**ORIGINAL ARTICLE**

# A Morphological Study of Inflammatory Bowel Disease; Manifestatons, Incidence and Management at Different Tertiary Care Hospitals at Lahore, Pakistan

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## ABSTRACT

**Background**: Inflammatory bowel disease is polygenetic disease and comprises of Crohn's Disease & Ulcerative Colitis. Its incidence is increasing in Asian countries over past many decades. Physiological and Biochemical alteration in the phenomenon of stress are also responsible for its increasing incidence.
**Methods**: Total 50 patients were selected from Mayo Hospital Lahore, Ganga Ram Hospital Lahore, Services Hospital Lahore and Fatima Memorial Hospital Lahore over the period of 3 months by following inclusion & exclusion criteria. Data was collected & analyzed on SPSS 20.0.
**Results**: Among 50 patients, 52% were male and 48% were females. 52% patients were in age group 15-30, 28% in 31-45 & 20% in 46-60 year age group. The most common oral presentation was aphthous ulcer 44.4%, Lip swelling with vertical fissures was seen in 16.7%, mucogingivitis in 27.8% and cobble stoning in 11.1 % cases. 40% patients taking corticosteroid, 30% amino salicylates and 30% antibiotics. 80% of these patients were taking antibiotics intermittently.
**Conclusion**: The rising incidence is most likely associated with the changing environmental conditions in developing countries such as with industrialization dietary habits, increased drugs intake and increasing stress.
**Keywords:** Inflammatory bowel disease, ulcerative colitis, Crohn's disease

## INTRODUCTION

Inflammatory bowel disease (IBD) results from complicated interaction of environmental, genetic and immune regulatory components. It comprises of 2 primary constituents; Crohn's Disease (CD) & Ulcerative Colitis (UC). Caucasians, Ashkenazic Jews, northern and industrialized countries are at risk populations (Hanauer, B.S., 2006). IBD is polygenetic disease and population based studies have described well established link between NOD2 variants and CD. (Hanauer, B.S., 2006).

The incidence of UC has increased in Western countries after the Second World War era and it is increasing in (previously) low- incidence parts of globe i.e. Asia, East European countries and developing countries. CD incidence is <1 per 100,000 (but increasing) in Asia and South America (Thia, et al., 2008).

Regardless of underlying genetic factor, nonfunctional mucosal immune response to commensal bacteria in the IBD pathogenesis is the emerging debate. Possible triggering factor is chronic inflammatory response initiated by infection or disrupted mucosal barrier. Infiltration of neutrophils and macrophages is followed by cytokines & chemokines release. These exacerbate dysfunctional immune response and TH1 or TH2 cells are activated in gut mucosa (Cho, 2008).

IBD occurs in genetically prone subjects by interaction between genes and environmental factors (still debatable). 5–10% of cases are familial while rests are sporadic cases (Kaseret al., 2010).

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The new idea of psychoneuroimmunology involvement in chronic stress and in acute experimental stress can disturb systemic immune and inflammatory function, and can increase disease process in humans with IBD. It is proved that thestress is able to initiate and reactivate gastrointestinal inflammation in animal models of colitis. There is a role of changed Physiology of the HPA axis and increased permeability of intestine. Psychological stress may speed upthe disease process in IBD.

IBD has broadspectrum of non-specific clinical features which can usually lead clinicians to misdiagnosis. Therefore, clinical presentation, histological, radiological, endoscopic and serological findings establish an accurate diagnosis. IBD patients having raised interleukin-6 (IL-6) levelsin saliva, predict that gastrointestinal tract involvement is encroaching to oral cavity. Therefore, IL-6 level monitoring can be an initial diagnostic tool for monitoring disease activity and progression level(Mortada et al., 2017).

In 1972, Varley described the presentation of CD only as Oral findings without any intestinal features. The prevalence rate is between 20-50% in most publications (Thia et al., 2008).

In most of the cases, intestinal lesions precede the oral involvement while oral lesions to be the first presenting sign are seen only in 5-10% cases. In CD oral lesions are more prevalent as compared to UC, more common in children than older, and with male predominance (Lankarani et al., 2013).

On microscopy, IBD lesions show granulomatous changes. The most commonly involved parts of oral cavity: buccal mucosa, gingiva, lips, vestibular, and retromolar areas (Boirivantand Cossu, 2010). There are four main types of lesions; cobblestoning, mucogngivitis, aphthous ulcers (aphthous stomatitis) & pyostomatitisvegetans (Katsanos et al., 2015).

