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Ulcerative Colitis: Psychosocial Factors Involved Cornelia Rada^{1*}, Mihai Andrei², Cristian Țieranu², Alexandru Teodor Ispas¹, Carmen C. Diaconu³ and Adina Baciu¹

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ABSTRACT

Background: This study aims to extend the knowledge regarding the psychological component of Ulcerative colitis (UC). **Materials and methods:** Eight questionnaires were completed and were performed deep psychosocial anamnesis, semi-structured interview, and observation, to reconstitute biography, critical incidents of the environmental conditions of the patient (MC) with ulcerative colitis from 2008. **Results:** Before the diagnosis he had a year bloody diarrhoea, abdominal pain, and a weight loss of 8 kg, that had greatly affected his work, his family and sexual life. The deviation from the socially encouraged norms regarding the life cycles-such as the successful completion of the studies, career, marriage, becoming a parent, children exceeding the socioeconomic and professional status of the family of origin, etc., perceived as catastrophes, frustrated the patient, and exhausted his energy. Psychological questionnaires showed tendency towards instability at the limit, tendency toward accentuation for emotivity and hyperthymia and was identified as the patient often feels tense. **Conclusion:** Is necessary a rigorous psychosocial anamnesis to reveal the emotional stresses, to introduce a psychologist, a psychotherapist in evaluating and treating the patients with UC.

Keywords: Ulcerative colitis, Crohn's disease, psychosomatic, psycho-emotional stress, psychotherapy

INTRODUCTION

Inflammatory bowel disease (IBD) comprises two main diseases: Ulcerative colitis (UC) and Crohn's disease (CD). In the rare situations when patients cannot be classified in one of these two categories, the pathology is called indeterminate colitis.

The aetiology of the chronic inflammatory bowel diseases remains incompletely elucidated, being incriminated environmental factors, a number of susceptible genetic variants, gut microbiome altered qualitatively or quantitatively, and a host's modified immune response. Up to now, no treatment is completely curative, various therapies having variable results [1,2]. For UC, the radical surgery (total proctocolectomy) can be considered curative, but patient's quality of life can be seriously altered.

Intensive genetic and molecular research in IBD have led to the identification of some genetic loci, which in the presence of certain environmental factors (smoking, antibiotic consumption, modifications of the composition of the gut microbiome etc.) predispose to the development of one of these affections [3,4]. Genetic factors seem to have an important role in IBD pathogenesis, as evidenced by familial aggregation, high rates of IBD in Ashkenazi, and increased concordance for IBD in monozygotic compared to dizygotic twin pairs [5]. Genetic research has advanced our understanding of the interactions between genetic risk factors and environmental risk factors in IBD. Various genetic variants may interfere differently with the metabolism of drugs and determine the clinical response however, they can be responsible also of the response to different environmental factors as it is known that the patients who smoke have usually an unfavourable evolution, even in the case of an appropriate drug treatment [3].

CD mainly manifests as diarrhoea and abdominal pain. During the active periods of the disease, patients present a

severe coprological syndrome, having to adapt their daily life to a high number of stools (sometimes even 15-20 per day); the sensation of defecation is imperative and extremely difficult to control. Stenosis of the intestinal lumen and formation of fistulas or abscesses may occur [6]. In some cases, it is necessary the resection of the affected segment (inflamed or stenosed). The long-term effects may mean the significant alteration of the patient's quality of life, and the relapse after the surgery is not at all rare [7].

There is no standard treatment to help all patients with CD, as the treatments differ according to the extent of disease, the severity of the endoscopic lesions, the prior history of response to different classes of molecules, and patient's preference given the different safety profile of the existing treatments. Drugs that can be administered depending on the case are systemic corticosteroids (e.g. Prednisone, Budesonide, Medrol), derivatives of 5-amino-salicylic acid (Mesalazine and Sulphasalazine), cyclosporine, thalidomide, immunosuppressants (azathioprine, 6-mercaptopurine and methotrexate), biological agents-Infliximab (Remicade), Adalimumab (Humira), Certolizumab pegol (Cimzia), Vedolizumab (Entyvio), Ustekinumab (Stelara), antibiotics (Ciprofloxacin, Metronidazole). The absence of response or the loss of the efficacy of the treatment with a certain molecule can lead in time to its replacement with a more powerful molecule, or, in the case of the biologic agents where there are no comparative data on efficacy, to its replacement with another biologic agent [8].

