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Evaluation of Autonomic Functions in Patients with Inflammatory Bowel Disease by using Electro Diagnostic Study and Composite Autonomic Symptom Score-31

Noor Jawad Kadhim[1*], Farqad Bader Hamdan[2], Raghad J. Hussain[3]

[1] Department of Neurophysiology, Baghdad Teaching Hospital, Medical City, Baghdad, Iraq. [2] Department of Medical Physiology, College of Medicine, Al-Nahrain University, Baghdad, Iraq
[3] Gastroenterology and Hepatology teaching hospital, Medical City, Baghdad, Iraq.

Corresponding Author Email: Noorjawad1987@gmail.com

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Abstract (Times New Roman Bold 11)

The autonomic nervous system may be involved in inflammatory bowel disease (IBD). Autonomic dysfunction is linked to systemic issues and altered gut motility, possibly contributing to symptoms. This study evaluates autonomic function using electrodiagnostic measures and examines its relationship to factors such as age, sex, disease duration, treatment type, and the Composite Autonomic Symptom Score-31. A case–control design included 75 individuals, consisting of 45 patients diagnosed with Crohn's disease or Ulcerative colitis and 30 healthy controls, aged 18 to 60 years, of either sex. Subjects fasted overnight and did not take any medications for IBD or those that might affect heart rate from noon the day before testing. Smokers were asked to abstain on the morning of testing. Patients exhibited lower heart rate variability during normal breathing and Valsalva maneuvers, with a prolonged palmar sympathetic skin response latency compared to controls. 22 (48.9%) showed early dysfunction, 3 (6.7%) had definite dysfunction, and 3 (6.7%) had severe dysfunction. Eleven (50%) early autonomic dysfunction patients showed parasympathetic involvement (7 Ulcerative colitis, 4 Crohn's disease), 5 (22.7%) had sympathetic involvement (3 Crohn's, 2 Ulcerative colitis), and 6 (27.3%) had both (3 Ulcerative colitis, 3 Crohn's). The Composite Autonomic Symptom Score-31 was negatively linked to heart rate responses to deep breathing, Valsalva, and standing. Patients with IBD have lower autonomic functions. Patients with ulcerative colitis have significantly lower parasympathetic function in comparison to those with Crohn's disease and healthy controls.

1. General Guidelines

1.1. Structure

Your paper should be compiled in the following order: title page; abstract; keywords; main text introduction; materials and methods; results and conclusions; acknowledgments; and references.

1.2. Page Limits

Use Microsoft Office Word 2007 or later to write the article. Please include a page count for your paper.

1.3. Formatting and Templates

Papers should be submitted in Word format. Author details All authors of a manuscript should include their full name and affiliation on the first page of the manuscript. Where available, please also include the ORCiDs code. One author will need to be identified as the corresponding author. Authors' affiliations are the affiliations where the research was conducted. Please note that no changes to affiliation can be made after your paper is accepted.

2. Preparing Your Submission

Authors are advised to consult a recent issue of the Journal for guidance on style and layout. All papers must be written in clear, concise English. In general, research papers should be in an impersonal form.

2.1. Title

Evaluation of Autonomic Functions in Patients with Inflammatory Bowel Disease by using Electro Diagnostic Study and Composite Autonomic Symptom Score-31

2.2. Author Names

Noor Jawad Kadhim MD[1], Farqad Bader Hamdan MD[2], Raghad J. Hussain MD[3]

1. Department of Neurophysiology, Baghdad Teaching Hospital, Medical City, Baghdad, Iraq. Email: Noorjawad1987@gmail.com
2. Department of Medical Physiology, College of Medicine, Al-Nahrain University, Baghdad, Iraq. Email: farqadbhamdan@colmed-alnahrain.edu.iq
3. Gastroenterology and Hepatology teaching hospital, Medical City, Baghdad, Iraq. Email: raghadjawad2011@yahoo.com