Cobblestoning lesions may cause pain. Pyostomatitisvegetans can present in both UC and CD, but more commonly seen in UC (Muhvić-Urek et al., 2016).

Aphthous stomatitis are oral ulcers which occur commonly in both UC and CD and it is a nonspecific finding indistinguishable from other oral ulcers (Laranjeria et al., 2015).

Extra intestinal manifestations (EIM) of IBD are prevalent in both UC & CD. Skin involvement &musculoskeletal features are commonest findings. Other systems involved are hepatopancreatobiliary, ocular, renal, and pulmonary systems (Kaser et al., 2010).

Patient can present with abdominal pain, vomiting, diarrhea, weight loss andextra intestinal manifestations. Duration of these symptoms should be noted (Baumgart&Sandborn, 2007).

Mood disorders are also present. Family history and history of cigarette smoking also should be asked (Halme et al., 2006).

Diagnosis of IBD needs a complete physical examination and detailed history. Different base line tests like blood test, stool examination, endoscopy, biopsy, and imaging studies are performed to rule out other causes and reach the definitive diagnosis (Trikudanathan et al., 2012).

The objective of our study was to calculate the frequency of IBD among local population, frequency of different clinical features and rational therapy for management of IBD.

## MATERIAL AND METHODS

Total 50 patients were selected from Mayo Hospital Lahore, Ganga Ram Hospital Lahore, Services Hospital Lahore and Fatima Memorial Hospital Lahore over the period of 3 months. We included patients of both sexes (male and female) with age range of 15-60 years diagnosed with IBD. Data was collected on specially designed proformas. SPSS 20.0 was used to analyze the data and results were recorded.

## RESULTS

Graph 1: Graph showing male and female distribution

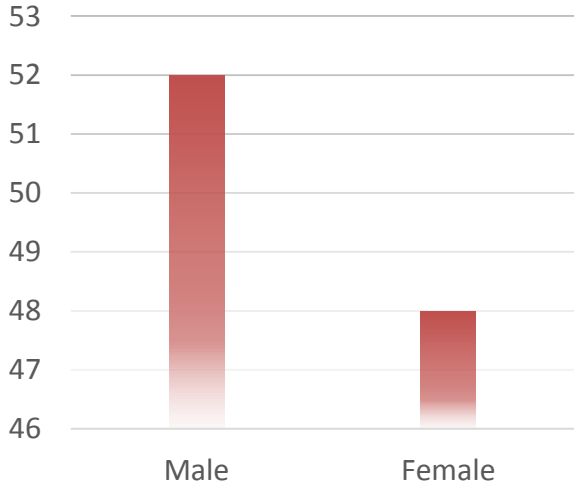


Table 1: Percentages of patients in different age groups. Among 50 patients, 52% were male and 48% were females. Patients were categorized into 3 age groups.

| Age of IBD Patients | %age |
|---|---|
| Between 15-30 years | 52 |
| Between 31-45 years | 28 |
| Between 46-60 years | 20 |

40% patients had positive family history by having any family member diagnosed with IBD while 60% had no family history. To observe the level of awareness about IBD in our community, its causes and treatment and to study the risk factors following data was obtained: 36 % patients were aware of the term IBD and had understanding about their medical condition while 64 % had no knowledge what they were suffering from. Among the 50 patients who were suffering from IBD, 32% fully aware about the management of IBD and 68% had no idea about IBD management.

70% patients tried to take symptomatic treatment by self-medication only before being diagnosed IBD by a consultant. 70% patients had history of smoking while 30 % never smoked. Among all patients, 60% patient had positive hypertension history while 40% were not hypertensive as stress is the major factor triggering the IBD. 26% patients belonged to high class and 45% patients belonged to lower socioeconomic status.

Among all BD cases, 36% were diagnosed by colonoscopy, 44% by stool analysis and 20% by CT scan. Among the 50 patients of IBD whose data was collected, the medications used by the patients at the time of data collection were as follow: 40% patients taking corticosteroid, 30% amino salicylates and 30% antibiotics. 80 % of these patients were taking antibiotics intermittently.