Although in the age of increasingly potent biologic treatments the incidence of surgery decreased, confirming that the natural history of this disease can be changed with these treatments, it remains an occurrence of approximately 48% of surgery in 10 years [9].

The surgery for removing the diseased part of the intestine should be delayed as much as possible because stenosis and inflammation may recur. In the case of UC, surgery is more successful. The diet does not cure the disease but can relieve the symptoms and help regaining the weight, as CD is associated with malabsorption and various vitamin deficiencies. CD affects different segments of the intestine and as a result digestion is affected differently; sometimes the diet can be individualized. The studies on homeopathic and folk remedies are still few and irrelevant. Probiotics and unsaturated fatty acids have a minimum adjuvant effect, without conferring real benefits as regards amelioration and the possibility of healing [8].

"Topographically, UC affects strictly the colon and the mucosa layer (the inner lining of the intestine); when inflammation is limited to the rectum (the terminal segment of the intestine), the condition is called proctitis. UC may manifest through abdominal pain, persistent diarrhoea with frequent severe episodes, the stools usually contain blood and mucus, and the patient may feel tired and lethargic. Occasionally, ulcerative haemorrhagic proctitis may lead to constipation" [10]. The medical literature and the European and American guides use rather the term of UC than haemorrhagic rectocolitis as it begins at the level of the rectum but has tendency to extend to the same colic framework, in the absence of a prompt treatment adapted to the severity [11].

The treatment is similar to that for CD. In case of colitis with severe complications which do not respond to medical therapy, partial or total colectomy is indicated, with or without external stoma (temporary or permanent) [12].

UC is characterized by a dysfunction of the intestinal epithelial barrier, resulting in chronic inflammation [13,14]. It is assumed that the disease is caused by an imbalance between the immune system and the microbial flora in genetically susceptible individuals [15,16].

It has been identified a link between the summer temperature and the prevalence of ulcerative colitis, which functions as an instrumental variable through the effect on the microbial species involved in the development of the ulcerative colitis [17]. It has also been established that the incidence rates were higher in Northern Europe than in Southern Europe [18]. It is suggested that the microbial richness could be a protective factor both against the gastrointestinal pathogens and against the autoimmune diseases such as ulcerative colitis and Crohn's disease [19].

Certainly, there is a neurogenic component in UC remarked since 1949 by Portis. Certain conflict situations transmit a vegetative nervous excitement through the vegetative centres on the parasympathetic pathway toward colon. Thus, lysozyme, a mucolytic enzyme, increases in quantity and leaves mucosa without its protective lining. Hence, mucosa becomes vulnerable to the action of the triptych enzyme present in the intestinal contents. Originally the location of the ulceration is in that part of the large intestine which is under the nervous control of the pelvic-sacral segment of the parasympathetic system. Also, a superficial digestion at the level of the intestinal mucosa opens the way for bacterial infections so that ulceration appears [20].

From the psychosomatic perspective, the specific dynamics in diarrhoea has the following pattern: Frustration of the intense wishes of oral dependency \rightarrow oral-aggressive reactions \rightarrow guilt \rightarrow anxiety \rightarrow overcompensation for the oral aggressiveness through the need to give (restitution) and to accomplish \rightarrow inhibition and failure to give and accomplish \rightarrow diarrhoea [21].

Personality traits are involved in aetiology and pathogenesis of UC. Ionescu states that unlike other psychosomatic diseases in which cases it is not known if they are the cause or effect of the disease, in the case of the ulcerative colitis the structure of personality precedes the disease and the traits are exacerbated in the presence of the symptoms [22].

Although it has been suspected a link between psychological factors on the one hand and initiation and exacerbation of IBD on the other hand, this fact was not clearly established. Meta-analysis conducted by Schoultz et al. on relevant studies up to November 2012 has not found a consensus as concerns the impact on IBD of the psychological variables such as anxiety, aggression, major life events, stress (Life Financial, Family), Coping, Personality, quality of life [23].

