week and once a day ☐ Once a day or more	☐ Not at all ☐ Less than once a month ☐ Between once a month and once a week ☐ Between once a week and once a day ☐ Once a day or more
4. Nausea Nausea is a feeling of sickness without actually being sick.	☐ Not at all ☐ Less than once a month ☐ Between once a month and once a week ☐ Between once a week and once a day ☐ Once a day or more	☐ Not at all ☐ Less than once a month ☐ Between once a month and once a week ☐ Between once a week and once a day ☐ Once a day or more
5. Which, if any, of these symptoms has been the most troublesome to you in the last 2 months? **Please tick one box only**	☐ Heartburn ☐ Regurgitation ☐ Indigestion ☐ Nausea	

OBSERVATION:



60% *GI disturbances*

- *60% of patients had GI disturbances*

20% *Hyper salivation*

- *More than 20% had hyper salivation*

10% *Dysphagia*

- *Dysphagia was found in 10% of patients*

80% *Constipation*

- *Constipation was found in almost 80% of patients*

30% *Heartburn*

- *Heartburn in 30% of patients*

60% *Indigestion*

- *Indigestion in 60% of patients.*

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60% of patients had non specific GI disturbances.More than 20% had hyper salivation .Dysphagia was found in 10% of patients.Constipation was found in almost 80% of patients.Heartburn in 30% of patients.Indigestion in 60% of patients. Patients with PD indicate that their NMS are more difficult to manage than their motor problems and may sometimes may need hospitalisation. NMS was also more predominant in the "off" medication state and some were alleviated by Dopaminergic therapy or, on the contrary, were exacerbated by the latter Attenuating NMS greatly improves the quality of life of patients, particularly those who positively respond to a Dopaminergic therapy. Thus, the recently developed awareness on the detection of the different NMS early in the course of PD has led to a more critical appraisal of its etiology.

GI Disturbances which correlated with the disease duration more or less than 5 years of onset.

More than 5 yrs	Less than 5 yrs
Constipation 50%	60%
Heartburn10%	18%
Hypersalivation 40%	12%
Indigestion 30%	10%
Dysphagia 15%	30%

Anism or complete muscular obstruction is very rarely a cause of constipation .GI disorders such as malnutrition,aspiration pneumonia ,megacolon,intestinal obstruction and intestinal perforation are the frequent cause of hospitalisation in parkinsonsdisease.A higher mean Leed dyspepsia questionnaire for PD patients indicate increased symptom severity.
GI disorders, such as malnutrition, aspiration pneumonia, megacolon, intestinal obstruction and intestinal perforation, are a frequent cause of hospitalisation in PD

CONCLUSION:

With these observations, PD can no longer be viewed solely as a complex disorder of motor **and nonmotor** functions, but rather as a progressive condition involving both motor and nonmotor features with earlier GIT manifestations.

In some patients, nonmotor problems can be reminiscent of complications resulting from pharmacological and surgical interventions for the treatment of motor symptoms.. Dietary components and dietary patterns have a considerable effect on the composition of the gut microbiome [(7)]. The com-mensal gut microbiota thrive on the substrates that escape absorp-tion in the small intestine and are available for colonic bacterial fermentation (8). For example, fiber-rich diets can enhance the growth of colonic bacteria that produce short-chain fatty acids (SCFA). These SCFA have systemic anti-inflammatory effects (9)and could therefore influence PD pathogenesis through this gut-mediated mechanism. Another example is Western diet (high in saturated fat and refined carbohydrates) that might result in dysbiotic microbiota (e.g., lower bifidobacteria, higher firmicutes, and proteobacteria) (10) and that could ultimately lead to a pro-inflammatory response and promote αSynpathol-ogy. Therefore, it is essential to continue to research specific foods and dietary patterns that can improve gut health for the reduction of risk of PD . Furthermore, the high costs associated with medical care and the aging population strongly stress the need to expand our knowledge base on all aspects of PD. The various effects of which NMS are complex and their highly divergent patterns of progression between PD patients further raise the challenge imposed by NMS in the management of PD . Therapeutic efforts are limited when it is disturbed motility of upper GIT.Hypersalivation is reduced by anticholinergics and now botulinium toxin injections are being tried. Behavioral modifications such as chewing gum have been suggested and this may increase the rate of swallowing. An anticholinergic such as glycopyrrolate may be useful and local treatment options including oral atropine solutions and hyoscine patches are useful.Domperidone has only a minor impact.In constipation polyethylene glycol leads to marked impairment.Physical activities are considerably reduced in Parkinsons disease and if they are promoted they considerably reduce the GIT dysfunction in PD.PD therapies has to be rationalised for optimum patient care.

