Development of Gastroenterology and Hepatology in Iran: Part II-Advances in Research and Therapeutic Modalities

Mehdi Saberifiroozi MD*, Seid-Hossein Mir-Madjlessi MD***

Abstract

Following the establishment of Gastroenterology and Hepatology Fellowship Programs in 1987, significant developments in research and health care delivery have been achieved. The number of published articles has increased significantly and now more than 10 approved research centers are involved in several longitudinal and population based studies in GI epidemiology, viral hepatitis and GI oncology around the country.

Before 1987 less than 50 gastroenterologists were working in the country, but now more than 300 gastroenterologists are involved in public and private health care delivery systems. Advanced diagnostic and therapeutic endoscopic procedures and complex surgical procedures such as liver transplantation are a routine now.

These achievements are indicative of hard work and determination of dedicated physicians after the Islamic Revolution, and the support of governmental and non-governmental sectors. The future prospect of development in the discipline of gastroenterology and hepatology in Iran seems to be very encouraging.

Keywords: Gastroenterology • history of medicine • Iran

Introduction

Before the establishment of subspecialty training program in gastroenterology and hepatology in 1976, which was a major step in the progress of this subspecialty in Iran, there were few published articles in international peer reviewed journals in this field.1 The first attempts to start research activities and try to publish papers in this field were started in Shiraz and Tehran after 1960.2,3 According to published articles, the major diseases during 1970’s were upper GI cancers, liver cirrhosis of liver, immunoproliferative small intestinal disease (IPSID), and peritoneal tuberculosis. According to K. Nasr important factors which promoted the research activities in Shiraz University in the 1960s and 1970s were: requirement of publication in good journals for academic promotion, full time system for academic staff, good medical charts in hospitals, good laboratory, pathology and radiology services, and very high rates of autopsy, which were available in a few academic centers at that time.4 It should be emphasized that in the 90s and after 2000, significant improvements have been done in the quantity and quality of research in all universities of Iran, which can be related to increasing number of academic staff and research centers, more longitudinal and population based studies and positive attitude of the government to research for development of the country.5 The list of scientists who have published more than 20 papers and their corresponding h-factor are shown in Table 1 and the list of highly cited papers in gastroenterology and digestive oncology are shown in Tables 2 and 3. In Table 4 the research centers with at least 5 years of age are shown with their scientific output and the corresponding h-factor. The accomplishments in the field of research can be summarized as follows:

Viral hepatitis and cirrhosis

Cirrhosis and its complications have been the most common diagnosis among patients admitted in GI wards from 1960s2,3 to the present time6 (Table 1). Dr. Borhammanesh in Shiraz was among the first scientists who did clinical research on cirrhosis and published papers about viral etiology.
and complications of cirrhosis. No major progress happened before 1980 when following availability of serologic tests for diagnosis of viral hepatitis it was recognized that HBV is the etiology of nearly 70% of cirrhosis with its complications in Iran.

During the last 30 years after revolution a major progress happened in the field of viral hepatitis and cirrhosis with more than 100 papers published about viral hepatitis and cirrhosis in international journals reporting advances in diagnosis and treatment of HBV. A new journal in the field of viral hepatitis named “Hepatitis Monthly” was founded in 2002 by S.M. Alavian. This clinical journal is published by the “Research Center for Gastroenterology and Liver Diseases” of Baqiyatallah University of Medical Sciences, in Tehran. It is the official journal of the “Iranian Hepatitis Network” and is indexed in the web of science (http://hepmon.com).

Liver transplantation was established for the first time in Nemazee Hospital, Shiraz, by Ali Malekhosseini and his team. This center is doing more than 150 transplants each year. The second center for Liver Transplant has already been started in Imam Khomeini Hospital in Tehran. Iranian scientists were among the first group of researchers who started Stem cell transplant for

Table 1. Scientists in the field of clinical gastroenterology with their corresponding h-factor (2000 – 2009) from Scopus July 2009.