The difference between the results is due to several reasons such as: measurements regarding the disease activity with different questionnaires, undifferentiated analysis of UC and CD, different methodologies, stage of disease activity, different definition of stress (chronic, acute) [24,25]. In IBD physio pathological stress is involved; in fact, from the psychological viewpoint the way people interact with the environment and the stress perception have effects on the intestine [26].

However, there are studies that do not support the hypothesis that stress affects IBD and others that do not have clear conclusions in this regard. The reasons for these unclear results are: different perspective of defining stress, inclusion in studies of people in various stages of the disease, introduction into the same batch analysis both of patients with UC and of those with CD [27,28].

Simply defined, the term "stress" is used "to describe almost everything that is bad psychologically and physically; stress is what body and mind feel when life demands are greater than what people think can bear" [29].

In the case of IBD medication to relieve physical symptoms is mandatory, and this aspect has been well-studied, promoted in the treatment guides and by most gastroenterologists [30]. As discussed above, the studies on the psychosocial aspects involved in triggering and maintaining IBD are few and partly inconclusive. Moreover, until now no article addressing this affection from this perspective has been identified in Romania. This study aims to extend the knowledge regarding the psychological component of UC, enabling in the future the creation of a psychotherapy plan.

MATERIALS AND METHODS

During 2013 and 2015, Elias University Emergency Hospital, Department of Gastroenterology and Francis I. Rainer Institute of Anthropology of the Romanian Academy in Bucharest, conducted the research project entitled Psychosociomedical Study on the inflammatory bowel disease having as a general objective of this pilot study was a quantitative and qualitative identification and evaluation of some psychological characteristics, existential events and some risk behaviours for the patients with IBD.

Starting from the hypothesis that the debut of the disease, the flare-ups and the symptoms are closely related to the biopsychosocial factors, participants completed eight questionnaires as follows.

An Omnibus survey was created and used, with open and closed questions, divided into four sections: 1. Sociodemographic data, 2. Sex, Sexuality, Gender, 3. Relationships, Family, 4. Health. Then we applied the following psychological questionnaires: echogram of communication style that assesses the use of the ego states [31]. Hospital Anxiety and Depression Scale [32], Woodworth-Mathews Personal Data Sheet (76 items) [33], the Aggression Questionnaire [34], the Schmieschek Questionnaire for accentuated personality traits (88 items) [35], 13 items from the Jenkins Activity Survey [36], and the Family Adaptability and Cohesion Scale III [37].

The qualitative assessment was performed by anamnesis, semi-structured interview (based on an interview guide) and observation, with the aim to reconstitute biography, to analyze the social and educational conditioning of the personality, to reveal attitudes, conflicts, feelings, critical incidents of the environmental conditions, the subject's

modality of communication, the effects of past experience and their influence on presence, as well as the objective somatic changes.

The questionnaires were handed out by the doctor to the patients during hospitalization for diagnostic and evaluation. They could fill them in during hospitalization or at home. The questionnaires were taken back from the patients, and the doctor and the psychologist-psychotherapist checked the degree of completeness. The qualitative assessments were carried out by the psychologist-psychotherapist in the psychology department.

Out of the patients who were hospitalized for diagnostic or control between 2010 and 2015, only 39 agreed to be included in the study. Out of these, from 6 patients have been collected data only partially because meanwhile they renounced to participate, and one patient died.

Ethical considerations

These evaluations were carried out on a voluntary basis for all the involved parties. Informed written consent was obtained from each participant at the time of recruitment. The subjects were informed that they could withdraw from the study at any stage, and they were ensured of confidentiality.

The study was approved by the Ethics Commission of Francisc I. Rainer Anthropological Institute of the Romanian Academy. No 2/26.04.2013.

This article examines some psychosocial elements, the role of the psycho-emotional stress in initiating and maintaining mucosal inflammation in a patient with UC.

RESULTS

The history of the patient's disease

The patient (MC) was diagnosed with ulcerative colitis in 2008 and was interviewed on September 2015 when he returned to the hospital for a check-up, being in a mild form according to the gastroenterologist. Before the diagnosis, he had had digestive problems for a year consisting of bloody diarrhoea, abdominal pain, and a weight loss of 8 kg.

