

The contribution of Greek gastroenterologists in the international clinical and basic research of inflammatory bowel disease

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SUMMARY

Aim: To assess the contribution of Greek gastroenterologists in the international literature as far as the epidemiology, diagnosis and treatment of inflammatory bowel disease (ulcerative colitis and Crohn's disease) are concerned. **Materials-Methods:** Scientific articles published by Greek gastroenterologists were identified in the international scientific data base PubMed using the key-words: Greece, gastroenterology, inflammatory bowel disease, ulcerative colitis, Crohn's disease. The studies were divided according to their subject of interest in epidemiological, clinical, case reports, therapy, and studies of basic research. The journal and year of publication, the impact factor of the journal and the origin of the study were recorded. Reviews concerning IBD were not taken into account. **Results:** During a period of 20 years (1986-2006) 91 research papers were identified. The geographic area in which the study was performed, the type and the number of studies as well as the total number of studies in each geographic area, are shown in the table.

Geographic area	Incidence-Prevalence	Clinical characteristics and diagnosis	Case-report	Treatment	Basic research	TOTAL
Athens	2	4		7	6	19
Crete	3	2	5		18	28
Ioannina	3	2	4	1	5	15
Nicea	2	5	8	8	4	27
Larissa	1				1	2
TOTAL	11	13	17	16	34	91

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Studies originated mainly from 4 geographic departments of the country with almost equal contribution concerning the number of papers but with quite different kind of research. All studies were published in 30 different medical journals with impact factor ranging from 1 to 12. The gastroenterology department of University of Crete contributed with basic research and epidemiological studies, the gastroenterology department of the general hospital of Nicea (Piraeus) with clinical studies and studies concerning treatment and case report studies, the department of gastroenterology of "Evangelismos" hospital with studies concerning treatment and the gastroenterology department of the University of Ioannina with studies of basic research and epidemiology. During the 5-year period of 1986-1990, ten studies were published, during 1991-1995 eight studies, during 1996-2000 twenty-two studies and during 2001-2005 fifty-one studies. **Conclusion:** The contribution of Greek gastroenterologists in the research of IBD in Greece is quite satisfactory mainly during the last decade. Most of the studies were performed in four centers of the country having special interest in IBD research.

Key Words: Inflammatory bowel disease, Ulcerative colitis, Crohn's disease, Clinical research, Basic research

INTRODUCTION

The volume of basic and clinical research in the field of inflammatory bowel disease (IBD) is rapidly growing all over the world. This assumption can easily be reached, as many specialized international medical journals devoted exclusively to the study of IBD – such as "Inflammatory Bowel Disease" – are regularly edited. Moreover, quite a large number of congresses are organized each year exploring the current perspectives of IBD, and a continuously increasing number of gastroenterologists have special interest in diagnosing and treating this fascinating and

important disease.

The gastroenterological community of Greece has exhibited a special interest in this disease dating back to the early 50's. Subsequently, some years ago, the Hellenic IBD study group was founded aiming to promote research in this scientific field.

The aim of this study was to assess the contribution of the Greek gastroenterologists in the international literature as far as the epidemiology, etiology, diagnosis and treatment of IBD (ulcerative colitis and Crohn's disease) are concerned.

MATERIALS - METHODS

Scientific articles published in the international literature by Greek gastroenterologists, were searched in the scientific data base PubMed using the key-words Greece, gastroenterology, inflammatory bowel disease, ulcerative colitis, and Crohn's disease.

Identified studies were divided according to their subject of research in epidemiological, clinical, case reports, studies devoted to treatment, and studies of basic research. The journal and year of publication, the impact factor of the journal and the origin of the study (the center in which the study was performed) were also recorded. Reviews concerning IBD were not taken into account.

RESULTS

During a period of 20 years (1986-2005) 91 research papers were identified. From these papers, 11 were referring to the incidence and prevalence of the disease, 13 were referring to the clinical characteristics and diagnosis of the disease, 17 were referring exclusively to case reports, 16 were referring to treatment, while the number of studies referring to basic research was 34.

Studies originated mainly from 4 geographic departments of the country. The geographic areas in which the study was performed and the corresponding number of pa-

pers published were: Athens 19, Crete 28, Ioannina 15, Nicea 27 and Larissa 2 papers, respectively (Table 1).