2.3. Abstract

Background: The autonomic nervous system may be involved in inflammatory bowel disease (IBD). Autonomic dysfunction is linked to systemic issues and altered gut motility, possibly contributing to symptoms. This study evaluates autonomic function using electrodiagnostic measures and examines its relationship to factors such as age, sex, disease duration, treatment type, and the Composite Autonomic Symptom Score-31.
Method: A case–control design included 75 individuals, consisting of 45 patients diagnosed with Crohn's disease or Ulcerative colitis and 30 healthy controls, aged 18 to 60 years, of either sex. Subjects fasted overnight and did not take any medications for IBD or those that might affect heart rate from noon the day before testing. Smokers were asked to abstain on the morning of testing.
Results: Patients exhibited lower heart rate variability during normal breathing and Valsalva maneuvers, with a prolonged palmar sympathetic skin response latency compared to controls. 22 (48.9%) showed early dysfunction, 3 (6.7%) had definite dysfunction, and 3 (6.7%) had severe dysfunction. Eleven (50%) early autonomic dysfunction patients showed parasympathetic involvement (7 Ulcerative colitis, 4 Crohn's disease), 5 (22.7%) had sympathetic involvement (3 Crohn's, 2 Ulcerative colitis), and 6 (27.3%) had both (3 Ulcerative colitis, 3 Crohn's). The Composite Autonomic Symptom Score-31 was negatively linked to heart rate responses to deep breathing, Valsalva, and standing. Patients with IBD have lower autonomic functions. Patients with ulcerative colitis have significantly lower parasympathetic function in comparison to those with Crohn's disease and healthy controls.

2.4. Keywords

Autonomic nervous system; Inflammatory bowel disease; Sympatho-vagal imbalance.

2.5. Introduction

Inflammatory Bowel Disease (IBD) is a chronic, relapsing inflammatory disorder of the gastrointestinal tract, mainly caused by an abnormal immune response to intestinal microbiota, leading to mucosal damage and systemic inflammation [1]. Although it usually affects young adults, IBD can appear at any age, with around 25% of cases occurring before age 20, and a significant rise in very early onset cases reported globally [2, 3].
Beyond gastrointestinal symptoms, IBD is increasingly linked to neurological complications affecting both the central and peripheral nervous systems, significantly contributing to patient morbidity [4]. The reported prevalence of neurological involvement varies from 0.25% to 47.5%, including cerebrovascular events, demyelinating disorders, neuromuscular diseases, and different forms of peripheral and autonomic neuropathies [5, 6]. Peripheral neuropathy, especially sensorimotor and autonomic types, is more common in IBD than in the general population and may involve demyelination or axonal damage [7, 8]. There are links between IBD and autoimmune neurological disorders such as myasthenia gravis, polymyositis, and dermatomyositis [6, 9]. Furthermore, systemic inflammation in IBD may impair the blood-brain barrier, lower seizure thresholds, and disrupt gut-brain axis signaling, increasing the risk of seizures and EEG abnormalities [10-13]. Emerging evidence points to autonomic nervous system (ANS) dysfunction in IBD, often presenting

as orthostatic intolerance, tachycardia, sudomotor issues, and gastrointestinal dysmotility, even without obvious autonomic symptoms [14, 15]. However, the full extent and clinical importance of autonomic impairment are still not well understood. This study aims to evaluate autonomic function in IBD patients using electrodiagnostic methods and the Composite Autonomic Symptom Score-31 (COMPASS-31), as well as to examine links with demographic and clinical factors, such as age, sex, disease duration, and treatment approaches.

2.6. Methodology and Approaches

Study design

This is a case-control study conducted in the Neurophysiology Unit at Baghdad Teaching Hospital from January 2024 to November 2024. The study followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines [16]. Seventy-five participants took part, including 45 patients referred and diagnosed by specialists from the Gastroenterology and Hepatology Teaching Hospital in Baghdad.

Inclusion and Exclusion Criteria

Patients were excluded if they had a history of peripheral or autonomic neuropathy caused by medical conditions such as diabetes, amyloidosis, thyroid disorders, renal failure, or alcoholism. Additional exclusion criteria included significant mental illness , use of medications known to affect heart rate (e.g., beta-blockers, antiarrhythmics), drugs that induce peripheral neuropathy (e.g., metronidazole), or those impacting autonomic function (e.g., tricyclic antidepressants). Individuals with a history of IBD-related surgery, those taking analgesics, or those with severe liver disease or chronic pancreatitis were also excluded. The control group consisted of 30 healthy individuals aged between 18 and 60 years, with a mean age of 37.86 ± 9.62 years.

All autonomic testing was conducted in a quiet, dimly lit room with the temperature maintained at 22–24 °C and skin temperature ≥35 °C. Participants fasted overnight and abstained from caffeine, nicotine, and heavy meals for at least 12 hours prior to testing. The electromyography and autonomic testing equipment were calibrated before each session according to the manufacturer's specifications.

Composite Autonomic Symptom Score

The COMPASS-31 (Composite Autonomic Symptom Score-31) scale measures neurodegenerative system symptoms using 31 patient-reported questions. Assessment is done through six weighted domains: orthostatic intolerance (10 points); vasomotor (6 points); secretomotor (7 points); gastrointestinal (28 points); bladder (9 points); and pupillomotor (15 points). A higher score on the scale indicates a more pronounced level of autonomic dysfunction.

