

# State and trait anxiety and depression in patients affected by gastrointestinal diseases: psychometric evaluation of 1641 patients referred to an internal medicine outpatient setting

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## SUMMARY

**Objectives:** To evaluate state and trait form of anxiety and current depression in patients affected by gastrointestinal diseases. **Methods:** We studied 1641 outpatients with gastrointestinal disorders, consecutively referred to our Internal Medicine outpatients from 1997 to 2005. State and trait anxiety were assessed by the State and Trait Anxiety Inventory. Current depression was assessed by the Zung self-rating depression scale. **Results:** Among patients, 1379 (84.1%) showed state anxiety, 1098 (67%) showed trait anxiety and 442 (27%) showed current depression. The number of gastrointestinal diseases was directly correlated to state anxiety ( $p < 0.001$ ) and trait anxiety ( $p = 0.04$ ). Females showed higher levels of anxiety and depression than males ( $p < 0.001$ ). State anxiety was related to food allergies ( $p < 0.001$ ), small intestinal bacterial overgrowth (SIBO) ( $p = 0.001$ ), Hp infection ( $p = 0.01$ ) and ulcerative colitis in active phase ( $p = 0.03$ ). Trait anxiety was related to irritable bowel syndrome (IBS) ( $p < 0.001$ ), *Helicobacter pylori* (Hp) infection ( $p = 0.001$ ), food allergies ( $p = 0.001$ ) and SIBO ( $p = 0.001$ ). Current depression was related to IBS ( $p < 0.001$ ) and coeliac disease ( $p = 0.01$ ), SIBO ( $p = 0.02$ ). A predicted probability of  $0.77 \pm 0.16$  to have state anxiety, of  $0.66 \pm 0.12$  to have trait anxiety and of  $0.39 \pm 0.14$  to have depression was found in these patients. **Conclusions:** Most of the patients who seek medical consultation for gastrointestinal problems show an associated affective disorder. These patients should be managed by a team including gastroenterologists, psychologists and/or psychiatrists, or by a gastroenterologist having expertise in the treatment of psychological disorders.

## Introduction

Anxiety and depression represent a common feature in patients affected by gastrointestinal diseases (1,2). In some cases as in patients with functional gastrointestinal disorders, anxiety and depression are present particularly as a personality trait (3) and they seem to play a main role in the genesis and/or the perception of symptoms (1). Recent studies showed that in these subjects, medical consultation is necessary because of the 'healthcare seeking behaviour' strictly related to the anxious trait, more than to the organic symptoms (4,5). In this case, the socio-economic impact resulting from consultations with several gastroenterologists and from undergoing

clinical examinations and consumption of drugs, is very high (6).

On the other hand, few information are at present available about anxiety and depression in patients in whom an organic cause for their symptoms has been found (2). In these cases, anxiety and/or depression could be present mainly in the 'state' and/or 'current' form, reactive to the symptoms (7), to the long-term diseases (8), to long-term therapies and dietary restrictions (9), to the necessity of frequent medical control and to the reduction of the quality of life and of general well-being (10,11).

However, at present, few data about the prevalence of state and trait form of anxiety and of current depression are available in large sample of patients

### What's known

Anxiety and depression represent a common feature in patients affected by gastrointestinal diseases. These affective disorders can be present as a personality trait or in a reactive form.

### What's new

The study supports that the approach to patients affected by gastrointestinal diseases should be managed by a team including gastroenterologists, psychologists and/or psychiatrists, or alternatively they should be managed by gastroenterologist having expertise in the treatment of psychological disorders.

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### Disclosure

The authors have declared that they have no interest which might be perceived as posing conflict or bias.

affected by gastrointestinal disorders. In addition, in these patients, the role played by affective disorders is still discussed.

Aim of this study was to evaluate the presence of state anxiety, trait anxiety and current depression in patients affected by gastrointestinal diseases, referred consecutively to an Internal Medicine outpatient setting for several consecutive years.

## Patients and methods

The study was performed on 1641 outpatients; mean age  $43.9 \pm 15.9$  years (range: 15–92, median value 42.0), 948 (57.8%) females (mean age  $\pm$  SD  $44.5 \pm 16.1$ , range: 15–92, median value 44.0) and 693 (42.2%) males (mean age  $\pm$  SD  $43.1 \pm 15.7$ , range: 15–85, median value 40.5) affected by gastrointestinal diseases, consecutively referred to the specialists including gastroenterologists in our Internal Medicine outpatient setting during the period of 8 years (1997–2005). This study was approved by the Ethics Committee of the 'Università Cattolica' in Rome.