INTRODUCTION: Over the course of PD progression, motor features in this disease are generally preceded by nonmotor symptoms (NMS) such as depression, olfactory deficit, sleep behavior disorder, and constipation, sometimes by up to ten years Among the non motor manifestations ,GUT BRAIN AXIS which is of growing interest in Parkinsons disease which is a multisystem disorder as evidenced by several neuropathologic studies

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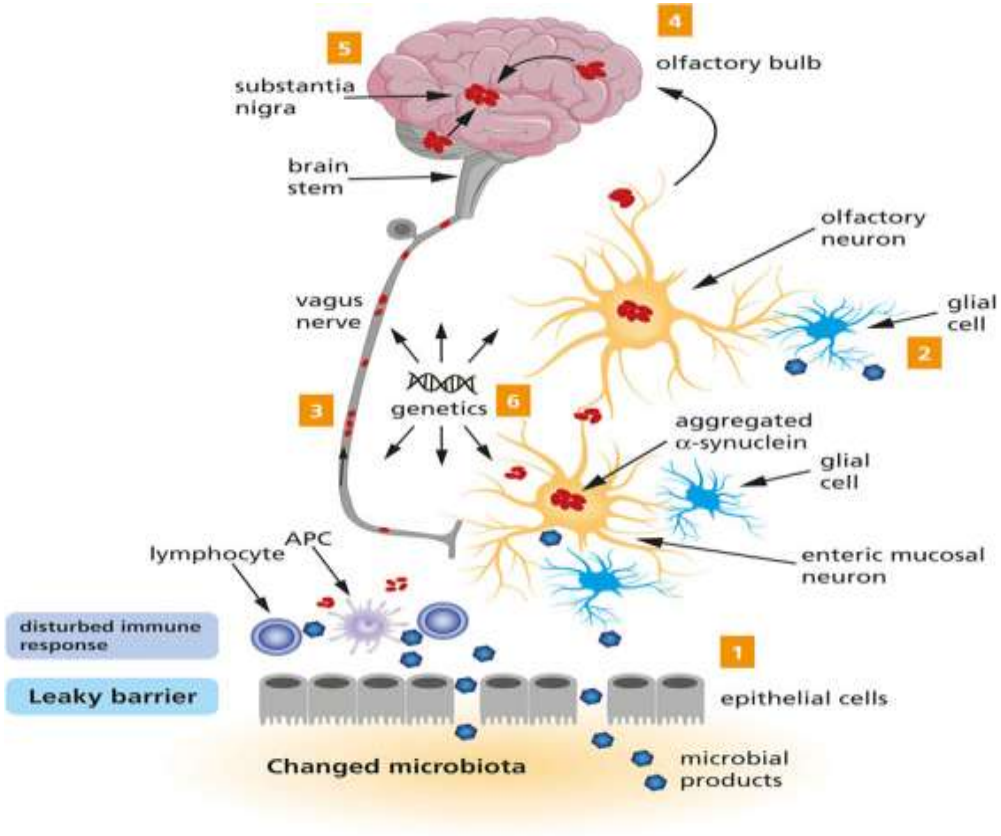
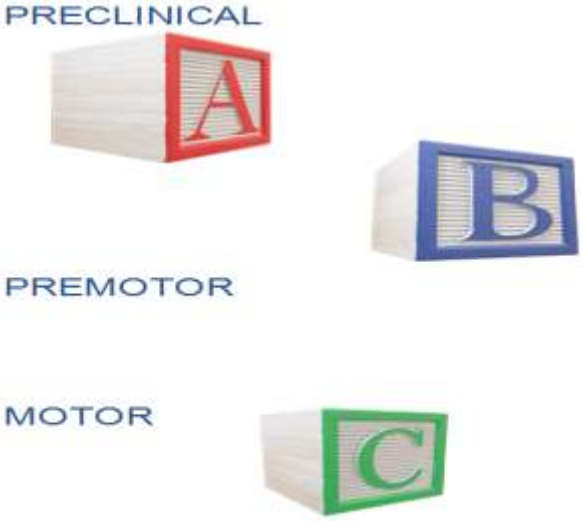
which have found lewy body accumulation in the enteric nervous system in the early stages of PD.Hence GIT dysfunction in parkinsons disease preceeds motor symptoms for decades hence presenting as early biomarkers.As per the braaks hypothesis ,the disease is postulated to originate in the intestine,spread to the brain via the vagus nerve . That's why nondopaminergic neurons and nonmotor symptoms preceed the onset of motor symptoms in parkinsons disease.