<table>
<thead>
<tr>
<th>Rank</th>
<th>Name of scientist</th>
<th>Affiliation</th>
<th>All documents</th>
<th>h-factor</th>
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<tr>
<td>1</td>
<td>Reza Malekzadeh</td>
<td>DDRC/TUMS</td>
<td>162</td>
<td>19</td>
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<td>2</td>
<td>Mohammad Reza Zali</td>
<td>GLRC/SBUMS</td>
<td>100</td>
<td>8</td>
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<tr>
<td>3</td>
<td>Sadegh Massarrat</td>
<td>GLRC/SBUMS</td>
<td>88</td>
<td>9</td>
</tr>
<tr>
<td>4</td>
<td>Kamran Bagheri Lankarani</td>
<td>GERC/SUMS</td>
<td>43</td>
<td>6</td>
</tr>
<tr>
<td>5</td>
<td>Seyed Moid Alavain</td>
<td>BRCG/BUMS</td>
<td>40</td>
<td>9</td>
</tr>
<tr>
<td>6</td>
<td>Shahin Merat</td>
<td>DDRC/TUMS</td>
<td>30</td>
<td>12</td>
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<tr>
<td>7</td>
<td>Mehdih Mohamadnejad</td>
<td>DDRC/TUMS</td>
<td>37</td>
<td>9</td>
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<td>8</td>
<td>Siavosh Nasser-Mohammadm</td>
<td>DDRC/TUMS</td>
<td>28</td>
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<td>9</td>
<td>Mehdih Saberifiroozi</td>
<td>GERC/SUMS</td>
<td>27</td>
<td>7</td>
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<td>10</td>
<td>Pourshams Akram</td>
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<td>23</td>
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<td>11</td>
<td>Nasser Ebrahimia Daryani</td>
<td>DDRC/TUMS</td>
<td>22</td>
<td>5</td>
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</table>

RC=research center; DDRC=digestive disease research center; TUMS=Tehran University of Medical Sciences; GLRC=gastroenterology and liver disease research center; SBUMS=Shaheed Beheshti University of Medical Sciences; GEHRC=gastroenterology and hepatology research center; SUMS=Shiraz University of Medical Sciences; RCGL=research center for gastroenterology and liver disease; BUMS=Baqiyatallah University of Medical Sciences

Table 2. Top Ten highly cited gastroenterology or hepatology papers from Iran during 1995 – 2009. Source: Scopus July 2009.

<table>
<thead>
<tr>
<th>Rank</th>
<th>Title of manuscript</th>
<th>Type of research</th>
<th>First and CC authors</th>
<th>Affiliation</th>
<th>Journal/year</th>
<th>Numbers of citations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Omeprazole in reducing re-bleeding in peptic ulcer</td>
<td>RCT</td>
<td>Kaviani, Hashemi SUMS/DDRC</td>
<td>SUMS/DDRC</td>
<td>Alim Pharm Ther 2003</td>
<td>63</td>
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<td>2</td>
<td>Probucol in treatment of Nash</td>
<td>RCT</td>
<td>Merat, Malekzadeh DDRC/TUMS</td>
<td>DDRC/TUMS</td>
<td>J Hepatol 2003</td>
<td>50</td>
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<tr>
<td>3</td>
<td>Prevalence APD and IBS In Iran</td>
<td>Observational</td>
<td>Massarrat, Saberfiroozi</td>
<td>SUMS</td>
<td>Eur J Gastro Hep 1995</td>
<td>47</td>
</tr>
<tr>
<td>4</td>
<td>Botax/ PD in Achalasia</td>
<td>RCT</td>
<td>Mikaeli, Malekzadeh DDRC/TUMS</td>
<td>DDRC/TUMS</td>
<td>Alim Pharm Ther 2001</td>
<td>46</td>
</tr>
<tr>
<td>5</td>
<td>Clarith vs. furazol in HP eradication</td>
<td>RCT</td>
<td>Fakheri, Malekzadeh DDRC/TUMS</td>
<td>DDRC/TUMS</td>
<td>Alim Pharm Ther 2001</td>
<td>43</td>
</tr>
<tr>
<td>6</td>
<td>Celiac in IBS</td>
<td>CCS</td>
<td>Shahbakhshani, Malekzadeh DDRC/TUMS</td>
<td>DDRC/TUMS</td>
<td>Alim Pharm Ther 2001</td>
<td>43</td>
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<tr>
<td>7</td>
<td>Prevalence of celiac in Iranian blood donors</td>
<td>observational</td>
<td>Shahbakhshani, Malekzadeh DDRC/TUMS</td>
<td>DDRC/TUMS</td>
<td>Eur J Gastro Hep 2003</td>
<td>42</td>
</tr>
<tr>
<td>8</td>
<td>Effect of triple therapy ... eradication of Helicobacter pylori</td>
<td>RCT</td>
<td>Saberi-Firoozzi, Massarrat</td>
<td>SUMS</td>
<td>Am J Gastroenterol 1995</td>
<td>41</td>
</tr>
<tr>
<td>10</td>
<td>HCV risk factors in blood donors</td>
<td>CCS</td>
<td>Alavian, Massarrat</td>
<td>RCG/L/DDRC</td>
<td>J Gastro Hep 2002</td>
<td>35</td>
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</table>