However, the kind of research was quite different. The gastroenterology department of University of Crete contributed mainly with basic research and epidemiological studies, the gastroenterology department of the general hospital of Nicea with clinical studies and studies concerning treatment as well as case report studies, the department of gastroenterology of "Evangelismos" hospital with studies mainly concerning treatment, and the gastroenterology department of the University of Ioannina with studies of basic research and epidemiological studies (Table 1).

These studies were published in 30 different medical journals with impact factor ranging from 1 to 12 (Table 2).

Concerning the number of papers published during the period of 20 years, it was found that during the surveyed period of 1985-1990 ten studies were published, during the period of 1991-1995 eight studies, during the period 1996-2000 twenty-two studies and during the period 2001-2005 fifty-one studies were published. Table 3 shows the number of papers published each year (from 1986 to 2005).

Table 4 shows all studies referring to the incidence and the prevalence of IBD in various parts of Greece. As the table indicates five epidemiological studies, performed in Crete, Ioannina and central Greece respectively, were published. The remaining six studies were referring to other epidemiological parameters such as incidence of *Helicobacter pylori* infection, appendectomy, suicide, gluten enteropathy and seasonal variation of IBD.

Table 5 shows all studies referring to the clinical characteristics and diagnosis of patients with IBD. As the table indicates almost the whole spectrum of clinical behavior of both Crohn's disease and ulcerative colitis, was covered by these publications.

Table 6 shows all studies related to medical or surgical treatment of patients with IBD. The main topics covered by these publications were devoted to the use of antibiot-

Table 1. Number of studies performed in different geographical areas according to the topic of research

Geographical area	Incidence Prevalence	Clinical characteristics and diagnosis	Case-report	Treatment	Basic research
Athens	2	4		7	6
Crete	3	2	5		18
Ioannina	3	2	4	1	5
Nicea	2	5	8	8	4
Larissa	1				1
Total	11	13	17	16	34

Table 2. International Journals in which studies related to IBD were published by Greek gastroenterologists during the surveyed period

Journal	Number of published papers
Abdom Imaging	1
Am J Gastroenterol	17
BMC Gastroenterol	1
Clin Exp Rheumatol	1
Clin Gastroenterol Hepatol	1
Digestion	4
Dis Colon Rectum	3
Dig Dis Sci	8
Dig Liver Dis	3
Eur J Clin Investig	1
Eur J Gastroenterol Hepatol	11
Eur J Intern Med	2
Eur Radiol	1
Gastroenterology	1
Growth Horm IGF Res	1
Gut	2
Hepatogastroenterol	7
Histol Histopathol	1
Inflamm Bowel Dis	2
Ital J Gastroenterol	4
J Clin Pathol	1
J Clin Gastroenterol	2
J Endocrinol Invest	1
J Gastroenterol	3
Int J Colorectal Dis	2
Med Sci Monit	1
Proc Roy Soc	1
Radiology	1
Scand J Gastroenterol	4
World J Gastroenterol	3

ics (ornidazole and ciprofloxacin), mesalazine, azathioprine, infliximab, and butesonide. One study was referring to the surgical treatment of a series of patients with ulcerative colitis and one on the surgical treatment of a series of patients with Crohn's disease.

Table 7 shows all studies referring to interesting IBD case-reports. A whole spectrum of interesting combinations of IBD with autoimmune disorders, acute leukaemia, thyroid disorders, varicella infection and other disorders was covered.

Table 8 shows all studies referring to basic research in IBD. This part of research covers more than one-half of all studies published during the surveyed period of 20

Table 3. Number of studies published each year, during the surveyed period

Year of publication	Number of published studies
1986	1
1987	2
1988	2
1989	1
1990	2
1991	0
1992	2
1993	1
1994	4
1995	1
1996	4
1997	4
1998	6
1999	3
2000	6
2001	8
2002	11
2003	17
2004	8
2005	8
Total	91

years. It must be emphasized that two university departments –for obvious reasons related to the availability of personnel and resources- were responsible for these publications. It must be emphasized that 25 out of 34 research studies (76.5%) were published during the last 5 years (from 2001 to 2005).

DISCUSSION

The analysis of the results showed that:

- i) The number of articles related to IBD published in the international literature by the Greek gastroenterologists is increasing year by year,
- ii) The vast majority of these studies originate from 4 geographical areas and actually from 4 IBD centers situated in these 4 geographical areas named Ioannina, Athens, Piraeus and Heraklion (Crete),
- iii) The kind of research differs in each center being mainly basic research in the two university hospitals and clinical research in the other two hospitals, and;
- iv) The research concerning IBD over the last decade is changing from clinical to basic research.