Electrophysiological Examination

Throughout the investigation, an electromyography machine from Key Point (Medtronic, Denmark) was utilized. To ensure optimal electrical conduction, the individual was grounded using a specialized surface-grounding electrode (H658 NM-550B, Denmark) that had been soaked in water. The recording electrode is a disposable bipolar surface (H690 NM-317Y3, Denmark). The bipolar stimulating electrode (DK-2740, Denmark) was used to stimulate the nerves. To guarantee optimal conductivity, the tips were soaked in water prior to usage.

Nerve Conduction Study

According to the protocol described by Preston and Shapiro [17], the following electrophysiological tests were conducted: sensory nerve conduction studies of the median, ulnar, radial, and sural nerves; motor nerve conduction studies of the median, ulnar, peroneal, and tibial nerves, recorded from the abductor digiti minimi, abductor pollicis brevis, extensor digitorum brevis, and abductor hallucis brevis muscles, respectively. F-wave responses were assessed for the median, ulnar, peroneal, and tibial nerves. Additionally, the sural/radial amplitude ratio (SRAR) was calculated. Electrophysiological parameters included a sweep speed of 5 msec/division for motor studies with a band-pass filter range of 10 Hz to 10 kHz and a sensitivity of 5 mV. For sensory studies, the band-pass filter was set to 20–2000 Hz, with a sweep speed of 2 msec/division and a sensitivity of 20 μV.

Electromyography

Electromyographic activity of cervical muscles (first dorsal interosseus, brachioradialis, and deltoid) and lumbosacral muscles (tibialis anterior, gastrocnemius, and vastus medialis or lateralis) was examined utilizing concentric needle electrodes (Medtronic, Denmark) to exclude myopathy. Twenty MUAPs were analyzed for duration and amplitude during rest, minimal, and maximal volitional effort. The setup used in this test was as follows: gain at 200 μV/division, sweep speed of 20 msec/division, and band-pass filter of 20Hz to 10 kHz.

Autonomic Function Tests

Patients should avoid heavy meals, coffee, and nicotine for at least three to four hours prior to ANS testing. Autonomic testing sessions typically last between sixty and ninety minutes.

Heart Rate Recording and the RR Interval

A three-lead electrocardiograph (ECG) device is commonly used to record heart rate (HR). HR variability (HRV) tests can only be conducted in a sinus rhythm environment. The active recording electrode is fixed to the left anterior chest area at the intercostal area between the fourth and fifth ribs. The reference electrode is fixed at the left anterior axillary line over the fifth or sixth rib. The ground electrode was placed on the midline of the sternum.

Parasympathetic tests

This test evaluates respiratory sinus arrhythmia, which is most noticeable at a breathing rate of six breaths per minute. Subjects first breathe normally for one minute to record baseline R-R interval variability, then perform deep breathing (5 seconds inhalation, 5 seconds exhalation) while the percentage difference between the shortest and longest R-R intervals is calculated. For the Valsalva maneuver, patients exhale forcefully for 15 seconds against a 40 mmHg pressure while lying down or with a 30° head elevation; heart rate is monitored during and after the strain, and the Valsalva ratio is determined from the highest and lowest heart rates. After 20

minutes of rest, the 30:15 ratio is measured by dividing the longest R-R interval (about 30 beats after standing) by the shortest (about 15 beats after standing); a ratio of ≥1.04 is considered normal and tends to decrease with age.

Sympathetic Tests

This test evaluates blood pressure response to active standing, along with heart rate assessment. After 20 minutes of rest, baseline blood pressure is measured in the supine position using a mercury sphygmomanometer. After standing, blood pressure is monitored for 1–3 minutes, with responses assessed within the first 4 minutes. A systolic drop greater than 20 mmHg or a diastolic drop greater than 10 mmHg is considered abnormal. For sympathetic skin response (SSR), the active electrode is placed on the palm, the reference on the back of the hand, and the ground on the palm. Electrical stimulation (12–20 mA, 0.1 msec pulse) is applied to the opposite wrist. SSR amplitude (peak-to-peak, mV) and latency (onset time, msec) are recorded using a sensitivity of 200–1000 μV/div, a filter range of 0.5–2000 Hz, and a sweep speed of 500 msec/div. Normal upper limb SSR values are approximately 0.5 ± 0.1 mV for amplitude and 1.5 ± 0.1 seconds for latency.

Statistical analysis

To perform statistical analyses, SPSS software version 23.0 (SPSS, Chicago) was used. The Shapiro-Wilk test, a normality test, was applied to continuous data. The mean and standard deviation of normally distributed data were reported, and the Student t test and ANOVA were employed for analysis. Non-normally distributed data were presented as median and range, and they were analyzed using the Kruskal-Wallis test or the Mann-Whitney U test. The Chi-square test was used to analyze categorical variables, which were expressed as numbers and percentages. The potential relationship between COMPASS 31 and age and normally distributed autonomic function tests was examined using Pearson's correlation test. A difference was considered statistically significant if the p-value was less than 0.05.