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treatment of liver cirrhosis in the world.14–16

Following universal neonatal HBV vaccination (1995) and later on adult mass vaccination (2007) the incidence and prevalence of new HBV infection declined sharply17 while treatment of more than 1000,000 subjects already infected with HBV remained a major challenge for practicing gastroenterologist.5 Realizing that almost all HBV isolates in Iran are of the genotype D1, 18 cohort studies of chronically infected HBV subject is now going on to define the best strategy for early therapy of these patients. The face of liver disease is changing in the country in the near future with increasing numbers of HCV infected individuals19, and the emergence of obesity epidemic 20 and non alcoholic fatty liver disease21 in the country. Autoimmune liver disease seems to be on the rise as well.5,22

Immuno-proliferative small intestinal disease (IPSID)

Dr. Khosrow Nasr and his colleagues from Shiraz published important papers about gastrointestinal cancers,23–25 IPSID26 and the so called idiopathic or subtropical enteropathy27 in the 1970s. During the same period, Farhad Navab from Tehran university of Medical sciences also published papers on IPSID.28 The most common etiology for malabsorption during the 70s was thought to be idiopathic enteropathy, IPSID and Tuberculosis. Recently, in a descriptive paper in “Gut” Kamran Bagheri-Lankarani and his colleagues have clearly shown that there has been a sharp decline in the incidence of IPSID. It seems that this decline followed the establishment of healthy drinking water in rural areas along with improvement in socioeconomic condition in the country after Islamic 1979 revolution.29 On the other hand, Reza Malekzadeh and Bijan Shahbazi have demonstrated that Celiac disease is not uncommon in Iran and it is probably the most common cause of malabsorption now a days.30,31

Upper gastrointestinal cancer

A major concern for gastroenterologists practicing in Tehran and other major cities during the 70s was the very high rate of esophageal squamous cell carcinoma (ESC) and its rather dismal prognosis in spite of surgery.23,32 The earliest reports about incidence of ESC in Iran were published in the mid 1960s and early 1970s from Tehran33 and Shiraz.23,34 There was no population-based cancer registry system, which could determine the exact incidence or mortality of ESC in different parts of the country, but anecdotal reports indicated a high rate of esophageal cancer in the Northeastern provinces of Mazandaran and Khorasan. In 1967 Janez Kmet, from the “International Agency for Research on Cancer

<table>
<thead>
<tr>
<th>Rank</th>
<th>Title of Manuscript</th>
<th>Type of Research</th>
<th>First &amp;CC authors</th>
<th>Affiliation</th>
<th>Journal/year</th>
<th>Number of citations</th>
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<tr>
<td>1</td>
<td>Esoph. cancer in the Caspian littoral initial studies</td>
<td>Observational</td>
<td>Kmet, Mahboubi</td>
<td>IPHR/TUMS/IARC</td>
<td>Science 1972</td>
<td>130</td>
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<td>Esophageal cancer in the Caspian littoral</td>
<td>Observational</td>
<td>Mahboubi</td>
<td>IPHR /TUMS</td>
<td>JNCI 1977</td>
<td>52</td>
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<td>Ardabil Cancer registry</td>
<td>Observational</td>
<td>Sadjadi, Malekzadeh</td>
<td>DDRC/TUMS</td>
<td>Int J Cancer 2003</td>
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<td>5</td>
<td>Precancerous lesions in Ardabil</td>
<td>Interventional</td>
<td>Malekzadeh</td>
<td>DDRC/TUMS</td>
<td>JCP 2004</td>
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<td>6</td>
<td>Caspian Cancer Registry</td>
<td>Observational</td>
<td>Mahboubi, Kmet</td>
<td>IPHR/TUMS/IARC</td>
<td>BJC 1973</td>
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<td>7</td>
<td>Esophageal cancer in NE Iran</td>
<td>Interventional</td>
<td>Saadi, Sepehr</td>
<td>SBUMS</td>
<td>BJC 2000</td>
<td>30</td>
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<td>8</td>
<td>Epidem. of upper GI Cancer</td>
<td>Observational</td>
<td>Islami, Malekzadeh</td>
<td>DDRC/TUMS</td>
<td>BJC 2004</td>
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<td>9</td>
<td>Golestan cohort Pilot Phase study</td>
<td>Observational</td>
<td>Pourshams, Malekzadeh</td>
<td>DDRC/TUMS</td>
<td>BJC 2005</td>
<td>21</td>
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<td>10</td>
<td>Cancer occurrence in Iran in 2002</td>
<td>Observational</td>
<td>Sadjadi, Malekzadeh</td>
<td>DDRC/TUMS</td>
<td>ACP/C 2005</td>
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<td>11</td>
<td>Colorectal in cancer</td>
<td>Observational</td>
<td>Ansari, Malekzadeh</td>
<td>DDRC/TUMS</td>
<td>Cancer Letter 2006</td>
<td>16</td>
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Source: Scopus January 2009