He followed a nine-month treatment with Medrol (methylprednisolone as the active substance) with breaks, and the treatment was resumed because of the relapses. He also had a continuous treatment with Salofalk (mesalazine as the active ingredient). For six months, he had been having four-five stools, with a tendency toward formation, without blood.

Socio-demographic data

When he was interviewed, MC was 64 years old, with higher education, and lived in the urban area. He was first married at 23, then divorced and got married again at 31. He has three daughters: one from the first marriage, 40 years old (married with a child of 15 years of age), the other two from the second marriage-one 32 years old (married with a child of 9 years old) and one of 24 years old (married, attending a master program). He lived with his second wife and his younger daughter, and the average income per month was between 220 and 440 Euros. He appreciated that he was getting along well with the current family and had good relationships with his first daughter and her son. The patient said he had divorced from his first wife because they always quarrelled and she had not respected him enough.

The description of the manifestations and the assessment of UC impact on the patient

The patient considered that in the past his disease had greatly affected his work, his family and sexual life, and that currently was still affecting to some extent his family life. The following passage from the interview highlights the physical and psychological stress experienced by the patient during the active period of the disease: "I do not want to think about how terrible it was to go at least 10 times a day at toilet. I only left home when I had to go to work. Sometimes I had the urgent need to go to the toilet during the classes. I did no longer sleep with my wife in the same bed at night because I had to go to the toilet and woke her up. I tended to eat less, I was on the diet, I was on pills and nothing happened. It was better with Medrol, but at some time after the end of the treatment the diarrhoea and stomach aches relapsed."

Relevant sociopsychomedical aspects for the disease: The stress

The interview has revealed that in the period before the onset of the disease and in the period of disease activity, 2004-2008, the patient felt stress because of several causes and for a longer period of time as follows:

1. Regarding the youngest daughter, the patient reported emotions, anxiety, and stress due to the cost of the private lessons for the entrance exams in high school and college: "From our wages of high school and elementary school teachers it was really hard" (our note: between 70 and 150 Euros/person/month).

2. The birth of the middle daughter's son has been reported as a stressful event due to the fact that it was an unplanned pregnancy and the daughter was in the third year of college. The patient outlined the situation as follows: "It was a disaster for me that she did not focus on her studies. She turned her life and our life upside down. She could hardly pass her exams and after giving birth she could not continue the college and then the Bologna system was implemented. Only when the child was three years old and entered the nursery school could she continued her studies. It was very hard ... she did not have any income; moreover, tensions occurred between my son-in-law and my daughter. He continued his university studies, went to work, and had little time for his child. He wanted to stay with his parents but my daughter did not want to. We could hardly handle the financial situation and the space in a threeroom apartment with a baby. I felt like I did not want to come home, but at work the situation was not great either. Now things have settled; my daughter graduated her master degree, they both work, and have moved from our home. Now there is another situation which worries us and makes us sad: they want to go to work and settle abroad". Here are a few clarifications on the system of school education in Romania at that time. In 2004, the youngest daughter was in seventh grade (13 years old), when children usually begin to have private lessons for the entry examination to high school (in the ninth grade). Then, in about the tenth grade, pupils start to have private lessons for baccalaureate (the graduation examination at the end of the twelfth grade, which is the end of the high school) and to enter a good college without taxes. The Bologna process, initiated by the Bologna Declaration, a document signed in 1999 by the ministers responsible for higher education from 30 European countries, aimed to introduce inter alia a common framework for higher education in Europe by 2010. Romania became a member process in 1999 and the implementation began in 2005. It introduced a two-stage university structure: undergraduate (3-4 years) and master degree (1-2 years), followed by PhD. Most students attend a master program because only this way the university studies are considered concluded. The PhD is optional, but for various degrees in research, or in higher education it is mandatory [38,39]. Before that, the university studies ended after 4-5 years of studies and the simple recognition of qualifications in the entire European area was not possible.

3. Other stress factors which MC specified were the strained relations with the former principal of the high school where he was a professor and the change of the work place. In this regard, here is a passage from interview with the patient: "We had a big fight when my middle daughter gave birth to her son; the principal did not want to arrange my classes in the afternoon so that I could help my daughter to take care of my grandson. I had an agreement with a colleague and for about half a year, in a great tension, I had classes clandestinely only in the afternoon. As I was in a conflict with my conscience as regards the lies and the correctness, after the holiday I left the high school and started to teach at an elementary school with a lower grade than I previously had had".