Ethical Statement

The Iraqi Council approved this study for Medical Specialization under Order No. 626, dated January 30, 2024. Written informed consent was obtained from all participants prior to enrollment, and all procedures were conducted in accordance with the ethical standards of the institutional and national research committee, as well as the Declaration of Helsinki.

2.7. Results and Conclusions

Demographics characteristics of study population

The demographic features of the population under study are displayed in **Table 1**. Regarding age and sex, there was no discernible difference between the patients and controls.

Autonomic Function Tests

Patients with IBD had substantially lower HR responses to Valsalva and normal breathing compared to the control group ($p < 0.042$ and $p = 0.012$, respectively). However, there was no difference between the two groups in terms of the HR response to standing and deep breathing. The palmar SSR latency was significantly prolonged ($p = 0.03$) in patients with IBD compared to the controls. The other sympathetic NS parameters were not different between the studied groups (**Table 2**).

Distribution of patients according to the number of abnormal autonomic function tests

Seventeen (37%) of the total patients show no abnormality in ANS function. Twelve (26.7%) have one abnormal autonomic function test, 10 patients (22.2%) have two, 3 patients (6.7%) have three, and 3 patients (6.7%) have four abnormal autonomic function tests.

Distribution of patients according to the severity of autonomic dysfunction

Seventeen (37%) of patients show no abnormal ANS function test results. Twenty-two (48.9%) exhibit early autonomic dysfunction, 3 (6.7%) display definite dysfunction, and only 3 (6.7%) present with severe autonomic dysfunction. Eleven (50%) have parasympathetic autonomic dysfunction, 5 (22.7%) have sympathetic involvement, and 6 (27.3%) show both sympathetic and parasympathetic involvement. All three (100%) with definitive autonomic dysfunction have both sympathetic and parasympathetic involvement, while none show only parasympathetic or only sympathetic dysfunction. Regarding severe dysfunction, all three (100%) patients have both sympathetic and parasympathetic involvement, with none exhibiting solely parasympathetic or sympathetic dysfunction.

Correlation Analysis

Age, length of illness, severity score, and kind of treatment did not correlate with sympathetic and parasympathetic autonomic function testing. COMPASS-31 score was negatively correlated with HR response to deep breathing ($r = -0.665$; $p = 0.0003$), HR response to Valsalva ($r = -0.640$; $p = 0.0001$), and HR response to standing ($r = -0.684$; $p = 0.004$), as shown in **Figure 1**.

Association of Autonomic Function Tests with Sex Difference

Table 3 shows that the only HR response to Valsalva was strongly correlated with sex difference ($p = 0.032$).

Association of Autonomic Function Tests with Disease Duration

No significant association was demonstrated between all autonomic function tests and disease duration and treatment type (**Table 4**).

Discussion

The ANS, through its parasympathetic and sympathetic branches, plays a pivotal role in maintaining gut–brain axis integrity. In this study, the mean age of patients with IBD was 36.9 ± 13.0 years, consistent with the well-recognized early adulthood peak of IBD onset

[18]. Males comprised 75.6% of the cohort, a distribution that mirrors reports of higher ulcerative colitis prevalence among men in some populations, although sex patterns vary globally by disease subtype and geography [19].

Our findings demonstrated reduced heart rate responses during normal breathing and Valsalva maneuvers, accompanied by prolonged palmar SSR latency in IBD patients. Although the prolongation of SSR latency appeared modest compared with controls, it indicates impaired sympathetic sudomotor function. Evidence from prior studies suggests that even subclinical latency prolongation may represent early stages of autonomic involvement, which can subsequently progress to symptomatic dysfunction. Such alterations may contribute to gastrointestinal dysmotility, orthostatic intolerance, and reduced quality of life in patients with IBD.

Importantly, 62.3% of patients in our cohort exhibited some degree of autonomic dysfunction, with parasympathetic impairment being the most prominent feature. This aligns with earlier work highlighting diminished vagal tone, reduced HRV, and sympatho–vagal imbalance in IBD, particularly in ulcerative colitis [20]. The predominance of parasympathetic dysfunction raises the possibility that impaired vagal regulation may not only exacerbate symptom burden but also contribute to disease pathogenesis through altered gut–brain signaling.