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(IARC)” and Ezatollah Mahboubi, from “Tehran University Institute of Public Health Research (IPHR)” made an exploratory visit to the Caspian littoral in the north of Iran, during which they got the “clinical impression” that rates in the Eastern part of this littoral were much higher than those in the Western part. They were successful to confirm their impression with a well-designed cancer registry in the area and later on (1968 – 1978) did several ecologic studies to compare the environmental factors between the high versus low-risk areas. They tested the results in a subsequent case-control study and published several papers, including a highly-cited paper in “Science”. They reported very high rates of ESC; higher than any single cancer rate ever reported anywhere in the world (age-adjusted rates > 100/10^5 /year). Majority of cancers (>90%) were of squamous cell type and rates were at least as high in women as in men. During the same period, other scientists made some effort to investigate possible options for early detection of esophageal cancer. 

ESC studies in the North of Iran came to a halt for approximately 17 years (1979 – 1996) after the revolution in 1979. In 1996, Farrokh Saidi and his team from “Shaheed Beheshti University, Tehran, Iran” resumed these studies by conducting a large-scale screening study. In the 2000, Reza Malekzadeh and his colleagues also started collaborations with several newly established national (Golestan, Mazandaran, Gilan, and Mashhad) Universities of medical sciences and international cancer research groups, including the “National Cancer Institute (NCI), Bethesda, Maryland, USA”, IARC, the Cambridge University, the Karolinska Institute (Sweden), the University of Toronto (Canada) and the University of Glasgow (UK). This effort involves a full range of several very well designed studies including, cancer surveillance, cancer registry programs, ecologic, case-control studies, and a very large prospective cohort study covering 50,000 subjects planned to be followed for 15 years along with several genetic and molecular epidemiologic studies. Several elegant reports have been published based on the results of the cancer surveillance, registry, ecologic, case-control and the pilot phase of the cohort, but the full-scale studies have not yet been completed. In addition to the DDRC, several other Iranian research groups have recently conducted epidemiologic and molecular studies albeit in smaller scales. These studies have shown that male to female ratio is still close to one and the majority of cancers are of squamous type. Rates are still high (ASR: 45); however, they seem to have declined sharply in the past 30 years, perhaps to half or a third as low as what they were in the past most likely due to socioeconomic improvement especially in rural areas after the 1979 Islamic revolution.

**Acid peptic disease, acid reflux and Helicobacter pylori infection**

Professor Sadegh Massarrat was the first one to start research on Helicobacter pylori and acid peptic disease (APD). He was very helpful to encourage the new generation of gastroenterologists in the post revolution Iran to collaborate with each other and do multicenter studies. He and

<table>
<thead>
<tr>
<th>No.</th>
<th>Name of RC and university</th>
<th>Date of establishment</th>
<th>Chairman and Founder</th>
<th>Scientific output</th>
<th>h-factor</th>
</tr>
</thead>
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<tr>
<td>1</td>
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<td>Mohammad Reza Zali</td>
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<td>3</td>
<td>GEHRC/SUMS</td>
<td>2002</td>
<td>Mehdi Saberifiroozi</td>
<td>43</td>
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<td>4</td>
<td>RCGL/BUMS</td>
<td>2005</td>
<td>Said Moid Alavian</td>
<td>53</td>
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</table>

