Original Article

Establishment and Development of the First Biobank of Inflammatory Bowel Disease, Suspected to Primary Immunodeficiency Diseases in Iran

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Access this article online

Website: www.advbiores.net

DOI: 10.4103/abr.abr_278_16

Quick Response Code:

Abstract

Background: Inflammatory bowel disease (IBD) might be an immunodeficiency rather than an excessive inflammatory reaction. IBD, suspected to primary immunodeficiency diseases biobank (IBDSPIDB) as a resource for researches can help improve the prevention, diagnosis, and illness treatment and the health promotion throughout the society. Therefore, we launched the biobank of IBDSPID for the first time in Iran. **Materials and Methods:** This study was designed to provide the IBDSPIDB to have a high-quality DNA, RNA, and cDNA. Among of 365 patients, 39 have inclusion criteria that were as below: (1) IBD diagnosis before 5 years of age. (2) Resistance to conventional therapy of IBD. (3) Severe IBD. (4) Signs of SPID (including ear infections or pneumonia or recurrent sinus within the 1-year period; failure to thrive; poor response to the prolonged use of antibiotics; persistent thrush or skin abscesses; or a family history of PID). **Results:** Out of 39 patients, 51.3% were males. The mean age was 32.92 ± 15.90 years old. Ulcerative colitis (79.5%) was more than Crohn's disease. The majority of patients (50.0%) had severe IBDSPID. Resistance to drugs and consanguinity was 12.9% and 47.4%, respectively. Age at onset in 65.8% of patients was after 17 years old. Patients with autoimmune, allergy, and immunodeficiency disease history were 33.3%, 33.3%, and 10.36%, respectively. RNA and cDNA yields large quantities of high-quality DNA obtained and stored. **Conclusion:** Our biobank would be valuable for future genetic and molecular study to be more about the relation between IBD and PID.

Keywords: *Biobank, inflammatory bowel diseases, primary immunodeficiency diseases*

Introduction

Inflammatory bowel diseases (IBDs) is one of the heterogeneous group of disorders that is characterized as Crohn's disease (CD) and ulcerative colitis (UC) and IBD unclassified.[1,2]

Several genetic and environmental factors as well as alterations in microbial composition and the intestinal mucosal immune response reactivity of the gut intervene in IBD pathogenesis.[3]

Interactions between the immune system and the commensal bacterial flora of the gut are influenced in the development of IBD.[4] However, there is a document that CD might be the result of a decreased release of pro-inflammatory cytokines and an impaired acute inflammatory response, thereby it can be expressed IBD might be an immunodeficiency rather than an excessive inflammatory reaction. This opinion has been trusted by observations in patients with primary immunodeficiencies such as the immune dysregulation, Wiskott–Aldrich syndrome, enteropathy, polyendocrinopathy, and X-linked syndrome. On the contrary, defects in the anti-inflammatory downregulation of the immune response as they are seen in patients with Mendelian defects in interleukin-10 (IL-10) signaling pathway confirm the hyperinflammatory theory.[5]

Previous studies indicate the increased occurrence of this disease in Asian countries in the last two decades.[6] Although lack of the prevalence and incidence of that have not been properly studied in Iran, there is an increasing number of IBD patients reported in our country.[7]

As previous studies utilized more hospital-based and retrospective data rather than national registry system, epidemiological data are not clearly available in Iran, especially with suspected to primary immunodeficiency diseases (SPIDs).[8,9]

Public studies and focus groups illustrate strong confirmation for medical

How to cite this article: Sherkat R, Rostami S, Yaran M, Emami MH, Saneian H, Tavakoli H, *et al*. Establishment and Development of the First Biobank of Inflammatory Bowel Disease, Suspected to Primary Immunodeficiency Diseases in Iran. Adv Biomed Res 2018;7:45.

Received: December, 2016. Accepted: February, 2017.

investigation,[10] yet there is a little understanding and perceptions of biobanking patients with certain chronic disease states including IBDSPIDs.