An additional novel aspect of this study is the observed negative correlations between COMPASS-31 scores and heart rate responses to deep breathing, Valsalva, and standing. While COMPASS-31 has been validated in conditions such as cardiac autonomic neuropathy and small fiber neuropathy [21, 22], evidence in IBD is sparse. Notably, no correlation has been demonstrated in systemic sclerosis [23], underscoring the disease-specific nature of autonomic involvement. Our findings suggest that COMPASS-31 may provide a simple, non-invasive adjunct to electrodiagnostic testing in IBD, particularly for capturing parasympathetic dysfunction. However, these associations should be considered preliminary given the modest sample size and require validation in larger, multicenter cohorts before definitive conclusions can be drawn.

Several methodological considerations warrant acknowledgment. Although no statistically significant differences were observed in age or sex distribution between groups, the controls were not strictly matched, and residual confounding cannot be fully excluded. Furthermore, while medications known to affect autonomic function were discontinued 24–48 hours before testing, this period may be insufficient for drugs with longer half-lives, and residual effects remain possible. These factors may have influenced autonomic test results and should be addressed in future studies with stricter matching and longer washout periods.

Taken together, our results provide further evidence that autonomic dysfunction is a clinically relevant, though often underrecognized, extra-intestinal manifestation of IBD. The predominance of parasympathetic impairment, coupled with the potential utility of COMPASS-31 as a screening tool, highlights a novel avenue for integrating autonomic assessment into the clinical evaluation of IBD patients.

Clinical Implications

This study reveals a significant autonomic dysfunction burden in IBD patients, especially parasympathetic impairment shown by reduced heart rate variability and prolonged sympathetic skin response. Autonomic testing, including heart rate assessments and the COMPASS-31 questionnaire, could help detect subclinical dysfunction early, even without symptoms. Routine screening may enable timely interventions to improve gastrointestinal symptoms, quality of life, and personalized management.

Limitations

The small sample size may limit the generalizability of the findings to broader IBD populations. Second, the cross-sectional design precludes assessment of causality or progression of autonomic dysfunction over time. Third, potential confounders such as psychological stress, subclinical nutritional deficiencies, or undiagnosed comorbidities were not fully accounted for, which may influence autonomic function. Another limitation of this study is the absence of a formal sample size and power calculation, which may have reduced the statistical strength of subgroup analyses, particularly between Crohn’s disease and ulcerative colitis.

Conclusions and Recommendations

This study demonstrates that ANS dysfunction is a prevalent extra-intestinal manifestation in patients with IBD, particularly among those with ulcerative colitis who show significantly reduced parasympathetic function compared to Crohn’s disease and healthy controls. The dysfunction was not associated with age, disease duration, or treatment type. Patients with a single abnormal autonomic test often showed sympathetic involvement only, whereas multiple abnormalities typically indicated combined sympathetic and parasympathetic dysfunction. Future studies with larger cohorts are needed to validate the observed associations. Incorporating advanced HRV metrics may improve detection sensitivity. Furthermore, assessing ANS function in newly diagnosed patients using standardized methods could clarify the role of autonomic imbalance in disease onset and flare-ups.

2.8. Tables

Each table should be numbered consecutively (1, 2, etc.). The Table header should be placed at the top (example).

Table 1: Demographic data of the study population

Characteristics	Patients (n=45)	Control (n=30)	P-value
Age, years			
Mean ±SD	36.96±13.01	39.43±8.79	0.35
Sex			
Male	34 (75.6%)	20 (66.7%)	0.57
Female	11 (24.4%)	10 (33.3%)	
Type of IBD			
Crohn's disease	18(40%)		
Ulcerative colitis	27(60%)		

Disease duration, years	
Newly diagnosed	12(26.6%)
< 5 years	17 (37.8%)
> 5 years	16 (35.6 %)
Smoking	
Yes	9 (20%)
No	36 (80%)
COMPASS-31 score Mean ±SD	16.08±12.00
Treatment Type	
No	12 (26.7%)
Biological	23 (51%)
Non biological	10 (22.2%)

Table 2: Autonomic Tests in Patients and Controls

Parameter	Patients (n=45)	Controls (n=30)	P-value
HRNB, beat/min			
Mean ± SD	22.72 ± 17.44	29.98± 5.13	0.042
Median	18.00	23.00	
Range	7.90-95.00	15-97	
HRDB, beat/min			
Mean ± SD	33.37 ± 22.40	40.66 ± 23.66	0.172
Median	24.00	28.500	
Range	11.00-98.00	23.00-99.00	
HRVals, beat/min			
Mean ± SD	1.72±0.37	2.25 ± 1.35	0.012
Median	1.66	1.87	
Range	0.98-2.90	2.0-5.65	
HRS, beat/min			
Mean ± SD	1.49±0.65	1.51±0.56	
Median	1.20	1.205	0.926
Range	0.50-2.86	1.05-3.10	
SBP drop, mmHg			
Mean± SD	0.55±11.57	0.16±5.94	0.772
DBP drop, mmHg			
Mean± SD	-2.66±12.92	-1.66±5.62	0.706
Palmar SSR Latency, sec			
Mean± SD	1.86±1.33	1.30±0.13	0.030
Palmar SSR amplitude, mV			
Mean± SD	3.14±2.63	4.04±1.85	0.140
Planter SSR latency, sec			
Mean± SD	1.85±1.33	1.30±0.13	0.100
Planter SSR amplitude, mV			
Mean± SD	1.71±0.84	1.96±0.56	0.250