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Table 4. Gastroenterology and hepatology research centers with at least 5 years of age and scientific output and h-factor.
his colleague, Mehdi Saberifiroozi performed a very interesting survey for APD and irritable bowel syndrome in Qashqaei Nomadic tribe in Southern Iran and industry workers in Tehran and published the first epidemiologic study about these two common disease in 1995. Their landmark paper has been extensively cited since its publication (Table 2). Duodenal ulcer was the most common pathologic endoscopic finding during 1980 – 2000. Dr. Massarrat designed and conducted several randomized controlled trials testing different combinations of antibiotics in Shiraz and Yazd. He finally joined the DDRC at TUMS in Shariati Hospital where he established the *H. pylori* research group and with collaboration of Dr. Malekzadeh designed and conducted more than 10 randomized controlled trials (RCTs) to find the most effective HP eradication regimens. He also started a very important RCT to test the hypothesis of beneficial effect of HP eradication in first degree relatives of gastric cancer patients in Tehran. Mohammad-Javad Kaviani, a graduate of DDRC, did an interesting research at GEHRC/SUMS about non-variceal gastrointestinal bleeding and confirmed the effect of oral omeprazole for prevention of rebleeding after endoscopic therapy.

The declining incidence of APD after year 2000 coincided with an epidemic of gastro-esophageal reflux disease (GERD) which presently is the most common GI disease in Iran. Siavosh Nasserimoghaddam from the DDRC/TUMS established the GERD research group and conducted several observational study followed by a cohort study to look for possible etiologies and the best management of this very common disease. Several other colleagues from Shaheed Beheshti University of Medical sciences (SBUMS) gastroenterology and liver research center (GLRC), Tabriz university of Medical sciences, and GEHRC of SUMS conducted several observational studies. Among them Ali-Reza Taghavi from GEHRC of SUMS published a highly cited paper in *Gut* which won the Iranian Academy of Medical Sciences prize as the best clinical paper in the year 2007.

**Colorectal cancer and inflammatory bowel disease (IBD)**

Inflammatory bowel disease was almost nonexistent in Iran during the 70s. Hossein Mirmadjlessi was the first Iranian scientist who studied IBD characteristics in Shariati Hospital at TUMS and published the first case series of ulcerative colitis in 1985 from Iran. He could not find any case of Crohn’s disease in his careful study. In the year 2000 the first series of Crohn’s disease was reported by Reza Malekzadeh from Shariati hospital DDRC/TUMS and in the year 2006 a larger series of IBD cases was reported by Rahim Aghazadeh and Mohammad-Reza Zali from the “Gastro-Intestinal and Liver Disease Research Center (GLRC)” of “Shaheed Beheshti University of Medical Sciences (SBUMS), Tehran, Iran.”

Colorectal cancer was also rare before 1980 but the incidence has increased significantly during the last two decades and has special high percentage of familial clustering which is more frequent in younger probands with more prevalent right sided tumors.

Mohammad Reza Zali the director and founder of GLRC/SBUMS has established a very well equipped molecular laboratory to study the genetic epidemiology of colon cancer in Iran and other GI and liver diseases. He is presently running these studies and we are expecting more publication in future. Pooneh Mokarram and her colleagues in GEHRC/SUMS also designed some researches for colon cancer genetics.

Dr. Zali group has already published an interesting study on genetic of hereditary hemochromatosis and has shown that the frequency of C282Y mutations is very low in Iran. Even the few cases reported with homozygous H63D mutation did not have any abnormality in iron metabolism.

**Other research area**

Pancreaticobiliary diseases research has been growing parallel to availability of MRCP, therapeutic ERCP, and endoscopic ultrasonography (EUS) in academic centers. Morteza Khatibian expert in Therapeutic ERCP and R. Sotoudehmanesh the pioneer of EUS in Iran have already published several elegant papers in this field. Amir Mirbagher also an expert in EUS and therapeutic ERCP from TUMS has published an interesting paper in the field.

Dr. Mikaeli has established Achalasia research group in DDRC/TUMS and did several RCT comparing different therapy for this disease some of the paper are among highly cited papers in field of GI in Iran.