With regard to the effect of immune system alterations on IBD and also need to samples donated by affected patients and collecting data for researching the genetic and microbial factors on this disease, IBDSPID biobank (IBDSPIDB) was lunched for the first time in Iran.

Materials and Methods

Inflammatory bowel disease, suspected to primary immunodeficiency disease biobank

Inflammatory bowel disease, suspected to primary immunodeficiency disease biobank's management and database

IBDSPIDB is constructed under the support of AAA of BBB and other colleagues involved in IBDSPID management.

The Medical Ethics Committee of the BBB approved this research protocol under approval no. 293217.

Among the 365 patients who were referred to AAA, CCC, and DDD, from March 2014 to March 2015, 39 patients have inclusion criteria and were enrolled in this prospective study.

The inclusion criteria were as follows:

- IBD diagnosis before 5 years of age
- Resistance to conventional therapy of IBD
- Severe IBD
- Signs of SPID (including recurrent sinus or ear infections or pneumonia within a 1-year period; failure to thrive; poor response to prolonged use of antibiotics; persistent thrush or skin abscesses; or a family history of PID)[11]
- Autoimmune diseases (such as Sjögren's syndrome, autoimmune thyroiditis diseases, autoimmune gastritis, diabetes mellitus, alopecia, autoimmune liver diseases, dermatomyositis, connective-tissue diseases such as vitiligo, rheumatoid arthritis, systemic lupus erythematosus, and pernicious anemia).

All individuals were given an information sheet to read and understand why the IBDSPIDB is being created. Each patient who agreed to participate in the project was asked to sign a consent form and was given a unique code by that specimen tube, and data sheet is labeled.

Questionnaire was used to collect demographic information (age and sex), forms of diseases (CD or UC), intensity, age at onset, drugs resistance, consanguinity, history of autoimmune disease, immunodeficiency disease, and allergy. Medical data and interviews with patients have been stored in their clinical documents.

Inflammatory bowel disease, suspected to primary immunodeficiency disease biobank sampling

After informed consent was obtained from donors, 10 ml blood is drawn into anticoagulated tube to extract DNA and RNA.

The process of extraction was performed using calibrated instruments and standard protocols.

High Pure PCR Template Preparation Kit (QIAGEN, Germany) was used for DNA and RNA.

These genetic materials were frozen and saved in −70°C. To prevent any contamination, DNA samples were aliquoted and stored at two different sites.[12]

As cDNA is more stable than RNA, cDNA was synthesized with reverse transcriptase enzyme and kept at −20°C. All experiments were made by a trained team of general physicians, researcher, nurses, and technicians. Specimens are coded according to each individual's code in biobank to ensure that anonymity is preserved.

Data analysis

SPSS program (version 18.0, Chicago, IL, USA, IBM company) was used for statistical analyses.

Age variable was descriptive by descriptive statistics, and descriptive statistics were used to determine the frequency of other variables.

Results

The biobank of IBDSPID consists of 39 samples that all their reported data including age and sex are presented in Table 1. Included recipients in our study had a mean age of 32.92 ± 15.90 years old (range, 5-67 years) with 20 males (51.3%) and 19 females (48.7%).

The patients' characteristics [Table 2] indicate that the UC was the most common type of diagnosed IBD (79.5%) while frequency of CD was 20.5%.

The patients with severe IBDSPID (50.0%) were more than patients with the other severity of IBDSPID (mild [23.1] and moderate [29.4]).

In our study, the consanguinity rate was 47.4% at the total number and 52.6% of patients did not have parental consanguinity.

Age at onset of IBD in the majority of patients was after 17 years old (65.8%). Age at onset, before age 6 was 2.6% and patients aged between 6 and 17 were 31.6%.