The number of IBD related articles published by the

Table 4. Studies referring to incidence and prevalence of patients with IBD in various parts of Greece

Author	Year	Journal	Study	Area
Tsianos et al	1994	Gut	UC and Crohn's disease	Ioannina
Manousos et al	1996	Scand J Gastroenterol	Crohn's disease	Crete
Manousos et al	1996	Eur J Gastro-enterol Hepatol	Ulcerative colitis	Crete
Karamanolis et al	1997	Hepatogastro-enterology	Seasonal variation of IBD	Pireaus
Koutroubakis et al	1999	Dis Colon Rectum	Appendectomy & tonsillectomy	Crete
Triantafillidis et al	2002	Am J Gastroenterol	Suicide and IBD	Nicea
Triantafillidis et al	2003	Am J Gastroenterol	H pylori infection in IBD	Athens
Tsianos et al	2003	Dig Liver Dis	UC & Crohn's disease	Ioannina
Katsanos et al	2005	Eur J Intern Med	Dysplasia and cancer	Ioannina
Mantzaris et al	2005	Inflamm Bowel Dis	Incidence of gluten enteropathy	Athens
Ladas et al	2005	World J Gastroenterol	Ulcerative colitis	Larissa

Table 5. Studies related to clinical characteristics and diagnosis of patients with IBD

Author	Year	Journal	Study	Topic	Area
Zevgolatis et al	1969	Proc R Soc Med	Clinical	Characteristics of UC	Athens
Emmanouilidis et al	1988	Digestion	Clinical	Clinical course of UC	Athens
Manousos et al	1989	Scand J Gastroenterol	Clinical	Data UC	Athens
Gossios et al	1997	Abdom Imaging	Clinical	CT in Crohn's disease	Ioannina
Triantafillidis et al	1998	J Clin Gastroenterol	Clinical	Data UC	Nicea
Triantafillidis et al	2000	Dig Liver Dis	Clinical	Crohn's disease in the elderly	Nicea
Triantafillidis et al	2000	Digestion	Clinical	Clinical characteristics of Crohn's disease	Nicea
Triantafillidis et al	2001	J Gastroenterol	Clinical	UC in the elderly	Nicea
Archimandritis et al	2002	Med Sci Monit	Clinical	Characteristics of 172 UC cases	Athens
Christodoulou et al	2002	Dig Liver Dis	Clinical	Extraintestinal manifestations	Ioannina
Triantafillidis et al	2003	Am J Gastroenterol	Clinical	Acute pancreatitis in Crohn's disease	Nicea
Koutroubakis et al	2003	Radiology	Prospective	Evaluation of ^{99m} Tc scinti-graphy in IBD	Crete
Gourtsogiannis et al	2004	Eur Radiol	Prospective	MR enteroclysis in IBD	Crete

Greek gastroenterologists is far below the number of corresponding articles coming from other developed western European countries even after adaptation of the number of practising gastroenterologists in these countries. However, the number of articles published by the Greek gastroenterologists during this period was quite higher compared to the neighbouring Balkan countries. Indeed the corresponding number of the relevant articles performed in the Balkan countries (PubMed database) was Serbia 0, Albania 0, FYROM 1, Bulgaria 4, Croatia 9, Romania 9, and Turkey 20. If we accept the assumption that the level of medical research in a certain research field is reflected by the number of articles published in peer review journals, then the level of research concerning IBD in Greece

is better compared to the neighbouring Balkan countries, but lower compared to the developed western European countries. In other words, Greece seems to possess the middle ground between developed and developing European countries in the field of research in IBD.