Shahin Merat has established NASH and HCV research groups and has conducted elegant RCT in treatment of these disease some of them novel and
are among the top highly cited papers in GI in Iran. 

**Diagnosis and therapy**

**Fiberoptic endoscopy**

Before 1971 the endoscopes were rigid and used only in operating theaters by surgeons; in 1971 for the first time a semi-flexible gastroscope (Olympus D-series with deviation of the endoscope tip only on one side) was brought to Iran and used by British gastroenterologist, Peter Cotton in Nemazi Hospital when he was in Shiraz for 6 months as part of a newly established visiting professorship program of Shiraz Medical School University. In 1972 Farhad Navab a Cambridge graduated physician who came to Imam Khomeini Hospital at Tehran University after completion a gastroenterology fellowship at the University of Rochester, N.Y. was the first Iranian gastroenterologist who bought a fiberscope; the first generation of Olympus gastrointestinal fiberscope and used it in his private clinic and occasional used the same scope in the Imam Khomeini University Hospital.

**Diagnosis of viral hepatitis B and C**

The viral etiologic diagnosis of chronic liver diseases (viral hepatitis B and C) in Iran belonged to implementation of screening of donated bloods and then patients for these viral infections. In the laboratory of universities and private labs there was no facility for detection of viral hepatitis. So, the Blood Bank and Iranian Transfusion Organization for the first time checked HBs antigen at 1980 and anti-HCV antibody at 1996 and most carriers of these viruses from the Transfusion Organization referred for screening to university and private clinics. The oldest HBV registry was founded before 1978 in Faghihi’ (Saadi’s) Hospital in Shiraz University by Fath Ali Borhammanesh. Iranian Blood Transfusion Organization has done important role in detection of diseased persons and development of lab tests for diagnosis of viral hepatitis. In the new era some important activities such as increasing awareness of community and health personnel and preparing practical guidelines for disinfection of endoscopic instruments and guideline for management of viral hepatitis by Iranian Association of gastroenterology and hepatology along with the activities of Iranian Hepatitis Network (IHN) founded by Moayyed Alavian, from Baqiyatallah Gastroenterology and Hepatology Research Center with collaboration of other centers. The most important and effective step was taken by the Ministry of Health and Medical Education with the program of universal neonatal vaccination since 1995 followed by adulthood vaccination in 2007.

**Diagnostic laparoscopy**

The Late Rayhanollah Sarlati the pioneer of laparoscopy in the field of gastroenterology was one of the Tehran University academic staff who was trained in Germany under supervision of Prof. Kalk in 1960 and returned to Iran and developed this procedure and done a lot of diagnostic laparoscopies in Imam Khomeini Hospital. During the last 10 years with the development of diagnostic manners which replaced diagnostic laparoscopy, and more use of laparoscopy as therapeutic modality in biliary and GI disorders, laparoscopy have been done mostly by surgeons for therapeutic measures and now few gastroenterologists do diagnostic laparoscopy in gastroenterology departments.

**Endoscopic retrograde cholangiopancreatography (ERCP)**

Hossein Eshraghi was one of the pioneers of the Endoscopic Retrograde Cholangiopancreatography procedure in Iran; who has done more than 500 ERCP before 1978 in Sina, and Imam Khomeini Hospitals. Second generations who continued this procedure in Iran was Rahim Aghazadeh, Soheil Fadaei, Bahram Forzandeh, H. Khatibian in Tehran University. Later on Aghazadeh established ERCP unit in Taleghani Hospital at Shaheed Beheshti University. Sadehg Masserrat helped faculties of Shiraz University for development of this procedure. He brought a fluoroscopy from Germany by him and started ERCP procedure in Nemazee Hospital in Shiraz and trained the academic staff in Shiraz and then in Tabriz City. He also helped faculties of Tabriz University for starting this procedure. Dr. Khatibian and Dr. Aghazadeh have important role for implementing Therapeutic ERCP and teaching this procedure to other colleagues. With training of young colleagues, now therapeutic ERCP can be done in Tehran, Mashed, Shiraz, Tabriz, Yazd, and Rasht.

**Therapeutic endoscopy**

Surgical myotomy was the main therapeutic measure for achalasia before 1978, but after starting balloon dilatation in Shiraz University by Dr. Malekzadeh at 1985, and then training of
younger colleagues by him in Shiraz and Tehran Universities, this procedure became a common therapeutic modality for these patients. Now the Shariati Hospital is a well-equipped center for treatment of achalasia.