4. Another stressful aspect for the patient was the lack of trust and appreciation at the work place.

Emotional feelings, the need of psychotherapist

When asked how he feels, how he normally reacts when someone violates his boundaries, contradicts him, and does not appreciate him, he answered that he feels upset and angry, but he does not show his feelings.

The patient was asked about what he believed to have triggered his disease, and he answered: "my temper, as I care too much, I cannot stand injustice, that is why I had various discussions with the school principal; I cannot be silent when something is unfair. I care about order, punctuality, conscientiousness and compliance with the rules". It should be noted that MC's purpose in life is to be "useful to the community".

Asked about the need to talk to a psychologist therapist, he said: "I would have needed, maybe he could have taught me a technique to manage my stomach aches. I have heard that there is such a thing, but how can I not get angry, when injustice upsets me so much".

Significant results from questionnaires

Echogram of communication style showed that the patient uses mostly nurturing parent ego state. Hospital Anxiety and Depression Scale did not indicate depression, and possible case anxiety, Woodworth-Mathews. Personal Data Sheet showed that Psycho-behavioural tendency towards instability was at the limit, Scores on Aggression Questionnaire were low, the tendency toward accentuation was registered for Emotivity and Hyperthymia and of the 13 items from the Jenkins Activity Survey was identified as the patient often feels tense, in his work often feels defeated and that it is less confident about future.

DISCUSSION

A pioneer in the field of psychoanalysis and psychosomatic medicine Alexander F. considers that the disease recurrence is due to two emotional factors.

1. The frustrating tendency to fulfil any duty, which can be biological (childbirth), moral (to reach the standard of the parents' requirements), or material (financial obligations).

2. The frustration of the ambition to achieve something that requires sustained energy consumption [21].

Both emotional factors existed in the case of the patient presented in this paper: the desire to fulfil moral and financial obligations, and the aspiration to educational and professional achievements took possession of the thoughts of the patient, exhausting his energy.

From MC's accounts, it results that the psychologically stressful events that contributed to UC included those connected to loss and to narcissistic trauma, such as the situations that involved something he felt unable to achieve, hostility repression, anger finalized by passing to the state of helplessness-despair.

One aspect that needs further study is that his wife was very little mentioned, as if she had not existed. Although scores at the circumplex model indicate a middle functional family, the patient seems to have fought everything alone. It remains to be clarified whether it was a voluntary choice, or a fortuitous circumstance as a result of his wife's features. The studies show the importance of the family environment on all levels of life, the fact that the healthy balanced expression (neither too large nor too small) of the flexibility and cohesion in the family or in the couple are resilience factors which help the family system to cope better with stress [40].

It seems that the patient feels and acts as if all the responsibilities are on his shoulders, but with the pride of the person that has a mission-a true philosophy of life. It is possible that when the patient's internalized mission is blocked, he loses his self-esteem and feelings of uncertainty and insecurity are activated.

Attitudinal ambivalence and certain irrational beliefs make MC susceptible to experience most dysfunctional emotions, such as: anxiety, depressive feelings, anger, guilt, shame.

The analysis of the interview reveals rigid expectations for the self, the others and the world, the living conditions. Basically, this patient UC enters clearly the pattern ABC, the core of Rational Emotive Behavioural Therapy: Activating event or the individual interpretations of the activator event-A, Beliefs-B, Consequence, gained from the belief (behaviours, emotions)-C [41].

These events in the patient's life cannot be denied but what led to the behaviours and negative emotions were mostly the beliefs.

Between the activity of the colon and the emotional anal-regressive stimuli there is a specific connection. As it can be seen in this case, life situations, which involved an achievement for which the patient did not feel ready, can be considered triggers.

"Just as there is a biological clock, there is also a social clock, represented by social norms connected to each stage of development to which the individual relates in order to evaluate the degree of similitude of one's own evolution. An event occurring prematurely or with delay most often creates discomfort" [42]. Thus, the deviation from the socially encouraged norms regarding the life cycles-such as the successful completion of the studies, career, marriage, becoming a parent, children exceeding the socioeconomic and professional status of the family of origin, etc., perceived as catastrophes, frustrated the patient and exhausted his energy.