Table 2: Different medications prescribed to the patients at the study time

| Medication | Frequency | %age |
|---|---|---|
| Aminosalicylates | 15 | 30 |
| Corticosteroids | 20 | 40 |
| Antibiotics | 15 | 30 |

Common presenting complaints at the time of presentations were as follow: 13% bloody stool,16% severe abdominal pain, 2% fever,11% vomiting, 35% diarrhea, 23% weight loss. Among 50 patients, only 18 presented with oral lesions at the time of study.

Table 3: Oral lesions frequency and Percentages among IBD patients

| Oral lesions | Frequency | %age |
|---|---|---|
| Aphthous Ulcers | 8 | 44.4 |
| Lip swelling with vertical fissures | 3 | 16.7 |
| Mucogingivitis | 5 | 27.8 |
| Cobblestoning | 2 | 11.1 |
| Total | 18 | 100 |

## DISCUSSION

IBD affects both men and women and age of presentation is around 16- 25 years. Abnormal trigger of immune system, unhealthy diet plans and stress cumulatively aggravate and worsen the condition. Thia et al., 2008, reported the mean age for CD is 20-30 years while for UC

30-40 years in West. CD in Asia is also diagnosed at early age than UC. In our study, the most common age group affected was 15-30 years for CD and 45-60 for UC.

Halme et al, 2006 described family history in IBD cases in only 0.0–3.4% of IBD patients while Thia et al., 2008 reported familial history in 10–25% cases. In our study, 40 % patients had positive family history by having any family member diagnosed with IBD while 60% had no family history.

Thia et al., 2008 reported in review of data from China, Hong Kong,Japan, Korea,Singapore, Indiaand Sri Lanka male predominance for CD. In our study, among 50 patients, 52% were male and 48% were females.

Bernstein et al., 2010 narrated that among all risk factors, smoking and stress are the most commonly found risk factors in history of IBD patients. Gregersen & Olsson in 2009 described that certain foods and stress worsen the IBD.

Patient awareness is an important factor in the disease. Patients who don't respond to steroids for 2 weeks, they should be hospitalized. Patients should be on low residue diet to avoid diarrheaand other abdominal complaints (Bernstein et al., 2010).

Remarks of many patients were found satisfactory for their treatment.. Besides treatment, there is need for awareness program. Patients should be educated about course of disease, possible responsible risk factors and effects of IBD on patients overall health.

## CONCLUSION

The rising incidence is most likely associated with the changing environmental conditions in developing countries such as with industrialization, dietary habits, increased drugs intake and increasing stress.