At the start of endoscopic control of upper GI bleeding; 1990, the most common cause of non-variceal UGI bleeding was peptic (duodenal) ulcer, when for the first time endoscopic control of bleeding performed by ethanalamine (Thrombovar) and then by ethanol in Shiraz and Tehran Universities for peptic ulcer and esophageal varices. Sadegh Masserrat has an important role in training this procedure to young clinicians. Now rubber band ligation is a routine and frequently used procedure which is done by GI fellows, and different endoscopic modalities such as heater probe, Argon Plasma Laser, and injection therapies are performed frequently in endoscopic divisions of governmental and private hospitals. Endo Clip by Kamran Bagheri Lankarani and cyanoacrylate glue (Histoacryl) injection for fundal varices by Alireza Taghavi were popularized in Shiraz University. Endoscopic mucosal resection (EMR) for the first time done by Shahin Merat and Siavash Nasser-Moghaddam in Tehran University.

**Endoscopic ultrasonography (EUS)**

The pioneers who used the EUS for diagnosis of GI and pancreatobiliary lesions and staging of GI cancers were Rassol Sotoudehmanesh in Shariati Hospital, and Amir Mir-Bagheri, since 2000. Shariati Hospital then with the attempts of Dr. Sotoudehmanesh became the teaching center for this procedure and trained more than 10 young graduates from different cities. Now EUS can be done in more than 10 centers, in Tehran, Shiraz, Mashhad, and other cities.

**Liver transplantation**

The first orthotopic liver transplantation in Iran was performed in Nemazee Hospital, Shiraz, on 4 May 1993 by Ali Malekhosaini and his colleagues. At the end of 2008 more than 500 liver transplants was done in the Shiraz Liver Transplant Group, which both adult and pediatrics hepatologists have a significant role in management of transplanted patients.

The Shiraz Organ Transplantation Group as a whole has developed their experiences significantly during past few years and attained an important status in the region as an active member of MESOT, and regarding liver transplantation is one of major centers in the Middle-East region. According to the published data about one fourth of patients who were enrolled to the liver transplant waiting list were transplanted during the last 10 years. The most common etiology of end stage liver disease in transplant cases was hepatitis B virus. In this center more than 20 successful living related liver transplantation were done till now. Another liver transplant center which was established for a few years has done around 30 liver transplants in Imam Khomeini Hospital, Tehran University of Medical Sciences. A few transplants were done in Mashhad University also with the help of some Iranian surgeons from abroad. At least three active liver transplants in addition to Shiraz Center are needed for transplanting the enrolled patients in the country, which can be accomplished by training more surgeons in Nemazee Hospital, the only transplant fellowship training program in Iran. Pancreate transplantation was performed successfully in 40 patients on Shiraz Organ transplant Center since 2006 by Saman Nikeghbalian and his coworkers.

**Other diagnostic and therapeutic procedures**

According to our information esophageal manometry has been performing before 1990 for diagnosis of achalasia, in some centers such as Shiraz University; however, after initiation of fellowship programs significant improvements has been done and now esophageal and anorectal manometry, and ambulatory PH monitoring can be done in various universities and private centers. Evaluation of small bowel pathologies can be done in multiple centers by push enteroscopy, double balloon enteroscopy (DBE) and capsule endoscopy (CE) since 2005.

**Human resource and facilities**

It should be mentioned that the number of gastroenterologists increased significantly during the last 20 years from less than 100 persons with subspecialty degree to more than 300 persons. In addition around 700 internists also are working in the field of gastroenterology and doing diagnostic procedures according to the license of IAGH and Ministry of Health. Simultaneously the facilities for subspeciality activities have improved in different parts of the country. So, the availability of digestive disease services improved significantly for our people.

**Conclusion**

The research in the field of Gastroenterology
and Hepatology in I. R. Iran has expanded dramatically in the past two decades, which is the result of improving the quality and quantity of research activities, more budget supply by the government, increased number of research centers and scientists in this field, and more collaborative works in the international level. This trend of improvement can become more effective with more collaborative work in research activities in different centers, with development of research networks. The growth and development of research and educational programs in I.R. Iran and training of new gastroenterologists during the last 20 years, improved the quality and availability of gastrointestinal and hepatology services in different parts of the country.

Acknowledgements

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