Socio-demographic characteristics of the patients are reported in Table 1. Exclusion criteria were the presence of non-gastrointestinal disease. Patients affected by cancer diseases were also excluded to avoid bias on the prevalence of anxiety (12) and depression (13). Anamnesis and medical observation were performed by Internal Medicine (GG, GA) and Gastroenterology (GG) specialists. Evaluation of blood cell count, serum electrolytes, glycaemia, creatinine, blood nitrogen, electrophoresis pattern of serum proteins, transaminases, gamma-glutamyl-transferase, alkaline phosphatase, lactate dehydroge-

nase, albumin, bilirubin, amylasaemia, total cholesterol, high-density lipoprotein-cholesterol, low-density lipoprotein-cholesterol, triglycerides, erythrocyte sedimentation rate, reactive-C-protein, activated partial thromboplastin time, international normalized ratio (INR), urine analysis, anti-gliadin antibodies (AGA) and anti-endomysial antibody (EMA) antibodies, was performed in all patients. Instrumental examination was carried out in patients on the basis of the suspected disease. Based on the frequency, the following diseases were found (Table 2).

*Helicobacter pylori* (Hp) infection,  $n = 559$  (38.5%):  $^{13}\text{C}$ -Urea Breath test was performed to assess Hp infection (14). Chronic gastritis was present in 367 patients (65.6%) and peptic ulcer in 59 patients (10.5%). The diagnosis of chronic gastritis or peptic ulcer was obtained based on endoscopic and biopsy examinations of stomach and duodenum.

Small intestinal bacterial overgrowth (SIBO),  $n = 554$  (33.8%): the diagnosis was based on glucose (15) and/or lactulose (16) hydrogen breath tests.

Sugar malabsorption,  $n = 394$  (24%): In all cases, the presence of malabsorption of both lactose (20 g) and fructose plus sorbitol (20 + 3.5 g respectively) was assessed by hydrogen breath test (17).

Irritable bowel syndrome (IBS),  $n = 309$  (18.9%): the IBS was diagnosed based on Rome criteria (Rome I from 1997 to 1999 and Rome II from 2000 to 2005) (18). Liver steatosis,  $n = 227$  (13.8%): The diagnosis was based on abdominal ultrasonography (19).

Celiac disease,  $n = 168$  (10.2%): The diagnosis was based on the positivity of AGA and of EMA antibodies and was confirmed by histological evidence of subtotal or total duodenal villous atrophy (9).

Inflammatory bowel disease (IBD),  $n = 135$  (8.2%): The diagnosis was based on abdominal ultrasonography and endoscopic and biopsy examinations of the intestine (7). The clinical disease activity was assessed with the simplified Crohn's Disease Activity Index for patients affected by Crohn's disease (20) and with the Truelove–Witts criteria for patients affected by ulcerative colitis (21).

Chronic hepatitis,  $n = 122$  (7.4%): the diagnosis was based on the serological Hepatitis B virus (HBV) and Hepatitis C virus (HCV) tests, HBV-DNA, HCV-RNA, serum-free copper, 24 h urinary copper, ceruloplasmin, iron, serum ferritin, transferring saturation, unsaturated iron-binding capacity. Abdominal ultrasonography was performed in all these patients. Liver biopsy was performed when necessary (22). Liver cirrhosis was present in 35 (2.1%) patients.

Gastro-esophageal reflux disease (GERD),  $n = 107$  (6.5%): the diagnosis was based on accurate clinical

**Table 1** Socio-demographic characteristics of the gastrointestinal patients evaluated

<b>Sex</b>	
Female	948 (57.8%)
Male	693 (42.2%)
<b>Mean age (SD)</b>	43.9 (15.9)
<b>Education level</b>	
Grade school	389 (23.7%)
High School	720 (43.9%)
University	532 (32.4%)
<b>Employment status</b>	
Full time	668 (40.7%)
Part time	476 (29.0%)
Not employed	497 (30.3%)
<b>Marital status</b>	
Married	822 (50.1%)
Divorced	284 (17.3%)
Never married	535 (32.6%)

**Table 2** Diseases, their frequency (*n*) and percentage (%), mean age with standard deviation of the affected patients, percentage of patients positive to the tests administered (STAI *y*1: state anxiety; STAI *y*2: trait anxiety; Zung: current depression) and statistical significance (*p*-value) of diseases in ANOVA for each test