One explanation for the significant improvement in the bulk of papers devoted to basic research in Greece during the last five to ten years is probably related to a variety of reasons including the steady improvement of the economic level in Greece and thus the availability of grants for research, the increased number of researchers, especially those of other related fields of science (biologists, molecular biologists, etc), the progress made in many scientific fields including imaging and immunohistochemi-

Table 6. Studies related to medical or surgical treatment of patients with IBD

Author	Year	Journal	Study	Topic	Area
Triantafillidis et al	1988	Am J Gastroenterol	Clinical	Ornidazole in CD	Nicea
Mantzaris et al	1994	Am J Gastroenterol	Prospective randomized	Antibiotics in IBD	Athens
Mantzaris et al	1994	Dis Colon Rectum	Randomized	Mesalazine enemas vs mesalazine peros	Athens
Triantafillidis et al	1996	Ital J Gastroenterol	Prospective	Ornidazole in active CD	Nicea
Mantzaris et al	1997	Am J Gastroenterol	Prospective, randomized, controlled	Ciprofloxacin in active UC	Athens
Triantafillidis et al	1998	It J Gastro-enterol hepatol	Prospective	Ornidazole in maintenance treatment of CD	Nicea
Triantafillidis et al	1998	Hepatogastro-enterology	Clinical	Surgery for UC	Nicea
Triantafillidis et al	2000	Am J Gastroenterol	Clinical	Infliximab in acute pancreatitis	Nicea
Triantafillidis et al	2001	Hepatogastro-enterology	Clinical	Surgery for Crohn's disease in Greece	Nicea
Triantafillidis et al	2001	Am J Gastroenterol	Clinical	Toxicity of ornidazole	Nicea
Triantafillidis et al	2001	Dig Liver Dis	Clinical	Influence of ornidazole on immune system	Nicea
Mantzaris et al	2001	Scand J Gastroenterol	Prospective, randomized, placebo-controlled	Ciprofloxacin vs placebo in severe acute UC	Athens
Triantafillidis et al	2002	Scand J Gastroenterol	Clinical	Infliximab in pyoderma gangrenosum	Athens
Christodoulou et al	2003	Hepatogastro-enterology	Clinical	Efficacy and safety of AZ in IBD	Ioannina
Mantzaris et al	2003	Clin Gastroenterol Hepatol	Clinical	Budesonide vs mesalazine for maintenance in steroid depended CD	Athens
Mantzaris et al	2004	Am J Gastroenterol	Prospective randomized	AZ monotherapy vs AZ & Olsalazine in UC	Athens

Table 7. Studies referring to interesting IBD case-reports

Author	Year	Journal	Topic	Area
Triantafillidis et al	1987	Am J Gastroenterol	Acute leukaemia & UC	Nicea
Triantafillidis et al	1990	Am J Gastroenterol	Thyreotoxicosis & UC	Nicea
Kamberoglou et al	1990	Am J Gastroenterol	Balantidiasis & UC	Nicea
Triantafillidis et al	1992	Ital J Gastroenterol	Hyperthyroidism & UC	Nicea
Pomonis et al	1992	Am J Gastroenterol	Eales' disease & UC	Nicea
Triantafillidis et al	1994	Ital J Gastroenterol	Sjogren's syndrome & UC	Nicea
Tsianos et al	1995	J Clin Gastroenterol	Hidradenitis suppurative & Crohn's disease	Ioannina
Giannadaki et al	1997	Am J Gastroenterol	Autoimmune hemolytic anemia & UC	Crete
Koutroubakis et al	1998	Eur J Gastro-enterol Hepatol	Systemic Lupus Erythematosus & UC	Crete
Koulentaki et al	1999	Dig Dis Sci	Primary biliary cirrhosis & UC	Crete
Potamianos et al	2000	Eur J Gastro-enterol Hepatol	Idiopathic fibrosing pancreatitis & Crohn's disease	Crete
Triantafillidis et al	2002	Dig Liver Dis	Varicella infection & Crohn's disease	Nicea
Christodoulou et al	2002	Eur J Gastro-enterol Hepatol	Small bowel adenocarcinoma & Crohn's disease	Ioannina
Georgiadis et al	2003	Clin Exp Rheumatol	Reumatoid arthritis & Crohn's disease	Ioannina
Roussomoustakaki et al	2003	J Gastroenterol	Hidradenitis suppurative & Crohn's disease	Crete
Kalambokis et al	2004	J Endocrinol Invest	ACTH deficiency and Crohn's disease	Ioannina
Parasiet al	2005	Ann Ital Chir	Crohn's disease and inflammatory fibroid polyp	Nicea