BRAAKS HYPOTHESIS:



Some investigators have even proposed that PD could be divided into three phases, namely, preclinical, premotor (corresponding to the NMS), and motor phases].



Degeneration of dorsal vagal nucleus and the intramural plexus of the intestine are the reasons for the nonmotor features.These degenerations develop prior to the degeneration of dopaminergic neurons of the substantia nigra which is the cause of the motor features of Parkinsons disease such as bradykinesia ,rigidity and tremor.Therapeutic measures to overcome the GIT disturbance in parkinsons disease particularly the disturbed motility which responds to certain extent to domperidone and cisapride.Hypersalivation responded to anticholinergics, but botulinium toxin was not used in our center.

CONCLUSION:

With these observations, PD can no longer be viewed solely as a complex disorder of motor and nonmotor functions, but rather as a progressive condition involving both motor and nonmotor features with earlier GIT manifestations..

In some patients, nonmotor problems can be reminiscent of complications resulting from pharmacological and surgical interventions for the treatment of motor symptoms.. Dietary components and dietary patterns have a considerable effect on the composition of the gut microbiome [(7)]. The com-mensal gut microbiota thrive on the substrates that escape absorp-tion in the small intestine and are available for colonic bacterial fermentation (8). For example, fiber-rich diets can enhance the growth of colonic bacteria that produce short-chain fatty acids (SCFA). These SCFA have systemic anti-inflammatory effects (9)and could therefore influence PD pathogenesis through this gut-mediated mechanism. Another example is Western diet (high in saturated fat and refined carbohydrates) that might result in dysbiotic microbiota (e.g., lower bifidobacteria, higher firmicutes, and proteobacteria) (10) and that could ultimately lead to a pro-inflammatory response and promote αSyn pathol-ogy. Therefore, it is essential to continue to research specific foods and dietary patterns that can improve gut health for the reduction of risk of PD . Furthermore, the high costs associated with medical care and the aging population strongly stress the need to expand our knowledge base on all aspects of PD. The various effects of which NMS are complex and their highly divergent patterns of progression between PD patients further raise the challenge imposed by NMS in the management of PD . Therapeutic efforts are limited when it is disturbed motility of upper GIT.Hypersalivation is reduced by anticholinergics and now botulinium toxin injections are being tried. Behavioral modifications such as chewing gum have been suggested and this may increase the rate of swallowing. An anticholinergic such as glycopyrrolate may be useful and local treatment options including oral atropine solutions and hyoscine patches are useful.Domperidone has only a minor impact.In constipation polyethylene glycol leads to marked impairment.

Small intestinal bacterial overgrowth and altered microbiome in PD patients are active fields of investigation . Constipation is among the most common non-motor symptoms in PD, but research in this field is limited by a lack of standardization and the symptoms of anorectal dysfunction are often overlooked. Benefits of these treatments and their adverse effects are still poorly understood and this was the inspiration to present this paper

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