Diseases	<i>n</i> (%)	Mean age ± SD	STAI <i>y</i> 1 (%)	STAI <i>y</i> 2 (%)	Zung (%)	STAI <i>y</i> 1 <i>p</i> -value	STAI <i>y</i> 2 <i>p</i> -value	Zung <i>p</i> -value
Hp infection	559 (38.5)	43.0 ± 15.5	89.8	70.5	18.7	0.01	0.001	0.46
SIBO	554 (33.7)	44.1 ± 15.9	88.0	68.5	23.1	0.001	0.001	0.02
Sugar malabsorption	394 (24.0)	38.2 ± 13.9	88.0	69.0	20.0	0.79	0.57	0.06
IBS	309 (18.8)	43.9 ± 16.9	86.0	78.6	51.7	0.91	< 0.001	< 0.001
Liver steatosis	227 (13.8)	46.6 ± 13.4	84.1	65.6	15.4	0.79	0.75	0.60
Coeliac disease	168 (10.2)	36.1 ± 14.5	75.0	52.3	38.1	0.26	0.06	0.01
Chronic hepatitis	122 (7.4)	52.8 ± 13.6	81.9	57.3	21.3	0.54	0.53	0.26
GERD	107 (6.5)	43.6 ± 15.7	84.1	69.1	21.5	0.93	0.61	0.73
Gastritis Hp negative	60 (3.6)	47.9 ± 16.7	88.3	75.0	28.3	0.17	0.18	0.21
UC, active phase	53 (3.2)	34.0 ± 12.7	92.4	47.1	15.0	0.03	0.26	0.59
Food allergies	43 (2.6)	36.1 ± 13.2	93.0	86.0	44.1	< 0.001	0.001	0.35
Crohn's, active phase	41 (2.5)	36.6 ± 14.5	87.8	58.5	21.9	0.05	0.13	0.94
UC, remission phase	21 (1.3)	37.5 ± 11.1	66.6	47.6	0.0	0.09	0.08	0.02
Crohn's, remission phase	20 (1.2)	40.6 ± 12.9	55.0	35.0	15.0	0.29	0.01	0.39

STAI, State and Trait Anxiety Inventory; SIBO, small intestinal bacterial overgrowth; IBS, irritable bowel syndrome; GERD, gastro-esophageal reflux disease; Hp, *Helicobacter pylori*; UC, ulcerative colitis.

evaluation, endoscopy and oesophageal pH-metry examination (23).

Chronic gastritis without Hp infection, *n* = 60 (3.7%): the diagnosis was based on endoscopic and biopsy examinations of stomach and duodenum.

Food allergy, *n* = 25 (1.5%): the diagnosis was based on the measurement of food-specific immunoglobulin E antibodies, the skin prick tests, elimination diet and oral provocation tests (24). Endoscopic examinations as well as the histopathological findings were performed and evaluated always by the same investigators.

### Psychometric evaluation

Anxiety was assessed by the State and Trait Anxiety Inventory (STAI), made up of two axes (*y*1 for state anxiety and *y*2 for trait anxiety), both consisting of 20 multiple-choice items; each item has a score from one to four so that the total point score of *y*1 and *y*2 axes can range from 20 to 80 (25). This test was selected based on simplicity, validity and reliability (26) and also because it was already used by our group in studies aimed to evaluate anxiety levels and distinguish 'state' anxiety from 'trait' anxiety in gastrointestinal diseases (3,7–9,11). In particular, the STAI test permits a distinction between existing anxiety and the predisposition to the anxious reaction as a personality characteristic, as previously described (3). This theory is based on the conceptual distinction between anxiety as a transitory state and anxiety as a relatively stable personality trait. State anxiety is

conceptualised as an emotive state characterised by subjective feelings perceived on a conscious level, such as apprehension and tension, which vary with time; anxiety as a trait refers to individuals with continuous disposition towards anxiety (9). The subjects evaluated were grouped as high- and low-anxious and a value of 40 was used to distinguish between the two groups, according to Spielberg et al. (25) and to Weinstein (27).

The presence of depression was assessed by the Zung self-rating Depression Scale (Zung-SDS) (28). The Zung-SDS contains 20 multiple items with a score from one to four each, so that the total point score of more than 49 is considered high (29). The point score is based on the frequency of depressive symptoms: minor symptoms which occur frequently and therefore have a high score. This test constitutes an effective instrument in screening for depression in a clinical setting and its positive predictive value of a diagnosis of depression is between 88.7% and 92.3% (30).