Normally distributed variables are presented as mean ± SD, while non-normally distributed variables are presented as median and range, according to the results of the Shapiro–Wilk test.

Table 3: Association of Autonomic Function Tests with Sex of the patients

Parasympathetic tests	Males	Females	p-value
HRNB (beat/min)			
Mean ± SD	21.42 ± 15.13	26.74 ± 23.66	0.927
Median	18.00	18.00	
Range	7.90-95.00	20-80	
HRDB (beat/min)			
Mean ± SD	36.67±13.17	25.90±25.36	0.277
Median	32.50	16.00	
Range	13-98	11-69	
HRVals	2.45±1.43	1.63±0.86	0.032

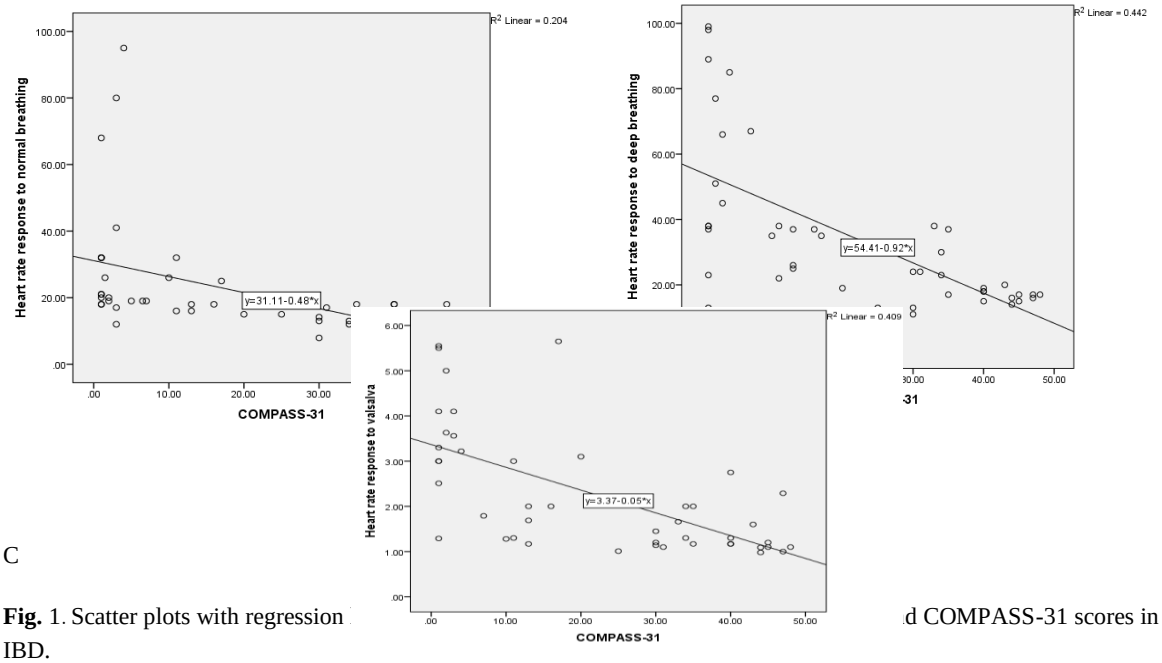
Mean ± SD	1.66	1.17	
Median	0.98-5.65	1.00-2.52	
Range			
HRS			
Mean ± SD	1.47±0.61	1.24±0.46	
Median	1.285	1.200	0.302
Range	0.50-2.86	0.70-2.24	
Palmar SSR Latency, ms			
Mean ± SD	1.73±1.26	1.69±0.40	0.277
Median	1.44	1.500	
Range	0.00-7.57	1.20-2.28	
Plantar SSR Latency, ms			
Mean ± SD	1.60±0.94	1.78±0.88	0.203
Median	1.85	1.98	
Range	0.78-3.57	0.79-2.60	

Table 4: Association of Autonomic Function Tests with Disease Duration and Treatment Type