Table 3 shows disease history of IBD patients. History of autoimmune, allergy, and primary immunodeficiency

Table 1: Demographic variables of inflammatory bowel diseases, suspected to primary immunodeficiency diseases patients

Demographic variable	Frequency (%)	Mean±SD
Age		32.92±15.90
Sex		
Female	19 (48.7)	
Male	20 (51.3)	

SD: Standard deviation

Table 2: Characteristics of inflammatory bowel diseases, suspected to primary immunodeficiency diseases patients

Characteristic	Frequency (%)
Type of disease	
Ulcerative colitis	31 (79.5)
Crohn's disease	8 (20.5)
Intensity	
Mild	9 (23.1)
Moderate	10 (29.4)
Severe	17 (50.0)
Age at onset	
Before age 6	1 (2.6)
Age 6-17	12 (31.6)
After age 17	25 (65.8)
Consanguinity	
Yes	18 (47.4)
No	20 (52.6)

Table 3: Concomitant disease with inflammatory bowel diseases

Concomitant disease	Frequency (%)
Autoimmune	
Yes	13 (33.3)
No	26 (66.7)
Allergy	
Yes	13 (33.3)
No	26 (66.7)
Primary immunodeficiency disease	
Yes	4 (10.3)
No	35 (89.7)

disease was 33.1%, 33.1%, and 10.3%, respectively, on the cases.

The use of whole-blood specimens to obtain genomic DNA yields large quantities of high-quality DNA that provides sufficient material for the current and future molecular applications at a sustainable cost of storage. RNA and cDNA extracted from whole-blood specimens were large quantities of high quality, obtained, and stored.

Discussion

With regard to homeostasis changes in the gut, IBD can be developed as the result of variety in different irregularities of the immune system.[13,14]

Recently, Mendelian forms of IBD have been detection, as exampled by IL-10 deficiency or its receptor subunits.

In addition, other types of PID might be as one of their leading clinical presentations with intestinal inflammation association.[14]

According to the previous study, CD may be an immunodeficiency due to a macrophage malfunction with faulty release of cytokines and subsequent impaired acute inflammatory response to bacteria and foreign material in the intestine.[5]

Although research progression carried out about IBD and developmental knowledge achieved about the intestinal mucosal immunity and the components, there are still many other factors that need to be studied and identified to understand complex ecosystem of the gut.[5]

Samples donated by affected patients require to research about microbial and genetic factors involved in IBD pathogenesis. Such IBD researches have a high importance, and for this need, a national biobank containing samples of serum, saliva, and stool for genetic and microbial analyses.[15]

Previous studies indicate the establishment of different biobanks worldwide.

For example, Mota-Vieira *et al*.[16] established a human DNA bank with 997 healthy blood samples. Sex, age, parental birthplaces, birth, and current place of living of each case were reported in this DNA bank.

The Spanish HIV BioBank processed, stored, and provided distinct samples from HIV/AIDS patients by García-Merino *et al*.[17] and has nearly 50,000 vials containing various sample types.

Nineteen national and international research projects are used of more than 1700 of these samples.

Isaian *et al*.[18] established the DNA banking and analyzed the information of 31 immunodeficient patients and their families (total of 92 samples). This biobank was used for molecular genetic testing, detection of mutation of these diseases, and prenatal diagnosis.

Furthermore, biobanks organized collections containing biological samples and associated data have gained great importance for research and personalized medicine.

In summary, in recent years, it has been needed for suitable biological material for the conduct of research, and biobanks are being used due to consisting of a large number of biological well-documented samples that selected with appropriate scientific criteria.

Our biobank would be valuable for future genetic and molecular study to be more about the relation between IBD and PID.

The current study was limited in one of the way that deserves careful attention: this study does not yet cover all IBDSPID in our country. Therefore, our biobank will be progressed in future; more sample data will be added and could be achieved valuable results.

Conclusion

Our biobank would be valuable for future genetic and molecular study to be more about the relation between IBD and PID.

Acknowledgments

The authors would like to thank the Gastroenterology Clinics and Research Centers of Isfahan University of Medical Sciences for their cooperation in the process of data collection. Furthermore, the authors gratefully acknowledge the authorities at the Isfahan University of Medical Sciences for financial support of this study.

Financial support and sponsorship

This study was financially supported by Isfahan University of Medical Sciences.