## REFRENCES


1. Halme L, Paavola-Sakki P, Turunen U, Lappalainen M,. 2006. Family and twin studies in inflammatory bowel disease. World J. Gastroenterol. 12:3668–72.
2. Tsironi E, Feakins RM, Probert CS, Rampton DS, Phil D. 2004. Incidence of inflammatory bowel disease is rising and abdominal tuberculosis is falling in Bangladeshis in East London, United Kingdom. Am. J. Gastroenterol. 99:1749–55.
3. Thia KT, Loftus EV Jr, Sandborn WJ, Yang SK. 2008. An update on the epidemiology of inflammatory bowel disease in Asia. Am. J. Gastroenterol. 103:3167–82.
4. Sadlack B, Merz H, Schorle H, Schimpl A, Feller AC, Horak I. 1993. Ulcerative colitis-like disease in mice with a disrupted interleukin-2 gene. Cell 75:253–61.
5. Baumgart DC, Sandborn WJ. 2007. Inflammatory bowel disease: clinical aspects and established and evolving therapies. Lancet 369:1641–57.
6. Gregersen PK, Olsson LM. 2009. Recent advances in the genetics of autoimmune disease. Annu. Rev. Immunol. 27:363–91.
7. Peterson DA, Frank DN, Pace NR, Gordon JI. 2008. Metagenomic approaches for defining the pathogenesis of inflammatory bowel diseases. Cell Host Microbe 3:417–27.
8. Van Limbergen J, Wilson DC, Satsangi J. 2009. The genetics of Crohn's disease. Annu. Rev. Genomics Hum. Genet. 10:89–116.
9. Cho, J.H. 2008. The genetics and immunopathogenesis of inflammatory bowel disease. Nat. Rev. Immunol. 8:458–66 www.annualreviews.org • Inflammatory Bowel Disease 605 Annu. Rev. Immunol. 2010.28:573-621.
10. Zhernakova A, van Diemen CC, Wijmenga C. 2009. Detecting shared pathogenesis from the shared genetics of immune-related diseases. Nat. Rev. Genet. 10:43–55 16.
11. Budarf ML, Labbe C, David G, Rioux JD. 2009. GWA studies: rewriting the story of IBD. Trends Genet. 25:137–46 17. Zielenski J. 2000.
12. Defects in mucosal immunity leading to ulcerative colitis. Immunol. Rev. 206:296-305.
13. Revisiting Crohn's disease as a primary immunodeficiency of macrophages. J. Exp. Med. 206:1839–43.
14. Lankarani KB, Sivandzadeh GR and Hassanpour, S. Oral manifestation in inflammatory bowel disease: A review. World J Gastroenterol 2013; 19:85717-9.
15. Katsanos KH, Torres J, Roda G, Brygo A, Delaporte E, Colombel JF. Review article: non-malignant oral manifestations in inflammatory bowel diseases. Aliment PharmacolTher 2015; 42:40-60.
16. Skrzat A, Olczak-Kowalczyk D, Turska-Szybka A. Crohn's disease should be considered in children with inflammatory oral lesions. ActaPaediatr 2017; 106:199-203.
17. Muhvić-Urek M, Tomac-Stojmenović M, Mijandrušić- Sinčić B. Oral pathology in inflammatory bowel disease. World J Gastroenterol 2016; 22:5655-67.
18. Laranjeira N, Fonseca J, Meira T, Freitas J, Valido S, Leitao J. Oral mucosa lesions and oral symptoms in inflammatory bowel disease patients. ArqGastroenterol 2015; 52:105-10.
19. Trikudanathan G, Venkatesh PG, Navaneethan U. Diagnosis and therapeutic management of extraintestinal manifestations of inflammatory bowel disease. Drugs 2012; 72:2333-49.
20. Maynard CL, Elson CO, Hatton RD, Weaver CT. Reciprocal interactions of the intestinal microbiota and immune system. Nature 2012; 489:231-41.
21. Harty S, Fleming P, Rowland M, Crushell E, McDermott M, Drumm B, Bourke B. A prospective study of the oral manifestations of Crohn's disease. ClinGastroenterolHepatol 2005; 3:886-91.
22. Boirivant M and Cossu A. Inflammatory bowel disease. Oral Dis 2012; 18:1-15. 14. Rowland M, Fleming P, Bourke B. Looking in the mouth for Crohn's disease. Inflamm Bowel Dis, 2010; 16:332-37.
23. Hanauer, B.S., 2006. Inflammatory Bowel Disease: Epidemiology, Pathogenesis, and Therapeutic Opportunities. *Inflammatory Bowel Diseases*, Volume 12, Issue suppl_1, 1 January 2006, Pages S3–S9.
24. Kaser, A., Zeissig, S., Richard S. and Blumberg, S. R., 2010. Inflammatory Bowel Disease. Annu. Rev. Immunol. 2010. 28:573–621.
25. Mortada., Leone. A., GEAGEA, G. 2017. Oral manifestation in inflammatory bowel disease. Vol. 31, no. 3, xx-xx (2017)
26. Hussein, T.P., Bologna, S.B., Sipahi, A.M. and Nico, M.M. 2010. Oral manifestations of inflammatory bowel disease: a review based on the observation of six cases. *J Eur Acad Dermatol Venereol*. 2010;**24**: 204-207.
27. Fatahzadeh M. Inflammatory bowel disease. *Oral Surg Oral Med Oral Pathol Oral RadiolEndod*. 2009;**108**:e1-10.
28. Thrash B, Patel M, Shah KR, Boland CR, Menter A. Cutaneous manifestations of gastrointestinal disease: part II. *J Am AcadDermatol*. 2013;68:211.e1-33; quiz 244-246
29. Prideaux, L., Kamm, A.M., Cruz, D.P., Chan, K.L.F. and Ng, C.S. 2012. Inflammatory bowel disease in Asia: A systematic review. 13 April 2012.
30. Bernstein, N.C., Fried, M., Krabshuis, H.J., Cohen, H. and Hamid S. 2010. World Gastroenterology Organization Practice Guidelines for the Diagnosis and Management of IBD. Clinical Guidelines. 2010.