Parasympathetic function tests	Disease Duration Newly diagnosed	< 5 years	> 5 years	p-value
HRNB, beat/min				
Mean ± SD	21.17±10.61	24.20±19.50	22.31±19.99	0.975
Median	18.0	18.0	18.0	
Range	7.90-41.0	10.0-80.0	11.0-95.0	
HRDB, beat/min				
Mean ± SD	30.83±15.76	30.29±23.61	40.43±28.78	0.322
Median	30.50	18.0	27.50	
Range	13.00-66.0	13.0-77.0	11.0-98.0	
HRVals				
Mean ± SD	2.41±1.55	1.95±1.24	2.45±1.33	0.333
Median	1.48	1.28	2.0	
Range	1.0-5.50	1.01-5.65	0.98-5.55	
HRS				
Mean ± SD	1.75±0.99	1.37±0.60	2.14±0.96	
Median	1.17	1.20	1.49	0.287
Range	0.50-2.0	0.70-2.31	0.90-2.86	
Palmar SSR Latency, ms				
Mean ± SD	1.43±0.38	1.81±0.83	1.86±1.65	0.319
Median	1.30	1.45	1.52	
Range	1.06-2.19	1.23-4.00	0.00-7.57	
Planter SSR latency, ms				
Mean ± SD	1.64±0.99	1.78±0.98	1.52±0.84	0.902
Median	1.85	1.85	1.87	
Range	0.98-3.57	0.99-3.40	0.00-2.50	
Test	Treatment type None	Non-biological	Biological	p-value
HRNB, beat/min				
Mean ± SD	21.17±10.61	20.96±17.02	25.22±21.56	0.580
Median	18.0	18.0	19.0	
Range	7.90-41.0	10-80	11.0-95.0	
HRDB, beat/min				
Mean ± SD	30.83±15.76	25.60±19.43	43.22±29.07	0.061
Median	30.50	17.0	32.5	
Range	13.0-66.0	13.0-89.0	11.0-98.0	
HRVals				
Mean ± SD	2.41±1.55	2.18±1.57	2.20±1.05	0.537
Median	1.48	1.20	1.89	
Range	1.0-5.50	0.98-5.65	1.09-5.0	
HRS				
Mean ± SD	1.29±0.48	1.44±0.56	1.49±0.67	
Median	1.17	1.40	1.33	0.786
Range	0.50-2.0	0.70-2.79	0.78-2.86	

Palmar SSR Latency, ms				
Mean ± SD	1.43±0.38	1.90±0.87	1.77±1.54	0.205
Median	1.30	1.48	1.47	
Range	1.06-2.19	1.23-4.0	0.0-7.75	
Planter SSR latency, ms				
Mean ± SD	1.64±0.99	1.66±0.93	1.65±0.92	
Median	1.85	1.85	1.90	0.975
Range	0.78-3.57	0.78-3.37	0.98-3.40	

2.9. Figures



C

Fig. 1. Scatter plots with regression d COMPASS-31 scores in patients with IBD.

A: Scatter plot and Regression line between HR Response to Normal Breathing and COMPASS-31 in the IBD Patients

B: Scatter plot and Regression line between HR Response to Deep Breathing and COMPASS-31 in the IBD Patients.

C: Scatter plot and Regression line between HR Response to Valsalva and COMPASS-31 in IBD Patients

The Figure in the manuscript should be given in the following format. For example, Fig. 1. in the manuscript should be written as Fig. 1

Acknowledgments

None

REFERENCES

[1] Colombel JF, Shin A, Gibson PR. AGA Clinical Practice Update on Functional Gastrointestinal Symptoms in Patients With Inflammatory Bowel Disease: Expert Review. Clin Gastroenterol Hepatol. 2019 Feb;17(3):380-390.

[2] Rosen MJ, Dhawan A, Saeed SA. Inflammatory bowel disease in children and adolescents. JAMA Pediatr. 2015; 169:1053–60.

[3] Kuenzig ME, Fung SG, Marderfeld L, Mak JW, Kaplan GG, Ng SC, Wilson DC, Cameron F, Henderson P, Kotze PG, Bhatti J. Twenty-first century trends in the global epidemiology of pediatric-onset inflammatory bowel disease: systematic review. Gastroenterology. 2022 Apr 1;162(4):1147-59.

[4] Ferro JM, Oliveira Santos M. Neurology of inflammatory bowel disease. J Neurol Sci. 2021; 424:117426.

[5] Benavente L, Morís G. Neurologic disorders associated with inflammatory bowel disease. Eur J Neurol. 2011; 18(1):138-143.

[6] Ferro JM, Oliveira SN, Correia L. Neurologic manifestations of inflammatory bowel diseases. Handb Clin Neurol. 2014; 120:595-605.