Table 8. Studies referring to basic research in IBD

Author	Year	Journal	Topic	Area
Koutroubakis et al	2005	Dig Dis Sci	Pancreatic autoantibodies in IBD	Crete
Hyphantis et al	2005	J Gastroenterol	Defence mechanisms in IBD	Nicea - Ioannina
Gazouli et al	2005	World J Gastroenterol	Polymorphisms in the Toll-like receptor 4, and CARD15/NOD2 & IBD	Athens
Triantafillidis et al	2005	World J Gastroenterol	Administration of Infliximab in rats	Nicea
Gazouli et al	2004	Gastroenterology	C3435T MDR1 gene polymorphism	Athens
Gazouli et al	2004	Eur J Gastroenterol Hepatol	Association of NOD2/CARD15 variants with Crohn's disease	Athens
Koutroubakis et al	2004	Dig Dis Sci	Serum angiogenin in IBD	Crete
Koutroubakis et al	2004	Eur J Gastroenterol Hepatol	Enhanced soluble CD40 ligand and pro-thrombotic state in IBD	Crete
Koutroubakis et al	2004	Dig Dis Sci	Total and corrected antioxidant capacity in IBD patients	Crete
Roussomustakaki et al	2003	Gastroenterology	NOD2 insertion mutation in Crohn's disease	Crete
Koutroubakis et al	2003	J Clin Pathol	Serum laminin and Collagen IV in IBD	Crete
Koutroubakis et al	2003	Int J Colorectal Dis	Serum levels of YKL-40 in IBD patients	Crete
Pallis et al	2003	Digestion	Quality of health care in IBD patients	Crete
Vlachonikolis et al	2003	Am J Gastroenterol	Validation of IBD Questionnaire	Crete
Skopelitou et al	2003	Eur J Gastroenterol Hepatol	Immunohistochemical expression of FHIT gene product in IBD	Ioannina
Ioachim et al	2003	Histol Histopathol	Expression of metallothionein in IBD	Ioannina
Triantafillidis et al	2003	Hepatogastro- enterology	Serum gastrin levels in IBD patients	Nicea
Kapsoritakis et al	2003	Int J Colorectal Dis	Vascular endothelial growth factor in IBD	Larissa
Pallis et al	2002	BMC Gastroenterol	Health related quality of life in IBD patients	Crete
Roussomoustakaki et al	2002	Gastroenterology	NOD2 insertion mutation	Crete
Kyriakou et al	2002	Eur J Gastroenterol Hepatol	inhibitors to coagulation factors	Crete
Koutroubakis et al	2002	Eur J Gastroenterol Hepatol	Circulating soluble vascular adhesion protein	Crete
Katsanos et al	2001	Growth Horm IGF Res	Insulin-like Growth factor-1 and IGF-binding protein-3 in IBD	Ioannina
Kapsoritakis et al	2001	Am J Gastroenterol	Platelet Volume as a marker of IBD activity	Crete
Koutroubakis et al	2001	Eur J Gastroenterol Hepatol	Increased levels of lipoprotein (a) in Crohn's disease	Crete
Koutroubakis et al	2000	Dig Dis Sci	Hyperhomocysteinemia in IBD patients	Crete
Kapsoritakis et al	2000	Am J Gastroenterol	Thrombopoietin levels in IBD patients	Crete
Koutroubakis et al	1998	Dig Dis Sci	Anticardiolipin & anti-beta2-glycoprotein I antibod- ies in IBD	Crete
Dalekos et al	1998	Eur J Gastroenterol Hepatol	Zinc, copper and immunological markers in UC	Ioannina
Karamanolis et al	1996	Eur J Gastroenterol Hepatol	Systemic absorption of 5-ASA in patients with inac- tive UC	Pireaus
Dalekos et al	1993	Gut	Interleukin-2 receptors, ANCA and other autoanti- bodies in UC	Ioannina
Triantafillidis et al	1987	Dis Colon Rectum	Cutaneous delayed hypersensitivity in IBD	Athens
Papasteriadis et al	1986	Digestion	HLA-A, B and UC in a Greek population	Athens
Triantafillidis et al	1985	Ital J Gastroenterol	Immunology	Athens

cal techniques, improvements in endoscopy (imaging capsule, magnifying endoscopy etc), and the increased use of sophisticated blood and serum examinations.

One of the interesting findings of this study was the fact that the published research in IBD comes from only 4 centers, -two university and two general hospitals- located in quite different geographical areas of Greece. The explanation is probably related to the existing tradition and the special interest of these departments in the IBD.

In conclusion, the contribution of Greek gastroenterologists in the research of IBD in Greece could be considered as satisfactory, mainly during the last decade. Most of the studies were performed mainly in four centers with special interest in the IBD research.

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