### Statistical analysis

Several standard analyses were first carried out to summarise variables and to explore the relationships among them. Results from such analyses are widely reported throughout the paper.

A multifactor ANOVA was then run to assess the influence of gender and each of the gastrointestinal diseases on STAI *y*1, STAI *y*2 and Zung-SDS scores respectively. The three tests were considered in their

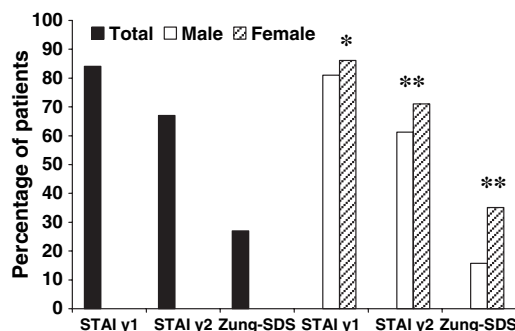
original scale total scores to obtain the most complete information from the data. Only main effects of factors were considered, discounting the possibility of interactions. Statistical significance of effects was judged through the corresponding p-values.  $p < 0.05$  was considered statistically significant.

Finally, a logistic regression analysis was performed for each of the three tests considered, to predict the probability that a specific patient is positive to the test. To obtain parsimonious models, factors emerging as influential in the corresponding ANOVA were used as predictors in the logistic regression models without constant term. Stepwise logistic regression, both forward and backward, applied to the entire set of candidate explanatory variables, led to somewhat similar sets of predictors as those identified from ANOVA procedures. For descriptive purposes, predicted probabilities for the 1641 patients examined in this paper are summarised in the Results section. These results seem to indicate that the fitted equations tend to overestimate predicted probabilities that the test is positive for STAI  $\gamma 1$  and STAI  $\gamma 2$  tests, and to underestimate those probabilities in the case of Zung-SDS. Further research is needed on this topic. All the computations were carried out using SPSS 14.0 (SPSS Inc., Chicago, IL).

## Results

Among examined patients, 1379 patients (84.1%) showed high levels of state anxiety, 1098 (67%) showed high levels of trait anxiety and 442 (27%) showed current depression (Figure 1).

Regarding single specific diseases, Table 2 shows the percentage of patients in which a high score of



**Figure 1** Percentage of patients affected by gastrointestinal disorders who showed state anxiety (STAI  $\gamma 1$ ), trait anxiety (STAI  $\gamma 2$ ) and current depression [Zung self-rating Depression Scale (Zung-SDS)], and differences between male and females. A very high percentages for the two forms of anxiety and of depression was found in the sample evaluated. State anxiety, trait anxiety and depression were present in a significantly higher percentage in female than in male. \* $p < 0.01$ ; \*\* $p < 0.001$

**Table 3** Number of diseases per number of patients (and relative percentage)

Number of diseases	Number of patients (%)
1	778 (47.3)
2	372 (22.7)
3	294 (17.9)
4	137 (8.4)
5	49 (3.0)
6	9 (0.6)
7	2 (0.1)
Total	1641 (100)

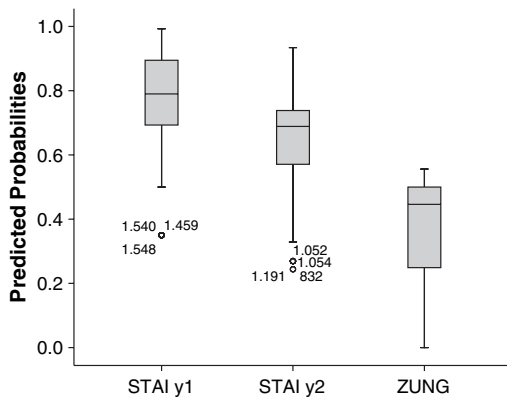
the psychometric scales indicating state anxiety, trait anxiety and current depression was found.

Number of pathologies affecting the patients evaluated are reported in Table 3. The mean of pathologies for patients was of  $1.97 \pm 1.1$  (median 2.00; range: 1–7),  $1.98 \pm 1.1$  (median 2.00; range: 1–7) for females and  $1.96 \pm 1.1$  (median 2.00; range: 1–7) for males. There was no statistical difference in number of pathologies between the genders ( $p = 0.74$ ). Although with a slight r-value, a direct correlation between the number of diseases and state anxiety ( $r = 0.086$ ,  $p < 0.001$ ) and trait anxiety ( $r = 0.050$ ,  $p = 0.04$ ) was found.