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Behaviourally it can be inferred that the patient appreciates order, punctuality, conscientiousness, conformism, and when they do not occur he becomes irritated, angry, frustrated. The events are described catastrophically, sometimes with obstinacy.

Taking into account the quantitative evaluation could be held as follows. The patient tends to be concerned with caring, loving, helping. Also, the patient tends to have high sensitivity reactions and depth within feelings subtle, spiritual, does not react strongly, but rather sentimental, feel fast pity, enjoy art, nature, cry easily, have reactions of fear (hyperirritability of neuro-vegetative system), is at risk of psycho-behavioural instability, and also tends to be tense and less optimist.

CONCLUSION

A rigorous psychosocial anamnesis is necessary to reveal the emotional stresses preceding the first flare-up. The anamnesis during the treatment may reveal why some patients enter remission more easily and others hardly respond to treatment. It should be taken into account that IBD is a condition that causes itself a distress to the individual.

It is necessary to introduce a psychologist, a psychotherapist in evaluating and treating the patients with UC and CD, as psychotherapy is a complement to pharmacological treatment.

It is assumed that the acute need to go to the toilet, sometimes over ten times a day, because of the diarrhoea stools, the perspective that IBD does not heal, that sometimes surgery with permanent external stoma is necessary and the idea of cancer risk predispose these patients towards depression and anxiety. Mikocka-Walus, et al. in a study conducted between 2006 and 2015 on 2007 patients with IBD find an association between symptoms of depression or anxiety and clinical recurrence [43].

Anxiety and depressive disorders are more common in people with chronic diseases such as IBD and this fact may have a negative effect on the development of the disease [44,45]. This is one reason for which these patients should be screened so that such a problem could be discovered, in order to establish a psychological treatment, possibly pharmacologically against anxiety and depression.

To increase the positive effects of the treatment, and longer remission is necessary that the doctors should encourage the patients to try psychotherapy too. This is especially important because many patients with IBD should follow a treatment with corticosteroids with negative neuropsychologic effects [46,47].

Simultaneously with the drug therapy, these patients need psychotherapy to increase tolerance to frustration, improve the ability to cope with conflict situations and life events, for cognitive behavioural changes and for pain management.

More than in the case of other conditions, for UC and CD the doctor, the psychotherapist should establish an empathic relation and have willingness to listen, offering the patients the permission to search for him anytime they are in a crisis, within a reasonable schedule. The patients will feel this as a "safety net".

The opinions regarding the causes and the evolution of IBD should not be polarized on the biological and genetic factors on the one hand [48] and the psychological factors involved in pathogenesis on the other hand [49]. For the benefit of the patients the opinions should be harmonized and all data, genetic, environmental, and psycho-emotional, should be integrated. Although there are disease categories, the patients have specific manifestations over the common elements of the IBD.

To determine the usefulness of psychotherapy in managing the symptoms, for improving the quality of life of the patients with IBD, more studies are needed. It is certain, however, that in the case of the patient analyzed in this article the psycho-emotional stress had an important role in triggering and maintaining the mucosal inflammation.

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REFERENCES

[1] Ciurezu, Adelina-Roxana, Laura Diana Lupu, and Dan Olteanu. "Current Issues in Crohn's disease." *Romanian Medical Journal* 56.1 (2009). Romanian.

[2] de Souza, Heitor S. P., and Claudio Fiocchi. "Immunopathogenesis of IBD: Current state of the art." *Nature Reviews Gastroenterology & Hepatology* (2015).

[3] Abraham, Clara, and Judy H. Cho. "Inflammatory bowel disease." N Engl J Med 361.21 (2009): 2066-2078.

[4] Duerr, Richard H., et al. "A genome-wide association study identifies IL23R as an inflammatory bowel disease gene." *science* 314.5804 (2006): 1461-1463.

[5] Vermeire, Severine, and Paul Rutgeerts. "Current status of genetics research in inflammatory bowel disease." *Genes and immunity* 6.8 (2005): 637-645.