[7] Zois CD, Katsanos KH, Kosmidou M, Tsianos EV. Neurologic manifestations in inflammatory bowel diseases: current knowledge and novel insights. Journal of Crohn's and Colitis. 2010 Jun 1;4(2):115-24.

[8] Babali A, Terzoudi A, Vadikolias K, et al. Peripheral neuropathy electrophysiological screening in inflammatory bowel disease. Eur J Gastroenterol Hepatol. 2013; 25(5):539- 542.

[9] Finnie IA, Shields R, Sutton R, Donnelly R, Morris AI. Crohn's disease and myasthenia gravis: a possible role for thymectomy. Gut. 1994 Feb 1;35(2):278-9.

[10] Rana A, Musto AE. The role of inflammation in the development of epilepsy. Journal of neuroinflammation. 2018 May 15;15(1):144.

[11] Musto AE, Rosencrans RF, Walker CP, Bhattacharjee S, Raulji CM, Belayev L, Fang Z, Gordon WC, Bazan NG. Dysfunctional epileptic neuronal circuits and dysmorphic dendritic spines are mitigated by platelet-activating factor receptor antagonism. Scientific reports. 2016 Jul 22;6(1):30298.

[12] Casella G, Tontini GE, Bassotti G, Pastorelli L, Villanacci V, Spina L, Baldini V, Vecchi M. Neurological disorders and inflammatory bowel diseases. World Journal of Gastroenterology: WJG. 2014 Jul 21;20(27):8764.

[13] De Caro C, Leo A, Nesci V, Ghelardini C, di Cesare Mannelli L, Striano P, Avagliano C, Calignano A, Mainardi P, Constanti A, Citraro R. Intestinal inflammation increases convulsant activity and reduces antiepileptic drug efficacy in a mouse model of epilepsy. Scientific reports. 2019 Sep 27;9(1):13983.

[14] Mogilevski T, Burgell R, Aziz Q, Gibson PR. the role of the autonomic nervous system in the pathogenesis and therapy of IBD. Alimentary pharmacology & therapeutics. 2019 Oct;50(7):720-37.

[15] Lindgren S, Lilja B, Rosen I, Sundkvist G. Disturbed autonomic nerve function in patients with Crohn's disease. Scandinavian journal of gastroenterology. 1991 Jan 1;26(4):361-6.

[16] Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. The lancet. 2007 Oct 20;370(9596):1453-7.

[17] Preston DC & Shapiro BE. Routine Upper Extremity, Facial, and Phrenic Nerve Conduction Techniques. In: Electromyography and Neuromuscular Disorders: Clinical–Electrophysiologic Correlations. Basic Nerve Conduction Studies. SECTION IV. Detailed Nerve Conduction Studies. 3rd edition, Chapter 10, Elsevier Inc. 2021; p. 105, 119.

[18] Rasquin A, Di Lorenzo C, Forbes D, et al. Childhood functional gastrointestinal disorders: child/adolescent. Gastroenterology. 2006; 130(5):1527-1537.

[19] Ott C, Obermeier F, Thieler S, Kemptner D, Bauer A, Schölmerich J, Rogler G, Timmer A. The incidence of inflammatory bowel disease in a rural region of Southern Germany: a prospective population-based study. European journal of gastroenterology & hepatology. 2008 Sep 1;20(9):917-23.

[20] Sadowski A, Dunlap C, Lacombe A, Hanes D. Alterations in heart rate variability associated with irritable bowel syndrome or inflammatory bowel disease: a systematic review and meta-analysis. Clinical and translational gastroenterology. 2021 Jan 1;12(1):e00275.

[21] Zhang Z, Ma Y, Fu L, Li L, Liu J, Peng H, Jiang H. Combination of composite autonomic symptom score 31 and heart rate variability for diagnosis of cardiovascular autonomic neuropathy in people with type 2 diabetes. Journal of Diabetes Research. 2020;2020(1):5316769.

[22] D'Ippolito I, Menduni M, D'Amato C, Andreadi A, Lauro D, Spallone V. Does the relationship of the autonomic symptoms questionnaire COMPASS 31 with cardiovascular autonomic tests differ between type 1 and type 2 diabetes mellitus?. Diabetes & Metabolism Journal. 2024 Nov 1;48(6):1114-25.

[23] Maghraby GG, Khalil AS, Fawzi MM, Hegazy MT. Heart rate variability stands up to bedside tests and composite autonomic symptom score-31 (COMPASS-31) questionnaire: Diagnostic tools for autonomic dysfunction in systemic sclerosis patients. The Egyptian Rheumatologist. 2025 Jan 1;47(1):41-5.