State anxiety ( $p < 0.01$ ), trait anxiety ( $p < 0.001$ ) and current depression ( $p < 0.001$ ) were present in a significantly higher percentage of females than in males (Figure 1). Moreover, females when compared with males showed significantly higher levels of state anxiety ( $51.1 \pm 10.6$  vs.  $48.1 \pm 9.8$ ;  $p < 0.001$ ), trait anxiety ( $46.5 \pm 10.7$  vs.  $43.2 \pm 10.2$ ;  $p < 0.001$ ) and current depression ( $43.5 \pm 13.8$  vs.  $37.4 \pm 11.4$ ;  $p < 0.001$ ). The age of patients directly correlated to trait anxiety ( $r = 0.069$ ,  $p = 0.005$ ) and to current depression ( $r = 0.143$ ,  $p < 0.001$ ). STAI  $\gamma 1$  correlates directly with STAI  $\gamma 2$  ( $r = 0.618$ ,  $p < 0.001$ ) and Zung scale ( $r = 0.428$ ;  $p < 0.001$ ).

Results from ANOVA showed that state anxiety was significantly related to food allergies ( $p < 0.001$ ), SIBO ( $p = 0.001$ ), Hp infection ( $p = 0.01$ ) and ulcerative colitis in active phase ( $p = 0.03$ ), (Table 2). Trait anxiety was significantly related to IBS ( $p < 0.001$ ), Hp infection ( $p < 0.001$ ), food allergies ( $p = 0.001$ ) and SIBO ( $p = 0.001$ ), (Table 2). Current depression was significantly related to: IBS ( $p < 0.001$ ), SIBO ( $p = 0.02$ ) and coeliac disease ( $p = 0.01$ ) (Table 2). Female gender was significantly related to the presence of state anxiety ( $p < 0.001$ ), trait anxiety ( $p < 0.001$ ) and current depression ( $p < 0.001$ ).

The presence of Crohn's disease in remission phase showed an inverse relation with trait anxiety



**Figure 2** Box-plots for the predicted probabilities on examined patients positive to the tests. These probabilities turned out to be  $0.77 \pm 0.16$  for state anxiety (STAI y1),  $0.66 \pm 0.12$  for trait anxiety (STAI y2) and  $0.39 \pm 0.14$  for current depression [Zung self-rating Depression Scale (Zung-SDS)]. Patient numbers 832, 1052, 1054, 1191, 1459, 1540 and 1548 (numbers in figure) showed outliers probability

( $p = 0.01$ ). The presence of ulcerative colitis in remission phase showed an inverse relation with current depression ( $p = 0.02$ ).

Finally, logistic regression gave for each patient the predicted probability to have state anxiety, trait anxiety and current depression. These probabilities turned out to be  $0.77 \pm 0.16$  for state anxiety,  $0.66 \pm 0.12$  for trait anxiety and  $0.39 \pm 0.14$  for depression (Figure 2).

## Discussion

This study shows that anxiety and depression are frequent psychiatric comorbidities in patients affected by chronic gastrointestinal diseases. The use of the STAI test allowed to distinguish between patients with state and trait form of anxiety. A high prevalence of state and trait form of anxiety was found both in patients affected by functional gastrointestinal disease and in patients in whom an organic cause for their symptoms was found. Among the patients examined, 84.1% showed presence of state anxiety, 67% showed trait anxiety and 27% showed current depression. In healthy subjects, epidemiological data show the presence of anxiety disorders in 10.6% (31) and of depression in 4.1% (32). The lack of a non-gastrointestinal control population restricted us to draft definitive conclusions about the specific relationship between affective disorders and gastrointestinal diseases. However, the very high percentages for the two forms of anxiety and of depression found in our subjects could indicate that most of the patients seeking medical consultation for gastrointestinal

problems show an associated affective disorder. These affective disorders could be present as a cofactor, or as psychiatric comorbidity, or as the main disorder that bring patients for the medical consultation. Our data are supported by recent studies showing that the presence of anxiety and depression seems to be able to increase the intensity and the perception of the gastrointestinal symptoms and consequently the need for medical consultation (5,33–35).