[6] Stenson, W. F., and Korzenik, J. R. "Inflammatory bowel disease." Alpers, David H., et al. *Textbook of gastroenterology*. Tadataka Yamada, Ed. New Jersey: John Wiley & Sons, 2011.

[7] Nos, Pilar, and Eugeni Domènech. "Postoperative Crohn's disease recurrence: A practical approach." World J Gastroenterol 14.36 (2008): 5540-5548.

[8] Dignass, A., et al. "The second European evidence-based consensus on the diagnosis and management of Crohn's disease: Current management." *Journal of Crohn's and Colitis* 4.1 (2010): 28-62.

[9] Frolkis, A. D., et al. Risk of surgery for inflammatory bowel diseases has decreased over time: A systematic review and meta-analysis of population-based studies. *Gastroenterology* 145.5 (2005): 996-1006.

[10] Association of patients with autoimmune diseases, all you need to know if you suffer from inflammatory bowel disease. Available from: www.apaa.ro.

[11] Danese, Silvio, and Claudio Fiocchi. "Medical progress ulcerative colitis." *New England Journal of Medicine* 365.18 (2011): 1713-1725.

[12] Biancone, Livia, et al. "European evidence-based consensus on the management of ulcerative colitis: Special situations." *Journal of Crohn's and Colitis* 2.1 (2008): 63-92.

[13] Vatn, Morten H. "Natural history and complications of IBD." Current gastroenterology reports 11.6 (2009): 481-487.

[14] Baumgart, Daniel C., and Simon R. Carding. "Inflammatory bowel disease: Cause and immunobiology." *The Lancet* 369.9573 (2007): 1627-1640.

[15] Cho, Judy H. "The genetics and immunopathogenesis of inflammatory bowel disease." *Nature Reviews Immunology* 8.6 (2008): 458-466.

[16] Barrett, Jeffrey C., et al. "Genome-wide association defines more than 30 distinct susceptibility loci for Crohn's disease." *Nature genetics* 40.8 (2008): 955-962.

[17] Aamodt, Geir, May-Bente Bengtson, and Morten H. Vatn. "Can temperature explain the latitudinal gradient of ulcerative colitis? Cohort of Norway." *BMC public health* 13.1 (2013): 530.

[18] Shivananda, S., et al. "Incidence of inflammatory bowel disease across Europe: Is there a difference between north and south? *Results of the European Collaborative Study on Inflammatory Bowel Disease* (EC-IBD)." *Gut* 39.5 (1996): 690-697.

[19] Rook, G. A. W., and Brunet, L. R. "Microbes, immunoregulation, and the gut." Gut 54.3 (2005): 317-320.

[20] Portis, Sidney A. "Idiopathic ulcerative colitis: Newer concepts concerning its cause and management." *Journal of the American Medical Association* 139.4 (1949): 208-214.

[21] Alexander, Franz, et al. Psychosomatic medicine: With a chapter on sexual device functions and their disorders: Principles and its applicability. *Editura Trei*, 2008. Romanian.

[22] Ionescu, George. "Medical psychology and psychotherapy." Publisher Asklepios (1995): 404-408. Romanian.

[23] Schoultz, Mariyana, et al. "Assessment of causal link between psychological factors and symptom exacerbation in inflammatory bowel disease: A protocol for systematic review of prospective cohort studies." *Systematic reviews* 2.1 (2013): 8.

[24] Schoultz, Mariyana. "The role of psychological factors in inflammatory bowel disease." *British journal of community nursing* 17.8 (2012): 370.

[25] Sajadinejad, M. S., et al. "Psychological issues in inflammatory bowel disease: An overview." *Gastroenterology research and practice* 2012 (2012).

[26] Collins, Stephen M. "IV. Modulation of intestinal inflammation by stress: Basic mechanisms and clinical relevance." *American Journal of Physiology-Gastrointestinal and Liver Physiology* 280.3 (2001): G315-G318.

[27] Cámara, Rafael J. A., et al. "The role of psychological stress in inflammatory bowel disease: Quality assessment of methods of 18 prospective studies and suggestions for future research." *Digestion* 80.2 (2009): 129-139.

[28] Keefer, Laurie, Ali Keshavarzian, and Ece Mutlu. "Reconsidering the methodology of "stress" research in inflammatory bowel disease." *Journal of Crohn's and Colitis* 2.3 (2008): 193-201.