Conflicts of interest

There are no conflicts of interest.

References

1. Abraham C, Cho JH. Inflammatory bowel disease. N Engl J Med 2009;361:2066-78.
2. Podolsky DK. Inflammatory bowel disease. N Engl J Med 2002;347:417-29.
3. Fiocchi C. Inflammatory bowel disease pathogenesis: Where are we? J Gastroenterol Hepatol 2015;30 Suppl 1:12-8.
4. Malys MK, Campbell L, Malys N. Symbiotic and antibiotic interactions between gut commensal microbiota and host immune system. Medicina (Kaunas) 2015;51:69-75.
5. Glocker E, Grimbacher B. Inflammatory bowel disease: Is it a primary immunodeficiency? Cell Mol Life Sci 2012;69:41-8.
6. Fujimoto T, Kato J, Nasu J, Kuriyama M, Okada H, Yamamoto H, *et al.* Change of clinical characteristics of ulcerative colitis in Japan: Analysis of 844 hospital-based patients from 1981 to 2000. Eur J Gastroenterol Hepatol 2007;19:229-35.
7. Cosnes J, Gower-Rousseau C, Seksik P, Cortot A. Epidemiology and natural history of inflammatory bowel diseases. Gastroenterology 2011;140:1785-94.
8. Aghazadeh R, Zali MR, Bahari A, Amin K, Ghahghaie F, Firouzi F. Inflammatory bowel disease in Iran: A review of 457 cases. J Gastroenterol Hepatol 2005;20:1691-5.
9. Vahedi H, Merat S, Momtahen S, Olfati G, Kazzazi AS, Tabrizian T, *et al.* Epidemiologic characteristics of 500 patients with inflammatory bowel disease in Iran studied from 2004 through 2007. Arch Iran Med 2009;12:454-60.
10. Trauth JM, Musa D, Siminoff L, Jewell IK, Ricci E. Public attitudes regarding willingness to participate in medical research studies. J Health Soc Policy 2000;12:23-43.
11. McCusker C, Warrington R. Primary immunodeficiency. Allergy Asthma Clin Immunol 2011;7 Suppl 1:S11.
12. de Montgolfier S, Moutel G, Duchange N, Theodorou I, Hervé C, Leport C; APROCO Study Group. Ethical reflections on pharmacogenetics and DNA banking in a cohort of HIV-infected patients. Pharmacogenetics 2002;12:667-75.
13. Rohr J, Pannicke U, Döring M, Schmitt-Graeff A, Wiech E, Busch A, *et al.* Chronic inflammatory bowel disease as key manifestation of atypical ARTEMIS deficiency. J Clin Immunol 2010;30:314-20.
14. Salzer E, Kansu A, Sic H, Májek P, Ikinciogullari A, Dogu FE, *et al.* Early-onset inflammatory bowel disease and common variable immunodeficiency-like disease caused by IL-21 deficiency. J Allergy Clin Immunol 2014;133:1651-9.e12.
15. Denson LA, Long MD, McGovern DP, Kugathasan S, Wu GD, Young VB, *et al.* Challenges in IBD research: Update on progress and prioritization of the CCFA's research agenda. Inflamm Bowel Dis 2013;19:677-82.
16. Mota-Vieira L, Pacheco PR, Almeida ML, Cabral R, Carvalho J, Branco CC, *et al*. Human DNA bank in Sao Miguel Island (Azores): A resource for genetic diversity studies. Int Congr Ser 2006;1288:388-90.
17. García-Merino I, de Las Cuevas N, Jiménez JL, Gallego J, Gómez C, Prieto C, *et al.* The Spanish HIV BioBank: A model of cooperative HIV research. Retrovirology 2009;6:27.
18. Isaian A, Moin M, Pourpak Z, Rezaei N, Aghamohammadi A, Movahedi M, *et al.* DNA banking of primary immunodeficiency disorders in Iran. Iran J Allergy Asthma Immunol 2006;5:201-2.