Our data are in line with several studies performed in patients affected by functional gastrointestinal diseases (5,33,35). A high prevalence of psychiatric disorders such as anxiety, depression, panic and somatisation has been reported in these patients (1,35). Moreover, our data also seem to be in line with the few data reported in patients affected by organic gastrointestinal diseases. In particular using hospital anxiety and depression scale (HADS) psychometric scale in a large cohort of patients, Van Kerkhoven et al. (2) recently showed the presence of anxiety and depression in subjects referred to digestive endoscopy outpatient setting. In this study evaluating patients referred for lower gastrointestinal endoscopy, there were no differences in anxiety and depression between patients with functional disorders and those with organic causes for their symptoms.

In the present study, the logistic regression analysis showed that patients affected by gastrointestinal disorders have a very high probability to have state anxiety (about eight of 10) and/or trait anxiety (about six of 10). The probability of having depression in these patients was not so elevated (about four of 10) but in any case higher than in general population (32). The incidence of depression lower than that of anxiety disorder in our patients could also be in line with recent data showing that depression is a risk factor for non-compliance to medical treatment (36) and consequently for non-compliance to medical consultation. These findings could also support the inverse correlation between the number of diseases and current depression found in this study.

The number of diseases correlated directly to state anxiety. This data led to hypothesise that a higher number of pathologies represents a greater reason of worry for one's own health with respect to a single disease, consequently resulting in a higher anxious reaction.

However, also trait anxiety directly correlates to the number of pathologies, although with less intensity. This effect could be related to the observation that a patient with an anxious trait could have a higher perception of symptoms becoming more predisposed to seek medical consultation and clinical examination, being part of 'consulters' cluster (5,34). However, it could also be hypothesised that a

prolonged state anxiety could influence trait anxiety (9) and our findings may, at least in part, be related to some increase in trait anxiety score associated with chronic illness. This hypothesis could be also supported by the direct correlation between STAI  $y_1$  and STAI  $y_2$  that was observed in this study.

ANOVA results showed that state anxiety was more common in patients affected by food allergies, SIBO, Hp infection and ulcerative colitis in active phase, while trait anxiety was more common in patients affected by IBS, Hp infection, food allergies and SIBO. Current depression was more common in patients affected by IBS, coeliac disease and SIBO. On the other side, trait anxiety was less frequent in patients with Crohn's disease in remission phase and current depression was less common in patients with ulcerative colitis in remission phase.

These data may indicate that patients with different gastrointestinal diseases, as well as patients with the same disease but in a different clinical phase, could have different psychometric characteristics supporting our previous observations (3,7–9). Regarding gender differences, state and trait anxiety and current depression, are significantly higher in females than in males supporting previous observation (37).

This study emphasises that the patients affected by gastrointestinal diseases should be managed by a team including gastroenterologists, psychologists and/or psychiatrists, or alternatively by a gastroenterologist having expertise in treating psychological disorders. In this view, the psychometric evaluation, other than anamnesis, medical observation and exams, acquire a great value. Accordingly, the efficacy of the approach made to solve psychological problems in improving the therapeutic outcome in patients with gastrointestinal functional disorder was recently underlined by Levy et al. (1). Moreover additional therapeutic strategies such as psychotherapy (11,38,39), hypnosis (40) and/or psychoactive drugs (41) have been found to play a role in these patients. These evidences suggest that the management of gastrointestinal diseases by a team of professionals could improve the quality of life of these patients and could reduce the costs related to frequent medical consultations.

### Authors' contributions

**Giovanni Addolorato**, MD participated in the conception and design of the study, acquisition of data, drafting and critical revision and supervision of the manuscript for important intellectual contents. **Antonio Mirijello**, MD participated in the design of the study, analysis and interpretation of data, drafting and revision of the manuscript. **Cri-**

**stina D'Angelo**, MD participated in the design of the study, drafting and critical revision of the manuscript. **Lorenzo Leggio**, MD participated in the design of the study, drafting and critical revision of the manuscript. **Anna Ferrulli**, MD gave technical support in data collection, participated in the drafting and critical revision of the manuscript. **Ludovico Abenavoli**, MD gave technical support in data collection, participated to the drafting and critical revision of the manuscript. **Luisa Vonghia** MD, **Silvia Cardone**, MD, **Veruscka Leso**, MD: gave technical support in the study. **Anthony Corsari**, MSc participated in the analysis and interpretation of data with statistical expertise. **Esmeralda Capristo**, MD participated in the data collection, drafting and critical revision of the manuscript. **Giovanni Gasbarrini**, MD participated in the conception and design of the study, and supervised the manuscript for important intellectual contents.

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