[29] Moore Bret A. How to control your anxiety. Gets the best of worry, stress and fear. Trei (2016): 248. Romanian.
[30] Bonaz, Bruno L., and Charles N. Bernstein. "Brain-gut interactions in inflammatory bowel disease." *Gastroenterology* 144.1 (2013): 36-49.

[31] de Graaf, Anne, and Klaas Kunst. Einstein art of sail: An exploration of modern leadership. Bucharest: Editura CODECS. Romanian.

[32] Zigmond, Anthony S., and Philip Snaith, R. "The hospital anxiety and depression scale." Acta psychiatrica scandinavica 67.6 (1983): 361-370.

[33] Dafinoiu, Ion. Personality. Method of Approach. Polirom, 2016. Romanian.

[34] Buss, Arnold H., and Mark Perry. "The aggression questionnaire." *Journal of personality and social psychology* 63.3 (1992): 452.

[35] Minulescu, Mihaela. "Psychodiagnosis modern. "Personality questionnaires, Ed. Tomorrow Foundation Romania, Bucharest (2004): 286-288. Romanian.

[36] Jenkins, C. David, Stephan J. Zyzanski, and Ray H. Rosenman. "Progress toward validation of a computerscored test for the type A coronary-prone behavior pattern." *Psychosomatic medicine* 33.3 (1971): 193-202.

[37] Olson, D. H. "Clinical assessment and treatment interventions using the Circumplex Model. (Chapter 5), In: Kaslow, F. W. (Ed.) Handbook of Relational Diagnosis and Dysfunctional Family Patterns." (1996): pp. 59-80.

[38] Alianța Națională a Organizațiilor Studențești din România. Reprezentăm Viitorul! 2009 Raport: Implementarea Procesului Bologna în România: Perspectiva studenților. Romanian. Available from: http://www.anosr.ro/wp-content/uploads/2012/07/2009-Raport-Implementare-Proc-Bologna-in-Romania-Perspectiva-Studentilor-1.pdf.

[39] Gavra, Alina C., Daniela Alexe, and Irina Drexler. Quality assurance review for higher education, quality assurance review. 2010; Available from: http://www.aracis.ro/fileadmin/ARACIS/Revista_QAR/Aprilie_2010/Gavra Alexe Drexler.pdf.

[40] Olson, David H. "Circumplex model of marital and family systems." *Journal of family Therapy* 22.2 (2000): 144-167.

[41] Dryden, W., and Di Giuseppe R. "Guide rational emotive behavioral therapy." (2003). Romanian.

[42] Rada, Cornelia, and Olson, D.H., Circumplex model of marital and family systems (Faces III) in Romania, Roumain Annuaire D'Anthropologie, Bucarest: Romanian Academy Publishing. Tome 53 (2016): 11-29.

[43] Mikocka-Walus, Antonina, et al. "Symptoms of depression and anxiety are independently associated with clinical recurrence of inflammatory bowel disease." *Clinical Gastroenterology and Hepatology* 14.6 (2016): 829-835.

[44] Scott, Kate M., et al. "Depression-anxiety relationships with chronic physical conditions: Results from the world mental health surveys." *Journal of affective disorders* 103.1 (2007): 113-120.

[45] Graff, Lesley A., John R. Walker, and Charles N. Bernstein. "It's not just about the gut: Managing depression and anxiety in inflammatory bowel disease." *Practical Gastroenterology* 34.7 (2010): 11-25.

[46] Buchman, Alan L. "Side effects of corticosteroid therapy." *Journal of clinical gastroenterology* 33.4 (2001): 289-294.

[47] Brown, E. Sherwood, et al. "Effects of chronic prednisone therapy on mood and memory." *Journal of affective disorders* 99.1 (2007): 279-283.

[48] Bouma, Gerd, and Warren Strober. "The immunological and genetic basis of inflammatory bowel disease." *Nature Reviews Immunology* 3.7 (2003): 521-533.

[49] Maunder, Robert G., and Susan Levenstein. "The role of stress in the development and clinical course of inflammatory bowel disease: Epidemiological evidence." *Current molecular medicine* 8.4 (2008): 247-252.